JSMB2016

Ito Campus, Kyushu University

Fukuoka, Japan

September 7 - 9

Sep 7 (Wed)	Sep 8 (Thu)	Sep 9 (Fri)
9:00 - 10:30 minisymposia Oral presentations	**9:00 - 10:30** minisymposia Oral presentations	**9:00 - 10:30** minisymposia Oral presentations
10:45 - 12:15 minisymposia Oral presentations	**10:45 - 12:15** minisymposia Oral presentations	**10:45 - 12:15** minisymposia Oral presentations
12:15 - 14:00 Lunch Poster Session I *Core time for presenters with Odd number*	**12:15 - 14:00** Lunch Poster Session II *Core time for presenters with Even number*	**12:15 - 14:00** Lunch
14:00 - 16:00 Plenary Talks ［Room D］ Mark Rees Miles Davenport	**14:00 - 15:30** General meeting ［Room D］	**14:00 - 15:30** minisymposia Oral presentations
16:15 - 17:45 minisymposia Oral presentations	**15:45 - 17:15** mini-symposia Oral presentations Award Lectures ［Room D］ Takeshi Kano Yukihiko Nakata Takeshi Miki	
18:00 - 19:00 Board meeting ［Room D］	**19:00 - 21:00** banquet	

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The 2016 (26th) annual meeting of
The Japanese Society for Mathematical Biology

September 7(Wed.) - 9(Fri.), 2016

Shiiki Hall, Ito campus, Kyushu University

Message from Organizing Committee of JSBM2016

Welcome to the 25th annual meeting of Japanese Society for Mathematical Biology (JSMB2016) at Ito campus, Kyushu University. With over 200 participants, both domestic and overseas, we look forward to plenary lectures, many symposia, oral and poster sessions.

School of Science, Kyushu University has a long history of research and education activities in mathematical biology since early 1970's. Last autumn, we moved to Ito-campus, located in the west part of Fukuoka city. JSMB2016 is a very good opportunity to show this new campus to the participants.

We also hope that you enjoy your stay in Fukuoka -- rich with heritage, surrounded by picturesque countryside. Fukuoka is also a modern lively city with many tourist attractions.

We would like to thank JSMB and Japan Society for the Promotion of Science for their financial support.

Yoh Iwasa and Shingo Iwami
Co-chairs of the local organizing committee

Organizing Committee

Chairs: Yoh Iwasa, Shingo Iwami
(Department of Biology, Faculty of Sciences, Kyushu University)

HP of the Meeting:

http://bio-math10.biology.kyushu-u.ac.jp/jsmb2016/home.html

E-mail:

hello.jsmb2016@gmail.com

Schedule of the meeting

Sep 7 (Wed)	Sep 8 (Thu)	Sep 9 (Fri)
9:00 - 10:30 minisymposia Oral presentations	**9:00 - 10:30** minisymposia Oral presentations	**9:00 - 10:30** minisymposia Oral presentations
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16:15 - 17:45 minisymposia Oral presentations	**15:45 - 17:15** mini-symposia Oral presentations Award Lectures [Room D] Takeshi Kano Yukihiko Nakata Takeshi Miki	
18:00 - 19:00 Board meeting [Room D]	**19:00 - 21:00** banquet	

12:15 - 14:00, Sep. 7th : the core time for presenters with Odd numbers

12:15 - 14:00, Sep. 8th : the core time for presenters with Even numbers

Please check your number in the table below if you are a poster presenter.

Sep 7 Wed 9:00 – 10:30

7A1-O1	Epidemiology / Within-host dynamics i (Hisashi Inaba)		
7A1-O1-1	Genki Ichinose	(Shizuoka University)	Effect of peer pressure on the evolutionary vaccination game
7A1-O1-2	Masayuki Kakehashi	(Hiroshima University)	An analysis on the effect of school closure against influenza: 'Back Monte Carlo' data approach
7A1-O1-3	Takaaki Funo	(Kyushu University)	Correlation between malaria cases and rainfall
7C1-O2	Development / Pattern / Morphogen i (Takeshi Miura)		
7C1-O2-1	Yuji Sakai	(Interdisciplinary Theoretical Science Research Group, RIKEN)	Chromosome condensation effects on the organization and segregation
7C1-O2-2	Hisao HONDA	(Kobe University Graduate School of Medicine)	Mechanism of cardiac looping of the embryonic heart
7C1-O2-3	Kenichi Nakazato	(Theoretical biology lab, RIKEN)	Understanding vascular remodelling from the view of continuum mechanics
7B1-S1 (Special)	Complexity and coexistence of population in simple ecological systems (Malay Banerjeeand Yasuhiro Takeuchi)		
7B1-S1-1	Toshiyuki Namba	(Osaka Prefecture University)	Coexistence of predators in simple ecological systems of intra-guild predation
7B1-S1-2	Yasuhiro Takeuchi	(Aoyama Gakuin University)	Maturation delay for the predators can enhance stable coexistence in prey-predator model with Allee effect
7B1-S1-3	Malay Banerjee	(IIT Kanpur)	Maturation delay can stabilize the prey-predator dynamics
7D1-S2	Structure-based control of complex network systems (Atsushi Mochizuki)		
7D1-S2-1	Tatsuya Akutsu	(Kyoto University, Japan)	Minimum Dominating Set-Based Approaches for Controlling and Analyzing Biological Networks
7D1-S2-2	Ying-Cheng Lai	(Arizona State University)	Tipping point in networked dynamical systems: control, recovery, and early warnings
7D1-S2-3	Jorge Gómez Tejeda Zañudo	(Pennsylvania State University)	Cell fate reprogramming by control of intracellular network dynamics
7D1-S2-4	Atsushi Mochizuki	(RIKEN)	Controlling regulatory networks by feedback vertex sets
7E1-S3	Biological oscillations at diverse spatiotemporal scales (Takayuki Ohara and Akiko Satake)		
7E1-S3-1	Tomoaki Muranaka	(Nagoya University)	The plant circadian clock as a multi-oscillator system
7E1-S3-2	Takayuki Ohara	(Hokkaido University)	Phase response of circadian clocks optimizes the growth of Arabidopsis thaliana
7E1-S3-3	Sungho Hong	(OIST)	GABA-mediated phase couplings and seasonal time coding in the suprachiasmatic nucleus
7E1-S3-4	Akiko Satake	(Kyushu University)	Parameterization and validation of a resource budget model for masting using spatiotemporal flowering data of individual trees

Sep 7 Wed 10:45 – 12:15

7A2-O3	Evolution / Behaviour i (Hisashi Ohtsuki)		
7A2-O3-1	Joe Yuichiro Wakano	(Meiji University)	Traveling waves of cultural invasion
7A2-O3-2	Riccardo Pansini	(Kunming Institute of Zoology)	High cooperation levels in a PGG by Chinese subjects to mitigate climate change
7A2-O3-3	Cinthia Marie Tanaka	(University of Sao Paulo)	Persistence of local dialect in the face of a national standard language: a mathematical study
7C2-O4	Ecology / Environment i (Toshiyuki Namba)		
7C2-O4-1	Hiromi Seno	(Tohoku University)	Mathematical modeling of metapopulation dynamics: Revisiting its meaning
7C2-O4-2	Kei Tokita	(Nagoya University)	Species abundance patterns of a food web model
7C2-O4-3	Ryo Oizumi	(Ministry of Health, Labour and Welfare)	Twofold stochasticity in structured population models
7C2-O4-4	Takashi Shimada	(The University of Tokyo)	Robustness of evolving open systems with mutual interactions
7B2-S4	Cancer modeling (Hiroshi Haeno)		
7B2-S4-1	Hiroshi Haeno	(Kyushu University)	The evolution of tumor metastasis during clonal expansion with alterations inmetastasis driver genes
7B2-S4-2	Munechika Misumi	(Radiation Effects Research Foundation)	Cancer risk of Japanese Atomic bomb survivors: challenge in radiation epidemiology to investigate radiation carcinogenesis
7B2-S4-3	Lin L. Liu	(Harvard University)	A unified framework to model induced stem cell - a case study of generalized multi-type branching process and beyond
7B2-S4-4	Kimiyo N. Yamamoto	(Kyushu University)	Computational Modeling of Individualized Management in Pancreatic Adenocarcinoma
7D2-S5	Network and Timeline : Recent Topics in Complex Networks (Takaaki Aoki and Satoru Morita)		
7D2-S5-1	Takaaki Aoki	(Kagawa University)	Burst behavior and scale-free network emerging in adaptive temporal Networks
7D2-S5-2	Tomokatsu Onaga	(Kyoto University)	Controlling the emergence of event cascades in inhomogeneous networks
7D2-S5-3	Taro Takaguchi	(National Institute of Information and Communications Technology)	On uncertainty of epidemic spreading in complex networks
7D2-S5-4	Satoru Morita	(Shizuoka University)	Comparison among several types SIS epidemic models on networks

Sep 7 Wed 16:15 – 17:45

7A3-O5	Medicine / Immunology / Cancer i (Akira Sasaki)		
7A3-O5-1	Akane Hara	(Kyushu University)	When is the allergen immunotherapy effective?
7A3-O5-2	Yoshiki Koizumi	(Kanazawa University)	Mathematical modeling of drug administration schedule in HCV infection
7A3-O5-3	Tatsuya Kurusu	(Kyushu University)	Modeling Hepatitis B Virus entry
7A3-O5-4	Haru Negami	(JSMB)	Differential equation model with state-dependent delays for sleep disorder
7C3-O6	Other (Ken-ichi Hironaka)		
7C3-O6-1	Gen Kurosawa	(Theoretical Biology Laboratory, RIKEN)	Theoretical studies on temperature and biological clocks
7C3-O6-2	Koichiro Uriu	(Kanazawa University)	Genetic oscillations by positive and negative feedback loops interlocked at competitive binding sites
7C3-O6-3	Shingo Gibo	(Theoretical Biology Laboratory, RIKEN)	Toward understanding the mechanism of the regulation for circadian clocks by RNA methylation
7C3-O6-4	Prabhat Shankar	(RIKEN)	Inference of Gene Regulatory from Experimental Data
7B3-S6	Cancer Evolution (Kimiyo N. Yamamoto)		
7B3-S6-1	Subhajyoti De	(Rutgers University)	TBA
7B3-S6-2	Yoichiro Yamamoto	(Shinshu University)	Tumour and immune cell dynamics explain the PSA bounce after prostate cancer brachytherapy
7B3-S6-3	Benjamin Werner	(Cancer Research UK)	Identification of neutral tumor evolution across cancer types
7D3-S7	Ecosystem Dynamics and Management (Yoh Iwasa, Joung-Hun Lee)		
7D3-S7-1	Yoh Iwasa	(Kyushu University)	Coupled social and ecological models for ecosystem management
7D3-S7-2	Tae-Soo Chon	(Pusan National University)	Assessment of Communities Responding to Natural and Anthropogenic Variability in Aquatic Ecosystems
7D3-S7-3	Cindy Hauser	(University of Melbourne)	Optimisation and statistics used in an Australian weed eradication program
7D3-S7-4	Joung-Hun Lee	(Kyushu University)	Optimal management of tropical forests with high risk of illegal logging: role of agroforestry and profit sharing
7E3-S8	Infectious diseases in structured populations (Yukihiko Nakata and Ryosuke Omori)		
7E3-S8-1	Gouhei Tanaka	(The University of Tokyo)	Metapopulation epidemic models with heterogeneous patches
7E3-S8-2	Koichi Saeki	(SOKENDAI)	Evolution of global and local viral infection in the structured SIS model
7E3-S8-3	Diána Knipl	(University College London)	Challenges in control strategies of spatially explicit epidemic models
7E3-S8-4	Toshikazu Kuniya	(Kobe University)	Discretization approach for the global stability analysis of structured epidemic models
7E3-S8-5	Takehisa Hasegawa	(Ibaraki University)	Outbreaks in the SIR epidemics with multiple seeds - a statistical physics approach

Sep 8 Thu 9:00 – 10:30

8A1-O7	Evolution / Behaviour ii (Joe Yuichiro Wakano)		
8A1-O7-1	Hisashi Ohtsuki	(SOKENDAI)	Does spatiality hinder evolutionary branching?
8A1-O7-2	Ryo Yamaguchi	(Kyushu University)	A tipping point in speciation with gene flow
8A1-O7-3	Yuma Sakai	(Hokkaido university)	Pathogen propagation model with superinfection in lattice space
8B1-S9	Towards data-driven mathematical biology (Joung-Hun LEE and Marko JUSUP)		
8B1-S9-1	Madeleine BEEKMAN	(The University of Sydney)	Different bees, different needs – nest site selection in honeybees
8B1-S9-2	Kazunori YAMAHIRA	(The University of the Ryukyus)	Life-history adaptations and the latitudinal diversity gradient in medaka fishes
8B1-S9-3	Takashi KITAGAWA	(The University of Tokyo)	Electronic tagging applications and migration of Pacific bluefin tuna, Thunnus orientalis
8B1-S9-4	Yoshinori AOKI	(The University of Tokyo)	Change in energy intake and cost of skipjack tuna (Katsuwonus pelamis) with northward migration in the western North Pacific
8D1-S10	Mathematical modeling for viral infections within host (Yusuke Kakizoe)		
8D1-S10-1	Yusuke Kakizoe	(Kyushu University)	Modeling to quantify HIV-1 entry
8D1-S10-2	Alexey Martyushev	(Kyushu University)	Epitope-specific CD8+ T cell kinetics rather than viral variability determines the timing of immune escape in SIV infection
8D1-S10-3	Laura Liao	(Ryerson University)	The impact of influenza A defective interfering particles on plaque assays
8D1-S10-4	Catherine Beauchemin	(Ryerson University)	Something is wrong with the respiratory syncytial virus
8E1-S11	Plant phenotyping with morphometrics (Koji Noshita)		
8E1-S11-1	Koji Noshita	(The University of Tokyo)	Leaf surface reconstruction from “noisy” point cloud data for geometric analysis
8E1-S11-2	Dan Chitwood	(Donald Danforth Plant Science Center)	Morphometric analysis of leaves
8E1-S11-3	Wei Guo	(The University of Tokyo)	Low cost field based plant phenotyping with cameras and image analytics

Sep 8 Thu 10:45 – 12:15

8A2-O8	Ecology / Environment ii (Hiromi Seno)		
8A2-O8-1	Norio Yamamura	(Doshisha University)	Population Dynamics and Optimal Management of 4 Species (Grass, Shrub, Sheep and Goat) in Nomadism
8A2-O8-2	Shigeo Yachi	(Kyoto University)	Dynamics of community-based ecosystem management: the role of context-dependent ecosystem services
8A2-O8-3	Yuki Kubo	(Kyushu University)	Management of tropical forests with agroforestry and profit sharing
8A2-O8-4	Mayuko Nakamaru	(Tokyo Institute of Technology)	The evolution of cooperation in the division of labor: Industrial waste illegal dumping as an example
8C2-O9	Epidemiology / Within-host dynamics ii (Shingo Iwami)		
8C2-O9-1	Akira Sasaki	(SOKENDAI)	A Bayesian updating model for the antigenic escapes of influenza virus subtypes
8C2-O9-2	Kazunori Sato	(Shizuoka University)	Lattice model of foot-and-mouth disease revisited
8C2-O9-3	Noriyuki Suzuki	(Aoyama Gakuin university)	HIV infection dynamics with pyroptosis of target cells
8B2-S12	Horizon of mutualism studies (Hisashi Ohtsuki)		
8B2-S12-1	Jonas Schluter	(Memorial Sloan-Kettering Cancer Center)	The ecology of the microbiome: Networks, competition & cooperation, and stability
8B2-S12-2	Hideo Ezoe	(Osaka Prefectural University)	Coevolutionary dynamics of one-to-many mutualisms
8B2-S12-3	Yu Uchiumi	(SOKENDAI)	Resampling after discrimination destabilizes mutualism
8B2-S12-4	Atsushi Yamauchi	(Kyoto University)	Joint evolution of interspecific mutualism and developmental stability under directional selection in trait space
8D2-S13	Patterns and Dynamics in Partial Differential Equations appearing in Mathematical Biology (Toshiyuki Ogawa)		
8D2-S13-1	Hirokazu Ninomiya	(Meiji University)	Pattern formation through non-local interactions
8D2-S13-2	Keiichi Ueda	(University of Toyama)	Differentiation of behavioral type induced by environmental variations in an amoeba
8D2-S13-3	Harunori Monobe	(Tokyo Institute of Technology)	Convex traveling wave solutions to an interface equation
8D2-S13-4	Toshiyuki Ogawa	(Meiji University)	Bifurcation of traveling wave in Competition-Diffusion equations
8E2-S14	Extraordinary forms - exploring the limits of cell shape modeling (Shigeo Hayashi and Takashi Miura)		
8E2-S14-1	Takashi Miura	(Kyushu University)	Mechanism of jigsaw-puzzle pattern formation in plant leaf epidermal cell: modeling single cell shape by interface equation and convolution kernel
8E2-S14-2	Hideki Takahashi	(Hokkaido University)	Form and Function of Pollen Grains
8E2-S14-3	Ryuichi Nishinakamura	(Kumamoto University)	Recreating human podocytes in the kidney
8E2-S14-4	Hideru Togashi	(Kobe University)	Cellular Tessellation in Sensory Epithelia
8E2-S14-5	James Glazier	(Indiana University)	Simulating the Onset and Development of Polycystic Kidney Disease using Virtual Tissues

Sep 8 Thu 15:45 – 17:15

8A3-O10	Evolution / Behaviour iii (Satoru Morita)		
8A3-O10-1	Tsuyoshi Mizuguchi	(Osaka Prefecture University)	Spatial and temporal structure of flying bird flocks
8A3-O10-2	Yumino Hayase	(Hiroshima University)	An active undulation of centipede locomotion
8A3-O10-3	Nariya Uchida	(Tohoku University)	Collective dynamics of bacteria at interfaces
8A3-O10-4	Takahiro Kamioka	(Kyushu University)	Evolution of density dependence and juvenile hormone regulation in wing polymorphic insects
[Room D]	Award Lectures		
	Takeshi Kano	(Research Institute of Electrical Communication)	Toward Understanding of the Decentralized Control Mechanism Underlying Adaptive Locomotion of Animals
	Yukihiko Nakata	(Shimane University)	Analysis and applications of delay equations in mathematical epidemiology
	Takeshi Miki	(National Taiwan University)	Multiple modeling approaches for better understanding the roles of microbial diversity in community and ecosystem dynamics.
8B3-S15	Biological Relevances of Mathematical Models (Kunimochi Sakamoto)		
8B3-S15-1	Kunimochi Sakamoto	(Hiroshima University)	Bulk reaction versus Boundary flux in diffusive systems
8B3-S15-2	Fumio Nakajima	(Iwate University)	A mathematical approach to the economy of atomic power generation
8B3-S15-3	Masataka Kuwamura	(Kobe University)	Diffusion driven destabilization of a spatially homogeneous limit cycle in reaction-diffusion systems
8E3-S16 (Special)	Pattern formation in heterogeneous environments (Izumi Takagi and Fang Li)		
8E3-S16-1	Izumi Takagi	(Tohoku University)	Pattern formation in homogeneous media vs in heterogeneous media: cutting and grafting experiments on hydra
8E3-S16-2	Huicong Li	(East China Normal University)	Spiky steady states of a chemotaxis system with singular sensitivity
8E3-S16-3	Sohei Tasaki	(Tohoku University)	Self-organization of bacterial communities against environmental pH variation
8E3-S16-4	Fang Li	(East China Normal University)	Non-local effects in an integro-PDE model from population genetics

Sep 9 Fri 9:00 – 10:30

9A1-O11	Evolution / Behaviour iv (Sachi Yamaguchi)		
9A1-O11-1	Masato S. Abe	(National Institute of Informatics, JST ERATO Kawarabayashi Large Graph Project)	Detecting interaction patterns in ant society by cross-embedding method
9A1-O11-2	Wataru Nakahashi	(SOKENDAI)	Cost and benefit of emotional contagion in group-living animals
9A1-O11-3	Robert Schlicht	(Technische Universität Dresden)	Evidence for conditional cooperation in biparental care systems?
9A1-O11-4	Shinsuke Satoi	(Kyushu University)	Theoretical study of chemical mimicking strategy in ants
9B1-S17	Hans Meinhardt; The Loss of the Meister of Developmental Pattern Formation and Unachieved Discussions (Akiko Nakamasu)		
9B1-S17-1	Izumi Takagi	(Tohoku University)	Mathematical beauty of the activator-inhibitor system
9B1-S17-2	Shigeru Kondo	(Osaka University)	Simpler modelling of the biological pattern formation
9B1-S17-3	Masayasu Mimura	(Meiji University)	Notion of diffusion-induced instability
9B1-S17-4	Tatsuo Shibata	(RIKEN)	Pattern formation in chemotaxis cells and body axis formation
9D1-S18 (Special)	Unifying epidemiological and genomic approaches to infectious diseases (Yusuke Asai and Hiroshi Nishiura)		
9D1-S18-1	Cornelia Pokalyuk	(Universität Magdeburg)	The role of reinfection in a viral population subject to balancing selection
9D1-S18-2	Hiroshi Nishiura	(Hokkaido University)	Mathematical modeling of MERS using epidemiological and genomic data
9D1-S18-3	Yusuke Asai	(Hokkaido University)	Identifying the location of virus source by the effective distance approach
9D1-S18-4	Kiyeon Kim	(Hokkaido University)	Estimating the population dynamics of influenza viruses from genomic data
9E1-S19	Mathematical and statistical modeling to bridge the gap between empirical and theoretical research in ecology (Michio Kondoh)		
9E1-S19-1	Chih-hao Hsieh	(National Taiwan University)	Empirical dynamic modeling for understanding and forecasting dynamic systems
9E1-S19-2	Masayuki Ushio	(Ryukoku University)	Environmental triggers of general flowering in a tropical lowland forest in Borneo
9E1-S19-3	Koji Iwayama	(Ryukoku University)	Imputation of RNA-seq data toward modeling transcriptome dynamics in a field
9E1-S19-4	Takeshi Miki	(National Taiwan University)	Improved statistical recipe for evaluating microbial functional diversity from metabolic fingerprinting

Sep 9 Fri 10:45 – 12:15

9A2-O12	Evolution / Behaviour v (Atsushi Yamauchi)		
9A2-O12-1	Makoto Douge	(Kyushu University)	Advantage of sex due to sibling diversity in an environment fluctuating over space and time
9A2-O12-2	Shikayama Daisuke	(Shizuoka University)	Improvement of the overestimation for invasion speed in higher birth-rate population
9A2-O12-3	Takuji Oba	(Kyoto University)	When does invasion implies substitution?
9A2-O12-4	Shota Nishijima	(Fisheries Research Agency, National Research Institute of Fisheries Science, Research Center for Fisheries Management)	Eco-evolutionary dynamics of a plant-pollinator system under climate change
9C2-O13	Medicine / Immunology / Cancer ii (Koichi Saeki)		
9C2-O13-1	Mizuho Nagata	(Aoyama Gakuin University)	Mathematical model of T and NK cell therapy against cancer
9C2-O13-2	Shoya Iwanami	(Kyushu University)	Mathematical model of hematopoietic system with myeloid-restricted progenitors with long-term repopulating activity
9C2-O13-3	Yu Min	(Aoyama Gakuin University)	Dual role of delay effect in a tumor immune system
9B2-S20	The role of cost-benefit analysis in ecology (Marko Jusup)		
9B2-S20-1	Tin Klanjscek	(Ruđer Bošković Institute, Zagreb)	Cost-benefit analysis to guide management of tourist activities in nature protected areas
9B2-S20-2	Hiroyuki Matsuda	(Yokohama National University)	The tragedy of the mitigation policy on climate change
9B2-S20-3	Zhen Wang	(Kyushu University)	Statistical physics of vaccination
9D2-S21	Recent development of Lyapunov functional approaches in mathematical biology (Yoichi Enatsu and Toshikazu Kuniya)		
9D2-S21-1	Connell McCluskey	(Wilfrid Laurier University)	Lyapunov functionals for delayed epidemic models
9D2-S21-2	Jinliang Wang	(Heilongjiang University)	Dynamics of viral infection models incorporating cell-to-cell transmission
9D2-S21-3	Tsuyoshi Kajiwara	(Okayama University)	Mathematical theory of the global stability of age-structured models for pathogen-immune interactions
9D2-S21-4	Toru Sasaki	(Okayama University)	Asymptotic behaviour of solutions for a virus-immune dynamics model with diffusion
9D2-S21-5	Yoji Otani	(Okayama University)	Lyapunov functionals for multi-group models with delay
9D2-S21-6	Yasuhisa Saito	(Shimane University)	Lyapunov functions and some predator-prey differential equations
9E2-S22	Geometry and Patterning in Tissue, Cell, and Nucleus (Yoshihiro MORISHITA and Sungrim SEIRIN LEE)		
9E2-S22-1	Yoshihiro MORISHITA	(RIKEN)	An equation of chemical field to be satisfied for achieving optimal encoding of positional information during organ development
9E2-S22-2	Masatoshi NISHIKAWA	(Hosei University)	Controlling contractile instabilities in the actomyosin cortex
9E2-S22-3	Sungrim SEIRIN LEE	(Hiroshima University)	A challenging interdisciplinary approach to elucidate a mystery of remodeling process in nuclear architecture （Part I: Theory)
9E2-S22-4	Hiroshi OCHIAI	(PRESTO, JST)	A challenging interdisciplinary approach to elucidate a mystery of remodeling process in

Sep 9 Fri 14:00 – 15:30

9A3-O14	Ecology / Environment iii (Kazunori Sato)		
9A3-O14-1	Sachi Yamaguchi	(Kanagawa University)	Time required for sex change in teleost fishes: hormonal dynamics shaped by selection
9A3-O14-2	Kouki Uchinomiya	(RIKEN)	Modeling optimal resource allocation in plant-fungi mutualism
9A3-O14-3	Ross Booton	(University of Sheffield)	The Role of Cannibalism in Determining Insect Voltinism Patterns
9A3-O14-4	Osaki Toru	(Shizuoka university)	Spatial pattern and its stability formed by algal blooms
9C3-O15	Development / Pattern / Morphogen ii (Koichiro Uriu)		
9C3-O15-1	Hiroshi UENO	(Doshisha University)	Dynamical Cooperativity: A New Approach to Enzymatic Computing
9C3-O15-2	Yoshihiro Morishita	(RIKEN Quantitative Biology Center)	Reconstructing 3D deformation dynamics for curved epithelial sheet morphogenesis from positional data of sparsely-labelled cells
9C3-O15-3	Masashi Tachikawa	(RIKEN)	Cargo accumulation can physically trigger membrane trafficking
9C3-O15-4	Takashi Okada	(RIKEN)	Law of Localization in Chemical Reaction Networks
9B3-S23	The role of cost-benefit analysis in medicine (Shingo Iwami)		
9B3-S23-1	Naoko Tomita	(National Institute of Public Health)	Health technology assessment and mathematical biology: A possibility for better economic evaluation
9B3-S23-2	Eunha Shim	(Soongsil University)	Mathematica modeling vaccination against infectious diseases including dengue and influenza
9B3-S23-3	Shingo Iwami	(Kyushu University)	Characterization of cost-effectiveness of multidrug treatment - Case study on HCV treatment
9D3-S24	Real-time modeling approaches to emerging infectious diseases (Kenji Mizumoto and Hiroshi Nishiura)		
9D3-S24-1	Kenji Mizumoto	(Hokkaido University)	Estimating Seasonal Influenza-Associated Deaths in Japan
9D3-S24-2	Kyeongah Nah	(Hokkaido University)	Estimating risks of importation and local transmission of Zika virus infection
9D3-S24-3	Ryo Kinoshita	(Hokkaido University)	Optimizing vaccination program against rubella in Japan
9D3-S24-4	Ryota Matsuyama	(Hokkaido University)	A Meta-Analysis of Risk and Risk Factors related mortality of Middle East Respiratory syndrome
9D3-S24-5	Masaya Saitoh	(Institute of Statistical Mathematics)	Spatiotemporal forecasting of rubella and its vaccination
9E3-S25 (Special)	Wanders will never cease: the current and future studies of the evolutionary ecology of dispersal (Ryosuke Iritani and Yuuya Tachiki)		
9E3-S25-1	Ryosuke Iritani	(Kyushu University)	Who escapes from whom: disease transmission among kin can drive the evolution of conditional dispersal in viscous host populations
9E3-S25-2	Florence Débarre	(College de France)	Evolution of dispersal in spatially and temporally heterogeneous environments
9E3-S25-3	Allison K. Shaw	(University of Minnesota)	The evolution of marine larval dispersal kernels in spatially structured habitats
9E3-S25-4	Yuuya Tachiki	(Kyoto University)	Evolutionary and ecological consequences of individual decisions, whether they stay or go, under environmental fluctuations

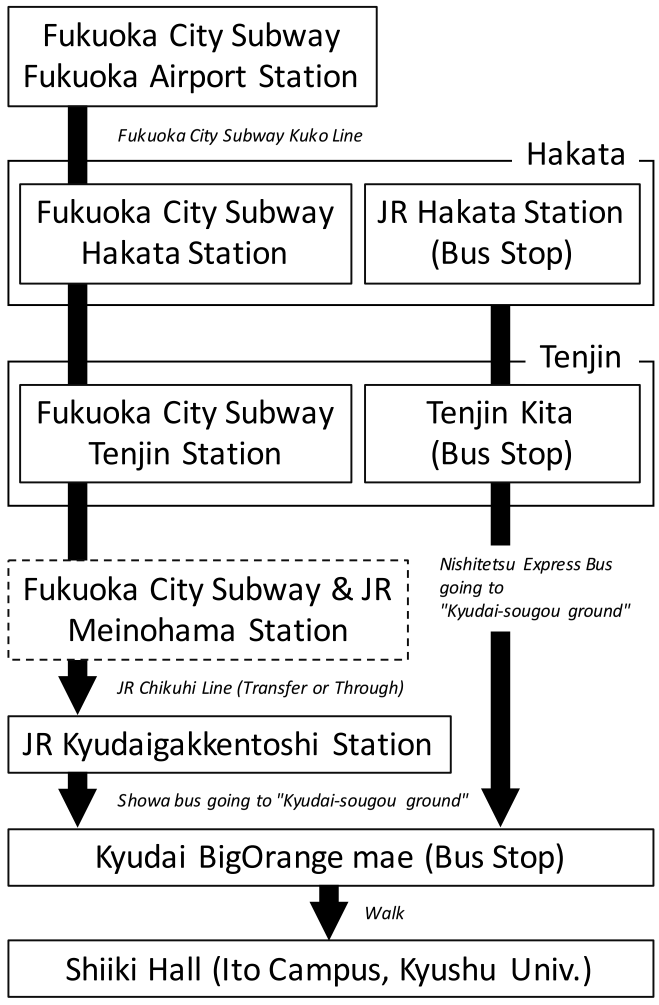
Poster Session List

No.	Name	Affiliation	Title of poster presentation
P-1	Kazumasa Kaneko	Department of Electrical Engineering and Information Systems, The University of Tokyo	Modeling and inferring dynamics of T cell population in thymus
P-2	Naoki Nakada	Aoyama gakuin university	Mathematical modeling and analysis of cancer immunotherapy: exploring the effect of cytokine mediated communication among T and NK cells
P-3	Shinji Nakaoka	Graduate School of Medicine, The University of Tokyo	Development of a computational grammar for immune cell processes
P-4	Seiya Nishikawa	Department of Electrical Engineering and Bioscience, Waseda University	Fate after ‘cell competition’ depending on initial states in tumor-suppressor system
P-5	Takayuki Hiraoka	University of Tokyo	Computational modeling of three-dimensional cell migration
P-6	Kentaro Inoue	RIKEN	Mathematical model for NF-kB signal transduction system
P-7	Masashi Kamo	Advanced Industrial Science and Technology	Explanation of non-additive effects in mixtures of similar mode of action chemicals
P-8	Isao Kawaguchi	NIRS, QST	Mathematical model approach to understand abscopal effect with radiotherapy.
P-9	Masahiko Higashi	Nagoya University	A Coevolution Model of Individual and Social Learning in a Rugged Fitness Landscape
P-10	Mariko Ito	The Graduate University for Advanced Studies	Emergence of opinion leaders in reference networks
P-11	Mitsuhiro Nakamura	Department of Evolutionary Studies of Biosystems, SOKENDAI	Learning processes and matching behavior in domestic chicks foraging
P-12	Junpei Okuno	Department of Electrical Engineering and Bioscience , Waseda University	Foraging strategy using multi-tentacles in plasmodial slime mold
P-13	Chikoo Oosawa	Dept of Biosci Bioinfor, Kyushu Inst of Tech	Gathering animals by escaping
P-14	Hemma Philamore	Kyoto University	Trophallaxis for Swarms of Energy-Scavenging Artificial Organisms.
P-15	Motohide Seki	Kyushu University	Optimality and evolutionary stability of life histories with stages for cultural transmission of information
P-16	Shohei Utsunomiya	Department of Electrical Engineering and Bioscience, Waseda University	Diversity of behavioral preference on cooperative transport in ants reduces obstacle passing time
P-17	Fumiko Ogushi	Math. Sci. group, AIMR, Tohoku Univ.	A mean-field analysis of the simple model of evolving open systems
P-18	Shota Shibasaki	Graduate School of Arts and Sciences, The University of Tokyo	The evolutionary game in sexual reproduction of the social amoeba
P-19	Masanori Tsuchiya	Graduate School of Information Science Nagoya University	An agent-based evolutionary model for diversification of phenotypic plasticity and personality in resource partitioning
P-20	Yu Uchiumi	Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies)	Evolution of vertical transmission of symbionts by reducing the rate of cell division
P-21	TakahiroYamagishi	Kyoto University	Joint Evolution of cytoplasmic male sterility and selfing rate in plant

No.	Name	Affiliation	Title of poster presentation
P-22	Nobuyuki Ishizuka	Aoyama University	Analysis of Lymph tissues network model of HIV infection dynamics
P-23	Yusuke Ito	Kyushu University	Estimating the number of HIV-1 to infect target cells in nonrandom co-infection
P-24	Nao Yamamoto	University of Hokkaido	How Does Correlation between Condom Use and Partner Type Influence the Transmission Dynamics of STI?
P-25	Kenta Yashima	The Graduate University for Advanced Studies (Sokendai)	Network centrality measure based on sensitivity analysis of the basic reproductive ratio
P-26	Shiori Abe	Nara Women's University	Population viability analysis of the Japanese rock ptarmigan
P-27	Miki Hamada	Nara Women's University	Spatial SIS model as a point pattern dynamics
P-28	Ikegawa Yusuke	Ryukyu Sankei Co., Ltd.	Effects of spatial and temporal homogeneity of releases of sterile insects on control of pests with limited dispersal ability
P-29	Takahiro Irie	The University of Tokyo	A hierarchical Bayesian estimation of wild population size from the neutral genetic information
P-30	Nariyuki Nakagiri	School of Human Science and Environment,University of Hyogo	Nest plate model for spacial effects and simulation of honey bees
P-31	Kenta Suzuki	National Institute for Environmental Studies	Resilience of hydrothermal vent communities: a metacommunity framework
P-32	Takenori Takada	Hokkaido University	Population statistics of random matrices
P-33	Takahiro Hiraga	Hiroshima University	Mathematical study of the rising movement and its support from the chair
P-34	Shigehide Iwata	Tokyo University of Marine Science and Technology	The catch control by the allocation of number of boat
P-35	Kodai Sato	Department of Electrical Engineering and Bioscience,Waseda University	zone planning for emergency evacuation using Physarum algorithm
P-36	Takuya Sekiguchi	National Institute of Informatics	How population clusters predict the population growth in Japan
P-37	Mayumi Seto	Nara Women's University	Cost-benefit analysis of food safety management: The case of radioactive contaminant

No.	Name	Affiliation	Title of poster presentation
P-38	Hironori Fujita	National Institute for Basic Biology	Pattern density control in Turing systems
P-39	Masatomo Matsushima	Doshisha Univ.	Classifying of synchronization pattern in oscillator circuits with optical signal
P-40	Noriaki Ogawa	RIKEN (Nishina Center / iTHES)	Dynamical Pattern Selection of Growing Cellular Mosaic in Fish Retina
P-41	Naoto Shingu	Kyushu University	Mathematical analysis for aging effects of endothelial cells on their self-organized pattern size.
P-42	Hiroto Shoji	Kyoto Prefectural University of Medicine	Physical Analysis of Branching Patterns of Sinusoidal Networks in Hepatic Lobule
P-43	Suguru Yaginuma	The univ. of Tokyo	Searching for 'ROP reaction system' which realizes Turing Pattern
P-44	Takaaki Yonekura	Botanical Gardens, Graduate School of Science, The University of Tokyo	Analysis of orixate phyllotactic pattern with expanded Douady and Couder's model
P-45	Yoshinori Hayakawa	Theoretical Biology Laboratory, RIKEN	Mathematical study of gene expression and morphogenesis coupling that realizes flat leaf formation
P-46	Kazuya Horibe	Osaka University Graduate School of Information Science and Technology	Curvature-driven splitting of a planar traveling wave
P-47	Osamu Iizuka	Kyushu University	Mechanism of Scaling law formation in developing retina vasculature
P-48	Sang-Woo Lee	RIKEN QBiC	Neutral cell competition and tissue growth efficiency
P-49	Fumito Mori	Theoretical Biology Laboratory, RIKEN	Origin of cell diversity: Analysis of fixed points in Boolean networks
P-50	Shigeru Moriyama	Department of Developmental Biology, Shimane University Faculty of Medicine	Mathematical representation and analysis of the number of cells in the intestinal epithelium of mouse embryos
P-51	Yuto Naroda	Kyushu University	Mathematical analysis of fractality of skull sutures
P-52	Toshiki Oguma	Kyushu University	The effect of cell dynamics on Delta-Notch pattern formation during retinal angiogenesis
P-53	Daiki Sasaki	Kyushu University	Mathematical Modeling for Meshwork Formation of Endothelial Cells in Fibrin Gel
P-54	Hisako Takigawa-Imamura	Kyushu University	Emergence of hierarchical structure of lung: a model and observation of cellular response to FGF
P-55	Emiko Ishiwata	Tokyo University of Science	Effect of time delay for an ultra-discretized logistic equation
P-56	Kohkichi Kawasaki	Doshisha Univ.	Exact traveling wave solution with minimum speed for nonlinear reaction-diffusion equation and its properties
P-57	Yohei Saito	Institute of Industrial Science, The University of Tokyo	Discreteness-induced transition in multi-body reaction systems
P-58	Yuki Sughiyama	Institute of Industrial Science, The University of Tokyo	Steady State Thermodynamics in Population Dynamics

Traffic



➢ From Fukuoka Airport

Fukuoka Airport → *Subway Kuko line* → **Meinohama Station** (Transfer or through) *JR Chikuhi Line* → **Kyudai-Gakkentoshi Station** (Transfer) *Showa Bus* → **Kyudai Big-orange bus stop** → *Walk* → **Shiiki Hall**

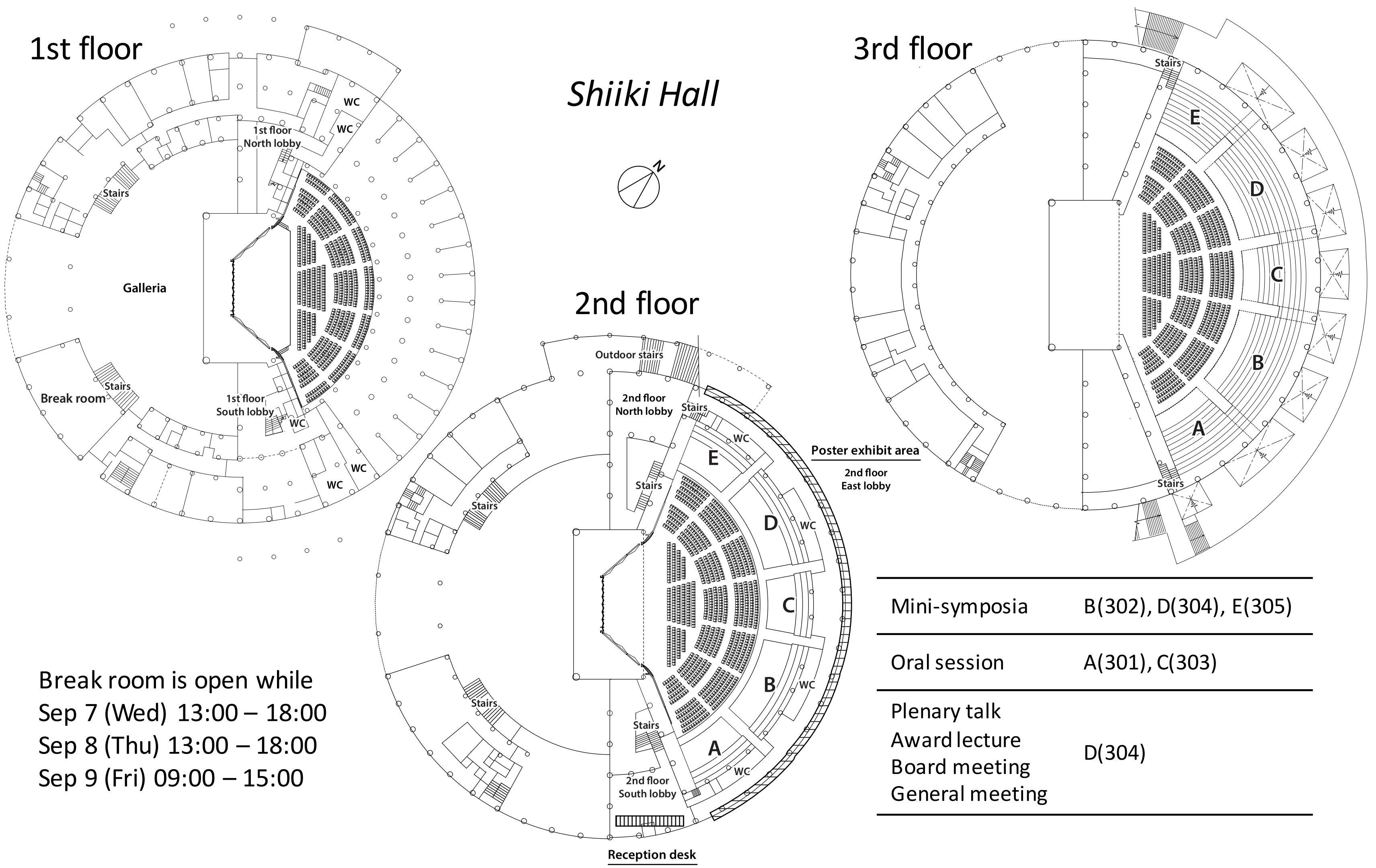
➢ From Hakata station

JR Hakata Station → *Subway Kuko Line* → **Meinohama Station** → = Same as "From Fukuoka Airport" = → **Shiiki Hall**
JR Hakata Station (at Hakata Station A bus stop) → *Nishitetsu Express Bus going to "Kyudai-sougou ground"* → **Kyudai Big-orange bus stop** → *Walk* → **Shiiki Hall**

➢ From Tenjin

Tenjin Station → *Subway Kuko Line* → **Meinohama Station** → = Same as "From Fukuoka Airport" = → **Shiiki Hall**
Tenjin (at Tenjin 2B or Tenjin-kita bus stop) → *Nishitetsu Express Bus going to "Kyudai-sougou ground"* → = Same as "From Hakata Station" = → **Shiiki Hall**

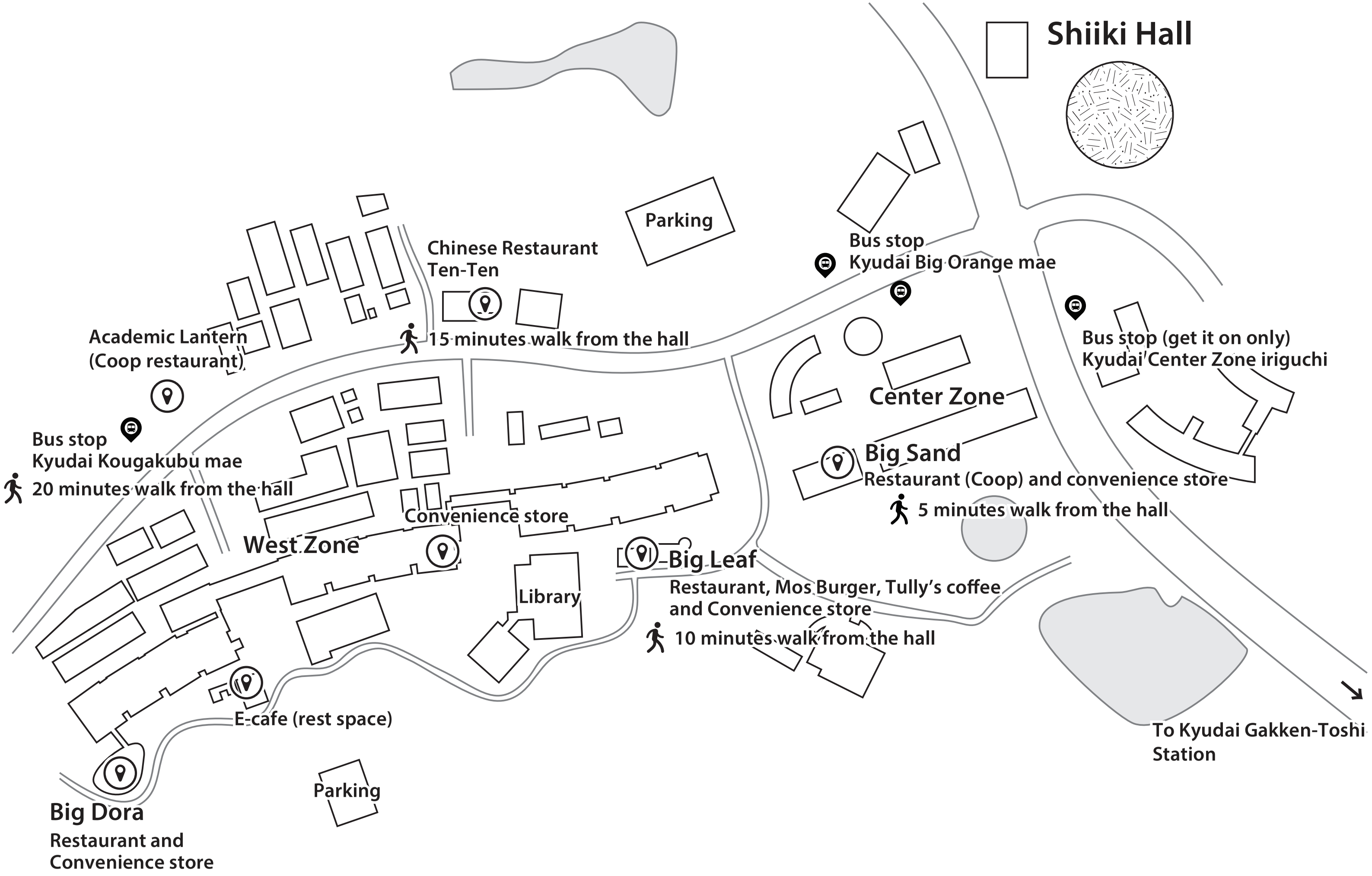
Map



Break room is open while
Sep 7 (Wed) 13:00 – 18:00
Sep 8 (Thu) 13:00 – 18:00
Sep 9 (Fri) 09:00 – 15:00

Mini-symposia	B(302), D(304), E(305)
Oral session	A(301), C(303)
Plenary talk Award lecture Board meeting General meeting	D(304)

Campus map & Lunch



General Information

Rooms

There are five rooms in Shiiki Hall:

A (301), B (302), C (303), D (304), E (305)

- Symposiums take place in room B, D and E.
- Oral Sessions take place in room A and C.
- Poster Sessions take place in room during launch time; 12:15 – 14:00 on Wednesday 7th and Thursday 8th September.

ID

Mini-symposia and oral sessions:

7	A	1	-	S or O	1	-	1
Day	Room	Time		Presentation Type	Serial number		Your order in the session

Posters: P-(number)

Banquet

Date: Thursday, September 8

Venue: 博多百年蔵（Hakata Hyakunenngura）

博多百年蔵 Website (in Japanese): http://www.ishikura-shuzou.co.jp/

Introduction of the venue

博多百年蔵（Hakata Hyakunenngura）is a great Japanese sake brewery built in 1870, the only one in Hakata city. It is a familiar place to Hakata residents, due to its traditional style of brewing Japanese sake, as well as the building of historical value. We hope that participants will join us for a delicious dinner and wonderful time at 博多百年蔵（Hakata Hyakunenngura）.

For vegitarians

We plan to prepare a vegetarian menu.

Presentation

Symposium

1. All talks in symposia will be delivered in English.
2. Organizers should manage their symposium at their own responsibility.
3. PC for presentations is not prepared. Please bring your own PC.
4. Display connecters of projectors are VGA. If the output of your PC is not VGA, please bring an appropriate display adapter.

Oral Presentation

1. In order to encourage attendance of non-Japanese researchers, presentation les must be prepared in English. We also strongly recommend speakers to talk in English.
2. Each talk must be delivered within 20 min, including questions and comments.
3. PC for presentations is not prepared. Please bring your own PC.
4. Display connecters of projectors are VGA. If the output of your PC is not VGA, please bring an appropriate display adapter.
5. Please test your projection before your session starts.

Poster Presentation

1. Posters must be prepared in English. We also strongly recommend presenters to explain in English.
2. Posters are numbered. Core times of odd and even numbered posters are 12:15 – 14:00 on Sep 7 and 8, respectively.
3. Please display before lunch time on Sep 7. To examine posters for prize, keep your poster displayed until 17:15 on Sep 8, then remove your poster before 14:00 on Sep 9.
4. Please keep in mind that posters left at the place will be discard by the organizing committee.

Poster Award

Prizes will be awarded for the best posters.

Special session

Plenary Talk

Award Lecture

Mark Rees
Sheffield University
e-mail: `m.rees@sheffield.ac.uk`

Evolutionary Demography an Integral Projection Approach

Integral projection models (IPMs) project a continuously structured population, where say individuals are characterized by their size, in discrete time. An overview of the application of IPMs to field populations will be given covering 1) model parameterization in both constant and stochastic environments, 2) populations where multiple traits influence an individual's fate (e.g. size and age), and 3) density dependence. The use IPMs to understand the evolution of traits in natural populations will then be explored. In these IPMs individuals are characterized by traits that vary over the organism's life, such as size and age, and invariant traits, such as genotype or breeding value. Methods of approximating the dynamics of both the mean and variance of the genotype/breeding value distribution will be presented. Methods for embedding quantitative genetics models into IPMs will be presented and used to explore the timing of reproduction in two plant populations. These models will be used to explore the maintenance of genetic variability in natural populations.

Miles Davenport
Centre for Vascular Research, University of New South Wales, Sydney, Australia.
e-mail: `m.davenport@unsw.edu.au`

Modeling “latent” Infection

When we think of infection, we usually think of active replication of a virus or parasite, causing illness. However, some infections can lie sleeping (latent) for many years before they re-activate to cause a new active infection. Understanding how infections become latent, and how they reactivate from latency, is important to controlling infection. Because it is not easy to measure the latent (sleeping) infection, modeling is needed to study how infection reactivates. This talk will discuss modeling applied to experimental data from patient and animal studies to better understand the dynamics of latency in HIV infection.

REFERENCES

[1] Pinkevych M, Cromer D, Tolstrup M, Grimm AJ, Cooper DA, Lewin SR, Søgaard OS, Rasmussen TA, Kent SJ, Kelleher AD, Davenport MP.HIV Reactivation from Latency after Treatment Interruption Occurs on Average Every 5-8 Days--Implications for HIV Remission.PLoS Pathog. 2015 Jul 2;11(7):e1005000.
[2] Reece J, Petravic J, Balamurali M, Loh L, Gooneratne S, De Rose R, Kent SJ, Davenport MP.An "escape clock" for estimating the turnover of SIV DNA in resting $CD4^+$ T cells.PLoS Pathog. 2012;8(4):e1002615.

Takeshi Kano

Research Institute of Electrical Communication
e-mail: `tkano@riec.tohoku.ac.jp`

Toward Understanding of the Decentralized Control Mechanism Underlying Adaptive Locomotion of Animals

In this presentation, I talk about my research activities up to now, mainly focusing on the decentralized control mechanism underlying animal locomotion.

Animals exhibit adaptive, versatile, and resilient locomotion under unpredictable and unstructured real-world constraints. They achieve such movements by successfully coordinating many points along their bodies, each of which has some degrees of freedom, even though their computational resources are limited. A key mechanism for the coordination of many body points is an autonomous decentralized control, whereby the non-trivial macroscopic behavior or functionality of an entire system emerges through the coordination of simple individual components. In fact, several biological findings indicate that animal locomotion depends on autonomous decentralized control mechanisms such as biochemical oscillators in true slime molds [1] and central pattern generators (CPGs) found in many animals [2].

We are trying to understand the decentralized control mechanism of various animals by using a synthetic approach: we propose a mathematical model based on the observation of real animals, and then we implement the propose mechanism in a robot to reproduce the locomotion of real animals. I introduce our recent results based on this approach, particularly focusing on the locomotion of snakes and ophiuroids [3,4].

REFERENCES

[1] Takamatsu, A., Tanaka, R., Yamada, H., Nakagaki, T., Fujii, T., and Endo, I., 2001. Spatio-temporal Symmetry in Rings of Coupled Biological Oscillators of Physarum Plasmodium, *Phys. Rev. Lett.*, **87**: 078102.

[2] Ijspeert, A.J., 2008. Central Pattern Generators for Locomotion Control in Animals and Robots: A Review, *Neural Networks*, **21**: 642–653.

[3] Kano, T., Sato, T., Kobayashi, R., and Ishiguro, A., 2012. Local Reflexive Mechanisms Essential for Snakes' Scaffold-based Locomotion, *Bioinsp. Biomim.*, **7**: 046008.

[4] Kano, T., Sato, E., Aonuma, H., Matsuzaka, Y., and Ishiguro, A., 2014. Mathematical Model of Inter-arm Coordination Mechanism of Ophiuroids, *JSMB/SMB 2014*.

Yukihiko Nakata
Department of Mathematics, Shimane University
e-mail: `ynakata@riko.shimane-u.ac.jp`

Analysis and applications of delay equations in mathematical epidemiology

Mathematical description of disease transmission dynamics often yields a nonlinear infinite-dimensional dynamical system ([1]). Many important mathematical theories for infectious diseases dynamics have been developed [2]. However, the waning immunity is a major challenge for mathematical modeling and analysis. We present our recent studies for epidemiological models with waning immunity [3]. Here we also discuss delay equation formulation in the spirit of Lotka's renewal equation. We then introduce an application of delay differential equations for modeling periodical outbreak of a childhood disease [4].

REFERENCES

[1] W.O. Kermack, A.G. McKendrick, A contribution to the mathematical theory of epidemics. Proc. R. Soc. Lond. B Biol. Sci. **115** (1927) 700-721
[2] O. Diekmann, H. Heesterbeek, and T. Britton, Mathematical tools for understanding infectious disease dynamics. Princeton University Press, (2012)
[3] Y. Nakata, Y. Enatsu, H. Inaba, T. Kuniya, Y. Muroya, Y. Takeuchi, Stability of epidemic models with waning immunity. SUT J. Math. Vol. 50, No. 2 (2014), 205–245
[4] R. Omori, Y. Nakata, H. L. Tessmer, S. Suzuki, K. Shibayama, The determinant of periodicity in Mycoplasma pneumoniae incidence: an insight from mathematical modelling. Scientific Reports 5, 14473 (2015)

Takeshi Miki
Institute of Oceanography, National Taiwan University
Research Center for Environmental Changes, Academia Sinica
tksmiki@ntu.edu.tw

Multiple modeling approaches for better understanding the roles of microbial diversity in community and ecosystem dynamics.

Microbial diversity in natural environments had been not observable for long time but microbial ecology and environmental microbiology have identified microbial diversity in the last two decades. General ecology also has just started investigating *in-situ* roles of microbial diversity, not only for using microbial community as *model* system. Major research interests include the roles of microbial community and diversity as the determinant of fitness of other organisms and their diversity through interactions, e.g, those between microbes and plants, their impacts on ecosystem functions (i.e. biogeochemical processes such as carbon and nutrient cycling), and community and ecoststem stability. In this presentation, after briefly summarizing my past studies on the roles of microbial community (bacteria and fungi) in plant-soil feedback in terrestrial ecosystems, I'm going to talk on recent achievements and developing ideas for better understanding the roles of bacterial diversity in ecosystem functions and their stability.

With a series of mathematical models, we have investigated the roles of microbes in the plant-soil feedback system where plant community alters soil abiotic and biotic environment that in turn affects plant growth, competition, and thus community and ecosystem dynamics. A model of two plant-two microbe species coupled with nutrient cycling demonstrated the roles of microbial diversity in buffering species-specific plant control on soil environments, and thus maintaining plant coexistence [1]. The buffering effect was later supported by the microcosm experiment. A model of the stage-structured plant population coupled with two distinct microbial functional groups (parasitic and mutualistic ones) demonstrated that different plant traits are the key determinants of plant fitness under the dominance of parasitic or mutualistic microbes, which could also explain the empirical pattern [2]. We have also reviewed the past achievement in the field of plant-soil feedback from the point of mathematical modeling [3].

For better understanding the roles of bacterial diversity in the maintenance of ecosystem functioning in aquatic ecosystems, we are developing an integrated framework that combines comparative genomic analysis, microcosm experiments, and model simulations [4]. The key index to predict the decline of ecosystem functionality due to species loss is called 'functional redundancy', i.e., how many functions are shared by coexisting species within a community. Our new approach succeeded in evaluating the functional redundancy through species loss simulation using whole genome information of bacteria, which can quantitatively explain the results from microcosm experiments. On-going study extends this framework for developing new indices to predict functional stability of ecosystem, as well as the magnitude of ecosystem functions. Finally, I will briefly address the importance of developing new statistical methods to quantify microbial functions, which will be the main topic in my presentation at the mini symposium "Mathematical and statistical modeling to bridge the gap between empirical and theoretical research in ecology" on Sep. 9.

REFERENCES

[1] T. Miki*, Masayuki Ushio, Shin Fukui, Michio Kondoh. (2010) Functional diversity of microbial decomposers facilitates plant coexistence in a plant-microbe-soil feedback model. Proceedings of the National Academy of Sciences, USA 107:14251-14256

[2] Po-Ju Ke, Takeshi Miki*, Tzung-Su Ding (2015) The soil microbial community predicts the importance of plant traits in plant-soil feedback. New Phytologist DOI: 10.1111/nph.13215

[3] Po-Ju Ke*, Takeshi Miki (2015) Incorporating the soil environment and microbial community into plant competition theory. frontiers in Microbiology http://dx.doi.org/10.3389/fmicb.2015.01066

[4] Takeshi Miki, Taichi Yokokawa, Kazuaki Matsui* (2014) Biodiversity and multifunctionality in a microbial community: a novel theoretical approach to quantify functional redundancy. *Proceedings of The Royal Society B* vol.281 no.1776 20132498

Mini-Symposium Abstract

Special Symposium

Sep 7, 9:00 – 10:30, Room B

Complexity and coexistence of population in simple ecological systems

Organizer(s): **Malay Banerjee**
Associate professor of IIT Kanpur, Editorial Advisory board member of Ecological Complexity, Department of Mathematics and Statistics, Kanpur - 208016, INDIA
e-mail: `malayb@iitk.ac.in`

Yasuhiro TAKEUCHI
Aoyama Gakuin University, College of Science and Engineering, Department of Physics and Mathematics, Fuchinobe, ChuoKu, Sagamihara-shi, Kanagawa, 252-5258, Japan
e-mail: `takeuchi@gem.aoyama.ac.jp`

Lotka-Volterra (LV) model is fundamental in population dynamics. The two-species LV model admits no isolated periodic orbits. It is known the three-species LV model can exhibit periodic and even chaotic dynamics (2 prey, one-predator case and prey-predator with intra-guild predation by the top predator). If we modify two-species LV type prey-predator by adopting Holling type II functional response, the model can have a periodic solution but the appearance of large amplitude limit cycles leads to the paradox of enrichment. Recently several interesting bifurcation scenarios have been found when the logistic growth for prey is substituted with growth including Allee effect. The purpose of the symposium is to summarize the complex dynamics known in simple population models and how the modification of functional response or the growth with Allee effect or inclusion of maturation delay can change the bifurcation scenario. Also we discuss on the effect given by these modifications on the stable coexistence and persistence of population.

Time	**Title & Presenter**
09:00 – 09:30	**Coexistence of predators in simple ecological systems of intra-guild predation** **Toshiyuki Namba** (*Department of Biological Science, Graduate School of Science, Osaka Prefecture University*)
09:30 – 10:00	**Maturation delay for the predators can enhance stable coexistence in prey-predator model with Allee effect** **Yasuhiro Takeuchi** (*Department of Physics & Mathematics, College of Science & Engineering, Aoyama Gakuin University*)
10:00 – 10:30	**Maturation delay can stabilize the prey-predator dynamics** **Malay Banerjee** (*Department of Mathematics & Statistics, IIT Kanpur*)

Toshiyuki Namba
Department of Biological Science, Graduate School of Science, Osaka Prefecture University, Sakai, 599-8531 JAPAN
e-mail: tnamba@b.s.osakafu-u.ac.jp

Coexistence of predators in simple ecological systems of intra-guild predation

Prey-predator interactions are the basic building block of food-webs and food-chains. In a simple three-species module of intraguild predation, one of the two predators sharing common resources feeds on the other and three predator-prey interactions are included. Therefore, types of the functional responses and strengths of the interactions have significant effects on stability and persistence of the system.

In ecology, there is a controversial issue in a system of intraguild predation; Classical theory predicts that the intraguild prey goes to extinction at high productivity, but empirical observations do not support the prediction. In this talk, I will propose two hypotheses which can resolve the contradiction, using models with the functional responses of type II or type III. Importance of the relative profitability of two types of prey for the intraguild predator and the complex oscillations appearing through nonlinearity of the interactions will be emphasized.

REFERENCES

[1] Holt, R.D., and Polis, G.A., 1997. A theoretical framework for intraguild predation. American Naturalist, **149**:745–764.
[2] Tanabe, K., and Namba, T., 2005. Omivory creates chaos in simple food web models. *Ecology*, **86**: 3411–3414.
[3] Namba, T., Tanabe, K., and Maeda, N., 2008. Omnivory and stability of food webs. *Ecological Complexity*, **5**: 73-85.

Yasuhiro Takeuchi
Department of Physics & Mathematics, College of Science & Engineering, Ayoama Guykin University, Kanagawa, JAPAN

Malay Banerjee
Department of Mathematics & Statistics, IIT Kanpur, Kanpur, INDIA
e-mail: `malayb@iitk.ac.in`

Maturation delay for the predators can enhance stable coexistence in prey-predator model with Allee effect

We consider a prey-predator model with Allee effects in prey growth and Michaelis-Menten type functional response to describe the grazing pattern. We obtain the conditions for stable and oscillatory coexistence of prey and their specialist predator in case of strong and weak Allee effect in prey growth. Main objective of the present work is to show the stabilizing role of maturation delay in the presence of Allee effect in prey growth. We construct the delayed model by incorporating maturation delay parameter and juvenile predators death rate into the growth equation of predators. Apart from the analytical results for the non-delayed and delayed models, we perform extensive numerical simulations to construct the relevant bifurcation diagrams. We provide the biological implications of the current investigation in detail at the conclusion section.

REFERENCES

[1] Banerjee, M. and Takeuchi, Y., 2016. Maturation delay for the predators can enhance stable coexistence in prey-predator model with Allee effect. (under review).

Malay Banerjee
Department of Mathematics & Statistics, IIT Kanpur, Kanpur, INDIA
e-mail: `malayb@iitk.ac.in`

Yasuhiro Takeuchi
Department of Physics & Mathematics, College of Science & Engineering, Ayoama Guykin University, Kanagawa, JAPAN

Maturation delay can stabilize the prey-predator dynamics

Prey-predator type interaction model is the basic building block for several types of food-webs and food-chains. Two component prey-predator models are capable to exhibit a wide variety of complex dynamics which have relevance with the ecological phenomena we observe in real world ecosystems. There are several types of modeling approaches to construct the relevant models and analyze them to understand the system dynamics. It is well-known that delay differential equation models with such type of interactions are capable to produce oscillatory dynamics due to the introduction of delay in ordinary differential equation models. As a result it is common to believe that the delay is responsible for the destabilization of the system dynamics. This talk is intended to describe the construction of delayed prey-predator model with maturation delay and analysis of the complete model reveals that the delay can also stabilize the system dynamics. Furthermore, we emphasize that the construction of delayed model with appropriate ecological assumptions cannot always predict the destabilization although the incorporation of delay is ecologically justified. Conclusions are drawn based upon the analysis of two prey-predator model with Allee effect, one with prey-dependent functional response and another with ratio-dependent functional response.

REFERENCES

[1] Banerjee, M. and Takeuchi, Y., 2016. Maturation delay for the predators can enhance stable coexistence in prey-predator model with Allee effect. (under review).
[2] Sen, M., Banerjee, M. and Morozov, A., 2014. Stage-structured ratio-dependent predator-prey models revisited: When should the maturation lag results in systems' destabilization? *Ecological Complexity*, **19**: 23–34.

Mini-Symposium

Sep 7, 9:00 – 10:30, Room D

Structure-based control of complex network systems

Organizer(s): **Atsushi Mochizuki**
Theoretical Biology Laboratory, RIKEN, 2-1 Hirosawa, Wako 351-0198, JAPAN
e-mail: `mochi@riken.jp`

Controlling complex biological systems is one of the most important missions in basic biology and medical science. Especially in regenerative medicine, it is strongly required to establish non-empirical methods to regenerate cells or tissues artificially. Experimental methods have provided large information on interactions between bio-molecules. However, such network information is not sufficient to specify detail of the dynamics of systems. Recently, different theoretical methods were proposed independently, by which rational criteria to choose key nodes for controlling whole systems are given from structure of networks alone. In this symposium, we invite advanced researchers studying theoretical methods to control complex network systems. We discuss mathematical and practical aspects of these methods, and consider possible improvement and collaborations between different methods.

Time	**Title & Presenter**
09:00 – 09:20	**Minimum Dominating Set-Based Approaches for Controlling and Analyzing Biological Networks** **Tatsuya Akutsu** (*Kyoto University, Japan*)
09:20 – 09:40	**Tipping point in networked dynamical systems: control, recovery, and early warnings** **Ying-Cheng Lai** (*Arizona State University, USA*)
09:40 – 10:00	**Cell fate reprogramming by control of intracellular network dynamics** **Jorge Gómez Tejeda Zañudo** (*Pennsylvania State University, USA*)
10:00 – 10:20	**Controlling regulatory networks by feedback vertex sets** **Atsushi Mochizuki** (*RIKEN, Japan*)

Tatsuya Akutsu
Bioinformatics Center, Institute for Chemical Research, Kyoto University
e-mail: `takutsu@kuicr.kyoto-u.ac.jp`

Minimum Dominating Set-Based Approaches for Controlling and Analyzing Biological Networks

Extensive studies have recently been done on structural controllability of complex networks. Different from the well-studied approach based on bipartite matching, we have been studying an approach based on the minimum dominating set (MDS), where MDS is a well-known concept in graph theory and has been applied to analysis and control of engineering systems. We showed that if nodes in MDS are selected as control nodes and each of these nodes can control its connecting edges independently, the system is structurally controllable [1]. We also showed via theoretical analysis and computer simulation that the more heterogeneous a network degree distribution is, the easier it is to control the entire system [1]. Since then we have been extending this MDS-based approach as follows [2].

(1) Since many networks have bipartite network structure such as drug-disease networks and ncRNA-protein networks, we extended the MDS-based approach to bipartite networks in which controls are given for nodes in only one side.

(2) Jia et al. introduced the concepts of critical and redundant nodes in the maximum matching-based approach to controllability of complex networks. We applied these concepts to the MDS-based approach in both unipartite and bipartite networks.

(3) We introduced the robust MDS using which a network remains structurally controllable against arbitrary failures of up to a constant number of communication links (i.e., edges).

MDS has also been applied to analysis of various kinds of biological networks by us and by several other research groups, which include protein-protein interaction networks, drug-target protein network, non-coding RNA-protein network, and cancer metabolic network [2]. In this talk, we overview these extensions and applications of the MDS-based approach. This talk is based on joint work with Jose Nacher in Toho University.

REFERENCES

[1] Nacher, J.C. and Akutsu, T., 2012. Dominating scale-free networks with variable scaling exponent: heterogeneous networks are not difficult to control. *New Journal of Physics*, **14**:073005.
[2] Nacher, J.C. and Akutsu, T., 2016. Minimum dominating set-based methods for analyzing biological networks. *Methods*, **102**:57-63.

Ying-Cheng Lai
Arizona State University, USA
e-mail: `Ying-Cheng.Lai@asu.edu`

Tipping point in networked dynamical systems: control, recovery, and early warnings

A variety of complex dynamical systems, ranging from ecosystems and the climate to economic, social, and infrastructure systems, can exhibit a tipping point at which an abrupt transition to a catastrophic state occurs. To understand the dynamical properties of the system near a tipping point, to predict the tendency for the system to drift toward it, to issue early warnings, and finally to apply control to reverse or slow down the trend, are outstanding and extremely challenging problems. We consider two empirical bipartite mutualistic networks of pollinators and plants from the real world and investigate the issues of control, recovery, and early warning indicators. In particular, both networks exhibit a tipping point as a parameter characterizing the population decay changes continuously, at which the system collapses suddenly to zero abundance for all the species. We articulate two control strategies: (a) maintaining the abundance of a single influential pollinator and (b) eliminating the factors contributing to the decay of the pollinator. In both cases, we find that control can turn the sudden collapse into a more gradual process in the sense that extinction of the species occurs sequentially with variation of the parameter, indicating that control can effectively delay the occurrence of global extinction. We then investigate population revival as the bifurcation parameter varies in the opposite direction away from the tipping point. Without control, there is a hysteresis loop which indicates that, in order to revive the species abundance to the original level, the parameter needs to be further away from the tipping point, i.e., the environment needs to be fitter than before the collapse. However, with control the hysteresis behavior diminishes, suggesting the *positive role of control in facilitating species revival*. The issue of early warnings is also addressed. To develop effective control strategies to prevent the system from drifting towards a tipping point is an unsolved problem at the present, and we hope our work can shed light on the challenging and significant problem of understanding and controlling tipping point dynamics in nonlinear and complex systems.

This is a joint work with Mr. Junjie Jiang (PhD student at Arizona State University), Prof. Zigang Huang (Lanzhou University), Prof. Wei Lin (Fudan University), Prof. Tom Seager (Arizona State University), and Prof. Celso Grebogi (University of Aberdeen).

Jorge G. T. Zañudo
The Pennsylvania State University. Department of Physics. University Park, Pennsylvania, USA.
Dana-Farber Cancer Institute. Boston, Massachusetts, USA
Broad Institute of MIT and Harvard. Cambridge, Massachusetts, USA.
e-mail: `jgtz@phys.psu.edu`

Réka Albert
The Pennsylvania State University. Department of Physics. University Park, Pennsylvania, USA.
The Pennsylvania State University. Department of Biology. University Park, Pennsylvania, USA.

Cell fate reprogramming by control of intracellular network dynamics

Practical applications in modern molecular and systems biology, such as the search for new therapeutic targets for diseases and stem cell reprogramming, have generated a great interest in the cell fate reprogramming, i.e., controlling the internal state of a cell so that it is driven from an initial state to a final target state. Although the topic of controlling the dynamics of a system, of which cell fate reprogramming can be considered a subset, has a long history in control and systems theory [1, 2], most of this work is not directly applicable to intracellular networks. Among the main reasons for this are the nonlinear nature of intracellular dynamics and the lack of consideration of biologically admissible states [3]. Furthermore, most control methods rely solely on the structural or the functional information available for a system, and thus, do not take advantage of the full range of biological information available for intracellular networks.

Here we present a network control method that integrates the structural and functional information available for intracellular networks to predict control targets [4]. Formulated in a logical dynamic scheme [5, 6], our control method takes advantage of certain function-dependent network components, referred to as stable motifs [7], and their relation to steady states, in order to identify targets whose manipulation (upregulation or downregulation) ensures the convergence of the system towards or away from a steady state of interest. Among the noteworthy properties of our approach are that it drives any initial state to the target state with 100% effectiveness and needs to be applied only transiently for the network to reach and stay in the desired state [4]. We illustrate our method's potential to find intervention targets for cancer treatment and cell differentiation by applying it to a leukemia signaling network [8] and to the network underlying the epithelial-to-mesenchymal transition in liver cancer [9]. We show that stabilizing the expression or activity of a few select components in these models can drive the cell towards a desired fate or away from an undesired fate. Moreover, we confirm the validity of the predicted control targets in a differential equation version of the tested models and also find the predicted interventions are supported by experimental work, thus suggesting our control targets are effective in a broad dynamic sense. Overall, our approach provides new insights into how to control the dynamics of intracellular networks.

REFERENCES

[1] Luenberger DG (1979) Introduction to Dynamic Systems: Theory, Models, and Applications. Wiley.
[2] Slotine JJ, Li W (1991) Applied Nonlinear Control. Prentice-Hall.
[3] Müller FJ and Schuppert A (2011) Few inputs can reprogram biological networks. Nature 478, E4.
[4] Zañudo JGT, Albert R (2015) Cell Fate Reprogramming by Control of Intracellular Network Dynamics. PLoS Comput Biol 11(4): e1004193.
[5] Morris MK, Saez-Rodriguez J, Sorger PK, and Lauffenburger DA (2010). Logic-based models for the analysis of cell signaling networks. Biochemistry 49, 3216–24.
[6] Wang RS, Saadatpour A, and Albert R (2012). Boolean modeling in systems biology: an overview of methodology and applications. Physical Biology 9, 055001.
[7] Zañudo JGT and Albert R (2013) An effective network reduction approach to find the dynamical repertoire of discrete dynamic networks. Chaos 23 (2), 025111. Focus Issue: Quantitative Approaches to Genetic Networks.
[8] Zhang R, Shah MV, Yang J, et al. (2008) Network Model of Survival Signaling in LGL Leukemia. PNAS 105, 16308–16313.
[9] Steinway SN, Zañudo JGT, Ding W, et al. (2014) Network Modeling of TGFβ Signaling in Hepatocellular Carcinoma Epithelial-to-Mesenchymal Transition Reveals Joint Sonic Hedgehog and Wnt Pathway Activation. Cancer Research 74 (21), 5963–77.

Atsushi Mochizuki
Theoretical Biology Laboratory, RIKEN, Japan
CREST, JST, Japan
e-mail: `mochi@riken.jp`

Bernold Fiedler
Department of Mathematics, Free University of Berlin, Germany

Yutaka Satou
Graduate School of Science, Kyoto University, Japan

Kazuki Maeda
School of Science and Technology, Kwansei Gakuin University, Japan

Controlling regulatory networks by feedback vertex sets

Modern biology provides many networks describing regulations between a large number of species of bio-molecules. It is widely believed that the dynamics of molecular activities based on such regulatory networks are the origin of biological functions. In this study we present a mathematical theory to provide an important aspect of dynamics from information of regulatory linkages alone. We also present an application of our theory to a real biological network, and experimental results to verify our prediction.

In theoretical part, we show that the "feedback vertex set" (FVS) of a regulatory network is a set of "determining nodes" of the dynamics. It assures that i) any long-term dynamical behavior of the whole system, such as steady states, periodic oscillations or quasi-periodic oscillations, can be identified by measurements of a subset of molecules in the network, and that ii) the subset is determined from the regulatory linkage alone. The theory also claims that iii) dynamical behavior of the whole system can be switched from one attractor to others just by controlling the dynamics of the FVS.

In experimental application, we analyzed a gene regulatory network including 90 genes, which is responsible for cell differentiation in early development of ascidian. We identified five genes in minimum FVS of the network. We conducted a series of experiments to control activities of these five genes to verify our prediction. The exhaustive artificial activation/inhibition of five genes showed that the system of cell fate determination could be controlled totally just by controlling activities of five genes in FVS.

REFERENCES

[1] Mochizuki, A., Fiedler, B., Kurosawa, G. and Saito, D., 2013. Dynamics and control at feedback vertex sets. II: A faithful monitor to determine the diversity of molecular activities in regulatory networks. *J. Theor. Biol.*, **335**, 130-146.
[2] Kobayashi, K., Maeda, K., Tokuoka, M., Mochizuki, A. and Satou, Y. In Preparation.

Mini-Symposium

Sep 7, 9:00 – 10:30, Room E

Biological oscillations at diverse spatiotemporal scales

Organizer(s): **Takayuki Ohara**
Graduate School of Environmental Science, Hokkaido University, N10W5, Kita-ku, Sapporo 060-0810, Japan
e-mail: `t.ohara.63920@ees.hokudai.ac.jp`

Akiko Satake
Department of Biology, Faculty of Science, Kyushu University, 744, Motooka, Nishi-ku, Fukuoka 819-0395, Japan
e-mail: `akiko.satake@kyudai.jp`

Periodic or chaotic oscillations are observed in diverse biological phenomena at different spatiotemporal scales ranging from gene expression to mass flowering of forests.

These rhythmic phenomena are directly connected with the fitness of organisms, e.g. rhythmic patterns of plant starch metabolism to avoid carbon starvation.

In this session, recent findings about biological oscillations at different scales including cellular circadian rhythms of plants and mammals, growth patterns of plant tissue, and synchronization of plant reproduction will be presented.

The purpose of the session is (i) to provide the audiences with diverse topics of biological rhythms, and (ii) to develop our understanding of the oscillation phenomena by sharing different viewpoints obtained from the studies of distinct spatiotemporal scales.

Time	**Title & Presenter**
09:00 – 09:25	**The plant circadian clock as a multi-oscillator system** **Tomoaki Muranaka** (*Nagoya University*)
09:25 – 09:45	**Phase response of circadian clocks optimizes the growth of Arabidopsis thaliana** **Takayuki Ohara** (*Hokkaido University*)
09:45 – 10:10	**GABA-mediated phase couplings and seasonal time coding in the suprachiasmatic nucleus** **Sungho Hong** (*OIST*)
10:10 – 10:30	**Parameterization and validation of a resource budget model for masting using spatiotemporal flowering data of individual trees** **Akiko Satake** (*Kyushu University*)

Tomoaki Muranaka
Graduate School of Science, Nagoya University
e-mail: `muranaka.tomoaki@c.mbox.nagoya-u.ac.jp`

Tokitaka Oyama
Graduate School of Science, Kyoto University

The plant circadian clock as a multi-oscillator system

The circadian clock is the endogenous timing system based on self-sustained oscillations. In eukaryotes, the circadian clock is implemented in individual cells as a gene regulatory oscillator. Thus, the circadian system of multicellular organisms should be understood as a multi-oscillator system. For this purpose, the observation of circadian rhythms at a cellular level is essential. Recent bioluminescence imaging techniques using mammalian cells revealed noisy and heterogeneous circadian rhythms in isolated cells and tight coupling between neurons in the suprachiasmatic nucleus, the master clock organ.

In plants, a tendency of independence in behaviors of cellular clocks has been demonstrated. Previous studies reporting the intra-tissue desynchronization of circadian rhythms indicated the heterogeneous traits of cellular clocks and the weakness of cell-to-cell coupling. However, fundamental properties of the cellular clock, such as instability, heterogeneity, and the manner of cell-to-cell interaction, remain unclear because of the difficulty of monitoring the circadian gene expression in individual cells.

To address this problem, we developed a single-cell bioluminescence imaging system using duckweeds [1]. In this system, a circadian reporter, *AtCCA1::LUC*, was introduced into cells located near upper surface of a plant body by particle bombardment. Then the luminescence from transfected cells that dispersed on the same frond (leaf-like structure) was monitored by a high-sensitive CCD camera. The tiny and flat body of duckweeds was remarkable advantages for a long-term imaging of the entire body.

Using this system, we monitored cellular circadian rhythms under various light conditions for more than a week [2]. Under constant light conditions, each cellular rhythm was maintained but desynchronization between cells in the same frond was observed. Quantitative analysis of these asynchronous rhythms uncovered the heterogeneity and instability of cellular clocks and partial synchronization between neighboring cells. The extents of heterogeneity and instability of plant cellular clocks were comparable to those of cultured fibroblast cells of mouse. Then we exposed the plants at an asynchronous state to the external light-dark cycles. Cellular rhythms at any phase were synchronized to light-dark cycles within a couple of days. Interestingly, the luminescence traces in the first dark period was depended on their onset phases, suggesting that cellular clocks in the same tissue individually responded to the dark signal. Furthermore, we found that cellular clocks in the plant body under light-dark cycles showed a centrifugal phase pattern. Because there was no such spatial pattern in free-running periods of them, the locked phase of each cellular clock depended on its position rather than its free-running period.

Collectively, our studies revealed that cellular circadian clocks in intact plants work individually as heterogeneous oscillators under constant conditions and that the heterogeneity is corrected under light-dark cycles to coordinate the daily rhythms of the plant body. These findings provide a novel perspective on spatiotemporal architectures in the plant circadian system.

REFERENCES

[1] Muranaka, T., Kubota, S. and Oyama, T., 2013. A single-cell bioluminescence imaging system for monitoring cellular gene expression in a plant body. *Plant Cell Physiology*, **54**: 2085-2093

[2] Muranaka, T. and Oyama, T., 2016. Heterogeneity of cellular circadian clocks in intact plants and its correction under light-dark cycles. *Science Advances*, **2**: e1600500

Takayuki Ohara
Graduate School of Environmental Science, Hokkaido University, Sapporo, Japan
e-mail: `t.ohara.63920@ees.hokudai.ac.jp`

Akiko Satake
Department of Biology, Faculty of Science, Kyusyu University, Fukuoka, Japan

Phase response of circadian clocks optimizes the growth of *Arabidopsis thaliana*

Circadian clocks are internal pacemakers of living organisms that coordinate their physiology and metabolism to periodically changing environment. In higher plants, diverse biological processes such as flowering and gene expression are under the control of the circadian clocks [1]. Recent experimental studies have showed that growth rates of leaves and roots of *Arabidopsis thaliana* diurnally oscillate [2,3], which suggest the circadian regulation of the plant growth. One of the important characteristics of the circadian clocks is the regulation of their phase by external stimuli such as light and sugar [4]. In our previous study, we have showed that the phase response of plant circadian clocks to sugar signals reduces the variations of sucrose concentration [5]. This means that plants can avoid the situation where the amount of sucrose extremely decreases, i.e. starvation of sucrose occurs. In *pgm* mutants, which are not able to accumulate starch, sucrose largely fluctuates throughout a day, and depletes at night [6]. Moreover, the growth of *pgm* mutants is severely impaired compared with wild type plants [7]. These observations suggest that sucrose starvation causes the reduction of the plant growth. Taken together, there is a possibility that the phase response to sugar signals leads to the stable growth of plants.

In this study, we investigate the effect of the phase response of circadian clocks on the plant growth. We first construct the mathematical model describing the sugar dynamics in source leaves and sink tissues. In source leaves, sugar is produced by photosynthesis and is exported to growing sink tissues. In sink tissues such as root or young leaves, sugar is supplied from sources and is spent for growth. Carbon metabolism in the source region is regulated by the circadian clocks. In addition, based on the pressure flow hypothesis, we model the sucrose translocation between the source and the sink on the basis of the Hagen-Poiseuille law. Regarding the plant growth, we assume that the growth of sink tissues is proportional to the amount of sucrose existing in each sink and the growth is inhibited when the amount of sucrose falls below the threshold level of sucrose. We then simulate the long-term growth patterns of wild type plants and mutants, which are insensitive to sugar signals, in the presence of annual changes of day lengths. Based on the comparison of the growth patterns, we discuss whether the phase response of circadian clocks is effective in the achievement of the stable growth in the natural environment.

REFERENCES

[1] Harmer, S.L., 2009. The circadian system in higher plants. *Annu. Rev. Plant Biol.*, **60**: 357–377.
[2] Wiese, A., Christ, M.M., Virnich, O., Schurr, U. and Walter, A., 2007. Spatio-temporal leaf growth patterns of *Arabidopsis thaliana* and evidence for sugar control of the diel leaf growth cycle. *New Phytologist*, **174**: 752–761.
[3] Yazdanbakhsh, N., Sulpice, R., Graf, A., Stitt, M. and Fisahn, J., 2011. Circadian control of root elongation and C partitioning in *Arabidopsis thaliana*. *Plant Cell Environ*., **34**: 877–894.
[4] Haydon, M.J., Mielczarek, O., Robertson, F.C., Hubbard, K.E. and Webb, A.A.R., 2013. Photosynthetic entrainment of the *Arabidopsis thaliana* circadian clock. *Nature*, **502**: 689–692.
[5] Seki, M., Ohara, T., Hearn, T.J., Frank, A., da Silva, V.H., Caldana, C., Webb, A.A.R. and Satake, A., in preparation.
[6] Gibon, Y., Bläsing, O.E., Palacios-Rojas, N., Pankovic, D., Hendriks, J.H.M., Fisahn, J., Höhne, M., Günther, M. and Stitt, M., 2004. Adjustment of diurnal starch turnover to short days: depletion of sugar during the night leads to a temporary inhibition of carbohydrate utilization, accumulation of sugars and post-translational activation of ADP-glucose pyrophosphorylase in the following light period. *Plant J.*, **39**: 847–862.
[7] Caspar, T., Huber, S.C. and Somerville, C., 1985. Alterations in growth, photosynthesis, and respiration in a starchless mutant of *Arabidopsis thaliana* (L.) deficient in chloroplast phosphoglucomutase activity. *Plant Physiol.*, **79**: 11–17.

Sungho Hong
Computational Neuroscience Unit, Okinawa Institute of Science and Technology
e-mail: `shhong@oist.jp`

Jihwan Myung
Laboratory for Mental Biology, RIKEN Brain Science Institute

GABA-mediated phase couplings and seasonal time coding in the suprachiasmatic nucleus

The fundamental processes underlying the function and behavior of most life forms on Earth, such as plants and animals, are locked in a circadian rhythm that is synchronized with the 24-hour cycle of light and darkness. Furthermore, organisms can adapt the rhythm to changes in this cycle, such as seasonal variation in day length, which is crucial for survival.

I will present our recent findings [1] that can explain how the suprachiasmatic nucleus (SCN), a master clock for the circadian rhythm in the brain [2], can memorize and encode information about daylength. We have found that GABA-mediated signaling, which is dominant in the SCN neural circuit, organizes 24-hour rhythmic activity of gene expression networks within individual neurons into an oscillator network. Crucially, the network structure has asymmetrically distributed phase repulsive (desynchronizing) and attractive (synchronizing) couplings, and this leads to a unique computational property that can explain various features of the SCN dynamics and circadian behavior. Furthermore, the daylength-dependent shift in the balance between two different couplings, which can explain seasonal changes in the SCN oscillators and animal's circadian behavior, comes from the changes in GABAergic signaling due to plasticity in cellular mechanisms regulating intracellular chloride.

We suggest that these results show that the SCN is a memory for circadian information in the brain, governed by the *tunable* balance between excitation and inhibition in its neural circuit that regulates the balance between repulsive and attractive phase couplings within the network of gene expression oscillators.

REFERENCES

[1] Myung J, Hong S, DeWoskin D, De Schutter E, Forger DB, Takumi T. 2015. GABA-mediated repulsive coupling between circadian clock neurons in the SCN encodes seasonal time. *Proc Natl Acad Sci USA* **112**:E3290-9.
[2] Welsh DK, Takahashi JS, Kay SA. 2010. Suprachiasmatic Nucleus: Cell Autonomy and Network Properties. *Annu Rev Physiol* **72**: 551–577.

Akiko Satake
Department of Biology, Faculty of Science, Kyusyu University, Fukuoka, Japan
e-mail: `akiko.satake@kyudai.jp`

Tomoyuki Abe
Hirokazu Kon
Akiko Nagasaka
Kensuke Onodera
Kazuhiro Minamino
Hokkaido Research Organization, Forestry Research Institute, Higashiyama, Koshunai, Bibai 079-0198, Japan.

Yuuya Tachiki
Department of Biology, Faculty of Science, Kyusyu University, Fukuoka, Japan

Qingmin Han
Department of Plant Ecology, Forestry and Forest Products Research Institute, Tsukuba 305-8687, Japan.

Parameterization and validation of a resource budget model for masting using spatiotemporal flowering data of individual trees

Synchronized and fluctuating reproduction by plant populations, called masting, is widespread in diverse taxonomic groups. Proximally, many studies have suggested significant links between masting and climatic variables, such as temperature, the temperature difference in the two previous seasons and rainfall. Conversely, effects of internal factors such as carbon and nitrogen have been demonstrated to play an important role in the regulation of masting. These ecological findings for proximate factors of masting are, at least for the flowering process, consistent with recent findings from the molecular genetic studies of flowering time that indicate that requirements from both climatic cues and resource availability must be satisfied for a plant to switch from vegetative growth to flowering. Although the way climate factors influence seed production is not well understood, the interplay between climatic factors and resource dynamics could be found in the process of seed ripening that determines the quantity of mature seed production because seasonal precipitation and temperature influence plant nitrogen and carbon availability. Therefore, we need to study coupled effects of climatic factor and internal resource dynamics on masting [1].

A family of resource budget models would be an ideal tool to evaluate the coupled effect of climatic factors and resource availability on masting [2]. Here, we propose a new method to explore the proximate mechanism of masting by combining spatiotemporal flowering data, biochemical analysis of resource allocation, and the resource budget model [3]. Flowering data of 170 trees over 13 years showed the emergence of clustering with trees in a given cluster mutually synchronized in reproduction, which was successfully explained by resource budget models that consider dynamic allocation of carbon or nitrogen resources for reproduction [4]. Analysis of resources invested in the development of reproductive organs showed that parametric values used in the model are significantly different between nitrogen and carbon. Using a fully parameterized model, we showed that the observed flowering pattern is explained only when the interplay between nitrogen dynamics and climatic cues was considered. This result indicates that our approach successfully identified resource type-specific roles on masting and that the method is suitable for a wide range of plant species.

REFERENCES

[1] Monks, A., Monks, J.M. & Tanentzap, A.J. 2016. Resource limitation underlying multiple masting models makes mast seeding sensitive to future climate change. *New Phytologist,* 210, 419-430.

[2] Crone, E.E. & Rapp, J.M. 2014. Resource depletion, pollen coupling, and the ecology of mast seeding. *Ann. N.Y. Acad. Sci.,* 1322, 21-34.

[3] Satake, A. & Iwasa, Y. 2000. Pollen coupling of forest trees: forming synchronized and periodic reproduction out of chaos. *J. Theor. Biol.,* 203, 63-84.

[4] Abe, T, Tachiki, Y., Kon, H., Nagasaka, A., Onodera, K., Minamino, K., Han, Q., Satake, A. 2016. Parameterization and validation of a resource budget model for masting using spatiotemporal flowering data of individual trees. *Ecology Letter* DOI: 10.1111/ele.12651.

Mini-Symposium

Sep 7, 10:45 – 12:15, Room B

Cancer Modeling

Organizer(s): **Hiroshi Haeno**
Kyushu University, 744 Motooka, Nishi-ku, Fukuoka 819-0395, Japan
e-mail: `haeno@kyushu-u.org`

In the field of cancer research, the demand of mathematical and theoretical analysis has recently been increasing. Based on tons of genomic data and tumor growth data with/without drugs, lots of mathematical and statistical models have been investigated for revealing the theory of cancer dynamics and evolution. In this symposium, we will present the up-to-date mathematical models of cancer based on experimental and clinical data and spread the opportunities that theoretical researchers study cancer.

Time	**Title & Presenter**
10:45 – 11:08	**The evolution of tumor metastasis during clonal expansion with alterations in metastasis driver genes** **Hiroshi Haeno** (*Kyushu University*)
11:08 – 11:30	**Cancer risk of Japanese Atomic bomb survivors: challenge in radiation epidemiology to investigate radiation carcinogenesis** **Munechika Misumi** (*Radiation Effects Research Foundation*)
11:30 – 11:53	**A unified framework to model induced stem cell - a case study of generalized multi-type branching process and beyond** **Lin L. Liu** (*Harvard University*)
11:53 – 12:15	**Computational Modeling of Individualized Management in Pancreatic Adenocarcinoma** **Kimiyo N. Yamamoto** (*Kyushu University*)

Hiroshi Haeno
Department of Biology, Kyushu University
e-mail: `haeno@kyushu-u.org`

The evolution of tumor metastasis during clonal expansion with alterations in metastasis driver genes

Metastasis is a leading cause of cancer-related deaths. Carcinoma generally initiates at a specific organ as a primary tumor, but eventually metastasizes and forms tumor sites in other organs. In this report, we developed a mathematical model of cancer progression with alterations in metastasis-related genes. In cases in which tumor cells acquire metastatic ability through two steps of genetic alterations, we derive formulas for the probability, the expected number, and the distribution of the number of metastases. Moreover, we investigate practical pancreatic cancer disease progression in cases in which both one and two steps of genetic alterations are responsible for metastatic formation. Importantly, we derive a mathematical formula for the survival outcome validated using clinical data as well as direct simulations. Our model provides theoretical insights into how invisible metastases distribute upon diagnosis with respect to growth rates, (epi)genetic alteration rates, metastatic rate, and detection size. Prediction of survival outcome using the formula is of clinical importance in terms of determining therapeutic strategies.

Munechika Misumi
Department of Statistics, Radiation Effects Research Foundation
e-mail: `misumi@rerf.or.jp`

Cancer risk of Japanese Atomic bomb survivors: challenge in radiation epidemiology to investigate radiation carcinogenesis

The Life Span Study (LSS) of the Radiation Effects Research Foundation (RERF) has long been a primary resource for evaluation of health risks associated with exposure to ionizing radiation. Radiation risks are usually described by a parametric regression model in the LSS [1]. However, there are issues with imposing a parametric assumption on the dose-response, such as unrealistic uncertainty estimates due to the parametric constraint. If we are uncertain of the exact shape of the dose-response, a linear function passing through the origin provides unrealistically narrow confidence intervals especially in low dose range. Also, the risk estimate based on a simple linear dose-response function is strongly influenced by cases with high dose, which are actually very few in the LSS cohort due to the highly skewed distribution of radiation dose. In estimating the uncertainty based on a non-parametric function, such messages reflecting the reality of the data were revealed [2]. In addition to the radiation dose-response, the variables that modify the radiation risk have also traditionally been modeled with parametric functions which are used to describe risk. With regard to this conventional parametric modeling, there was a concern about risk estimates near the limits of ranges of the data. We recently applied a multi-dimensional smoothing for the radiation excess relative risk (ERR), simultaneously smoothing with respect to the dose and the modifiers of the radiation effect, such as age at exposure, to loosen the parametric constraints on the age trends of ERR with the results graphically described [3]. That method enabled us to have better insights about the risks of low dose exposure at young ages, which are of general public concern. However, in investigating and understanding radiation carcinogenesis, we are facing a big challenge with statistical limitations related to small effect size in the low radiation dose range.

REFERENCES

[1] Preston D, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M, Mabuchi K, Kodama K. Solid cancer incidence in atomic bomb survivors: 1958-1998. *Radiat Res* 2007; **168**: 1-64.
[2] Furukawa K, Misumi M, Cologne JB, Cullings HM, A Bayesian Semiparametric Model for Radiation Dose-Response Estimation., *Risk Analysis*, 2016 Jun;36(6):1211-23.
[3] Misumi M, Furukawa K, Multi-dimensional smoothing for age trends of radiation effects on the cancer risk of Japanese Atomic bomb survivors, unpublished.

Lin L Liu
Department of Biostatistics, Harvard University
e-mail: `lliu.hsph@gmail.com`

A unified framework to model induced stem cell - a case study of generalized multi-type branching process and beyond

Reprogramming of somatic cells to induced pluripotent stem cells (iPSCs) is a promising tool for novel therapeutic strategies in cancer research. A fundamental question that biologists working on iPSCs often ask is whether the reprogramming process is deterministic or stochastic. A variety of physical models have been employed to study such process as attempts to answer such question, albeit none of the previous works were analyzed altogether in a unified and interpretable mathematical framework. With such goal in mind, we modeled the system using generalized multi-type branching processes that can help us dissect the variability observed in the experiments into process-intrinsic noise (stochasticity in random proliferation/apoptosis/cell fate transition) and process-extrinsic noise (such as variability among cells or measurement noise). We found that reprogramming driven by the Yamanaka factors alone is a heterogeneous process due to cell-specific reprogramming rates, which can be homogenized by the addition of additional factors. We also validated our approach using all publicly available induced reprogramming time-series data with different types of information recorded, such as the distribution of some vague form of first passage time, direct cell counts and etc., and thus demonstrated the general utility and predictive power of our methodology for investigating reprogramming and other cell fate change systems. If time permits, I will also briefly talk about some other ongoing projects related to therapeutic optimization in cancer and models on antibody stimulation in cancer vaccine and germinal center reaction based on knowledge gained very recently on the newly discovered follicle regulatory T cells in the germinal center.

Kimiyo N. Yamamoto
Department of Biology, Kyushu University
e-mail: `kyamamoto@kyushu-u.org`

Computational Modeling of Individualized Management in Pancreatic Adenocarcinoma

Pancreatic ductal adenocarcinoma (PDAC) is one of the leading causes of cancer-related mortality. To treat patients with this malignancy most effectively, we propose individualizing management based on a mathematical framework validated by clinical data from two independent institutes. The computational model considers alterations in specific genes – *KRAS*, *CDKN2A*, *TP53*, and *SMAD4*. The model well represents the dynamics of PDAC regarding metastatic patterns, response to medical interventions, and the genetic evolution. Importantly, we succeed in identifying a potential predictive factor indicating a subgroup of patients with low metastatic efficiency. The marker is universally applicable throughout the range of detected sizes of tumors. From computational clinical trials with the predictive factor, we reveal that the selected subgroup obtains its best benefits from (i) complete resection, (ii) adjuvant chemoradiation therapy, and (iii) salvage treatment for isolated recurrence. Our computational approach provides insights into clinical decision making in PDAC.

Mini-Symposium

Sep 7, 10:45 – 12:15, Room D

Network and Timeline: Recent Topics in Complex Networks

Organizer(s): **Takaaki Aoki**
Faculty of Education, Kagawa University
e-mail: `aoki@ed.kagawa-u.ac.jp`

Satoru Morita
Department of Mathematical and Systems Engineering, Shizuoka University
e-mail: `morita.satoru@shizuoka.ac.jp`

The purpose of this symposium is to bring together some new topics in network science, which are expected to be associated with mathematical biology. We will discuss possibility of new models of temporal networks, adaptive networks and epidemics on networks.

Time	**Title & Presenter**
10:45 – 11:05	**Burst behavior and scale-free network emerging in adaptive temporal Networks** **Takaaki Aoki** (*Kagawa University*)
11:05 – 11:25	**Controlling the emergence of event cascades in inhomogeneous networks** **Tomokatsu Onaga** (*Kyoto University*)
11:25 – 11:45	**On uncertainty of epidemic spreading in complex networks** **Taro Takaguchi** (*National Institute of Information and Communications Technology*)
11:45 – 12:05	**Comparison among several types SIS epidemic models on networks** **Satoru Morita** (*Shizuoka University*)
12:05 – 12:15	**Discussion**

Takaaki Aoki
Kagawa University
e-mail :`aoki@ed.kagawa-u.ac.jp`

Burst behavior and scale-free network emerging in adaptive temporal Networks

The spread of information in society depends on communication networks between people. These networks are characterized by both structure, i.e. who is connected to whom, and by temporal patterns, i.e. the times when communication actually occurs. The increasing availability of large high-resolution data on human behavior revealed that these networks follow non-trivial structural and temporal patterns, such Bursting behavior of social contact patterns and the scale-free structure of social networks.

To study these patterns on human communication, previous research has treated structure and timings as different phenomena, even though they both originate from communication. From the physics perspective, we address a fundamental question that is to find a unified process able to reproduce both structural temporal patterns, telling us more on the nature of human dynamics. We propose a model based on a feedback between communication of information and adaptive network behavior that explains the emergence of structural and temporal patterns as observed in real-life.

In statistical physics, particles interact with each other and exchange energy. Our intuitive model, motivated by kinetic theory, considers that many interacting individuals exchange hypothetical resources that in turn regulate their own activation rate. We show that this model exhibits distinct behavior, reminiscent of real-life communication, by simply varying a control parameter, similarly to changes of temperature in kinetic theory.

This relatively simple and theoretically tractable physics model of stochastic processes opens up several opportunities to better understand human communication by using methods of statistical physics.

REFERENCES

[1] Takaaki Aoki, Luis E. C. Rocha, and Thilo Gross, 2016. Temporal and structural heterogeneities emerging in adaptive temporal networks. *Physical Review E Rapid Communication*, **93**, 040301(R) .

Tomokatsu Onaga
Department of Physics, Kyoto University, Kyoto 606-8502, Japan
e-mail: `onaga@scphys.kyoto-u.ac.jp`

Shigeru Shinomoto
Department of Physics, Kyoto University, Kyoto 606-8502, Japan

Controlling the emergence of event cascades in inhomogeneous networks.

There is a commonality among contagious diseases, tweets, and neuronal firings that past events facilitate the future occurrence of events. A key quantity representing the interaction in these various phenomena is the basic reproduction ratio, which is defined as the average number of additional events induced by a single event. The spread of events has been extensively studied such that the systems exhibit catastrophic chain reactions if the interaction represented by the ratio of reproduction exceeds the epidemic threshold [1]. In epidemics, a disease becomes a pandemic if the reproduction ratio is greater than the epidemic threshold, as in a nuclear chain reaction, and vanishes otherwise. Nevertheless, the event-occurrence does not cease if individuals are stimulated in external communities or exhibit spontaneous activity. In such situations, the system may still exhibit cascades of event-occurrences intermittently, even if the reproduction ratio is smaller than the epidemic threshold, as in tweets and neuronal firings *in vivo*.

Here, we report that these systems are possessed by nonstationary cascades of event-occurrences already in the subthreshold regime [2]. Event cascades can be a nuisance in some contexts, such as when the peak-demand causes vaccine shortages or heavy traffic on communication lines, but may be beneficial in other contexts; for example, spontaneous activity in neural networks may be used to generate motion or store memory [3]. Thus it is important to comprehend the mechanism by which such cascades appear, and consider controlling a system to tame or facilitate fluctuations in the event-occurrences. We use epidemic Markov process and Hawkes process to analyze event cascades and derive the condition in which event cascades emerge. The critical interaction for the emergence of cascades depends greatly on the network structure in which individuals are connected. We demonstrate that we can predict whether cascades may emerge, given information about the interactions between individuals. Furthermore, we suggest a systematic method for controlling systems to oppress or promote the event cascades. Accordingly we found that reciprocal connections and clustering tends to facilitate event cascades.

REFERENCES

[1] Pastor-Satorras, R., Castellano, C., Van Mieghem, P. and Vespignani, V., 2015. Epidemic processes in complex networks. *Rev. Mod. Phys.*, **87**: 925.
[2] Onaga, T. and Shinomoto, S., 2014. Bursting transition in a linear self-exciting process. *Phys. Rev. E*, **89**: 042817.
[3] Sussillo, D., Abbott, L. F., 2009. Generating coherent patterns of activity from chaotic neural networks. *Neuron*, **63(4)**: 544-557.

Taro Takaguchi
National Institute of Information and Communications Technology
Global Research Center for Big Data Mathematics, National Institute of Informatics
JST, ERATO, Kawarabayashi Large Graph Project
e-mail: `taro.takaguchi@nict.go.jp`

On uncertainty of epidemic spreading in complex networks

Threat of epidemic spreading in societies partly stems from the uncertain nature of its behavior. The uncertainty has been taken into account in mathematical modeling of spreading process by means of stochastic processes [1]. On the other hand, recent theoretical studies proved that a characteristic measure of epidemics converges to a deterministic function in a long-term limit [2]. We investigated this transition from stochastic to deterministic behavior on the basis of numerical simulations. The main results presented in this talk are based on the collaboration work [3] with Petter Holme (Sungkyunkwan University, Korea). In addition, we will discuss a future direction on predicting epidemics beyond model simulations by using additional information sources.

REFERENCES

[1] Romualdo Pastor-Satorras, Claudio Castellano, Piet Van Mieghem, and Alessandro Vespignani, 2015. Epidemic processes in complex networks. *Review of Modern Physics,* **87**: 925.
[2] Svante Janson, Malwina Luczak, and Peter Windridge, 2014. Law of large numbers for the SIR epidemic on a random graph with given degrees. *Random Structures & Algorithms,* **45**: 724-761.
[3] Petter Holme and Taro Takaguchi, 2015. Time evolution of predictability of epidemics on networks. *Physical Review* E **91**: 042811.

Satoru Morita
Shizuoka University
e-mail: morita.satoru@shizuoka.ac.jp

Comparison among several types SIS epidemic models on networks

Spreading phenomena are ubiquitous in nature and society. For example, disease and information spread over underlying social and information networks. Recently, spreading processes on scale-free networks have been intensively studied. In scale-free networks the distribution of degree obeys a power law, and high degree nodes are called hubs. It has been well known that the hubs can lead to the absence of an outbreak threshold. In the previous work [1], I introduced six types of SIS models on scale-free networks, where the links represent potential connections. It is assumed that a node is activated at random. Then, the activated node can contact its nearest neighbors on the network. Two possibilities for transmission are considered: an activated node is (a) the sender or (b) the receiver. I also consider the hybrid case (c): an active node plays both roles. In the previous work, I considered the two cases: (1) all neighbors or (2) only one neighbor is contacted at the same time. Thus, by combining the transmitting and contacting types, six models are constructed.

Here, I extend the models in the previous work and consider the case that activated individual contacts only one neighbor, but the rate of activation depends on the degree. Thus, the power exponent of the degree distribution can be different from that of the distribution of the contact number. I explore the equilibrium solution and calculate the outbreak threshold by using degree-based mean-field theory. I confirm that the features of prevalence depends on the details of contact and propagation mechanism.

REFERENCES

[1] Satoru Morita, Six Susceptible-Infected-Susceptible Models on Scale-free Networks. Scientific Report 6, 22506 (2016).

Mini-Symposium

Sep 7, 16:15 – 17:45, Room B

Cancer evolution

Organizer(s): **Kimiyo N. Yamamoto**
Kyushu University, 744 Motooka, Nishi-ku, Fukuoka 819-0395, Japan
e-mail: `kyamamoto[at]kyushu-u.org`

Cancer progression can be considered as the consequences of evolution. Recently, lots of genomic data have been acquired due to the advancement of sequencing technologies, and research of the evolutionary process of cancer by genomic analysis and mathematical modeling is in attention. In this symposium, we will present the up-to-date mathematical and statistical analysis with experimental and clinical data and spread the opportunities that theoretical researchers study cancer.

Time	**Title & Presenter**
16:15 – 16:45	**TBA** **Subhajyoti De** (*Rutgers University*)
16:45 – 17:15	**Tumor and immune cell dynamics explain the PSA bounce after prostate cancer brachytherapy** **Yoichiro Yamamoto** (*Shinshu University*)
17:15 – 17:45	**Identification of neutral tumor evolution across cancer types** **Benjamin Werner** (*Cancer Research UK*)

Yoichiro Yamamoto
Department of Pathology, Shinshu University School of Medicine
e-mail: `yoichiro@shinshu-u.ac.jp`

Tumour and immune cell dynamics explain the PSA bounce after prostate cancer brachytherapy

Background: Interstitial brachytherapy for localised prostate cancer may be followed by transient increases in prostate-specific antigen (PSA) that resolve without therapy. Such PSA bounces may be associated with an improved outcome but often cause alarm in the patient and physician, and have defied explanation.

Methods: We developed a mathematical model to capture the interactions between the tumour, radiation and anti-tumour immune response. The model was fitted to data from a large cohort of patients treated exclusively with interstitial brachytherapy. Immunohistological analysis for T-cell infiltration within the same tumours was also performed.

Results: Our minimal model captures well the dynamics of the tumour after therapy, and suggests that a strong anti-tumour immune response coupled with the therapeutic effect of radiation on the tumour is responsible for the PSA bounce. Patients who experience a PSA bounce had a higher density of CD3 and CD8 cells within the tumour that likely contribute to the PSA bounce and the overall better outcomes observed.

Conclusions: Our observations provide a novel and unifying explanation for the PSA bounce in patients with early prostate cancer and also have implications for the use of immune-based therapies in such patients to improve outcomes.

Benjamin Werner
Cancer Research UK
e-mail: werner@evolbio.mpg.de

Identification of neutral tumor evolution across cancer types

Despite extraordinary efforts to profile cancer genomes, interpreting the vast amount of genomic data in the light of cancer evolution remains challenging. Here we demonstrate that neutral tumor evolution results in a power-law distribution of the mutant allele frequencies reported by next-generation sequencing of tumor bulk samples. We find that the neutral power law fits with high precision 323 of 904 cancers from 4 types and from different cohorts. In malignancies identified as evolving neutrally, all clonal selection seemingly occurred before the onset of cancer growth and not in later-arising subclones, resulting in numerous passenger mutations that are responsible for intratumoral heterogeneity. Reanalyzing cancer sequencing data within the neutral framework allowed the measurement, in each patient, of both the in vivo mutation rate and the order and timing of mutations. This result provides a new way to interpret existing cancer genomic data and to discriminate between functional and non-functional intratumoral heterogeneity.

Mini-Symposium

Sep 7, 16:15 – 17:45, Room D

Ecosystem Dynamics and Management

Organizer(s): **Yoh Iwasa**
Department of Biology, Faculty of Science, Kyushu University, 744 Motooka, Nishi-ku, Fukuoka 819-0395, Japan
e-mail: `yohiwasa@kyudai.jp`

Joung-Hun Lee
Center for Decision Sciences, Kyushu University, 744 Motooka, Nishi-ku, Fukuoka 819-0395, Japan
e-mail: `clinamen2013@gmail.com`

Many ecosystems on earth have been formed under strong human activity. For the sustainable management of natural resources to be successful, we need to understand the coupling between social economic aspects and ecological and resource sciences. This is particularly important given the demands of increasing global population, environmental change and rising living standards (which lead to increased demand for resources). Mathematical and computational modeling has a great potential to improve our understanding of many aspects that are difficult to predict otherwise. In this symposium, we introduce several examples of coupled socio-economic and resource models, we discuss their common features and differences, and the future of this increasingly important section of mathematical biology.

Time	**Title & Presenter**
16:15 – 16:17	**Introduction**
16:17 – 16:39	**Coupled social and ecological models for ecosystem management** **Yoh Iwasa** (*Kyushu University, Japan*)
16:39 – 17:01	**Assessment of Communities Responding to Natural and Anthropogenic Variability in Aquatic Ecosystems** **Tae-Soo Chon** (*Pusan National University, Korea*)
17:01 – 17:23	**Optimisation and statistics used in an Australian weed eradication program** **Cindy Hauser** (*University of Melbourne, Australia*)
17:23 – 17:45	**Optimal management of tropical forests with high risk of illegal logging: role of agroforestry and profit sharing** **Joung-Hun Lee** (*Kyushu University, Japan*)

Yoh Iwasa
Department of Biology, Kyushu University
e-mail: `yohiwasa@kyudai.jp`

Coupled social and ecological models for ecosystem management.

Many ecosystems on earth have been formed under strong human activity. For the sustainable management of natural resources to be successful, we need to understand the coupling between social economic aspects and ecological and resource sciences. This is particularly important given the demands of increasing global population, environmental change and rising living standards (which lead to increased demand for resources). Mathematical and computational modeling have a great potential to improve our understanding of many aspects that are difficult to predict otherwise. In this symposium, we introduce several examples of coupled socio-economic and resource models, we discuss their common features and differences, and the future of this increasingly important section of mathematical biology.

For successful ecosystem management and biodiversity conservation, in addition to ecological and evolutionary processes, we need to consider social and economic influences on the management target. In this symposium, four speakers will talk on different systems in which socio-economic consideration is very important in ecosystem management.

After briefly explaining the structure of symposium "Ecosystem Dynamics and Management" (ogs. Y. Iwasa and J-H. Lee), Yoh Iwasa introduces two theoretical models.

The first model analyzes coupled socio-economical and ecological dynamics for lake water pollution. Players choose between cooperative (but costly) option and economical option, and their decision is affected by the fraction of cooperators in the community and by the importance of water pollution problem. When an opportunity for choice arrives, players take the option with the higher utility [5].

Results are: Oscillation of large amplitude is generated if social change occurs faster than ecosystem responses. The model can show "paradox of nutrient removal" [4]. If phosphorus is removed more effectively either from the inflow or from the lake water, the pollution level may increase (rather than decrease) due to the decline in people's willingness to cooperate.

The second model analyzes punishment as a mechanism to maintain cooperative behavior in a social group [3]. We discuss the efficiency of a graduated punishment system, in which the severity of the punishment applied to deviators increases with the amount of harm caused by the selfish action, which field research has shown to be essential for successful resource management.

We conclude that graduated punishment is the most efficient way to ensure cooperation when evaluation errors are unavoidable and when the social group is heterogeneous with respect to the sensitivity of its members to utility difference [3].

REFERENCES

[1] Lee, J-H., Kakinuma, K., Okuro, T. and Iwasa, Y. 2015. Coupled social and ecological dynamics for herders in the rangeland. *Ecological Economics,* **114**: 208-217.

[2] Iwasa, Y. and Lee, J-H. 2013. Graduated punishment is efficient in resource management if people are heterogeneous. *Journal of Theoretical Biology,* **333**:117-125.

[3] Lee, J-H. and Y. Iwasa. 2011. Tourists and traditional divers in a common fishing ground. Ecological Economics 70:2350-2360.

[4] Iwasa, Y., Suzuki-Ohno, Y. and Yokomizo, H. 2010. Paradox of nutrient removal in coupled socio-economic and ecological dynamics for lake water pollution. *Theoretical Ecology,* **3**:113-122.

[5] Iwasa, Y., Uchida, T. and Yokomizo, H. 2007. Nonlinear behavior of the socio-economic dynamics for lake water pollution control. *Ecological Economics* **63**: 219-229.

[6] Satake, A., Levin, S.A. and Iwasa, Y. 2008. Comparison between perfect information and passive-adaptive social learning models of forest harvesting. *Theoretical Ecology,* **1**: 189-197.

[7] Satake, A., Leslie, H.M., Iwasa, Y. and Levin, S.A. 2007. Coupled ecological-social dynamics in a forested landscape: spatial interactions and information flow. *Journal of Theoretical Biology,* **246**: 695-707.

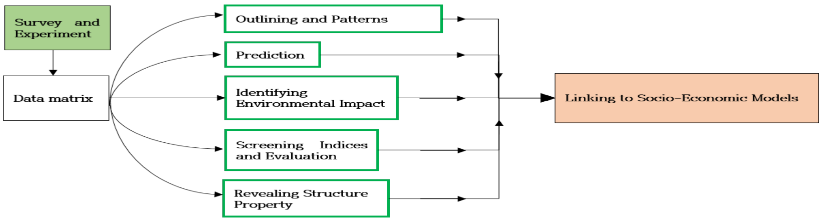
Tae-Soo Chon
Ecology and Future Research Association (EnFRA), Busan, Republic of Korea
Prof. (Emer.), Pusan National University, Busan, Republic of Korea
e-mail: `tschon.chon@gmail.com, tschon@pusan.ac.kr`

Dong-Hwan Kim
National Institute of Ecology, Republic of Korea

Woon-Seok Cho, Muyoung Heo
Pusan National University, Republic of Korea

Assessment of Communities Responding to Natural and Anthropogenic Variability in Aquatic Ecosystems

Two aspects should be linked effectively in achieving sustainable ecosystem management, social-economic management and ecological/resource sciences. Considering that numerous biological and environmental factors are involved in a complex manner, objective ecological assessment of ecosystems is a stepping stone for better human understanding of ecological systems for decision making in social-economic management. In this presentation, by taking aquatic communities as examples, objective assessment of ecological integrity is presented utilizing a series of informatics and computational methods. After collecting field data and establishment of data matrix, various aspects of community data are addressed in responding to natural (e.g., flooding) and anthropogenic (e.g., pollution) variability, including community patterns, responses to environmental impacts, prediction, determining indicators for water quality evaluation, and characterizing community structure properties. Initially self-organizing map (SOM) was used to outline community patterns and visualize relationships with environmental factors. SOM was further utilized to screen metrics of community data to indicate water quality according to discriminative power, redundancy, and responsiveness to disturbing factors pertaining to the community data in the surveyed area. Temporal prediction of communities was further performed using temporal neural networks. Subsequently community structure was analyzed based on species abundance distribution (SAD) models including log-normal distribution and geometric series. SADs and related parameters were feasible in indicating community response to natural and anthropogenic variability from the structure aspect. Hidden Markov model was additionally used to define the state of communities in relation with the observable events in field conditions including water quality and seasonal effect. Computational methods would be an efficient means of expressing ecological integrity that could serve as an objective reference system for applying socio-economic models for ecosystem management.



REFERENCES

[1] Kim D.-H., Cho, W.-S., and Chon, T.-S., 2013. Self-organizing map and species abundance distribution of stream benthic macroinvertebrates in revealing community patterns in different seasons. Ecological Informatics 17: 14–29.
[2] Kim D.-H., Song, M.-Y., and Chon, T.-S., 2016. Inferring pollution states based on community structure of benthic macroinvertebrates in streams. Ann. Limnol. - Int. J. Lim. 52: 91–108.
[3] Kim D.-H., Van Nguyen, T., Heo, M., and Chon, T.-S., 2015. Subsequent application of self-organizing map and hidden Markov models infer community states of stream benthic macroinvertebrates J. Ecol. Environ. 38: 1-13.

Cindy Hauser
University of Melbourne, Australia
e-mail: `chauser@unimelb.edu.au`

Katherine Giljohann, Inka Veltheim, Beth Crase, Gurutzeta Guillera-Arroita, Michael McCarthy
University of Melbourne, Australia

Joslin Moore
Monash University, Australia

Optimisation and statistics used in an Australian weed eradication program

Three species of hawkweed (*Hieracium* spp.) have invaded Australia's Alpine National Park. The first incursion was discovered by students of the University of Melbourne and since then, University researchers have had a strong collaborative role in hawkweed management.

Hawkweeds have a high capacity to outcompete other plant species, and are capable of long distance disturbance via wind and other vectors. They are an immediate threat to biodiversity within the National Park and, if they are left unmanaged, are also expected to reduce grazing productivity. Therefore state government agencies have funded an eradication program to remove hawkweed populations.

Finding and removing hawkweeds can be difficult in the vast and varied terrain of the Alpine National Park. We have used field observations, statistics, modelling and optimisation techniques to assist managers in the effective use of their resources.

First, modelling is used to predict where hawkweed seeds are likely to disperse by wind from the known infestations. Habitat information is used to identify which locations are most suitable for seed establishment. Together, these models predict where mature hawkweeds are most likely to occur in the landscape.

Second, hawkweeds cannot be found by searchers with 100% confidence, because they look similar to other plants and can also be hidden by shrubs and other vegetation. We have conducted observational experiments to assess the conditions under which human searchers and trained scent dogs can successfully detect hawkweeds. We use statistics to predict the probability of hawkweed detection in different scenarios.

Third, we bring together the above occurrence modelling and detection statistics in an optimisation. Here we seek to minimise the negative impacts of hawkweeds in the National Park by deploying limited search effort across the landscape.

This program demonstrates how managers and researchers can work together to develop efficient strategies for conservation work.

REFERENCES

[1] Williams, N.S.G. and Holland K.D, 2007. The ecology and invasion history of hawkweeds (*Hieracium* species) in Australia. *Plant Protection* Quarterly, 22: 76-80.
[2] Williams, N.S.G., Hahs, A.K. and Morgan, J.W., 2008. A dispersal-constrained habitat suitability model for predicting invasion of alpine vegetation. *Ecological Applications*, **18**: 347-359.
[3] Moore, J.L., Hauser, C.E., Bear, J.L., Williams, N.S.G. and McCarthy, M.A., 2011. Estimating detection-effort curves for plants using search experiments. *Ecological Applications*, **21**: 601-607.
[4] Hauser, C.E. and McCarthy, M.A., 2009. Streamlining 'search and destroy': cost-effective surveillance for invasive species management. *Ecology Letters* **12**: 683-692.
[5] Hauser, C.E., Giljohann, K.M., Rigby, M., Herbert, K., Curran, I., Pascoe, C., Williams, N.S.G., Cousens, R.D. and Moore, J.L., 2016. Practicable methods for delimiting a plant invasion. *Diversity and Distributions* **22**: 136-147.

Joung-Hun Lee
Kyushu University
e-mail: `clinamen2013@gmail.com`

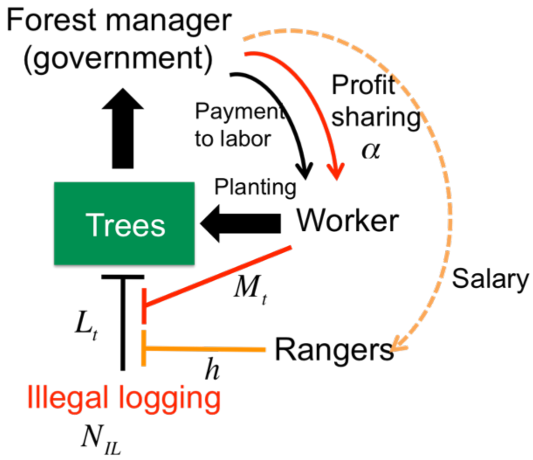
Y. Kubo, T. Fujiwara, Y. Iwasa
Kyushu University

Optimal management of tropical forests with high risk of illegal logging: role of agroforestry and profit sharing

Illegal logging is a serious threat for plantation management in tropics. Here we study the role of profit-sharing and agroforestry as management strategies. The owner chooses the age of trees to cut, and the workers choose their monitoring effort to prevent illegal logging.

Assumptions are: After the trees were removed, either by cutting, physical disturbances, or illegal logging, the owner hires workers to replant young trees. While trees are young, the land is also used as agriculture. In addition, the owner may share a fraction of profit obtained by selling logs with the workers. Illegal logging may be prevented by hiring forest guards or by monitoring effort of the workers. We derived recursive formulas for the values of a site with trees of age *t*, and solved it by iteration.

Results are: (1) Under the presence of illegal logging pressure, the owner may find it profitable to share the income with the workers to solicit their monitoring efforts. We discuss policy implications of these results. (2) As the fixed cost of harvesting increases, the owner should delay the tree harvesting age. It decreases mutual surveillance effort, and profit-sharing rate increases. Increased agricultural income has similar effect.



REFERENCES

[1] Lauren Persha, Arun Agrawal, Ashwini Chhatre, 2011. Social and ecological synergy: Local rulemaking, forest livelihoods, and biodiversity conservation. *Science*, **311:**1606–1608

[2] Ashwini Chhatre and Arun Agrawal, 2009. Trade-offs and synergies between carbon storage and livelihood benefits from forest commons. *PNAS*, **106**:17667–17670.

[3] Joung-Hun Lee, Kaoru Kakinuma, Toshiya Okuro and Yoh Iwasa, 2015. Coupled social and ecological dynamics of herders in Mongolian rangelands. *Ecol Econ*, **114**:208–217

Mini-Symposium

Sep 7, 16:15 – 17:45, Room ID

Infectious diseases in structured populations

Organizer(s): **Yukihiko Nakata**
Department of Mathematics, Shimane University
e-mail: `yunayuna.na@gmail.com`

Ryosuke Omori
Research Center for Zoonosis Control, Hokkaido University
e-mail: `omori@czc.hokudai.ac.jp`

When describing the complex dynamics of infectious diseases in the real world, heterogeneity, such as spatial heterogeneity and individual heterogeneity, is always an issue. Tons of structured population models have been proposed so far, we need to know what kind of model can reveal what. In this symposium five speakers will talk about the state-of-art analyses of the dynamics of infectious diseases at different scales from within-host to between host communities using the different model descriptions.

Time	**Title & Presenter**
16:15 – 16:32	**Metapopulation epidemic models with heterogeneous patches** **Gouhei Tanaka** (*The University of Tokyo*)
16:33 – 16:50	**Evolution of global and local viral infection in the structured SIS model** **Koichi Saeki** (*SOKENDAI*)
16:51 – 17:08	**Challenges in control strategies of spatially explicit epidemic models** **Diána Knipl** (*Department of Mathematics, University College London*)
17:09 – 17:26	**Discretization approach for the global stability analysis of structured epidemic models** **Toshikazu Kuniya** (*Graduate School of System Informatics, Kobe University*)
17:27 – 17:45	**Outbreaks in the SIR epidemics with multiple seeds - a statistical physics approach** **Takehisa Hasegawa** (*Department of Mathematics and Informatics, Ibaraki University*)

Gouhei Tanaka
The University of Tokyo
e-mail: `gouhei@sat.t.u-tokyo.ac.jp`

Metapopulation epidemic models with heterogeneous patches

Metapopulation models have been widely used to describe the spreading of epidemics on a network of spatially separated patches. The epidemic events such as infection and recovery of individuals in each patch follow a standard compartment epidemic model. Therefore, if a patch is isolated, the basic reproductive number computed from the model determines whether an epidemic outbreak occurs or not in the patch. However, when the patches are connected via complex migration pathways and individuals can move from one patch to another, it is not obvious whether a local epidemic outbreak grows and leads to a global outbreak in the entire network or not. One of the major concerns in the studies on metapopulation models with complex network topology is the derivation of the global invasion threshold [1, 2].

In many studies on metapopulation epidemic models, the patches have been assumed to be identical for simplicity. However, the environments of the patches, related to epidemics, are not necessarily homogeneous. Namely, the local basic reproductive number in patches can be different. We have incorporated patch heterogeneity into the metapopulation epidemic models [3]. Assuming that there exist high-risk patches with local basic reproductive number larger than 1 and low-risk patches with local basic reproductive number smaller than 1, we have analytically derived the critical fraction of low-risk patches, above which the global epidemic spreading is controlled. In this presentation, the recent developments in the metapopulation epidemic models with heterogeneous patches are introduced.

REFERENCES

[1] V. Colizza, R. Pastor-Satorras, and A. Vespignani. 2007. *Reaction-diffusion processes and metapopulation models in heterogeneous networks*. *Nature Physics*, **3**: 276–282.
[2] V. Colizza, and A. Vespignani. 2008. *Epidemic modeling in metapopulation systems with heterogeneous coupling pattern: Theory and simulations*. *Journal of Theoretical Biology*, **251**: 450–467.
[3] G. Tanaka, C. Urabe, and K. Aihara. 2014. Random and targeted interventions for epidemic control in metapopulation models. *Scientific Reports*, **4**: 5522.

Koichi Saeki
SOKENDAI (The Graduate University for Advanced Studies), Kanagawa, Japan.
e-mail: `saeki_koichi@soken.ac.jp`

Akira Sasaki
SOKENDAI (The Graduate University for Advanced Studies), Kanagawa, Japan.

Evolution of global and local viral infection in the structured SIS model

There are two types of viral infections in a host, one is global and the other is local. Global infection means that an infected cell produce viral particles that travel to susceptible cells somewhere. In contrast, local infection occurs via physical contact between an infected cell and a susceptible cell. The emergence of mutant virus that has a high ability of local infection is observed *in vitro*[1] and suggested *in vivo*[2], and those mutants are considered to have a relationship with a severe disease caused by virus infection[2]. In the previous study, the evolution of global versus local infection has been modeled, and it suggested that the spatial structure have an important effect to the evolution[3]. However, the emerged structure in that model is only a part of possible spatial structures, and the spatial structure has not been parameterized.

Here we attempt to reveal what is the evolutionarily stable proportion of global and local infection, and how it depends on the spatial parameters. We consider a lattice space in which each site is occupied by either a target or a non-target cell for virus, and assume that whether a site is occupied by a target cell or a non-target cell will never change. Then, how target and non-target cells are distributed over the lattice space is parameterized by the frequency of target cells and the pair frequency of target cells.

At first, the infection dynamics are modeled by pair approximation and the endemic condition for a virus with a certain proportion of global infection is calculated. Next, the evolutionarily stable strategy is obtained by an invasibility analysis using pair approximated dynamics. The results show that higher proportion of local infection is selected as target cells become clustered. We also observe the parameter region that even if global infection is more efficient than local one, using local infection at a certain rate becomes the optimal due to spatial clustering of target cells.

REFERENCES

[1] Shirogane Y., Watanabe S., Yanagi Y., 2012. Cooperation between different RNA virus genomes produces a new phenotype. *Nat.Commun*.

[2] Watanabe S., Shirogane Y., Suzuki SO., Ikegame S., Koga R., Yanagi Y., 2013. Mutant fusion proteins with enhanced fusion activity promote measles virus spread in human neuronal cells and brains of suckling hamsters. *J.Virol*. **87**(**5**): 2648-59.

[3] Kamo M., Boots M., 2006. The evolution of parasite dispersal, transmission, and virulence in spatial host populations. *Evol. Ecol. Res*. **8**: 1333-1347.

Diána Knipl,
Department of Mathematics, University College London
e-mail: `d.knipl@ucl.ac.uk`

Challenges in control strategies of spatially explicit epidemic models

Mathematical epidemiology is an important branch of mathematical biology, concerned with the propagation of infectious diseases in human populations. Through mathematical modeling we gain valuable insight into the spatio-temporal spread of infectious diseases, and by better understanding their dynamics we become capable of designing their intervention strategies, like vaccination and social distancing. In this talk we present some simple models for disease spread when individuals travel between different cities, and describe by mathematical analysis their control measures including travel restrictions.

Toshikazu Kuniya
Graduate School of System Informatics, Kobe University
e-mail: `tkuniya@port.kobe-u.ac.jp`

Discretization approach for the global stability analysis of structured epidemic models

In this talk, we focus on structured epidemic models with heterogeneity (age, sex, position etc.) written as partial differential equations. By discretization, they can be rewritten to multi-group models as ordinary differential equations. For multi-group epidemic models, a celebrated graph theoretic approach has recently been developed by Guo et al. (2006). By using the approach, in a relatively formal way, we can construct suitable Lyapunov functions for the global stability analysis of the discretized multi-group epidemic models. From the form of these Lyapunov functions, we can expect the form of corresponding Lyapunov functions for the original structured models as partial differential equations.

Specifically, in this talk, we focus on two SIR epidemic models with age-structure and space-structure, respectively. By constructing the Lyapunov functions, we prove that the global asymptotic stability of each equilibrium is completely determined by the size of the basic reproduction number Ro. That is, the infected population converges to zero as time goes to infinity if Ro < 1, and it converges to a positive distribution as time goes to infinity if Ro > 1. This is a joint work with Dr. Jinliang Wang (Heilongjiang University) and Prof. Hisashi Inaba (University of Tokyo).

REFERENCES

[1] Kuniya, T., 2011. Global stability analysis with a discretization approach for an age-structured multigroup SIR epidemic model. *Nonlinear Anal. RWA*, **12**: 2640–2655.

[2] Kuniya, T., Wang J., 2016. Lyapunov functions and global stability for a spatially diffusive SIR epidemic model. *Appl. Anal.*, **13**:15 DOI: 10.1080/00036811.2016.1199796.

[3] Kuniya T., Wang J., Inaba H., A multi-group SIR epidemic model with age structure. *Disc. Cont. Dyn. Syst. Series B,* under revision.

Takehisa Hasegawa
Department of Mathematics and Informatics, Ibaraki University
e-mail: `takehisa.hasegawa.sci@vc.ibaraki.ac.jp`

Koji Nemoto
Department of Physics, Hokkaido University

Outbreaks in the SIR epidemics with multiple seeds - a statistical physics approach

The threat of infectious disease is conspicuous for modern society, wherein there is a large amount of international travel all over the world. Understanding how infectious diseases spread in our society is crucial to the development of strategies for disease control. In recent years, many studies have been devoted to epidemic models, e.g., the susceptible-infected-removed (SIR) model and the susceptible-infected-susceptible model, with a network structure of individuals [1]. Diseases spread over the networks of physical contacts between individuals, and the structure of real networks has crucial effects on this spread. Many analytical approaches for epidemic models with network structures, such as the edge-based compartment model, the effective degree approach, and the pair approximation, have been proposed and have succeeded in describing epidemic dynamics. Numerical simulations have also revealed how epidemics spread in more realistic situations.

Most previous studies using the SIR-type epidemic models have assumed that the fraction of initial infection seeds is infinitesimally small. In contrast, there have been few studies on epidemic models with finite fractions of seeds. What we discuss here is a fundamental, but almost overlooked problem: How do epidemic models with finite fractions of seeds undergo phase transitions? In this talk, we consider the SIR model with finite fractions of seeds on the six-regular random graph [2]. In this case, the SIR model exhibits a kind of percolation transition. We regard the epidemic clusters generated from seeds as supernodes and study the percolation problem of these supernodes. We analytically and numerically obtain the percolation transition point of supernodes, λ_{c1}, to show a gap between this critical infection rate and so-called epidemic threshold, indicating that the percolation of epidemic clusters occurs before a single seed can induce a global outbreak (Fig.1). Our result also shows the sensitivity of the seed fraction on percolation transition point, i.e., that a small seed fraction drastically reduces the critical infection rate for the emergence of the infinite epidemic cluster.

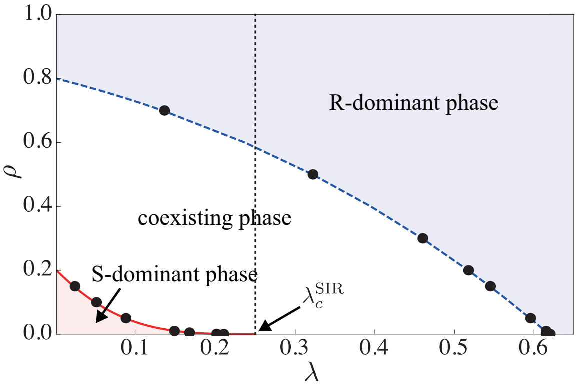


Figure 1

Phase diagram of the SIR model in the (ρ, λ)-space. Here ρ is the fraction of initial seeds and λ is the infection rate (the recovery rate is set to 1). In the S-dominant phase, there is no infinite epidemic cluster (no global outbreak occurs). In the coexisting and R-dominant phases, an infinite epidemic cluster appears (global outbreak occurs). In the latter, almost all nodes are removed so that residual components are disintegrated. Solid-red and dashed-blue lines represent the analytical estimates of the critical infection rates, λ_{c1} between the S-dominant and coexisting phases, and λ_{c2} between the R-dominant and coexisting phases, respectively.

REFERENCES

[1] R. Pastor-Satorras, C. Castellano, P. Van Mieghem, and A. Vespignani, 2015. Epidemic processes in complex networks. *Reviews of Modern Physics,* **87** 925.

[2] T. Hasegawa, and K. Nemoto, 2016. Outbreaks in susceptible-infected-removed epidemics with multiple seeds. *Physical Review E,* **193**: 032324.

Mini-Symposium

Sep 8, 9:00 – 10:30, Room B

Towards data-driven mathematical biology

Organizer(s): **Joung-Hun LEE**
Mathematical Biology Laboratory, Department of Biology, Kyushu University, 744 Motooka, Nishi-ku, Fukuoka 819-0395, Japan
e-mail: `clinamen2013@gmail.com`

Marko JUSUP
Center of Mathematics for Social Creativity, Hokkaido University, N12W7, Kita Ward, Sapporo, 060-0811 Japan
e-mail: `mjusup@gmail.com`

Mathematical biology is often driven by purely theoretical considerations. Although theoretical contributions in themselves are extremely valuable, there is a huge potential for mathematical biology to add value to existing and new empirical data. To realize this potential it is necessary to open up a continuous dialogue between experimentally and theoretically oriented researchers from various disciplines who share the interest in biology. The proposed mini-symposium is intended to establish such a dialogue by illustrating several interesting case studies which greatly benefited, or could benefit, from mathematical modeling. Challenging questions are posed for future developments.

Time	**Title & Presenter**
09:00 – 09:01	**Foreword** **Joung-Hun Lee** (*Kyushu University*)
09:01 – 09:21	**Different bees, different needs – nest site selection in honeybees** **Madeleine Beekman** (*The University of Sydney*)
09:21 – 09:41	**Life-history adaptations and the latitudinal diversity gradient in medaka fishes** **Kazunori Yamahira** (*Tropical Biosphere Research Center, University of the Ryukyus*)
09:41 – 10:01	**Electronic tagging applications and migration of Pacific bluefin tuna, Thunnus orientalis** **Takashi Kitagawa** (*The University of Tokyo*)
10:01 – 10:21	**Change in energy intake and cost of skipjack tuna (Katsuwonus pelamis) with northward migration in the western North Pacific** **Yoshinori Aoki** (*The University of Tokyo*)
10:21 – 10:30	**Discussion & comments** **Cindy Hauser** (*University of Melbourne*) & **Marko Jusup** (*Hokkaido University*)

Madeleine Beekman
Behaviour and Genetics of Social Insects Lab, School of Life and Environmental Sciences, The University of Sydney
e-mail: `madeleine.beekman@sydney.edu.au`

Different bees, different needs – nest site selection in honeybees

During reproductive swarming and seasonal migration, a honeybee swarm needs to locate and move to a new nest site. Our current knowledge of swarming and nest site selection in honeybees is based primarily on studies of just one species, *Apis mellifera*. Natural colonies of *A. mellifera* live in tree cavities. The quality of the cavity is often critical to the survival of a swarm. The scouts must search thousands of trees to ensure that they do not settle for a poor cavity when a better one is available. More recently another species of honeybee has been included in studies of nest site selection: the open-nesting dwarf honeybee *Apis florea*. *A. florea* builds a small nest comprised of a single comb suspended from a twig of a shrub or tree in the open. For a cavity-nesting species like *A. mellifera* there is only a limited number of potential nest sites that can be located by a swarm, simply because suitable nest sites are scarce. In contrast, for an open-nesting species like *A. florea* it seems that there is an abundance of shaded twigs that would be equally suitable for building a nest. Here I pull together recent research that shows that the nest site selection processes of *A. florea* and *A. mellifera* have been shaped by each species' nest site requirements. I argue that both species use the same behavioural algorithm, tuned to allow each species to solve their species-specific problem.

Kazunori Yamahira
Tropical Biosphere Research Center, University of the Ryukyus
e-mail: `yamahira@lab.u-ryukyu.ac.jp`

Life-history adaptations and the latitudinal diversity gradient in medaka fishes

Explaining the latitudinal diversity gradient has long been one of the central subjects in ecology and evolutionary biology [1,2]. In many taxa, species are more abundant in the tropics than in the temperate zone. Such a latitudinal pattern can be seen also in the family Adrianichthyidae, a freshwater fish group called “medaka” in Japan; many medaka species are distributed in the tropical regions of Southeast Asia, whereas only two species in the Japanese Archipelago. In this study, I focus on life-history adaptations along latitudes, which might result in the latitudinal gradient in population extinction rates.

In ectotherms such as fishes, lower temperatures in high-latitude environments would theoretically reduce the annual growth and reproduction rates of individuals. If smaller body size and lower fecundity reduce fitness, individuals in higher latitudes may evolve compensatory responses. Two alternative models of such latitudinal compensation are possible: adaptation-to-temperature model: thermal reaction norms for growth and reproduction rates of high-latitude individuals may be horizontally shifted to a lower range of temperatures, or adaptation-to-seasonality model: reaction norms may be vertically shifted so that high-latitude individuals can grow and reproduce faster across all temperatures. Common-environment experiments revealed that average thermal reaction norms for growth and reproduction rates of the Japanese medaka (*Oryzias latipes* species complex) differed primarily in elevation among latitudinal populations in a manner consistent with adaptation-to-seasonality model, suggesting that natural selection in high latitudes prefers individuals that grow and reproduce faster even within a shorter growing and reproductive season to individuals that have longer growing and reproductive seasons by growing and reproducing at lower temperatures. However, intrapopulation variation in reaction norms was also vertical: some full-sib families grew faster than others across all temperatures examined. This tendency in intrapopulation genetic variation for thermal reaction norms may have genetically constrained the evolution of latitudinal compensation, irrespective of the underlying selection pressure.

Comparative population ecological surveys in the wild revealed that latitudinal populations differ in population demography. As predicted from the adaptation-to-seasonality model, in high-latitude populations, reproduction concentrated during a shorter favorable period of a year, and young-of-the-year (YOY) individuals grew faster within a shorter period before long winter. In contrast, both reproduction and growth were slower but continued for a longer period in low-latitude populations. It was found that overwinter mortality of YOYs is size-dependent in the high-latitude populations; smaller individuals suffer cold death and starvation more frequently. Therefore, YOYs produced later in a season or YOYs growing slower are expected to suffer higher mortality, which is considered to be the main selection pressure on the adaptations to seasonality. As a result of the temporal synchronization of reproduction and growth within a shorter period of a year, high-latitude populations exhibited larger seasonal fluctuation in population size than low-latitude populations.

Theories predict that larger fluctuation in population size causes higher risk of stochastic extinction of the population [3,4]. The life-history adaptations to seasonality at high latitudes, therefore, will secondarily cause higher population extinction rates, which may reduce the number of species coexisting in high-latitude environments. Adaptation to temperature and resultant ability to reproduce and grow at lower temperatures would lessen the magnitude of population fluctuation, but the evolution of adaptation to temperature is genetically constrained as demonstrated above, resulting in inevitable high extinction risk in high-latitude populations.

REFERENCES

[1] Gaston, K. J., 2000. Global patterns in biodiversity. *Nature*, **405**: 220–227.
[2] Hillebrand, H., 2004. On the generality of the latitudinal diversity gradient. *American Naturalist*, **163**: 192–211.
[3] May, R. M. 1973. Stability in randomly fluctuating versus deterministic environments. *American Naturalist*, **107**: 621–650.
[4] Lande, R. 1993. Risks of population extinction from demographic and environmental stochasticity and random catastrophes. *American Naturalist*, **142**: 911–927.

Takashi Kitagawa
Atmosphere and Ocean Research Institute, The University of Tokyo, Chiba 277-8564, Japan
e-mail: `takashik@aori.u-tokyo.ac.jp`

Ko Fujioka
National Research Institute of Far Seas Fisheries, Japan Fisheries Research and Education Agency, Shizuoka 428-8633, Japan

Yoshinori Aoki
Atmosphere and Ocean Research Institute, The University of Tokyo, Chiba 277-8564, Japan

Electronic tagging applications and migration of Pacific bluefin tuna, *Thunnus orientalis*

Investigations of the migration and distribution of Pacific bluefin tuna (PBT) in the Pacific Ocean have used fisheries data analysis and/or conventional tagging experiments mainly in the 20th century, but these previous studies could not follow the detailed behavior of individuals at a higher resolution.

The electronic tags that were developed and applied to fish species at the end of the last century allowed the measurement of environmental and physiological variables by recording raw or processed data in their memory. The tags used for PBT research provide an estimation of fish geolocation using a light sensor and algorithms based on astronomy. To date, more than 800 PBT tuna tagged with the electronic tags have been released in the western Pacific Ocean (WPO). These fish range in size from 18 to 158 cm. Analyses of the retrieved tag data have showed that the vertical distributions and movements of immature PBT are affected by spatial and seasonal changes in the vertical temperature structure. PBT often make brief dives to depths below the thermocline for foraging and maintaining body temperature. Track durations ranged from 1 to 1285 days, and the location data indicate PBT in the WPO aggregate in the Kuroshio-Oyashio transition region where they spent more time at the surface feeding than in the other areas in the WPO. Archival tags have revealed the timing of trans-Pacific migrations from the transition region to the Eastern Pacific appears to depend on their specific wintering areas in the WPO. We also suggest directions of future research for investigating PBT migratory characteristics in the WPO.

REFERENCES

[1] Kitagawa, T., and Kimura, S. eds., 2015. *Biology and ecology of bluefin tuna*. CRC Press, pp 433.

[2] Kitagawa, T., 2013. Behavioral Ecology and thermal physiology of immature Pacific bluefin tuna (*Thunnus orientalis*). In Ueda, H., and Tsukamoto, K. eds.: *Physiology and ecology of fish migration*. CRC press, 152–178.

[3] Kitagawa, T., Boustany, A.M., Farwell, C.J., Williams, T.D., Castleton M., and Block, B.A., 2007. Horizontal and vertical movements of juvenile bluefin tuna (*Thunnus orientalis*) in relation to seasons and oceanographic conditions in the eastern Pacific Ocean. *Fisheries Oceanography*, **16**: 409–421.

[4] Kitagawa, T., Kimura, S., Nakata, H., and Yamada, H., 2004. Diving behavior of immature Pacific bluefin tuna (*Thunnus thynnus orientalis*) for feeding in relation to seasons and areas: the East China Sea and the Kuroshio-Oyashio transition region. *Fisheries Oceanography* **13**: 161–180.

[5] Kitagawa, T., Nakata, H., Kimura, S., Itoh, T., Tsuji, S., and Nitta, A., 2000. Effect of ambient temperature on the vertical distribution and movement of Pacific bluefin tuna (*Thunnus thynnus orientalis*). *Marine Ecology Progress Series*, **206**: 251–260.

Yoshinori, Aoki
Atmosphere and Ocean Research Institute, The University of Tokyo, Chiba 277-8564, Japan
e-mail: `aokiyoshinori@aori.u-tokyo.ac.jp`

Takashi, Kitagawa
Atmosphere and Ocean Research Institute, The University of Tokyo, Chiba 277-8564, Japan

Hidetada, Kiyofuji
National Research Institute of Far Seas Fisheries, Japan Fisheries Research and Education Agency, Shizuoka 428-8633, Japan

Suguru Okamoto
Hokkaido National Research Institute, Japan Fisheries Research Agency and Education Agency, Hokkaido 085-0802, Japan

Tomohiko Kawamura
Atmosphere and Ocean Research Institute, The University of Tokyo, Chiba 277-8564, Japan

Change in energy intake and cost of skipjack tuna (*Katsuwonus pelamis*) with northward migration in the western North Pacific

Skipjack tuna, *Katsuwonus pelamis*, are a highly migratory pelagic species distributed throughout tropical to temperate waters worldwide. In the western North Pacific, after hatching in subtropical ocean, juveniles travel long distances and extend their distribution through subtropical to temperate waters near Japan (northward migration) with their body composition changing especially in lipid content. In this study, we investigated their migration paths and behavior during the migration in terms of energy budgets measured with archival tags, which can record swimming depth, water and body temperatures, and light intensity, focusing on lipid composition changes between habitats. The tags were inserted into the stomach and 465 individuals with tag were released in total recording their migration from subtropical to temperate area. The tags were recaptured by fishermen and the data were retrieved from 16 individuals and used for analysis. The estimation of energy intake was based on the heat increment of feeding. As an indicator of use of the consumed energy, horizontal and vertical daily movement distances were also calculated. It was found that the daily energy intake increased with the northward movements, whereas the daily vertical distance was decreased, although the horizontal distances were not changed among habitats. This result suggests that skipjack spend less energy in acquiring prey in temperate than in subtropical waters since prey are available in higher densities, thereby providing excess energy for growth or lipid reserves.

Mini-Symposium

Sep 8, 9:00 – 10:30, Room D

Mathematical modeling for viral infections within host

Organizer(s): **Yusuke Kakizoe**
Systems Life Sciences, Graduate school of Kyushu University, 744 Motooka Nishi-ku Fukuoka, 819-0395, Japan,
e-mail: `yusuke.purple5@gmail.com`

Mathematical model of viral infections has a very important role in our quantitative understanding of viral dynamics. For instance, we can estimate the pathogenesis of viruses, evaluating the efficacy of anti viral drugs, predicting the viral dynamics, etc. In this symposium, we will present recent advances of mathematical modeling for viral infections.

Time	**Title & Presenter**
09:00 – 09:20	**Modeling to quantify HIV-1 entry** **Yusuke Kakizoe** (*Graduate School of Systems Life Sciences, Kyushu University*)
09:20 – 09:40	**Epitope-specific CD8+ T cell kinetics rather than viral variability determines the timing of immune escape in SIV infection** **Alexey Martyushev** (*Department of Biology, Faculty of Sciences, Kyushu University*)
09:50 – 10:10	**The impact of influenza A defective interfering particles on plaque assays** **Laura Liao** (*Department of Physics, Ryerson University*)
10:10 – 10:30	**Something is wrong with the respiratory syncytial virus** **Catherine Beauchemin** (*Department of Physics, Ryerson University*)

Yusuke Kakizoe
Systems Life Sciences, Graduate School of Kyushu University, Japan
e-mail: `yusuke.purple5@gmail.com`

Shingo Iwami
Faculty of Science, Kyushu University, Japan

Modeling to quantify HIV-1 entry

The entry of HIV-1 into a target cell is the first step of HIV-1 replication process, so entry inhibitor has advantages over the inhibition of steps in the viral life cycle after infection. Although we have *maraviroc*, one of the few entry inhibitor of HIV-1, the efficacy of the drug varies depending on CCR5 or CXCR4 co-receptor toropism, and patients need to take it twice a day contrary to other drugs once a day. More potent HIV-1 entry inhibitor is needed. So far, many researchers revealed HIV-1 entry processes qualitatively.

The entry of HIV-1 into a target cell is established between envelope glycoprotein (Env) on the surface of a virus and CD4 receptors on a target cell. The Env is a trimer composed of three gp120 and three gp41 envelope proteins, and it mediates virus entry by fusion. The entry of HIV-1 into target cells starts from binding of CD4 to gp120 protein. This binding induces conformational changes of Env that allows interactions with a coreceptor such as CCR5 or CXCR4. These interactions in turn trigger additional conformational changes in Env, which expose gp41 protein, and inserts into the membrane of host cell. Finally, the viral and target cell membranes are fusion.

In this way, we already know HIV-1 entry process qualitatively in detail. However, in order to develop a new entry inhibitor, we should quantitatively understand HIV-1 entry process. For example, Magnus et al. investigated the HIV-1 entry process using mathematical model, and estimated the number of gp120 trimmers on HIV-1 surface for the virus entry [1,2]. In this study, we focused on an interaction between HIV gp120 and CCR5 molecules during entry step and investigated how many number of CCR5 molecules are associated with HIV-1 entry. We made a mathematical model describing HIV entry and analyzed infectivity assay data using our model.

REFERENCES

[1] Carsten Magnus, Roland R. Rogoes: Estimating the Stoichiometry of HIV neutralization. PLoS Comput Biol 2010, 6(3): e1000713.
[2] Carsten Magnus, Roland R. Rogoes: Analysis of the Subunit Stoichiometry in Viral Entry. PLoS ONE 2012, 7(3):e33441.

Dr. Alexey Martyushev
Department of Biology, Faculty of Sciences, Kyushu University, Fukuoka 812-8581, Japan
e-mail: `martyushev.alexey.745@m.kyushu-u.ac.jp`

Epitope-specific CD8+ T cell kinetics rather than viral variability determines the timing of immune escape in SIV infection

Untreated human immunodeficiency virus (HIV) infection causes Acquired Immune Deficiency Syndrome (AIDS) that ultimately leads to death. Previous studies of HIV and its analogue in monkeys – Simian Immunodeficiency Virus (SIV) showed that CD8+ T cell responses are important for the control of infection [1, 2]. Virus-specific CD8 T-cells can detect and suppress HIV-infected cells, but they achieve only a temporary success. As soon as the virus mutates, viral variants can escape the established immune response. The strength of the CD8+ T cell response, as well as mutation rates, patterns of particular amino acids undergoing escape and growth rates of escape mutants may affect the time when escape occurs. However, this study demonstrates that the appearance of CD8 T-cell response, rather than viral variability, plays the dominant role in determining the time of immune escape.

This study is based on the analysis of epitope-specific CD8+ T cell response in 25 SIV-infected pigtail macaques at three SIV epitopes. Mathematical modeling and statistical analysis were applied in order to interpret and analyze the complex results of experiments. The rate of appearance of new mutants was firstly introduced in this research project and is defined by the following formula:

$$m'(t_i, t_{i+1}) = [m(t_{i+1}) - m(t_i)]/(t_{i+1} - t_i), \qquad (1)$$

where $m(t_i)$ is the number of mutants at a frequency above 1% in the sequence data at the time point t_i. The increase in mutants m' is discrete and takes values within time intervals defined by start and end time points, t_i and t_{i+1}, respectively, i.e. mutants with fraction less than 1% in the sequence were not taken into account in the values of $m(t_i)$ and $m(t_{i+1})$. For example, if the number of variants at >1% went from two to five in three days, this would be an average increase in variants of (5 mutants – 2 mutants) / 3 days = 1 mutant per day.

Two of the studied epitopes showed a variable escape pattern and one had a highly monomorphic escape pattern. Despite very different patterns, immune escape occurs with a similar delay of on average 18 days after the epitope-specific CD8+ T cells reach 0.5% of total CD8+ T cells. Moreover, the most delayed escape occurs in one of the highly variable epitopes, and that this is associated with a delay in the epitope-specific CD8+ T cells responding to this epitope. The kinetics of immune escape (see Eq. 1) demonstrated that multiple escape mutants emerge simultaneously during the escape, implying that a diverse population of potential escape mutants is present during immune selection. The similar effect has been previously observed in a HIV-1 study, however it was not deep investigated [3].

The results demonstrate that timing of escape is largely determined by the kinetics of epitope-specific CD8+ T cells. This discovery highlights a need of vaccines inducing immune response to conserved regions of HIV genome. In contrast, since vaccination aims to drive an earlier and stronger CD8+ T cell response, it seems possible that this would simply drive earlier immune escape at variable HIV genome regions.

REFERENCES

[1] Koup, R. A., Safrit, J. T., Cao, Y., Andrews, C. A., McLeod, G., Borkowsky, W., Farthing, C. and Ho, D. D., 1994. Temporal association of cellular immune responses with the initial control of viremia in primary human immunodeficiency virus type 1 syndrome. *J Virol*, **68(7)**: 4650–4655.
[2] Jin, X., Bauer, D. E., Tuttleton, S. E., Lewin, S., Gettie, A., Blanchard, J., Irwin, C. E., Safrit, J. T., Mittler, J., Weinberger, L., Kostrikis, L. G., Zhang, L., Perelson, A. S. and Ho, D. D., 1999. Dramatic rise in plasma viremia after CD8(+) T cell depletion in simian immunodeficiency virus-infected macaques. *J Exp Med*, **189(6)**: 991–998.
[3] Goonetilleke, N., Liu, J. F. Salazar-Gonzalez, G. Ferrari, E. Giorgi, V. V. Ganusov, B. F. Keele, G. H. Learn, E. L. Turnbull, M. G. Salazar, K. J. Weinhold, S. Moore, CHAVI Clinical Core B, N. Letvin, B. F. Haynes, M. S. Cohen, P. Hraber, T. Bhattacharya, P. Borrow, A. S. Perelson, B. H. Hahn, G. M. Shaw, B. T. Korber, and McMichael, A. J, 2009. The first T cell response to transmitted/founder virus contributes to the control of acute viremia in HIV-1 infection, *J Exp Med*, **206**: 1253–1272.

Laura Liao
Department of Physics, Ryerson University
e-mail: `laura.liao@ryerson.ca`

Catherine Beauchemin
Department of Physics, Ryerson University

The impact of influenza A defective interfering particles on plaque assays

Working stocks of influenza A virus are propagated in cell culture either from virus samples or existing virus stocks [1]. During propagation, unwanted defective interfering particles (DIP) –particles which competitively inhibit virus replication-- might be amplified from the initial inoculum itself, or spontaneously generated during infection [2]. To minimize the presence of DIPs, virus stocks can be passaged using a very dilute initial inoculum, in order to reduce instances of co-infection (i.e., when a cell receives both virus and DIP) which foster more DIPs. Despite this DIP depletion step, the virus stock obtained will still contain low levels of DIPs [3]. Furthermore, it is notoriously difficult to physically separate DIPs from virus, since they mainly differ in genomic content which is less than 0.8% of the total mass [2]. Hence, influenza virus stocks inevitably contain DIPs.

Since virus stocks contain DIPs, we are interested in how DIPs might impact the quantification of virus in the stock, specifically by plaque assay. In a plaque assay, virus stock dilutions are used to infect cell monolayers that are overlaid with agar. The agar restricts the diffusion of virus progeny to an infected cell's nearest neighbours. Hence, a single infected cell will infect its neighbours, and so on, and the infected patch of cells will spread radially outward. When the cells die, a circular void or "plaque" remains. Quantifying the number of plaques allows us to calculate the infectious virus concentration in the stock which is represented by the number of plaque-forming units per millilitre (PFU/mL).

As DIPs can alter the number of visible plaques through the arrest of early plaque growth [4], this research will use an agent-based model to investigate the degree of systematic error which leads to underestimation of stock virus concentration.

REFERENCES

[1] Szretter, K.J., Balish, A.L., and Katz, J.M., 2006. Influenza: propagation, quantification, and storage. *Curr. Protoc. Microbiol.*, Chapter 15:Unit 15 G.1.
[2] Nayak, D.P., Chambers, T.M., and Akkina, R. K., 1985. Defective-interfering (DI) RNAs of influenza viruses: origin, structure, expression, and interference. *Curr. Top. Microbiol. Immunol.*, **114**:103–151.
[3] Marcus, P.I., Ngunjiri, J.M., and Sekellick, M.J., 2009. Dynamics of biologically active subpopulations of influenza virus: Plaque-forming, noninfectious cell-killing, and defective interfering particles. *J. Virol.*, **83**(16):8122–8130.
[4] Janda, J.M., Davis, A.R., Nayak, D.P. and De, B.K., 1979. Diversity and generation of defective interfering influenza virus particles. *Virology*. **95**(1):48–58.

Catherine Beauchemin
Department of Physics, Ryerson University, Canada
iTHES, RIKEN, Japan
e-mail: `cbeau@ryerson.ca`

Something is wrong with the respiratory syncytial virus

Mathematical models of virus infection within a host or cell culture make assumptions about the properties of the virus. These assumptions are rarely validated when a model for one virus is applied to study another. Similarly, virology aims to rapidly develop vaccines and antiviral therapies by often learning only as much about the virus as is required to do so. In this haste, important characteristics are missed with sometimes devastating consequences, as was the case with the failed respiratory syncytial virus (RSV) vaccine. In this talk I will discuss the particularities of RSV and what we uncovered through mathematical analysis of available experimental data.

Mini-Symposium

Sep 8, 9:00 – 10:30, Room E

Plant phenotyping with morphometrics

Organizer(s): **Koji Noshita**
Graduate School of Agriculture and Life Science, The University of Tokyo, 1-1-1 Yayoi, Bunkyo, Tokyo, Japan
e-mail: `noshita@morphometrics.jp`

With recent advancements in genotyping, phenotyping is now a bottleneck in development of several research fields in plant science (e.g. agricultural science, developmental and evolutionary biology). Particularly, morphological properties are the most important information but hardest to treat in plant phenotyping. Morphometrics is one of the candidates to relieve the bottleneck by providing quantifying, visualizing, analyzing and summarizing techniques. In this minisymposium, we focus on how to understand and interpret the morphological data of plants with genomic, developmental, and physiological information.

Time	**Title & Presenter**
09:00 – 09:05	**Introduction** **Koji Noshita** (*The University of Tokyo*)
09:05 – 09:30	**Leaf surface reconstruction from "noisy" point cloud data for geometric analysis** **Koji Noshita** (*The University of Tokyo*)
09:30 – 10:00	**Morphometric analysis of leaves** **Dan Chitwood** (*Donald Danforth Plant Science Center*)
10:00 – 10:30	**Low cost field based plant phenotyping with cameras and image analytics** **Wei Guo** (*Institute for Sustainable Agro-ecosystem Services, The University of Tokyo*)

Koji Noshita
The University of Tokyo, Japan
e-mail: `noshita@morphometrics.jp`

Wei Guo
Institute for Sustainable Agro-ecosystem Services, The University of Tokyo, Japan

Bangyou Zheng
CSIRO Agriculture, Australia

Tao Duan
CSIRO Agriculture, Australia

Scott Chapman
CSIRO Agriculture, Australia

Hiroyoshi Iwata
The University of Tokyo, Japan

Leaf surface reconstruction from "noisy" point cloud data for geometric analysis

In recent years, 3D scanners, Depth cameras, LiDAR and etc. have become more widely available, and they have been used to acquire morphological and color information for target objects. A pipeline using Structure from Motion (SfM) and Multi-View Stereo (MVS) is a promising technique to reconstruct a surface as point cloud data from a set of 2D images. High-resolution point cloud data now can be acquired easily and cost-effectively because the pipeline has been implemented as several libraries and software products.

For estimating and evaluating biological traits (e.g. leaf area, leaf shape, curvature), not only point clouds but also 3D surfaces themselves need to be reconstructed. In this study, we propose a method to reconstruct 3D surfaces of leaves from "noisy" point clouds. In the proposed method, a leaf is modeled as a 2D closed surface embedded in the Euclidean space $\mathbb{R}^3$. Firstly, point cloud is parameterized by using isomap [1], which is one of the non-linear dimension reduction methods. Secondly, we fit a penalized B-spline surface to the point cloud based on the parameterized point cloud data. Finally, several biological traits can be estimated from the reconstructed surface. In this talk, we will show both computational and empirical researches on several crop species.

REFERENCES

[1] Tenenbaum, J.B., de Silva, V., Langford, J.C., 2000. A global geometric framework for nonlinear dimensionality reduction. *Science*, **290**: 2319–2323.

Dan Chitwood
Donald Danforth Plant Science Center, St. Louis, MO USA
e-mail: `dchitwood@danforthcenter.org`

Morphometric analysis of leaves

Natural variation in leaf shape is spectacularly diverse. Leaf shape is genetically specified within a complex developmental and environmental context. Leaf shape varies between species, changes between successive nodes on the same shoot, is altered between seasons in response to climate in long lived perennials, and even correlates with the paleoclimate in the fossil record. In this seminar I will talk about applying a variety of morphometric techniques—from Procrustes-adjusted landmarks to Elliptical Fourier Descriptors—to the genetic, developmental, and environmental analysis of leaf shape. I will end with a discussion of the caveats of each of these approaches and the application of a promising new technique, Persistent Homology, to more universally characterize the plant form.

Wei Guo
Institute for Sustainable Agro-ecosystem Services, The University of Tokyo, Japan
e-mail: email@address

Seishi Ninomiya
Institute for Sustainable Agro-ecosystem Services, The University of Tokyo, Japan

Low cost field based plant phenotyping with cameras and image analytics

Nowadays, field based plant phenotyping (investigates how a plant's genome, interacting with the environment, affects the observable traits of a plant) is becoming new bottleneck for plant breeding research. The measurements by image analytics allow the recording and monitoring of relevant phenotypes noninvasively, with higher precision, accuracy and throughput than manual measurement and at considerable reduced cost and human labors. In this talk, we will present some of the on-going field phenotyping researches using image analytics techniques. The image data collecting solutions which are integrating digital cameras into variance field sensing platforms such as field-server, ground moving vehicles and drones, image analyzing algorithms that aimed to measure the phenotypic traits of crops will be introduced. Then the futuristic challenges of field based phenotyping will also be discussed.

Mini-Symposium

Sep 8, 10:45 – 12:15, Room B

Horizon of mutualism studies

Organizer(s): **Hisashi Ohtsuki**
SOKENDAI (The Graduate University for Advanced Studies), Shonan Village, Hayama, Kanagawa 240-0193, Japan
e-mail: `ohtsuki_hisashi@soken.ac.jp`

Evolution of mutualism and its ecological consequences have recently been drawing a wider attention. For example, it is not obvious how mutualism is initially established between different species with different interests, how the evolutionary transition from parasitism to mutualism occurs, and how mutualism is stably maintained despite the possibility of exploitation by cheaters. In community ecology, it has been theoretically shown that mutualism destabilizes the community. This symposium aims to provide recent theoretical findings in mutualism studies and discuss future direction in this field.

Time	**Title & Presenter**
10:45 – 10:50	**Introduction** **Hisashi Ohtsuki** (*SOKENDAI*)
10:50 – 11:10	**The ecology of the microbiome: Networks, competition & cooperation, and stability** **Jonas Schluter** (*Memorial Sloan Kettering Cancer Center*)
11:10 – 11:30	**Coevolutionary dynamics of one-to-many mutualisms** **Hideo Ezoe** (*Osaka Prefecture University*)
11:30 – 11:50	**Resampling after discrimination destabilizes mutualism** **Yu Uchiumi** (*SOKENDAI*)
11:50 – 12:10	**Joint evolution of interspecific mutualism and developmental stability under directional selection in trait space** **Atsushi Yamauchi** (*Center for Ecological Research, Kyoto University*)
12:10 – 12:15	**General Discussion**

Jonas Schluter *+
Memorial Sloan Kettering Cancer Center
e-mail: `jonas.schluter+sokendai@gmail.com`

Katharine Z. Coyte*
Memorial Sloan Kettering Cancer Center

Kevin R. Foster+
University of Oxford

***These author contributed equally to this work**
+Corresponding authors

The ecology of the microbiome: Networks, competition & cooperation, and stability [1]

The human gut harbors a large and complex community of beneficial microbes that remain stable over long periods. This stability is considered critical for good health but is poorly understood. Here we develop a body of ecological theory to help us understand microbiome stability.

Although cooperating networks of microbes can be efficient, we find that they are often unstable. Counterintuitively, this finding indicates that hosts can benefit from microbial competition when this competition dampens cooperative networks and increases stability. More generally, stability is promoted by limiting positive feedbacks and weakening ecological interactions.

We have analyzed host mechanisms for maintaining stability—including immune suppression, spatial structuring, and feeding of community members—and support our key predictions with recent data.

REFERENCES

[1] Coyte KZ*, Schluter J *+, Foster, KR+, 2016 The ecology of the microbiome: Networks, competition, and stability. *Science*, **350**: 6261, p663-666.

Hideo Ezoe
Osaka Prefecture University, Sakai, Japan
e-mail: `hezoe@b.s.osakafu-u.ac.jp`

Coevolutionary dynamics of one-to-many mutualisms

One-to-many mutualisms—interspecific cooperations in which each host individual can potentially interact with multiple symbiont individuals while each symbiont individual can only one host individual—are ubiquitously found in nature and include well-known mutualistic systems such as fig–fig wasp, legume–rhizobium etc., although their evolutionary stability has not been explored. It has been often thought that partner choice by hosts can stabilize multi-player mutualisms [1][2]. However, in one-to-many mutualisms, partner choice is inevitably asymmetric between hosts and symbionts, which might destabilize the system.

In this study, I develop a simple mathematical model to describe the (co)evolutionary dynamics between host and symbiont populations in a one-to-many mutualism. I assume that each host chooses a constant number of symbionts from a potential symbiont population, a fraction of which are chosen through preferential choice on the basis of the cooperativeness of the symbionts and the rest are chosen randomly. After the associations between hosts and symbionts are established, the host offers a constant amount of resource to each associating symbiont. The symbiont spends a part of the resource to increase the fitness of the host in proportion to its cooperativeness, and the rest for its own reproduction.

First I fix the fraction and strength of the preferential symbiont choice of the host and concentrate on the evolutionary dynamics of cooperativeness of the symbiont. I show that the pure mutualist population is evolutionarily stable when the fraction of preferential choice c is large and the strength of preferential choice k is small, otherwise mutualists and cheaters receiving benefits from their host without a return coexist in the symbiont population. In the coexistence state the frequency of mutualists increases with c. In contrast, it decreases with k, while the cooperativeness of mutualists increases. The two factors offset against each other, so that the fitness gain of the host remains constant.

Next I examine coevolutionary dynamics of the traits of both hosts and symbionts, assuming that the preferential choice by the host incurs a cost. Using numerical calculations, I find that mutualism is maintained when the preferential choice by the host is not very costly and the mutation rate of the symbiont is sufficiently large. However, mutualist symbionts coexist with cheaters in the symbiont population when the cost of increasing the fraction of preferential choice is high. Moreover, hosts that do not engage in preferential partner choice (indiscriminator hosts) coexist with discriminator hosts when the cost of increasing the strength of preferential choice is high. As a result, the parameter domain of pure mutualism, i.e. the state free from cheater symbionts and indiscriminator hosts, can be much narrower than the whole domain where the mutualism can persist.

REFERENCES

[1] Bull, J. J. and Rice W. R., 1991. Distinguishing mechanisms for the evolution of co-operation. *J Theor Biol* **149**: 63–74.
[2] Noë, R. and Hammerstein, P. 1995. Biological Markets. *Trends Ecol Evol* **10**: 336–339.

Yu Uchiumi
Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Kanagawa, Japan
e-mail: `uchiumi_yu@soken.ac.jp`

Hisashi Ohtsuki
Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Kanagawa, Japan

Akira Sasaki
Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Kanagawa, Japan

Resampling after discrimination destabilizes mutualism

Mutualism based on the reciprocal exchange of costly services must avoid exploitation by free-riders, which exploit their partners without helping. Accordingly, hosts discriminate against free-riding symbionts in many mutualistic relationships. For example, it was experimentally shown by Kiers et al.[1] that soybeans (*Glycine max*) penalized non-N-fixing rhizobia (*Bradyrhizobium japonicum*) by halting oxygen supply to them. Such a mechanism is not limited to legumes. In fact, similar mechanisms have been reported in flowering plants in obligate pollination mutualism, ant plants with ants, and land plants with arbuscular mycorrhizal fungi (reviewed by Frederickson[2]). These mechanisms have been called "sanctioning", "partner choice", and/or "selective abortion". Here we call these phenomena "discrimination", regardless of their finer details. Because the selective advantage of discriminators comes from the presence of the free-riders that they eliminate, previous studies[3,4] have argued that free-riders must be frequently supplied by mutation or immigration to maintain such discrimination mechanisms in the population.

However, by rethinking the classification of discrimination, we found that the recurrent supply of free-riders is not always essential to maintaining discrimination. We classified discrimination into two types and analyzed the corresponding coevolutionary dynamics between host discrimination and symbiont cooperation. In the first type of discrimination, which we call "resampling" discrimination, a host terminates the symbiotic interaction with symbionts that it judges to be free-riders, and then resamples from the environment the same number of new symbionts as the ones that it rejected. In the second type of discrimination, called "one-shot" discrimination, a host terminates the symbiosis with free-riding symbionts, but does not resample new symbionts from the environment. We then asked whether mutational supply of free-riders must be frequent enough to evolutionarily maintain the discrimination, by comparing the differences in their coevolutionary outcomes.

Our comparison of the two discrimination types revealed two novel findings: (i) one-shot discriminators invade the resident populations consisting of free-riding symbionts and non-discriminating hosts, whereas resampling discriminators do not; (ii) one-shot discriminators are stably maintained regardless of the rate of mutation generating free-riders, whereas resampling discriminators are maintained only if the mutation rate is moderately high. Although previous studies[3-5] have emphasized the necessity of a recurrent supply of free-riders to maintain discrimination, our results strongly suggest that the type of actual discrimination mechanism should be focused on more than how the variability in a symbiont population is maintained.

REFERENCES

[1] Kiers, E.T., Rousseau, R.A., West, S.A. & Denison, R.F., 2003. Host sanctions and the legume-rhizobium mutualism. *Nature* **425**: 78–81.

[2] Frederickson, M.E., 2013. Rethinking mutualism stability: cheaters and the evolution of sanctions. *Q. Rev. Biol.* **88**: 269–295.

[3] Foster, K.R. & Kokko, H., 2006. Cheating can stabilize cooperation in mutualisms. *Proc. R. Soc. B Biol. Sci.* **273**: 2233–9.

[4] McNamara, J.M., Barta, Z., Fromhage, L. & Houston, A.I., 2008. The coevolution of choosiness and cooperation. *Nature* **451**: 189–92.

[5] Heath, K.D. & Stinchcombe, J.R., 2014. Explaining mutualism variation: a new evolutionary paradox? *Evolution* **68**: 309–17.

Atsushi Yamauchi
Center for Ecological Research, Kyoto University
Hirano 2-509-3, Otsu 520-2113, Japan
e-mail: `a-yama@ecology.kyoto-u.ac.jp`

Joint evolution of interspecific mutualism and developmental stability under directional selection in trait space

The present study theoretically examines the process by which interspecific mutualism is established with trait matching. The mathematical model for this process includes joint evolution of the mutualistic relationship between two species and developmental instabilities of relevant traits in one-dimensional trait space, assuming abiotic directional selection on the traits. The model indicates that the mutualism can evolve when (1) the scaled difference in directional selections on each species is small, (2) the scaled benefit of mutualism is large, and (3) the ratios of the cost coefficients of developmental stability to the benefits of mutualism are small. It also shows that the evolution of developmental stability can promote the evolution of mutualism with trait matching when the costs of stable development (which is a decreasing function of instability) have minimum thresholds at high instability that restrict unlimited increments in instability. In plant–pollinator interactions, it has recently been proposed that evolutionary surges of developmental stability in mutualistic relationships might promote species diversification. The present results partly support this theory with respect to the evolutionary relationship between mutualism and developmental instability.

Mini-Symposium

Sep 8, 10:45 – 12:15, Room D

Patterns and Dynamics in Partial Differential Equations appearing in Mathematical Biology

Organizer(s): **Toshiyuki Ogawa**
Meiji University, 4-21-1 Nakano, Nakano, 164-8525, Japan
e-mail: `togw@meiji.ac.jp`

Recent developments of the analysis for the PDE model relating to mathematical biology are discussed in this mini-symposia. Four speakers introduce reaction-diffusion approximation for non-local effects, amoeba behaviour, 2-dimensional traveling wave composed of convex curves and drift bifurcation of traveling waves.

Time	**Title & Presenter**
10:45 – 11:05	**Pattern formation through non-local interactions** **Hirokazu Ninomiya** (*Meiji University*)
11:05 – 11:25	**Differentiation of behavioral type induced by environmental variations in an amoeba** **Keiichi Ueda** (*University of Toyama*)
11:25 – 11:45	**Convex traveling wave solutions to an interface equation** **Harunori Monobe** (*Tokyo Institute of Technology*)
11:45 – 12:05	**Bifurcation of traveling wave in Competition-Diffusion equations** **Toshiyuki Ogawa** (*Meiji University*)

H. Ninomiya
Meiji University, 4-21-1 Nakano, Nakano-ku, Tokyo 164-8525, Japan
e-mail: hirokazu.ninomiya[at]gmal.com

Y. Tanaka
Hokkaido University, Kita 10, Nishi 8, Kita-ku, Sapporo, Hokkaido, 060-0810, Japan

H. Yamamoto
Meiji University, 4-21-1 Nakano, Nakano-ku, Tokyo 164-8525, Japan

Pattern formation through non-local interactions

Recent years have seen the introduction of non-local interactions in various fields. A typical example of a non-local interaction is where the convolution kernel incorporates short-range activation and long-range inhibition. This paper presents the relationship between non-local interactions and reaction-diffusion systems in the following sense:

(a) the relationship between the instability induced by non-local interaction and diffusion-driven instability;

(b) the realization of non-local interactions by reaction-diffusion systems.

To study these issues, we consider the following non-local evolution equation:

$$\begin{cases} u_t = d_u u_{xx} + g(u, J * u), & \text{in } [-L, L] \times \{t > 0\}, \\ u(x, 0) = u_0(x), & \text{on } [-L, L], \end{cases}$$

under suitable assumptions for the nonlinear function g where d_u is a positive constant, J is a kernel. To approximate this non-local evolution equation, we introduce the following reaction-diffusion system:

$$\begin{cases} u_t &= d_u u_{xx} + g\left(u, \sum_{j=0}^{M} \alpha_j v_j\right), \\ v_{j,t} &= \dfrac{1}{\varepsilon}\left(d_j v_{j,xx} + u - v_j\right), \quad (j = 0, \cdots, M) \end{cases}.$$

Using this reaction-diffusion system, we show that the non-local interaction of a Mexican-hat kernel destabilizes the stable homogeneous state and that this instability is related to diffusion-driven instability. Furthermore, a reaction-diffusion system that approximates the non-local interaction system with any even convolution kernel is shown to exist.

REFERENCES

[1] S. Amari, 1977, Dynamics of Pattern Formation in Lateral-Inhibition Type Neural Fields, Biol. Cybernetics, **27**, 77-87

[2] J. Furter, M. Grinfeld, 1989, Local vs. non-local interactions in population dynamics, J. Math. Biol. **27**, 65-80

[3] V. Huston, S. Martinez, K. Mischaikow, G.T. Vickers, 2003, The evolution of dispersal, J. Math. Biol. **47**, 483-517

[4] M. Iida, M. Mimura, H. Ninomiya, 2006, Diffusion, cross-diffusion and competitive interaction, J. Math. Biol. **53** 617-641

[5] C. R. Laing, W. Troy, 2003, PDE methods for nonlocal models, SIAM J. APPLIED DYNAMICAL SYSTEMS, **2**, 487-516

[6] H. Ninomiya, Y. Tanaka, H. Yamamoto, Reaction, diffusion and non-local interaction, submitted to J. Math. Biol.

[7] A.M. Turing, 1952, The chemical basis of morphogenesis. Phil. Trans. R. Soc. Lond. B, **237**, 37-72

Itsuki Kunita
Research Institute for Electronic Science, Hokkaido University, Sapporo, Japan

Keiichi Ueda
Graduate School of Science and Engineering, University of Toyama, Toyama, Japan
e-mail: `kueda@sci.u-toyama.ac.jp`

Dai Akita
Graduate School of Life Science, Hokkaido University, Sapporo, Japan

Shigeru Kuroda
Hokkaido University, Sapporo, Japan

Toshiyuki Nakagaki
Research Institute for Electronic Science, Hokkaido University, Sapporo, Japan

Differentiation of behavioral type induced by environmental variations in an amoeba

We experimentally found that statistical distribution of passage time across the quinine zone switched from unimodal to bimodal (two groups of crossing faster and not crossing at all) when the periodic perturbation of light stimulation is applied homogeneously in space in addition to the quinine-induced differentiation. Here, we develop a continuum mathematical model of the cell dynamics of amoeboid movement. Our model incorporates the dynamics of the mass flow of the protoplasmic sol, in relation to the generation of pressure based on the autocatalytic kinetics of pseudopod formation and retraction (mainly, sol-gel conversion accompanying actin-myosin dynamics). Based on the mathematical model, we succeeded to reproduce the stimulation-induced differentiation observed in the experiment. A possible mechanism originates from a saddle structure around a canard solution.

Harunori Monobe
Tokyo Institute of Technology
e-mail: `monobe.h.aa@m.titech.ac.jp`

Hirokazu Ninomiya
Meiji University

Convex traveling wave solutions to an interface equation

The *curve shortening flow* (CSF) is an interface equation and a geometric flow of hypersurfaces in two-dimensional spaces. CSF was originally proposed by Mullins [3] to analyze the motion of grain boundaries, and there are a lot of analysis results related to the flow. For instance, Grayson [2] showed that any Jordan curve (simple and closed curve) will be convex in a finite time. Moreover Gage-Hamilton[1] confirmed that any convex Jordan curves shrink to a single point at a finite time. From these two results, any Jordan curve will become to a convex shape and shrink to a single point in a finite time. We remark that there exists a traveling wave called *Grim Reaper* defined in the whole space.

In recent years, CSF with driving force F also appear in various physical and biological problems. The most simple one is that F is a positive constant, called *Eikonal-curvature flow*. This equation is related to a ray optics. Ninomiya and Taniguchi [4] showed that there exists a traveling wave, called *V-shaped traveling front*, defined in the whole space. Also this flow appears as a singular limit problem of some reaction-diffusion equations and systems, e.g., Allen-Cahn equation, FitzHugh-Nagumo equation and a kinematic model of excitable media. In addition, CSF with driving force is related to not only interface equations but also free boundary problems related to cell motility.

In this talk, we consider the existence of a traveling wave composed of a Jordan curve for CSF with driving force F. More precisely, we investigate the condition of driving force F such that CSF has traveling wave composed of Jordan curve. As a result, we obtain that

(1) If F is a Lipschitz function, all traveling waves are convex.
(2) In addition, when F is a positive, there exists a unique traveling wave.
(3) Assume that there exist traveling waves for CSF with a driving force F. Then there is at most one traveling wave.

REFERENCES

[1] M. E. Gage and R. S. Hamilton, 1986. The heat equation shrinking convex plane curves, *J. Differential Geom.,* **23**: 69–96.

[2] M. A. Grayson, 1987. The heat equation shrinks embedded plane curves to round points, *J. Differential Geom.,* **26**: 285–314.

[3] W. Mullins, 1963. Solid surface morphologies governed by capillarity, Metal Surface: Structure, Energetics and Kinetics. *Am. Soc. Metals.,* 17–66.

[4] H. Ninomiya and M. Taniguchi, 2005. Existence and global stability of traveling curve fronts in the Allen-Cahn equations, *J. Differential Equations,* **213**: 204–233.

Toshiyuki Ogawa
Meiji University, Nakano campus, 4-21-1 Nakano, Nakano-ku, Tokyo, Japan
e-mail: togw@meiji.ac.jp

Shin-Ichiro Ei
Hokkaido University, Kita 8, Nishi 5, Kita-ku, Sapporo, Japan
e-mail: Eichiro@math.sci.hokudai.ac.jp

Hideo Ikeda
Toyama University, Gofuku Campus, 3190 Gofuku, Toyama, Japan
e-mail: ikeda@sci.u-toyama.ac.jp

Masayasu Mimura
Meiji University, Nakano campus, 4-21-1 Nakano, Nakano-ku, Tokyo, Japan
e-mail: mimura.masayasu@gmail.com

Bifurcation of traveling wave in Competition-Diffusion equations

There have been a lot of studies on the traveling wave solutions to a reaction-diffusion system with 2 competing species. Let us consider, here, the situation where we have third competing species adding to the original two competing species. Since this system has a trivial traveling solution which consists of the traveling wave solution of 2 species, the question is the stability of this solution in the full 3 component system. It turns out there is one critical point by taking the birth rate of the third species as a bifurcation parameter and we study the bifurcation structure around this critical point.

REFERENCES

[1] H. Berestycki, O.Diekmann, C.Nagelkerke and P.A.Zegeling, Can a species keep pace with a shifting climate?, Bull. Math. Biol., **71**, 399-429, 2009.

[2] S.Ei, The motion of weakly interecting pulses in RD sysytems, J. Dyn.Diff. Eqs. **14(1)**, 2002.

[3] Y.Kan-on, Parameter dependence of propagation speed of traveling waves for competition-diffusion equations, SIAM J. Math. Anal., **26**, 340-363, 1995.

Mini-Symposium

Sep 8, 10:45 – 12:15, Room E

Extraordinary forms - exploring the limits of cell shape modeling

Organizer(s): **Shigeo Hayashi**
Laboratory for Morphogenetic Signaling, RIKEN Center for Developmental Biology,2-2-3 Minatojima-Minamimachi, Chuo-ku, Kobe, Japan, 650-0047
e-mail: `shayashi@cdb.riken.jp`

Takashi Miura
Department of Anatomy and Cell Biology, Kyushu University Graduate School of Medicine, 3-1-1 Maidashi Higashi-ku Fukuoka 812-0054 JAPAN
e-mail: `miura_t@anat1.med.kyushu-u.ac.jp`

Co-presented by Spontaneous pattern formation ex vivo, JST CREST

Cells have been extensively studied as a building block of living organisms in cell biology and mathematical biology. As a result, morphogenesis of standard cells like epithelia, fibroblasts or neurons are gradually understood. However, cells exhibit much diverse shape in the real world. In this symposium, we present several strange cell shapes which we cannot imagine from textbook knowledge together with current theoretical models that has been used to model cell form. By combining these biological examples and theoretical models, we try to clarify the possibility and limit of cell shape modeling in mathematical biology.

Time	**Title & Presenter**
10:45 – 11:03	**Mechanism of jigsaw-puzzle pattern formation in plant leaf epidermal cell: modeling single cell shape by interface equation and convolution kernel** **Takashi Miura** (*Kyushu University Graduate School of Medical Sciences*)
11:03 – 11:21	**Form and Function of Pollen Grains** **Hideki Takahashi** (*The University Museum, Hokkaido University*)
11:21 – 11:39	**Recreating human podocytes in the kidney** **Ryuichi Nishinakamura** (*Institute of Molecular Embryology and Genetics, Kumamoto University*)
11:39 – 11:57	**Cellular Tessellation in Sensory Epithelia** **Hideru Togashi** (*Kobe University Graduate School of Medicine*)
11:57 – 12:15	**Simulating the Onset and Development of Polycystic Kidney Disease using Virtual Tissues** **James Glazier** (*Department of Intelligent Systems Engineering and Biocomplexity Institute, Indiana University*)

Takashi Miura
Kyushu University Graduate School of Medical Sciences
e-mail: `miura_t@anat1.med.kyusu-u.ac.jp`

Takumi Higaki
Department of Integrated Biosciences, The University of Tokyo

Natsumaro Kutsuna
LPixel Inc. & Department of Integrated Biosciences, The University of Tokyo

Kae Akita
Department of Integrated Biosciences, The University of Tokyo

Hisako Takigawa-Imamura
Kyushu University Graduate School of Medical Sciences

Kenji Yoshimura
Department of Neurology, Osaka City General Hospital

Mechanism of jigsaw-puzzle pattern formation in plant leaf epidermal cell: modeling single cell shape by interface equation and convolution kernel

Plant leaf epidermal cell shows beautiful jigsaw-puzzle like pattern. Various molecules are known to be involved in this process. For example, two small rho GTPase ROP2 and ROP6, are involved in production and degradation of cell wall under the control of auxin [1]. However, how the interaction of these molecules results in pattern formation remain to be elucidated.

In the present study, we model this phenomenon using interface equation and convolution kernel [2]. We consider the movement of the boundary between cytoplasm and cell wall. At first we define the speed of growth normal to the interface as V. Next we define the effect of short-range signaling molecule (v) which is released from cytoplasm as convolution kernel k. Effect of surface tension is defined as $\sigma\kappa$, in which κ represents local curvature and σ represents strength of surface tension. The governing equation is

$$V = f(v) - \sigma\kappa$$
$$v = k \otimes u.$$

We use Heaviside function for kernel k and numerically calculate the equation using Phase field method. We reproduced the formation of cell wall interdigitation by this model, and analytically obtain the fastest growing wavenumber. We also reproduced the dynamics of three-way junction of cell wall and cell wall thickening by degradation of cellulose.

REFERENCES

[1] T. Xu, M. Wen, S. Nagawa, Y. Fu, J.-G. Chen, M.-J. Wu, C. Perrot-Rechenmann, J. Friml, A. M. Jones, and Z. Yang, “Cell Surface- and Rho GTPase-Based Auxin Signaling Controls Cellular Interdigitation in Arabidopsis,” *Cell*, vol. 143, no. 1, pp. 99–110, Oct. 2010.

[2] T. Higaki, N. Kutsuna, K. Akita, H. Takigawa-Imamura, K. Yoshimura, and T. Miura, “A Theoretical Model of Jigsaw-Puzzle Pattern Formation by Plant Leaf Epidermal Cells.,” *PLoS Comput Biol*, vol. 12, no. 4, p. e1004833, Apr. 2016.

Hideki Takahashi
The University Museum, Hokkaido University, Sapporo, 060-0810, JAPAN
e-mail: `hide@museum.hokudai.ac.jp`

Form and Function of Pollen Grains

Pollen grain is one of the most important cells in the plant life cycle. Genetic content of pollen grain is united with that of the female embryo sac, through the double-fertilization the next generation, the seed is formed. Thus if pollen grains could not reach the stigma of the pistils and they could not germinate the pollen tube, the next generation does not made.

Form and function of the pollen grains have been studied by Wodehouse (1935), Erdtman (1952), and Faegri et al. (1989) in light microscopic level (LM). They show many relationships between pollen morphology and plant taxonomic system and/or plant phylogeny and evolution. But mainly since 1970's, transmission electron microscope (TEM), and a little later scanning electron microscope (SEM) have worked as the useful tools for clarifying the fine pollen morphology. Especially TEM have worked well in clarifying the developmental processes of the exine (pollen wall) and aperture (lacking place of exine). Four cells derived from one mother cell is enclosed in the callose special wall, and the primexine works as template for making the exine.

We can divide the pollen morphology into several factors; size and shape of pollen grains, the number and position and structure of the pollen apertures, and structure and sculpture of pollen wall. Pollen grain is usually a single cell-size unit, but sometimes they unite into tetrad, polyad, or pollen mass (pollinia) in some special taxonomic groups.

In the spores (ancient pollen grains) of the mosses, ferns and fern allies, the single aperture is situated at the proximal pole on evely four cells that derived from one mother cell through the meiosis. In the first stage of the seed plant, i.e., Gymnospers, single aperture is changed to the distal pole. In the next evolutional stage, many angiospermous families show the three longitudinal, equatorially arranged colpi on the grain. This sudden change from one to three in the number of apertures is a very interesting problem in the plant evolution. And the pollen grains that have many apertures globally on the surface of the grains appeared in some special plant taxa.

Aperture shape is usually pore or colpus (slit-like). And in the next evolutional stage, colpus in the outer wall and pore in the inner wall are combined and form the 'colporate' apertures. Aperture is a thin wall area on the pollen surface and important in the pollen tube germination on the stigma, but during the pollen dispersal time, pollen grains have to maintain their own humidity, so shrinking shape by the intrusion of apertures work well in preserving the cell content. Structure of pollen wall and aperture is important in changing the cell shape both in dry and wet conditions. This function is called as 'hermomegathy'.

Structure and sculpture of the pollen wall works as the sticking method on the body of visiting insects. A layered structure of the pollen wall also work as the deposition space for some sticky materials for the pollinators and some efficient materials in incompatibility systems. Sculpture of the wall and shape and/or size of the pollen grain itself may include an important meaning in anemophily vs. entomophily.

REFERENCES

[1] Miyoshi, N., Fujiki, T. & Kimura, H. 2016. Pollen Flora of Japan (in Japanese), enlarged and 2nd ed. Hokkaido Univ. Press,

[2] Faegri, K., Kaland, P.E. and Krzywinski, K. 1989. Textbook of Pollen Analysis, 4th ed. John Wiley & Sons, Chichester.

[3] Erdtman, G. 1952. Pollen Morphology and Plant Taxonomy, Angiosperms. Almqvist & Wiksell, Stockholm.

[4] Wodehouse, R.P., 1935. Pollen Grains. McGraw-Hill Book Co., Inc., New York.

Hideru Togashi
Kobe University Graduate School of Medicine
e-mail: `htogashi@med.kobe-u.ac.jp`

Cellular Tessellation in Sensory Epithelia

Animal tissues are composed of multiple cell types arranged in complex and elaborate patterns. In sensory epithelia, including the auditory epithelium and olfactory epithelium, different types of cells are arranged in unique mosaic patterns. These mosaic patterns are evolutionarily conserved, and are thought to be important for hearing and olfaction. The complex patterns of cells in tissues often arise through self-organization of cells. Differential adhesion has been proposed to promote selective aggregation or rearrangement of cells, and these mechanisms could drive self-organized cell movements in the sensory epithelia. Recent progress has provided accumulating evidence that the cellular pattern formation in sensory epithelia involves cell rearrangements, movements, and shape changes. These morphogenetic processes are largely mediated by intercellular adhesion systems. Many different types of cells in tissues express various types of cell adhesion molecules. Although cooperative mechanisms between multiple adhesive systems are likely to contribute to the production of complex cell shapes and patterns, our current understanding is insufficient to entirely explain the complex mechanisms. Recent studies have revealed that nectins, in cooperation with cadherins, are crucial for the mosaic cellular patterning in sensory organs. The nectin and cadherin systems are physically and functionally associated with one another, and these associations provide cells with differential adhesive affinities for complex cellular pattern formations in sensory epithelia. In this symposium, I will introduce and discuss recent progress of our studies on cellular patterning and unique morphology of the cells in sensory organs.

REFERENCES

[1] Katsunuma, S., Honda, H., Shinoda, T., Ishimoto, Y., Miyata, T., Kiyonari, H., Abe, T., Nibu, K., Takai, Y., and Togashi, H. 2016. Synergistic action of nectins and cadherins generates the mosaic cellular pattern of the olfactory epithelium. *J. Cell Biol.*, **212**: 561–575.
[2] Fukuda, T., Kominami, K., Wang, S., Togashi, H., Hirata, K., Mizoguchi, A., Rikitake, Y., and Takai, Y. 2014. Aberrant cochlear hair cell attachments caused by Nectin-3 deficiency result in hair bundle abnormalities. *Development,* **141**: 399-409.
[3] Togashi, H., Kominami, K., Waseda, M., Komura, H., Miyoshi, J., Takeichi, M., and Takai, Y. 2011. Nectins Establish a Checkerboard-like Cellular Pattern in the Auditory Epithelium. *Science*, **333**: 1144–1147.

Ryuichi Nishinakamura
Institute of Molecular Embryology and Genetics, Kumamoto University
e-mail: `ryuichi@kumamoto-u.ac.jp`

Recreating human podocytes in the kidney

Recapitulating three-dimensional structures of the kidney in vitro is a major challenge for developmental biology and regenerative medicine. The kidney develops by the reciprocal interaction between the metanephric mesenchyme and the ureteric bud, the former of which contains nephron progenitors. We found that nephron progenitors are derived from posteriorly located T-positive population at the post-gastrulation stage, and succeeded in generating the three-dimensional nephrons in vitro from pluripotent stem cells both in mice and humans.

Nephrons consist of glomeruli and renal tubules, the former of which contribute to the filtration process of the kidney. Glomerular podocytes possess numerous cellular protrusions, and between these foot processes, the slit diaphragms are formed and prevent protein leakage into the urine. The podocytes induced from human iPS cells in vitro exhibit many of these features, suggesting that the basic morphology of the podocytes is generated cell-autonomously. However, the foot process become more complicated when glomeruli are vascularized upon transplantation, indicating that the interactions between the vascular endothelial cells and podocytes may be required for further maturation. These findings will be useful for dissecting human glomerular development and diseases.

Although many proteins, including nephrin and podocin, are involved in the formation of slit diaphragms, little is known how morphology of podocytes is regulated. I will update the podocyte biology to discuss whether the unique feature of the podocytes is a good target of mathematical biology.

REFERENCES

[1] Tanigawa S et al. Selective in vitro propagation of nephron progenitors from embryos and pluripotent stem cells. **Cell Rep** 15: 801-813, 2016
[2] Sharmin S et al. Human induced pluripotent stem cell-derived podocytes mature into vascularized glomeruli upon experimental transplantation. **J. Am. Soc. Nephrol.** 27: 1778-1791, 2016
[3] Taguchi A et al. Redefining the in vivo origin of metanephric nephron progenitors enables generation of complex kidney structures from pluripotent stem cells. **Cell Stem Cell** 14: 53-67, 2014

James A. Glazier
Department of Intelligent Systems Engineering and Biocomplexity Institute.
Indiana University
Bloomington, Indiana, USA
e-mail: `jaglazier@gmail.com`

Simulating the Onset and Development of Polycystic Kidney Disease using Virtual Tissues

In polycystic kidney disease (*ADPKD*), the normal structural organization of the kidney breaks down as cysts appear, grow and progressively impair kidney function. Mutations in PKD1 and PKD2 genes appear to cause ADPKD, but we do not know how mutations in these genes change cell behaviors to produce ADPKD pathogenesis. A clue to the mechanism of kidney disorganization is that human ADPKD cysts frequently express cadherin-8 (an adhesion molecule found in normal juvenile kidney but absent from normal adult kidney), and that ectopic expression of cadherin-8 *in vitro* initiates cystogenesis. To explore the possible roles of cadherin-8 in cyst initiation, we developed a virtual-tissue computer simulation using the open-source CompuCell3D modeling environment [1]. Our simulations showed that cadherin-8-induced reduction of either cell-cell adhesion or contact inhibition of proliferation could initiate cyst formation [2]. However, the dynamics and morphologies of the cysts differ between these two mechanisms, with reduced adhesion replicating the morphologies of *in vitro* cadherin-8-induced cysts. Decreased contact inhibition results in a disctinct morphology of “Saccular” cysts which have also been observed in some human patients, suggesting that cysts may form through multiple mechanisms in humans. We confirmed our simulation findings using *in vitro* experiments to show that ectopic cadherin-8 expression did, in fact, reduce cell-cell adhesion. Since adhesion loss due to cadherin type switching in ADPKD suffices to drive cystogenesis, control of cadherin type switching could provide an effective therapy for ADPKD.

REFERENCES

[1] http://www.compucell3d.org/

[2] Belmonte, J.M., Clendenon, S.G., Oliveira, G.M., Swat, M.H., Greene, E.V., Jeyaraman, S., Glazier, J.A., Bacallao, R.L., 2016. Virtual-Tissue Computer Simulations Define the Roles of Cell Adhesion and Proliferation in the Onset of Kidney Cystic Disease. *Molecular Biology of the Cell*, (2016), doi: 10.1091/mbc.E16-01-0059

Mini-Symposium

Sep 8, 15:45 – 17:15, Room B

Biological Relevances of Mathematical Models

Organizer(s): **Kunimochi Sakamoto**
Hiroshima University, 1-3-1 Kagamiyama, HigashiHiroshima, 739-8526, Japan
e-mail: `kuni@math.sci.hiroshima-u.ac.jp`

The purpose of the symposium is to investigate, by three talks, whether or not dynamical system models for biological phenomena are really relevant to, or capture certain aspects of, the biological systems which the differential equations are originally intended to model. It is not intended to assert that our views are the definite ones. Through our talks, we attempt to set a stage for open discussion.

Time	**Title & Presenter**
15:45 – 16:15	**Bulk reaction versus Boundary flux in diffusive systems** **Kunimochi Sakamoto** (*Hiroshima University*)
16:15 – 16:45	**A mathematical approach to the economy of atomic power generation** **Fumio Nakajima** (*Iwate University*)
16:45 – 17:15	**Diffusion driven destabilization of a spatially homogeneous limit cycle in reaction-diffusion systems** **Masataka Kuwamura** (*Kobe University*)

Kunimochi Sakamoto
Hiroshima University, Higashi-Hiroshima, Japan
e-mail: `kuni@math.sci.hiroshima-u.ac.jp`

Bulk reaction versus Boundary flux in diffusive systems

In dealing with the polarity and rhythmicity of a cell, several researchers have proposed reaction-diffusion systems with natural boundary conditions [2,3]. In addition, the proposed systems have another feature that they have a mass-conserving property. It should be emphasized that in these systems reaction takes place in the bulk (i.e., in the interior of domain).
On the other hand, the authors of [1] proposed a diffusive system with nonlinear boundary flux conditions, in order to account for rhythmic activities of cells. Although the system proposed in [1] contains bulk decay and growth, its essential innovation lies in the introduction of nonlinear boundary flux conditions into the modeling of cell activities. Following the same line of research area as in [1], a Turing type mechanism is extended for diffusive systems with boundary flux conditions by [4,5].

It is our interest to compare the behavior of solutions of two types of models:
(1) Diffusive systems with bulk reaction and the natural boundary conditions;
and
(2) Diffusive systems with flux boundary conditions.
It seems that the boundary flux in (2) has an effect similar to the bulk reaction in (1).

On one hand, systems of type (1) have solutions monotonic in one direction (or, traveling wave type solutions) and solutions with a single peak (so-called, a spike). On the other hand, the steady state solutions of systems of type (2) automatically have the characteristic of polarity. Therefore, stability property of steady states, studied in[4,5], is relevant in systems of type (2).

Exhibiting these features of solutions, the talk will propose that boundary flux conditions in diffusive systems may play an alternative modeling role of bulk reaction. Between bulk reaction and boundary flux, which mechanism is more relevant to biology depends on the phenomena one wish to understand. It is also natural that both of these effects, bulk reaction and boundary flux, should be appropriately combined in order to better describe processes taking place in cells. This is a challenge to both mathematics and biology.

REFERENCES

[1] Levine, H. and Rappel, W-J., 2005, Membrane-bound Turing patterns, *Physical Review E* **72**: 061912.
[2] Ishihara, S., Otsuji, M. and Mochizuki, A., 2007, Transient and steady state of mass-conserver reaction diffusion systems, *Physical Review E* **75**: 356--368.
[3] Mori, Y., Jilkine, A. and Edelshtein-Keshet, L., 2008, Polarity from a Bistable Reaction-Diffusion Systems, *Biophysical Journal* **94**: 3648--3697.
[4] Anma, A. and Sakamoto, K., 2013, Turing type mechanisms for linear diffusion systems under non-diagonal Robin boundary conditions, *SIAM Journal of Math. Anal.* **45**: 3611--3628.
[5] Sakamoto, K., 2016, Destabilization threshold curves for diffusion systems with equal diffusivity under non-diagomal flux boundary conditions, *Discrete and Continuous Dynamical Systems, Series B* **21**: 641--654.

Fumio Nakajima
Iwate University, Morioka, Japan
e-mail: `fnaka@iwate-u.ac.jp`

A mathematical approach to the economy of atomic power generation

In 1970's Dr. Schumacher appealed that the atomic power generation should be immediately abolished because of the various poisonous influence due to radiation [1]. Even at the present day, we have not found any safe disposal of the radio-active waste. The purpose of this paper is to innovate a mathematical model of the economy of the atomic power generation in our society, and then to conduct Schumacher's appeal as a theorem.

Now, setting $x(t)$ to be the population of the society at time t, and $y(t)$ and $z(t)$ to be the total power of the non-atomic power generation and atomic power generation demand by this society, respectively, we shall consider the system (1), (2) and (3) as follows.

(1) $x'=a(1-x)x+y+z$
(2) $y'=\theta x-by$
(3) $z'=(1-\theta)x-cz-d\int z(s)\,\mathrm{d}s,$

where the integral in s is between $s=0$ and $s=t$, while a, b, c, d and θ are positive constant with $0<\theta<1$. This system has the following meaning. First of all, (1) is the logistic equation when y and z are absent, and (1) implies that $x(t)$ increases by the addition of $y(t)$ and $z(t)$ to the society. In (2) and (3), the term θx and $(1-\theta)x$ are the incomes for the non-atomic power generation and the atomic power generation from the society, respectively, where the units of the power generation and the incomes are appropriately chosen, and terms by and cz are their immediate costs, respectively, for example the cost of the fossil fuel and the cost of the uranium, respectively. Finally the integral term in the right hand side of (3) is the cost for the treatment of the radio-active waste, which is a feature of the atomic power generation, where the lower limit of the integral, t=0, is the initial time for the atomic power generation to start, and hence our initial condition is as follows.

(4) $x(0)>0, \quad y(0)\geq 0, \quad z(0)=0.$

Clearly (1) (2) (3) are meaningful in the case where $x(0)>0$, $y(0)\geq 0$, $z(0)\geq 0$, and in fact by the conditions in (4),we have $x(t)>0$,$y(t)>0$ and $z(t)>0$ for small $t>0$. Therefore there exists the maximal number $\omega>0$ such that $x(t)>0$, $y(t)>0$ and $z(t)>0$ for $0<t<\omega$, where ω could be infinity.Our main result is the following.

Theorem 1
(i) *If ω is finite, then $x(t)$, $y(t)$ and $z(t)$ are defined for $t=\omega$, and $z(\omega)=0$, which $x(\omega)>0$ and $y(\omega)>0$.*
(ii) *If $\omega=\infty$, then the following hold as t goes to ∞:*

- *$z(t)$ converges to* 0; • *$x(t)$ converges to* $(\theta/ab)+1$; • *$y(t)$ converges to* $(\theta/b)\big((\theta/ab)+1\big)$;
- the integral of $z(t)$ on the non-negative half line $[0,\infty)$ is equal to $(1-\theta)\big((\theta/ab)+1\big)/d$.

Remark The conclusion of Theorem 1, that is either $z(\omega)=0$ or $z(\omega)=0$, claims that the atomic power generation should be abolished sooner or later.

REFERENCES

[1] E. F. Schumacher, Small is beautiful: A study of economics as if people matterd,
Blond and Briggs Ltd, London (1973).

Masataka KUWAMURA
Kobe University, Kobe, Japan
e-mail: kuwamura@main.h.kobe-u.ac.jp

Hirofumi IZUHARA
University of Miyazaki, Miyazaki, Japan
e-mail: izuhara@cc.miyazaki-u.ac.jp

Diffusion driven destabilization of a spatially homogeneous limit cycle in reaction-diffusion systems

In this talk, we study the diffusion driven destabilization of a spatially homogeneous limit cycle in 2-component reaction-diffusion systems defined on a finite size interval under the periodic boundary condition.

It is shown that a spatially homogeneous limit cycle becomes unstable and changes to a stable spatially nonhomogeneous limit cycle for appropriate diffusion coefficients.

This is analogous to the diffusion driven destabilization (Turing instability) of a spatially homogeneous equilibrium.

Our approach is based on a reaction-diffusion system with mass conservation and its perturbed system which is considered as an infinite dimensional fast-slow system.

It should be emphasized that the spatially nonhomogeneous limit cycle cannot be captured in the framework of the perturbation theory as seen in the previous works by Maginu [1] and Kuramoto [2].

Our approach would provide an useful and alternative viewpoint for studying the diffusion driven destabilization (Turing instability) of a spatially homogeneous limit cycle.

This is a first step for extending the scope of application of Turing's theory from stationary states to nonstationary states including limit cycles.

REFERENCES

[1] K. Maginu, Stability of spatially homogeneous periodic solutions of reaction-diffusion equations, J. Diff. Eqns. 31 (1979) 130-138.
[2] Y. Kuramoto, Chemical Oscillations, Waves, and Turbulence, Springer-Verlag, Berlin Heidelberg, 1984.
[3] M. Kuwamura, Y. Morita, Perturbations and dynamics of reaction-diffusion systems with mass conservation, Phys. Rev. E 92 (2015), 012908.
[4] S.-I. Ei, H. Izuhara, M. Mimura, Infinite dimensional relaxation oscillation in aggregation-growth systems, DCDS series B, 17 (2012) 1859-1887.
[5] H. Izuhara, M. Kuwamura, submitted.

Special Symposium

Sep 8, 15:45 – 17:15, Room E

Pattern formation in heterogeneous environments

Organizer(s): **Izumi Takagi**
Institute of Liberal Arts and Sciences, Tohoku University, 980-8576 Kawauchi 41, Aoba-ku, Sendai
e-mail: `takagi@m.tohoku.ac.jp`

Fang Li
Center for PDE, East China Normal University, No 500 Dongchuan Road, Center for PDE, Administration Building 12th floor, Minhang Campus, East China Normal University, Shanghai, 200241, China
e-mail: `fli@cpde.ecnu.edu.cn`

Turing used the principle of diffusion-driven instability (DDI, for short) to explain how a spatially homogeneous state can develop spontaneously a spatially nontrivial structure, i.e., pattern. However, actual biological phenomena take place in more or less non-uniform environments. In some cases organisms themselves create non-uniformity of the environment. Therefore, it is very important to understand quantitatively the effect of spatial heterogeneity on resulting patterns.

The purpose of this symposium is to explore the frontiers of mathematical researches on models of pattern formation that utilize partial differential equations, laying emphasis on how spatial heterogeneity influences patterns. Moreover, this mini-symposium is co-organized by Japanese and Chinese mathematicians in the hope of promoting collaboration not only between biologists and mathematicians, but also collaboration among young scientists in Eastern Asia.

Time	**Title & Presenter**
15:45 – 15:50	**Opening** **Izumi Takagi** (*Institute of Liberal Arts and Sciences, Tohoku University*)
15:50 – 16:10	**Pattern formation in homogeneous media vs in heterogeneous media: cutting and grafting experiments on hydra** **Izumi Takagi** (*Institute of Liberal Arts and Sciences, Tohoku University*)
16:10 – 16:30	**Spiky steady states for a chemotaxis system with singular sensitivity** **Huicong Li** (*Center for PDE, East China Normal University*)
16:30 – 16:50	**Self-organization of bacterial communities against environmental pH variation** **Sohei Tasaki** (*Frontier Research Institute for Interdisciplinary Sciences, Tohoku University*)
16:50 – 17:10	**Non-local effects in an integro-PDE model from population genetics** **Fang Li** (*Center for PDE, East China Normal University*)
17:10 – 17:15	**Closing** **Fang Li** (*Center for PDE, East China Normal University*)

Izumi Takagi
Institute of Liberal Arts and Sciences
Tohoku University
41 Kawauchi, Aoba-ku, Sendai 980-8576, JAPAN
e-mail: `takagi@morphos.jp`

Pattern formation in homogeneous media vs in heterogeneous media: cutting and grafting experiments on *hydra*

In their seminal paper [1] Gierer and Meinhardt derived their model equations by assuming that the interaction takes place in a spatially uniform environment. Once they obtained the equations, they proceeded to taking spatial heterogeneity into account. They wrote: “A shallow gradient of source distribution can lead to a striking pattern of activator concentration, with a maximum at the terminal of high source density, … . Thus the source density distribution determines the polarity of the pattern.” (p.34 of [1]). They applied their theory to transplantation experiments on hydra. Their computer simulations made use of the activator-inhibitor system with a fairly *steep* gradient of source density distribution, which suggests that to form a second head, strong heterogeneity in source distribution is needed.

Based on decades of mathematical studies on reaction-diffusion systems, we know that in spatially uniform environments, steady-state patterns are determined by the geometry of domain, while in spatially non-uniform environments, they are determined as a result of competition between the domain geometry and the spatial heterogeneity of the system. Hence, much more attention is required in modeling a phenomenon which involves the control of patterns by way of spatial heterogeneity. In this talk we present a modification of the activator-inhibitor system by Gierer and Meinhardt to explain hydra grafting experiments. Also, we compare our modification with receptor-based models by [5] and by Marciniak-Czochra [3, 4].

REFERENCES

[1] Gierer, A. and Meinhardt, H., 1972. A theory of biological pattern formation, *Kybernetik (Berlin)* **26**: 30–39.
[2] Maini, P.K., Takagi, I. and Yamamoto, H. (in preparation)
[3] Marciniak-Czochra, A. 2003. Receptor-based model with diffusion-driven instability for pattern formation in hydra. *J. Biol. Syst.* **11**, 293—324.
[4] Marciniak-Czochra, A. 2006. Receptor-based models with hysteresis for pattern formation in hydra. *Mathematical Biosciences* **199**, 97—119.
[5] Sherratt, J.A., Maini, P.K., Jäger, W. and Müller, W, 1995. A receptor-based model for pattern formation in hydra. *Forma* **10**, 77—95.

Huicong Li
Center for PDE, East China Normal University, Shanghai, China
e-mail: `hli7@tulane.edu`

Spiky steady states of a chemotaxis system with singular sensitivity

This project is concerned with the steady state problem of a chemotaxis model with singular sensitivity function in a one dimensional spatial domain. Using the chemotactic coefficient χ as the bifurcation parameter, we perform local and global bifurcation analysis for the system. It is shown that positive monotone steady states exist as long as χ is larger than the first bifurcation value. Then we use Helly's compactness theorem and Sturm's oscillation theorem to obtain basic and refined asymptotic profiles of these steady states, as χ becomes large. In particular, our results show that the cell density function forms a spike, which models the important physical phenomenon of cell aggregation.

Sohei Tasaki
Frontier Research Institute for Interdisciplinary Sciences (FRIS), Tohoku University, Sendai, Japan
Graduate School of Science, Tohoku University, Sendai, Japan
e-mail: `tasaki@tohoku.ac.jp`

Madoka Nakayama
Sendai National College of Technology, Natori, Japan

Wataru Shoji
Frontier Research Institute for Interdisciplinary Sciences (FRIS), Tohoku University, Sendai, Japan
Institute of Development, Aging and Cancer (IDAC), Tohoku University, Sendai, Japan

Self-organization of bacterial communities against environmental pH variation

As with many living organisms, bacteria often live on the surface of solids, such as foods, organisms, buildings and soil. Compared with dispersive behavior in liquid, bacteria on surface environment exhibit significantly restricted mobility. They have access to only limited resources and cannot be liberated from the changing environment. Accordingly, appropriate collective strategies are necessarily required for long-term growth and survival. However, in spite of our deepening knowledge of the structure and characteristics of individual cells, strategic self-organizing dynamics of their community is poorly understood and therefore not yet predictable. Here, we report self-organizing processes of *Bacillus subtilis* communities highly depending upon environmental pH, and present mathematical models for the spatio-temporal dynamics.

B. subtilis, one of the most well-studied bacteria, exhibits diverse colony patterns on the surface of nutrient agar media, which selectively develop in response to environmental conditions [1-3]. Among others, nutrition (e.g. peptone concentration) and surface moisture (inversely correlated with agar concentration) are known as principal environmental factors for the pattern selection. In the early 1990's, a phase diagram was described for *B. subtilis* strain OG-01, in which five distinct patterns were conditioned by nutrition and agar parameters [3]. However, little has been known if other environmental factors affect colony morphology. *B. subtilis* is also widely known to form thick biofilms in which cells are held together by a self-produced extracellular matrix. The wild-type strain OG-01 also creates thick biofilms on hard agar media, while swarming of motile cells results in rapid expansion of thin (almost one cell layer thick) colonies on soft media. We first focus on the thick biofilms of the same strain on hard plates (containing 1% agar), and report novel pH sensitive colony morphology. Self-generated directional motility depending upon pH underlies the morphological alteration, and our simulation model, based on the pH-dependent dose-response diagram, successfully explained the self-organizing dynamics of environment-sensitive biofilm morphology. Further, recent findings indicate that high pH sensitivity arises in a broad range of self-organizing processes such as cell migration, collective swarming and more detailed cell type heterogeneity, causing macroscopically morphologically diverse colonies in which sophisticatedly regulated collective behaviors maintain and rearrange the population structure for growth and survival in changing environment.

REFERENCES

[1] Ohgiwari, M., Matsushita, M. and Matsuyama, T., 1992. Morphological changes in growth phenomena of bacterial colony patterns. *J. Phys. Soc. Jpn.*, **61**: 816–822.
[2] Ben-Jacob, E., Schochet, O., Tenenbaum, A., Cohen, I., Czirók, A. and Vicsek T., 1994. Generic modeling of cooperative growth patterns in bacterial colonies. *Nature*, **368**: 46-49.
[3] Wakita, J., Komatsu, K., Nakahara, A., Matsuyama, T. and Matsushita, M., 1994. Experimental investigation on the validity of population dynamics approach to bacterial colony formation. *J. Phys. Soc. Jpn.*, **63**: 1205-1211.

Fang Li
Center for PDE, East China Normal University, Shanghai, China
e-mail: `fangli0214@gmail.com`

Non-local effects in an integro-PDE model from population genetics

In this talk, we discuss qualitative properties of a genetic model with partial panmixia. This model was proposed by T. Nagylaki in 2012 to describe the evolution of two alleles under the joint action of selection, migration and partial panmixia for the complete dominance case.

First, properties for general non-local problems are studied. Then, existence of non-trivial steady states, in terms of the diffusion coefficient d and the partial panmixia rate b, is obtained under different signs of the integration of g(x), which denotes the heterogeneous environment. Furthermore, stability and instability properties for non-trivial steady states, as well as the trivial steady states u = 0 and u = 1 are investigated. Our results illustrate how the non-local term – namely, the partial panmixia- helps the migration in this model.

Mini-Symposium

Sep 9, 9:00 – 10:30, Room B

Hans Meinhardt; The Loss of the Meister of Developmental Pattern Formation and Unachieved Discussions

Organizer(s): **Akiko Nakamasu**
Kyushu University, Japan
e-mail: `nakamasu@anat1.med.kyushu-u.ac.jp`

Co-presented by 3D morphologic, Scientific Research on Innovative Areas, JSPS

Hans Meinhardt was a giant and pioneer of mathematical biology in the field of developmental biology. He set up various mathematical models based on reaction-diffusion systems and was the first person who made systematic use of computer simulations in explanations of developmental phenomena. He had brought about positive impacts on this field; however we lost him last February. So, in this symposium scientists who have been working on subjects closely related to him get together and continue unachieved discussions with him. We will hope to deepen our understanding of current topics in the study of pattern formation and reaction-diffusion systems.

Time	**Title & Presenter**
09:00 – 09:05	**Opening** **Akiko Nakamasu** (*Kyushu University*)
09:05 – 09:25	**Mathematical beauty of the activator-inhibitor system** **Izumi Takagi** (*Tohoku University*)
09:25 – 09:45	**Simpler modelling of the biological pattern formation** **Shigeru Kondo** (*Osaka University*)
09:45 – 10:05	**Notion of diffusion-induced instability** **Masayasu Mimura** (*Meiji University*)
10:05 – 10:25	**Pattern formation in chemotaxis cells and body axis formation** **Tatsuo Shibata** (*QBiC RIKEN*)
10:25 – 10:30	**Closing** **Akiko Nakamasu** (*Kyushu University*)

Izumi Takagi
Institute of Liberal Arts and Sciences
Tohoku University
41 Kawauchi, Aoba-ku, Sendai 980-8576, JAPAN
e-mail: `takagi@morphos.jp`

Mathematical beauty of the activator-inhibitor system

In order to illustrate his idea that "Diffusion-Driven Instability" triggers spontaneous formation of patterns in a chemical system, Turing made use of a digital computer [7]. To do numerical simulation, he needed a system of equations and devised a hypothetical chemical reaction. Indeed, to find a real chemical reaction system which exhibits patterning was the most important step in his research project after the seminal paper [7], which was never done due to his death.

Twenty years later, Gierer and Meinhardt [1] found that interaction between a *slowly diffusing activator* and a *rapidly diffusing inhibitor* produces a pattern. They derived a two-species model system under the assumptions

(i) the interactions are described as a ratio of the power of the concentration of one species to that of the other,
(ii) the system has a uniform steady state which is stable under spatially uniform disturbances, and
(iii) one species is auto-catalytic.

They showed that these *local* requirements are sufficient to determine the nonlinearity. Here, "local" refers to a neighborhood of the uniform steady-state.

It is to be emphasized that they derived the activator-inhibitor system by purely mathematical arguments. (As a matter of fact, they found a family of reaction-diffusion systems, which has three subclasses [4].) This may account for the beautiful mathematical structures their model systems have.

There has been a sizable amount of literature on mathematical analysis of the activator-inhibitor model (e.g., boundedness of nonstationary solutions [6], a monograph on stationary solutions [8]). In this talk we review some results of mathematical analysis of the activator-inhibitor systems including

(a) classification of kinetic behavior ([4]);
(b) ultimate simplification of the system: right vs. wrong directions ([5, 2]).

As Turing did, Gierer and Meinhardt wrote down a few groups of partial differential equations which can generate patterns in order to do computer simulations ([1, 3]). What they wanted to say was the general statement "short-range activator and long-range inhibitor make patterns". Therefore, it is a mathematical challenge to justify their claim by identifying a class of nonlinearities which includes the activator-inhibitor system Gierer and Meinhardt proposed.

REFERENCES

[1] Gierer, A. and Meinhardt, H., 1972. A theory of biological pattern formation, *Kybernetik (Berlin)*, **26**: 30–39.
[2] Karch, G., Suzuki, K. and Zienkiewicz, J., 2016. Finite-time blowup of solutions to some activator-inhibitor systems. *Discrete and Continuous Dynamical Systems* **36**, 4997--5010.
[3] Meinhardt, H., 1982. Models of Biological Pattern Formation. Academic Press, London/New York.
[4] Ni, W.-M., Suzuki, K. and Takagi, I., 2006. The dynamics of a kinetic of activator-inhibitor system. *J. Differential Equaitons* **229**, 426--465.
[5] Ni, W.-M., Takagi, I. and Yanagida, E., 2001. Stability of least energy patterns of the shadow system for an activator-inhibitor model. *Japan J. Indust. Appl. Math.* **18**, 259--272.
[6] Suzuki, K. and Takagi, I., 2010. On the role of basic production terms in an activator-inhibitor system modeling biological pattern formation. *Funkcial. Ekvac.* **54**, 237--274.
[7] Turing, A.M., 1952. The chemical basis of biological pattern formation. *Phylos. Trans. Roy. Soc. London Ser. B* ***237,*** 37--72.
[8] Wei, J. and Winter, M., 2014. Mathematical Aspects of Pattern Formation in Biological Systems. Springer

Shigeru Kondo
Osaka University,Osaka,Japan
e-mail: `shigerukondo@gmail.com`

Simpler modelling of the biological pattern formation

In 1952, Turing presented the reaction-diffusion model that explains how the spatial patterns in organisms form autonomously. About 20 years later, Gierer and Meinhardt published their first paper about the pattern formation. Although the concept of their models was very similar, the models of Meinhardt assumed realistic cellular interactions that attracted many of experimental biologists. I (Kondo) am one of them. Another significant contribution of them are summarized the necessary conditions for the stable pattern formation in a short phrase, “local activation and long range inhibition (LALI)”. This is important because this “condition” does not need any specific cellular or molecular event. There are many variety of mathematical models those based on different cellular events. However, all of them share the same LALI condition. Owing to this simple formulation, we can recognize the variety of models as the brothers in the Turing model family. In short, Meinhardt made the reaction-diffusion model understandable for biologists, and established the basement for the wide acceptance of the model.

I think the task of the people following him is to proceed the way more. In my talk, I present an attempt to modify the reaction diffusion model.

Masayasu Mimura
Meiji Institute for Advanced Study of Mathematical Sciences
Meiji University
4-21-1 Nakano, Nakanoku, Tokyo 164-8525, Japan
e-mail: `mimura.masayasu@gmail.com`

Notion of diffusion-induced instability

From the understanding of pattern formation arising in biological, we know that there are two types of instability. One is diffusion-induced instability which is stated by Turing and independently by Gierer and Meinhardt. The instability is generated as the interaction of diffusion and suitable reaction. The other is cross-diffusion- induced instability which is observed in Shigesada-Kawasaki-Teramoto (SKT) model, for instance. It is generated as the interaction of diffusion and cross-diffusion. The mechanism of the two types of instabilities seems to be different. In this talk, we show that the singular limit analysis reveals the relation between these instabilities, that is, both of them possess the same mechanism to generate instability.

REFERENCES

[1] Turing, A. (1952). The basis of morphogenesis, Phil. Trans. R. Soc. Lond B **327**: 37-72–909.
[2] Gierer, A. and Meinhardt, H. (1972). A theory of biological pattern formation. Kybernetik **12**, 30-39.
[3] Shigesada, N., Kawasaki K. and Teramoto, E. (19979) Spatial segregation of interating species, J. Theor, Biol. **7**9, 83-99
[4] Iida, M., Mimura M. and Ninomiya M. Cross-diffusion and competitive interaction, J. Math. Biol. (2006), **53**, 617-641

Tatsuo Shibata
RIKEN Quantitative Biology Center & Center for Developmental Biology
e-mail: `tatsuo.shibata@riken.jp`

Pattern formation in chemotaxis cells and body axis formation

Meinhardt proposed numerous mathematical models on many processes from bacteria to development. I was in contact with him through models of single cell chemotaxis and body axis formation [1-2]. His last paper was on BMP-Chordin network published in June 2015 [2].. In my talk, I will introduce his contribution on both topics, together with the recent works in the fields.

REFERENCES

[1] Meinhardt, H., 1999. Orientation of chemotactic cells and growth cones: models and mechanisms. *Journal of Cell Science*, 112, pp.2867–2874.
[2] Meinhardt, H., 2015. Dorsoventral patterning by the Chordin-BMP pathway: a unified model from a pattern-formation perspective for Drosophila, vertebrates, sea urchins and Nematostella. *Developmental Biology*, 405(1), pp.137–148.

Special Symposium

Sep 9, 9:00 – 10:30, Room D

Unifying epidemiological and genomic approaches to infectious diseases

joint hosting symposium of the Japan Science and Technology Agency (JST) CREST big data application project "Detecting premonitory signs and real-time forecasting of pandemic using big biological data"

Organizer(s): **Yusuke Asai**
Hokkaido University
e-mail: `yusuke.asai@yahoo.de`

Hiroshi Nishiura
Hokkaido University, Kita 15 Jo Nishi 7 Chome, Kita-ku, Sapporo-shi, Hokkaido 060-8638, Japan
e-mail: `nishiurah@med.hokudai.ac.jp`

Our special symposium highlights the halfway achievements of abovementioned project that excels into prediction and premonitory sign detection of pandemic, unifying epidemiological, genetic and other diverse datasets, supported by Japan Science and Technology Agency. The symposium aims to share a mixture of different mathematical modeling approaches to infectious diseases and enhance cutting edge collaborations among researchers who share common interest in handling infectious disease data. Especially, the organizers are pleased to have invited Dr Cornelia Pokalyuk from Germany to share important insights of population genetic modeling to evolutionary dynamics of viruses.

Time	**Title & Presenter**
09:00 – 09:30	**The role of reinfection in a viral population subject to balancing selection** **Cornelia Pokalyuk** (*Universität Magdeburg*)
09:30 – 09:50	**Mathematical modeling of MERS using epidemiological and genomic data** **Hiroshi Nishiura** (*Hokkaido University*)
09:50 – 10:10	**Identifying the location of virus source by the effective distance approach** **Yusuke Asai** (*Hokkaido University*)
10:10 – 10:30	**Estimating the population dynamics of influenza viruses from genomic data** **Kiyeon Kim** (*Research Center for Zoonosis Control, Hokkaido University*)

Cornelia Pokalyuk
Institut für Mathematische Stochastik, Otto-von-Guericke-Universität Magdeburg
e-mail: `cornelia.pokalyuk@ovgu.de`

The role of reinfection in a viral population subject to balancing selection

The importance of balancing selection in evolution is still under discussion. However, there is general agreement that immunity genes, like the HLA locus of the humane genome, seem to be targeted by balancing selection. Hence, on the host site of a host-parasite system balancing selection seems to be significant.

In my talk I will focus on the parasite side of the system. Motivated by observations of DNA samples from the Human Cytomegalovirus I will introduce a model for the evolution of a viral gene locus being targeted by balancing selection in a host environment driven by primary infection and reinfection.

Hiroshi Nishiura
Graduate School of Medicine, Hokkaido University
e-mail: `nishiurah@med.hokudai.ac.jp`

Mathematical modeling of MERS using epidemiological and genomic data

OBJECTIVES:
To investigate the heterogeneous transmission patterns of Middle East respiratory syndrome (MERS) in the Republic of Korea, with a particular focus on epidemiological characteristics of superspreaders.
DESIGN:
Retrospective epidemiological analysis.
SETTING:
Multiple healthcare facilities of secondary and tertiary care centres in an urban setting.
PARTICIPANTS and OUTCOMES:
A total of 185 laboratory-confirmed cases with partially known dates of illness onset and most likely sources of infection. Superspreaders were identified using the transmission tree. The reproduction number, that is, the average number of secondary cases produced by a single primary case, was estimated as a function of time and according to different types of hosts.
RESULTS:
A total of five superspreaders were identified. The reproduction number throughout the course of the outbreak was estimated at 1.0 due to reconstruction of the transmission tree, while the variance of secondary cases generated by a primary case was 52.1. All of the superspreaders involved in this outbreak appeared to have generated a substantial number of contacts in multiple healthcare facilities (association: $p<0.01$), generating on average 4.0 (0.0-8.6) and 28.6 (0.0-63.9) secondary cases among patients who visited multiple healthcare facilities and others. The time-dependent reproduction numbers declined substantially below the value of 1 on and after 13 June 2015.
CONCLUSIONS:
Superspreaders who visited multiple facilities drove the epidemic by generating a disproportionate number of secondary cases. Our findings underscore the need to limit the contacts in healthcare settings. Contact tracing efforts could assist early laboratory testing and diagnosis of suspected cases.

REFERENCES

[1] Nishiura, Miyamatsu, Chowell, Saitoh, Eurosurveillance 2015:20:21181
[2] Nishiura, Endo, Saitoh, Kinoshita, Ueno, Nakaoka, Miayamatsu, Dong, Chowell, Mizumoto, BMJ Open 2016;6(2):e009936
[3] Chowell, Abdirizak, Lee, Lee, Jung, Nishiura, Viboud. BMC Medicine 2015;13:210
[4] Mizumoto, Saitoh, Chowell, Miyamatsu, Nishiura. International Journal of Infectious Diseases 2015;39:7-9
[5] Mizumoto, Endo, Chowell, Miayamtsu, Saitoh, Nishiura, BMC Medicine 2015;13:228
[6] Nishiura, Miyamatsu, Mizumoto, Emerging Infectious Diseases 2016;22(1):146-8

Yusuke Asai
Department of Hygiene, Graduate School of Medicine, Hokkaido University
e-mail: `yusuke.asai@yahoo.de`

Identifying the location of virus source by the effective distance approach

The large influenza pandemic occurred all over the world in 2009. More than 100,000 people were infected and 100 people died in Japan. In order to prevent next pandemic, the estimation of the import risk of the viruses plays an important role. Recently Nah et al. estimated the effective distance by the airline traffic network data and evaluated the import risk in each country.
In this talk, we apply the idea of the effective distance based on the domestic network data to the location and date of detection of the influenza viruses and identify the possible location of virus sources.

REFERENCES

[1] Shiino et al. Molecular evolutionary analysis of the influenza A(H1N1)pdm, May-September, 2009: Temporal and spatial spreading profile of the viruses in Japan, PLoS ONE, June 2010, Volume 5, Issue 6.
[2] Nah et al. Predicting the international spread of Middle East respiratory syndrome (MERS), BMC Infectious Diseases, 2016 16:356, DOI: 10.1186/s12879-016-1675-z

Kiyeon Kim
Research Center for Zoonosis Control, Hokkaido University
e-mail: `kiyeon@czc.hokudai.ac.jp`

Ryosuke Omori
Research Center for Zoonosis Control, Hokkaido University
e-mail: `omori@czc.hokudai.ac.jp`

Kimihito Ito
Research Center for Zoonosis Control, Hokkaido University
e-mail: `itok@czc.hokudai.ac.jp`

Estimating the population dynamics of influenza viruses from genomic data

The estimation of basic reproduction number is essential to understand the epidemic dynamics, and time-series data of infected individuals are usually used for the estimation of the basic reproduction number. However, such data is not always available, and methods to estimate epidemiological parameters using genealogy constructed from nucleotide sequences of pathogen have been proposed so far. Here, we propose a new method to estimate epidemiological parameters of outbreaks using time course of Tajima’s D statistic on the nucleotide sequences of their pathogens. We construct a parsimonious mathematical model describing the transmission process of pathogen among hosts and the evolutionary process simultaneously to compute the relation between time series of the number of infected individuals and Tajima’s D of pathogen sequences. Using this model, we estimated the basic reproduction number, recovery rate and mutation rate from Tajima’s D of field data of sequences of pandemic influenza A (H1N1) 2009 viruses. Our estimated basic reproduction number was consistent with the number estimated by birth–death skyline plot using the same sequence data, as well as with the number estimated from the time-series of the number of infected individuals, suggesting that Tajima’s D statistic on nucleotide sequences of pathogens could be useful to estimate epidemiological parameters of outbreaks.

Mini-Symposium

Sep 9, 9:00 – 10:30, Room E

Mathematical and statistical modeling to bridge the gap between empirical and theoretical research in ecology

Organizer(s): **Michio Kondoh**
Faculty of Science and Technology. Ryukoku University, 1-5 Yokotani, Seta Oe-cho, Otsu 520-2194, Japan
e-mail: `mkondoh@rins.ryukoku.ac.jp`

Ecological systems are highly dynamic and complex across a range of organization levels from individuals to ecosystems and usually consist of interactions between different organization levels. Empirical data to reveal the ecological complexity is accumulating, thanks to long-term ecological monitoring and recent technical revolutions (metagenomics, transcriptomics and stable isotope analysis, for example). However, mechanistic understanding of ecological system is still not straightforward, partly due to the difficulties in identifying the interactions, or causalities, between entities occurring at multiple spatio-temporal scales. This is especially true when a controlled experiment is not possible - which is often the case in ecological studies of higher organization levels. In this session, recent development in mathematical or statistical modeling to overcome the difficulty and its application to empirical data of a range of organization levels will be introduced and discussed.

Time	**Title & Presenter**
09:00 – 00:00	**Empirical dynamic modeling for understanding and forecasting dynamic systems** **Chih-hao Hsieh** (*National Taiwan University*)
00:00 – 00:00	**Environmental triggers of general flowering in a tropical lowland forest in Borneo** **Masayuki Ushio** (*Ryukoku University*)
00:00 – 00:00	**Imputation of RNA-seq data toward modeling transcriptome dynamics in a field** **Koji Iwayama** (*Ryukoku University*)
00:00 – 10:30	**Improved statistical recipe for evaluating microbial functional diversity from metabolic fingerprinting** **Takeshi Miki** (*National Taiwan University*)

Chih-hao Hsieh
Institute of Oceanography, Institute of Ecology and Evolutionary Biology, and Department of Life Science, National Taiwan University
chsieh@ntu.edu.tw

Empirical dynamic modeling for understanding and forecasting dynamic systems

Natural systems are often complex and dynamic (i.e. nonlinear), and are difficult to understand using linear statistical approaches. Linear approaches are fundamentally based on correlation and are ill posed for dynamic systems, because in dynamic systems, not only can correlation occur without causation, but causation can also occur in the absence of correlation. To study dynamic systems, nonlinear time series analytical methods have been developed in the past decades [1-5]. These nonlinear statistical methods are rooted in State Space Reconstruction (SSR), i.e. lagged coordinate embedding of time series data [6] (http://simplex.ucsd.edu/EDM_101_RMM.mov). These methods do not assume any set of equations governing the system but recover the dynamic from time series data, thus called Empirical Dynamic Modeling (EDM).

EMD bears a variety of utilities to investigating dynamic systems: 1) determining the complexity (dimensionality) of system [1], 2) distinguishing nonlinear dynamic systems from linear stochastic systems [1], 3) quantify the nonlinearity (i.e. state dependence) [7], 4) determining causal variables [3], 5) tracking strength and sign of interaction [8], 5) forecasting [5], 6) scenario exploration of external perturbation [4], and 7) classifying system dynamics [2, 9]. These methods and applications can be used for mechanistic understanding of dynamics systems and providing effective policy and management recommendations on ecosystem, climate, epidemiology, financial regulation, and much else.

REFERENCES

[1]Hsieh, C.H., S.M. Glaser, A.J. Lucas, and G. Sugihara (2005) Distinguishing random environmental fluctuations from ecological catastrophes for the North Pacific Ocean. Nature. 435: 336-340.

[2]Hsieh, C.H., C. Anderson, and G. Sugihara (2008) Extending nonlinear analysis to short ecological time series. American Naturalist. 171: 71-80.

[3]Sugihara, G., R. May, H. Ye, C. H. Hsieh, E. Deyle, M. Fogarty, and S. Munch (2012) Detecting causality in complex ecosystems. Science 338: 496-500.

[4]Deyle, E., M. F. Fogarty, C. H. Hsieh, L. Kaufman, A. MacCall, S. B. Munch, C. Perretti, H. Ye, and G. Sugihara (2013) Predicting climate effects on Pacific sardine. PNAS. 110: 6430-6435.

[5]Ye, H., R. J. Beamish, S. M. Glaser, S. C. H. Grant, C. H. Hsieh, L. J. Richards, J. T. Schnute, and G. Sugihara (2015) Equation-free mechanistic ecosystem forecasting using empirical dynamic modeling. PNAS. 112: E1569–E1576.

[6]Takens, F. 1981. Detecting strange attractors in turbulence. Pages 366-381 in D. A. Rand and L. S. Young, editors. Dynamic systems and turbulence. Springer-Verlag, New York.

[7]Anderson, C. N. K., C. H. Hsieh, S. A. Sandin, R. Hewitt, A. Hollowed, J. Beddington, R. M. May, and G. Sugihara. 2008. Why fishing magnifies fluctuations in fish abundance. Nature 452:835-839.

[8]Deyle, E. R., R. M. May, S. B. Munch, and G. Sugihara. 2016. Tracking and forecasting ecosystem interactions in real time. Proceedings of the Royal Society of London B: Biological Sciences 283.

[9]Liu, H., M. J. Fogarty, S. M. Glaser, I. Altman, C. Hsieh, L. Kaufman, A. A. Rosenberg, and G. Sugihara. 2012. Nonlinear dynamic features and co-predictability of the Georges Bank fish community. Marine Ecology Progress Series 464:195-207.

Masayuki Ushio
Joint Research Center for Science and Technology / Faculty of Science and Technology, Ryukoku University, Japan
e-mail: `ushio-masayuki@ad.ryukoku.ac.jp`

Environmental triggers of general flowering in a tropical lowland forest in Borneo

General flowering, one of the most fascinating phenomena in tropical biology, is a community-wide masting phenomenon unique to aseasonal dipterocarp forests in SE Asia. As general flowering has substantial influences on crop yield and reproductive status of forests, ecologists have studied proximate causes of the general flowering for decades. Long-term phonology census suggested changes in rainfall and/or air temperature associated with El Niño Southern Oscillation are correlated with the general flowering [e.g., 1]. However, as correlations usually do not imply causations, proximate causes of the mass flowering are still poorly understood. In this study, I applied recently developed statistical techniques, convergent cross mapping (CCM) [2] and multivariate S-map [3], in order to detect causal drivers of the general flowering in Borneo tropical forests.

In a tropical lowland forest in Lambir National Park in Sarawak, Borneo, reproductive activities of plant individuals were monitored since 1993. Approximately 440 plant individuals of 230 species have been monitored twice a month (40 species are Dipterocarpaceae). Plant phenology (i.e., the number of flowering tree individuals) and meteorological data (Southern Oscillation Index [SOI], daily mean temperature and rainfall and cumulative temperature and rainfall) were used for the time series analysis. To identify drivers of the general flowering, I applied CCM to the time series. In addition, multivariate S-map method was applied to quantify the influences of causal variables.

CCM showed that cumulative air temperature and rainfall had causal influences on the number of flowering trees in the forest, while SOI did not have causal influences. Multivariate S-map method suggested that both of cumulative air temperature and rainfall negatively influenced the number of flowering trees. The result indicated that low air temperature and drought triggered the general flowering in accordance with the previous studies. Changes in air temperature and rainfall associated with recent climate changes would result in changes in the magnitude and frequency of the general flowering in Borneo.

REFERENCES

[1] Sakai *et al*., 2006. Irregular drought trigger mass flowering in aseasonal tropical forests in Asia. *American Journal of Botany*, **93**: 1134–1139.
[2] Sugihara *et al*., 2012. Detecting causality in complex ecosystems. *Science*, **338**: 496–500.
[3] Deyle, E. R., May, R. M., Munch, S. B., Sugihara, G. 2016. Tracking and forecasting ecosystem interactions in real time. *Proceedings of the Royal Society B*, **283**:20152258

Koji Iwayama
Research Institute for Food and Agriculture, Ryukoku University, Japan
e-mail: `iwayama-kouji@ad.ryukoku.ac.jp`

Atsushi J. Nagano
Faculty of Agriculture, Ryukoku University, Japan
Center for Ecological Research, Kyoto University, Japan
JST PRESTO, Japan

Imputation of RNA-seq data toward modeling transcriptome dynamics in a field

The field environments is real and natural growth condition for crops and wild plants. In a field, environmental factors are continuously changing in complex manner and exhibit diurnal oscillations and seasonal changes. To reveal the effects of such environmental changes on organisms, transcriptome data in field environments have been collected and described by the statistical model [1]. However, the cost to obtain large-scale transcriptome data, required for construction, parameter fitting, and validation of a model, has restricted the modeling transcriptome dynamics.

Recently, RNA-Seq has become a widely-used technology to quantify transcriptomes [2]. The cost of RNA-Seq depends on sequencing depth. Whereas shallow-sequencing allows us to obtain transcriptome data from more samples, the information per sample would decrease. Here, we propose to use the topic model, which is the statistical model widely used for natural language processing, for precise estimation of whole gene expression from data obtained by shallow-sequencing. The topic model represents documents as a mixture of "topics." Hierarchical Dirichlet process (HDP) [3] is the nonparametric generalization of latent Dirichlet allocation [4], the most popular topic model, and automatically select the appropriate number of topics. We apply HDP to transcriptome data, considering a gene as a "word" and a sample as a "document". In our application to transcriptome data, the lack of information of each gene expression due to shallow-sequencing is complemented by co-expression information described by topics. In this talk, we demonstrate that the topic model can precisely estimate "true" expressions of genes from data obtained by shallow-sequencing.

Using the topic model, we can obtain information from transcriptome data quantified by shallow-sequencing comparable to deep-sequencing. Therefore, shallow-sequencing and the topic model enables quantification of transcriptome of more samples than deep-sequencing with the same cost. Large-scale transcriptome data obtained by this strategy will facilitate the modeling study of transcriptomic variation in field conditions.

REFERENCES

[1] Nagano, A. J., Sato, Y., Mihara, M., Antonio, B. a., Motoyama, R., Itoh, H., Nagamura, Y., and Izawa, T., 2012. Deciphering and prediction of transcriptome dynamics under fluctuating field conditions. *Cell,* **151**: 1358-1369.
[2] Wang, H., Gerstein, M., and Snyder, M., 2009. RNA-Seq : a revolutionary tool for transcriptomics. *Nature Reviews Genetics*, **52**: 5277-5286.
[3] Teh, Y. W., Jordan, M. I., Beal, M. J., and Blei, D. M., 2006. Hierarchical Dirichlet processes. *Journal of the American Statistical Association*, **101**: 1566–1581.
[4] Blei, D. M., Ng, A. Y., and Jordan, M. I., 2003. Latent Dirichlet allocation, *Journal of Machine Learning Research,* **3**: 993-1022.

Takeshi Miki
Institute of Oceanography, National Taiwan University
Research Center for Environmental Changes,　Academia Sinica
tksmiki@ntu.edu.tw

Improved statistical recipe for evaluating microbial functional diversity from metabolic fingerprinting

Fingerprinting methods are key tools to describe ecological structures and functions, such as phylogenetic community profiling (e.g. phylogenetic fingerprinting for microbes and plankton), community-level microbial functional profiling using EcoPlate or through quantifying multiple enzyme activities, and chemical fingerprinting of plant secondary metabolites such as defense chemicals and volatiles. For some indices, standard statistical methods have been developed but the statistical analysis on metabolic fingerprinting using EcoPlate has not been standardized despite the more and more studies use this technique for evaluating functional diversity and multifunctionality for microbial communities [1]. An EcoPlate is a 96-well microplate that composed with triplicates of 31 response wells with different sole carbon sources (with three blank wells). The utilization of each carbon source is coupled with the conversion from a chemical dye, which allows the quantification of carbon utilization by the color development in each well. The color developmental pattern is treated as multivariate (e.g. functional composition) and can also be converted to univariate (e.g. threshold-based multifunctionality).

The color development patterns from Ecoplate are highly variable because of variabilities in initial community size (inoculum size), those in initial species composition, and shifts in species composition during incubation. We need to develop an appropriate statistical method to overcome this issue to obtain reliable ecological signatures from the color development patterns. In addition, we need to consider the dissimilarity between carbon substrates in terms of chemical structure for better evaluating the functional diversity and functional dissimilarity between samples. In this study, we focused on two questions. 1. What is the best method for quantifying the color development pattern from 96 well microplates, depending on the data availability? 2. How is the chemical dissimilarity information between carbon substrates incorporated and whether does it improve the quantification of microbial functions? We hypothesized that using the information along the time evolution of color improves the quantification. For the second question, we calculated the dissimilarity between carbon substrates from their chemical structure by using chemoinformatic tools and weighted the ecoplate patterns through using exiting tools in community ecology analyses. We also hypothesized that consideration of chemical dissimilarity improves the quantification. In order to compare the performance of different calculation methods, we used two datasets: microcosm experiments and field observation. The basic idea for the evaluation was to compare the power of explanation (e.g. R2 values) under the identical statistical model, $Y \sim X1+X2+\dots$, where Xk is an explanatory variable such as temperature and treatment and Y is the univariate or multivariate index that is calculated from ecoplate patterns such as multifunctionality and functional composition. With different calculation methods, we had different Y values, which allowed the comparison of explanation power.

REFERENCES

[1 Takeshi Miki, Taichi Yokokawa, Kazuaki Matsui* (2014) Biodiversity and multifunctionality in a microbial community: a novel theoretical approach to quantify functional redundancy. *Proceedings of The Royal Society B* vol.281 no.1776 20132498

Mini-Symposium

Sep 9, 10:45 – 12:15, Room B

The role of cost-benefit analysis in ecology and beyond

Organizer(s): **Marko Jusup**
Center of Mathematics for Social Creativity, Hokkaido University, N12W7 Kita-ku Sapporo, 060-0812, Japan
e-mail: `mjusup@gmail.com`

To inform the audience of recent advances in our understanding of the cost-benefit analysis in biology, we discuss how mathematical modeling can help decision-making in various practical situations. The symposium is designed to be a fine example of how, using mathematics in the context of cost-benefit studies, we can extract unique and novel information that helps advance the knowledge in a number of subfields in biology (e.g. ecology, epidemiology, virology, etc.).

Time	**Title & Presenter**
10:45 – 11:01	**Foreword by Marko Jusup**
11:02 – 11:26	**Cost-benefit analysis to guide management of tourist activities in nature protected areas** **Tin Klanjscek** (*Ruđer Bošković Institute, Zagreb, Croatia*)
11:27 – 11:51	**The tragedy of the mitigation policy on climate change** **Hiroyuki Matsuda** (*Yokohama National University*)
11:52 – 12:15	**Statistical physics of vaccination** **Zhen Wang** (*Interdisciplinary Graduate School of Engineering Sciences, Kyushu University*)

Tin Klanjscek
Ruđer Bošković Institute, Zagreb, Croatia
e-mail: `tin@irb.hr`

Sunčana Geček
Ruđer Bošković Institute, Zagreb, Croatia

Jasminka Klanjšček
Ruđer Bošković Institute, Zagreb, Croatia

Tarzan Legović
Ruđer Bošković Institute, Zagreb, Croatia

Cost-benefit analysis to guide management of tourist activities in nature protected areas

Nature protected areas (PAs) are one of the most effective tools in protection of natural and, often, cultural heritage. The promise of increased well-being through recreation, education, and connection with nature in PAs attracts tourists who, in turn, benefit the local and regional economy. Since even limited tourist activities (e.g. sightseeing) have negative environmental impacts through pressures ranging from erosion to habitat fractionation to killing of plants and animals, the recent sharp increases of PA tourism seriously threatens the protection. Additionally, excessive crowding caused by large visitor numbers can cause stress to tourists and – ultimately – negate any positive effects of the visit. Therefore, managing visitor numbers to limit crowding can benefit both the environment, and the tourists.

Standard approaches to visitor management in PAs focus on preventing excessive environmental damage and unacceptable decrease in visitor satisfaction. Typically, the environment is considered well-protected if values of a number of indicators are better than a (somewhat arbitrary) critical value, and visitor satisfaction is considered to be in an acceptable range if a percentage (e.g. 80%) of visitors rate the experience with top marks (e.g. 4 and 5 on a 5-point Likert scale). Since both environmental damage and decrease in visitor satisfaction are monotonically increasing functions of visitor number, optimization is not possible. Therefore, the number of tourists that may visit any PA can increase up to the carrying capacity, i.e. the number of visitors for which the critical value of at least one indicator is reached. Managing visitor numbers to maximum carrying capacity can, therefore, be interpreted as managing for maximum acceptable environmental damage and minimum acceptable visitor experience. Clearly, neither goal should be considered optimal, and the underlying real-world maximization variable – monetary gain from tourism – is not even considered explicitly, but only implicitly through the idea that more is better. Approaches that do try to optimize monetary gain typically start by valuating the environment (e.g. approaches based on ecosystem services) – a step that is wrought with problems such as true monetary value of life.

We develop a new approach in which positive effects of tourism on the environment are taken as an additional constraint that makes optimization possible, and demonstrate the approach on the example of National Park Krka. We start by considering the management goals and analyzing both positive and negative aspects of tourist activities. Next, we estimate the carrying capacity taking into the account infrastructural limitations, and negative effects of crowding on the environment, infrastructure, and visitor experience. Finally, with environmental protection as the optimization target, we perform a cost-benefit analysis using socio-economic and environmental variables whilst avoiding the need to attach monetary value to the environment.

The new approach results in recommendations at odds with the traditional analysis. For example, while traditional analysis recommends distributing tourists throughout the PA to positively affect indicators and increase tourist satisfaction, the new approach recommends aggregating the visitors in as small of an area as possible without unacceptable impact on their satisfaction.

Hiroyuki Matsuda
Yokohama National University
e-mail: `matsuda-hioryuki-vj@ynu.ac.jp`

Rejaul Islam
Shota Nishijima
Fisheries Research Agency

The tragedy of the mitigation policy on climate change

Recently adaptation policy on climate change is becoming important because climate change is inevitable. To investigate the best mix of mitigation and adaptation policy, we need to evaluate the impact cost (I) due to climate change, mitigation cost (M) to prevent climate change, and adaptation cost (A) to climate change. We consider the mitigation-adaptation policy of each nation, as a non-cooperative game, although many studies consider the best solution for the world. Policy for climate change of nation s is characterized by mitigation and adaptation costs of nation s, denoted by M_i and A_i, respectively. The magnitude of climate change (t) depends on the sum of M_s of all nations, i.e., $t=t(\sum M_s)$. The magnitude of impact of nation s due to climate change depends on t and A_s. Therefore, the magnitude of impact is a function of the global mitigation cost and the national adaptation cost, i.e., $I_s = I_s[\sum M_s, A_s]$.

We simply assume that the net benefit of nation s (V_s) is $V_s = B - I_s[\sum M_s, A_s] - M_s - A_s$. We also assume that the total investment $C_s = M_s + A_s$ is constant.

If the world is unified (only nation 1 exists), the optimal solution that maximizes V_1 is obtained by $\partial I_1[M_1, A_1]/\partial M_1 - \partial I_1 [M_1, A_1]/\partial A_1 = 0$.
According to [1], $I_s[\sum M_s, A_s]=\mu(\sum M_s,)g(A_s)$, the optimal solution satisfies that $\mu'(\sum M_s,)/\mu(\sum M_s,) = g'[A_s]/g[A_s]$.
If $\mu(M) = \eta_1+ (\eta_2- \eta_1)e^{-bM}$ and $g(A)=g_0/A$, $M_1^* = \mathrm{Max}[0,\{C_1\mathrm{s} - 1 - P[\text{-}\mathrm{Exp}[C_1s\text{-}1]\, \eta_1/(\eta_2\text{-}\ \eta_1)]\}/s]$, where $P[x]$ is the product log function that satisfies $x =P(x)e^{P(x)}$. We can also numerically obtain C_1^* that maximizes $I_1[M_1^*, C_1 - A_1^*]$. This is a best mitigation-adaptation policy of the world for climate change.

In this paper we consider a multiple nation game:
$V_s = B - I_s[\sum M_s, A_s] - M_s - A_s$. We obtain the non-cooperative (Nash) solution:
$\partial I_s[\sum M_s, A_s]/\partial M_s=0$ and $\partial I_s[\sum M_s, A_s]/\partial A_s=0$ for all nations. We also assume that $I_s[\sum M_s, A_s]=\mu(\sum M_s)g(A_s)$. The Nash solution must satisfy:
$\mu'(\sum M_s)=1/g(A_s)$ and $\mu(\sum M_s)=1/g'(A_s)$ for all s. Note that $\mu(\sum M_s)$ and $\mu'(\sum M_s)$ are common for all nations. Therefore the adaptation cost A_s is common for all nations, while the mitigation cost M_s depends on the total cost C_s of each nation. This is a similar conclusion by the law of equalization in net incomes [2].

We sincere thank Prof. Managi for valuable information about the preceding studies that did not include our idea of non-cooperative game of mitigation-adaptation policy on climate change.

REFERENCES

[1] Bréchet, T., Hritonenko, N., Yatsenko, Y. 2013. Adaptation and mitigation in longterm climate policy. Environmental and Resource Economics, 55:217–243
[2] Matsuda, H., Harada, Y. 1990. Evolutionarily stable stalk to spore ratio in cellular slime molds and the law of equalization in net incomes. Journal of Theoretical Biology 147:329-344.

Zhen Wang
Interdisciplinary Graduate School of Engineering Sciences, Kyushu University
e-mail: `nkzhenwang@163.com`

Statistical physics of vaccination

Historically, infectious diseases caused considerable damage to human societies, and they continue to do so today. To help reduce their impact, mathematical models of disease transmission have been studied to help understand disease dynamics and inform prevention strategies. Vaccination–one the most important preventive measures of modern times–is of great interest both theoretically and empirically [1-3]. And in contrast to traditional approaches, recent research increasingly explores the pivotal implications of individual behavior and heterogeneous contact patterns in populations. I review the developmental arc of theoretical epidemiology with emphasis on vaccination, as it led from classical models assuming homogeneously mixing (mean-field) populations and ignoring human behavior, to recent models that account for behavioral feedback and/or population spatial/social structure. Many of the methods used originated in statistical physics, such as lattice and network models, and their associated analytical frameworks. Similarly, the feedback loop between vaccinating behavior and disease propagation forms a coupled nonlinear system with analogs in physics. I also review the new paradigm of digital epidemiology, wherein sources of digital data such as online social media are mined for high-resolution information on epidemiologically relevant individual behavior. Armed with the tools and concepts of statistical physics, and further assisted by new sources of digital data, models that capture nonlinear interactions between behavior and disease dynamics offer a novel way of modeling real-world phenomena, and can help improve health outcomes.

REFERENCES

[1] D. Henderson, P. Klepac, Lessons from the eradication of smallpox: an interview with da henderson, Philosophical Transactions of the Royal Society of London B: Biological Sciences 368 (1623) (2013) 20130113.
[2] D. M. Morens, G. K. Folkers, A. S. Fauci, The challenge of emerging and re-emerging infectious diseases, Nature 430 (6996) (2004) 242–249.
[3] P. Bonanni, Demographic impact of vaccination: a review, Vaccine 17 (1999) S120–S125.

Mini-Symposium

Sep 9, 10:45 – 12:15, Room D

Recent development of Lyapunov functional approaches in mathematical biology

Organizer(s): **Yoichi Enatsu**
Department of Mathematical Information Science, Faculty of Science, Tokyo University of Science 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan
e-mail: `yenatsu@rs.tus.ac.jp`

Toshikazu Kuniya
Graduate School of System Informatics, Kobe University 1-1 Rokkodai-cho, Nada-ku, Kobe 657-8501, Japan
e-mail: `tkuniya@port.kobe-u.ac.jp`

Recently, Lyapunov functional approaches for proving the global asymptotic stability of equilibria have been widely studied and developed by many researchers in the field of mathematical biology. The purposes of this minisymposium are to share and extend the knowledge on the theory of Lyapunov functions and their applications to mathematical models with various structures.

Time	**Title & Presenter**
10:45 – 11:00	**Lyapunov functionals for delayed epidemic models** **Connell McCluskey** (*Wilfrid Laurier University*)
11:00 – 11:15	**Dynamics of viral infection models incorporating cell-to-cell transmission** **Jinliang Wang** (*School of Mathematical Science, Heilongjiang University*)
11:15 – 11:30	**Mathematical theory of the global stability of age-structured models for pathogen-immune interactions** **Tsuyoshi Kajiwara** (*Okayama University*)
11:30 – 11:45	**Asymptotic behaviour of solutions for a virus-immune dynamics model with diffusion** **Toru Sasaki** (*Okayama University*)
11:45 – 12:00	**Lyapunov functionals for multi-group models with delay** **Yoji Otani** (*Okayama University*)
12:00 – 12:15	**Lyapunov functions and some predator-prey differential equations** **Yasuhisa Saito** (*Shimane University*)

Connell McCluskey
Wilfrid Laurier University (Canada)
e-mail: `ccmcc8@gmail.com`

Lyapunov functionals for delayed epidemic models

Recent work on modifying a Lyapunov function for an ODE to be a Lyapunov functional for a delay differential equation will be presented. The work generalizes the results of many specific examples in the field of mathematical epidemiology. We identify conditions under which delays are harmless: the delay does not disrupt the Lyapunov calculation, and therefore does not affect the global asymptotic stability.

Jinliang Wang
School of Mathematical Science, Heilongjiang University, P.R. China
e-mail: `jinliangwang@hlju.edu.cn`

Dynamics of viral infection models incorporating cell-to-cell transmission

In this talk, I will concern with viral infection model incorporating cell-to-cell transmission. For three types models with cell-to cell mechanism, ODEs with distributed delays and direct cell-to-cell transmission, infection-age model with cell-to-cell transmission, and reaction-diffusion model with cell-to-cell transmission, we study the global dynamic properties. Some mathematical arguments, such as the effect of cell-to-cell transmission on viral dynamics, relative compactness and persistence of the solution semi-flow, existence of a global attractor, and the principle eigenvalue problem will be addressed. This is a joint work with Dr. Toshikazu Kuniya (Kobe Univ.), Prof. Xianning Liu (Southwest Univ.) and Prof. Xingfu Zou (Western Univ. CANADA).

REFERENCES

[1] Jinliang Wang*, Min Guo, Xianning Liu and Zhitao Zhao, Threshold dynamics of HIV-1 virus model with cell-to-cell transmission, cell-mediated immune responses and distributed delay, Applied Mathematics and Computation, 291 (2016),149-161.
[2] Jinliang Wang, Jiying Lang and Xingfu Zou*, Analysis of a structured HIV infection model with both virus-to-cell infection and cell-to-cell transmission, Nonlinear Anal. RWA, Revision
[3] Jinliang Wang, Jie Yang, Toshikazu Kuniya*, Dynamics of a PDE viral infection model incorporating cell-to-cell tranmission, Journal of Mathematical Analysis and Applications, Accept

Tsuyoshi Kajiwara
Okayama University
e-mail: kajiwara`@okayama-u.ac.jp`

Mathematical theory of the global stability of age-structured models for pathogen-immune interactions

This talk is based on the joint work with Toru Sasaki and Yoji Otani.

Pathogen-immune interactions in vivo have been studied by ordinary differential equations and differential equations with time delay.

Recently, age-structured differential equations are used for the study of various infectious diseases in vivo. Lyapunov functional method developed by Korobeinikov in ordinary differential equations and McCluskey in differential equations with time delay for the global stability is now used in age-structured differential equations.

Browne and Pilygin [4], Browne [5] and Demasse and Ducrot [3] studied age-structured models of infectious diseases in vivo. Especially, Browne [5] and Demasse and Ducrot [4] treated multi- strain models. They proved the competitive exclusion principle for age-structured models. Their model do not contain immune variables explicitly.

In this talk, we consider multi-strain age-structured models of pathogen-immune interactions. Ordinary differential equation models of multi-strain pathogen-immune interactions are treated by Iwasa et al. [1] and Inoue et al. [2] Models with infinite delay for multi-strain pathogen-immune interactions are treated by Otani et al. [6]. By the existence of strain specific immunity, the coexistence of multiple strains are possible. We show the similar results for the age-structured models. Especially, we present mathematical detail of the global stability.

REFERENCES

[1] Iwasa Y., Michor F. and Nowak M., 2004. Some basic properties of immune selection, *J. Theor. Biol.* **229:**3093–3114.

[2] Inoue T., Kajiwara T., and Sasaki T., 2010, Global stability of models of humoral immunity against multiple viral strains, *J. Biol. Dyn.*, **4**: 282–295

[3] Demasse R.D., and Ducrot A., An age-structured within-host model for multistrain, *SIAM J. Appl. Math.*, **73**: 572–593.

[4] Browne C.J. and Pilygin S.S., 2013. Global analysis of age-structured within-host virus models, *Disc. Cont. Dyn. Sys. Ser.* **18**: 1999–2017.

[5] Browne C.J., A multi-strain virus model with infected cell age structure: Application to HIV, *Nonl. Anal. RWA*, **22**: 353–372.

[6] Otani Y., Kajiwara T., and Sasaki T, 2016. Lyapunov functionals for multistrain virus-immune models with infinite delay, submitted.

Toru Sasaki
Okayama University
e-mail: `sasaki@ems.okayama-u.ac.jp`

Takashi Suzuki
Osaka University

Asymptotic behaviour of solutions for a virus-immune dynamics model with diffusion

In this talk, we consider a virus-immune dynamics system with diffusion

$$\begin{aligned}\frac{\partial u_1}{\partial t} &= d_1\Delta u_1 + \lambda - mv_1 - \beta u_1 u_3,\\ \frac{\partial u_2}{\partial t} &= d_2\Delta u_2 + \beta u_1 u_3 - au_2,\\ \frac{\partial u_3}{\partial t} &= d_3\Delta u_3 + aru_2 - bu_3 - pu_3 u_4,\\ \frac{\partial u_4}{\partial t} &= d_4\Delta u_4 + qu_3 - du_4\end{aligned} \tag{1}$$

with $u_i = u_i(x,t),\ t \geqq 0, x \in \Omega$, where Ω is a bounded set in $\mathbf{R}^3$, with smooth boundary. Here u_1, u_2, and u_3 denote the populations of uninfected cells, of infected cells, of infectious agents, respectively. The variable u4 represents the amplitude of the humoral immunity.

On the boundary of the domain, we impose the Neumann condition:

$$\frac{\partial u_i}{\partial t} = 0 \text{ on } \partial\Omega \quad (i = 1,2,3,4)$$

For the ODE model that corresponds to the model (1), a Liapunov function is obtained by Inoue, Kajiwara, and Sasaki [1]. With a Liapunov function that is derived from that in [1], we can apply the methods described in [2] and [3] to our model, and obtain some basic results on the asymptotic behaviour.

REFERENCES

[1] Inoue, T., Kajiwara, T., and Sasaki T., 2010, Global stability of models of humoral immunity against multiple viral strains. J. Biol. Dyn., 4: 282–295

[2] Latos, E., Suzuki, T., and Yamada, Y., 2012, Transient and asymptotic dynamics of a prey-predator system with diffusion. Math. Meth. Appl. Sci. 35: 1101–1109,

[3] Sasaki, T. and Suzuki, T., Asymptotic behaviour of solutions for virus dynamics models with diffusion, in preparation.

Yoji Otani
Graduate School of Environmental and Life Science, Okayama University
e-mail: `gev421104@s.okayama-u.ac.jp`

Tsuyoshi Kajiwara
Graduate School of Environmental and Life Science, Okayama University

Toru Sasaki
Graduate School of Environmental and Life Science, Okayama University

Lyapunov functionals for multi-group models with delay

For the multi-group models with infinitely distributed delay, the global stability of the equilibria can be shown by using well-known Lyapunov functionals. We refine the proof of the nonpositivity of those Lyapunov functionals.

When $R_0>1$ we show the well-definedness of the Lyapunov functionals for good solutions. It completes the mathematical proof of the global stability.

The irreducibility of the next generation matrix and the properties of the Laplace transform play important roles.

REFERENCES

[1] Y. Otani, T. Kajiwara, T. Sasaki, 2015. Lyapunov functionals for virus-immune models with infinite delay. *Dsicrete Contin. Dyn. Syst. Ser. B*, **9**: 3093–314.
[2] M. Y. Li, Z. Shuai, C. Wang, 2010. Global stability of multi-grup epidemic models with distributed delays. *J. Math. Anal. Appl.*, 36**1**: 38–47.
[3] C. J. Browne, 2015. A Multi-Strain Virus Model with Infected Cell Age Structure Application to HIV. *Nonlinear Analysis: Real World Applications* **22**: 354–372.

Yasuhisa Saito
Department of Mathematics, Shimane University
e-mail: `ysaito@riko.shimane-u.ac.jp`

Lyapunov functions and some predator-prey differential equations

Lyapnov methods can be used to determine local stability and asymptotic stability of equilibria, but also global behavior of solutions such as global stability and permanence for ecological models described by ordinary differential equations. However, the problem of how to find an appropriate Lyapunov function is even more challenging in global behavior than in local behavior for their solutions. This talk mainly presents a Lyapunov method to show that the classical Lotka-Volterra predator-prey model (which has the neutrally stable equilibrium surrounded by a family of periodic orbits whose amplitudes depend on the initial population sizes) can be permanent by species migration.

Mini-Symposium

Sep 9, 10:45 – 12:15, Room E

Geometry and Patterning in Tissue, Cell, and Nucleus

Organizer(s): **Yoshihiro MORISHITA**
Laboratory for Developmental Morphogeometry, RIKEN, Quantitative Biology Center, Japan
e-mail: `morishita@cdb.riken.jp`

Sungrim SEIRIN LEE
MLS, Hiroshima University
e-mail: `seirin@hiroshima-u.ac.jp`

Mathematical studies have contributed to biology from different aspects. For example, one direct contribution is to find tendencies or rules by analyzing data, which can be bases for revealing mechanisms underlying focal phenomena. In addition to this, proving concepts by developing minimal models that can reproduce observations, and providing testable hypotheses or predictions for issues unsolved or difficult to experimentally approach. The purpose of this symposium is to show those different approaches to cellular and developmental biological phenomena with different theories such as differential geometry, cellular mechanics, and dynamical system.

Time	**Title & Presenter**
10:45 – 11:15	**An equation of chemical field to be satisfied for achieving optimal encoding of positional information during organ development** **Yoshihiro MORISHITA** (*RIKEN*)
11:15 – 11:45	**Controlling contractile instabilities in the actomyosin cortex** **Masatoshi NISHIKAWA** (*Hosei University*)
11:45 – 12:00	**A challenging interdisciplinary approach to elucidate a mystery of remodeling process in nuclear architecture (Part I: Theory)** **Sungrim SEIRIN LEE** (*Hiroshima University*)
12:00 – 12:15	**A challenging interdisciplinary approach to elucidate a mystery of remodeling process in nuclear architecture (Part II: Experiment)** **Hiroshi OCHIAI** (*PRESTO, JST*)

Yoshihiro Morishita
Laboratory for Developmental Morphogeometry, RIKEN, Quantitative Biology Center, Japan
e-mail: `yoshihiro.morishita@riken.jp`

An equation of chemical field to be satisfied for achieving optimal encoding of positional information during organ development

Robust positioning of cells in a tissue against unavoidable noise is important for achieving normal and reproducible morphogenesis. The position in a tissue is represented by morphogen concentrations, and cells read them to recognize their spatial coordinates. From the engineering viewpoint, these positioning processes can be regarded as a problem of information coding. Organisms are conjectured to adopt good coding designs with high reliability, and to answer the questions of how good coding is adopted, and subsequently when, where, and to what extent each morphogen contributes to positioning, we need a way to evaluate the goodness of coding. In this study, we tried to find a general rule that the chemical field or concentration distribution should satisfy for achieving an optimal coding. In physics, using tensorial or differential-geometrical description, coordinate-free general forms of fundamental equations governing diverse physical phenomena have been derived. After this, we here differential-geometrically formulated the process of morphogen-dependent positioning and then derived a general equation for optimal encoding. We also discuss the interpretation of the equation and the possibility of extending our theory.

REFERENCES

[1] Hironaka, K. and Morishita, Y. (Review) Encoding and decoding of positional information in morphogen-dependent patterning, Current Opinion in Genetics & Development, 22: 553?56, (2012)
[2] Morishita, Y. and Iwasa, Y. Coding design of positional information for robust morphogenesis, Biophysical Journal, 101: 2324-2335, (2011)
[3] Morishita, Y. and Iwasa, Y. Accuracy of positional information provided by multiple chemical gradients with correlated noises, Phys. Rev. E, 79: 061905, (2009)
[4] Morishita, Y. and Iwasa, Y. Optimal placement of multiple morphogen sources, Physical Review E, 77: 041909, (2008)

Masatoshi Nishikawa[1, 2, 3, 4]
1. BIOTEC Technical University Dresden, 2. Max Planck Institute for the Physics of Complex Systems, 3 Max Planck Institute of Molecular Cell Biology and Genetics, 4. Hosei University
e-mail: `masatoshi.nishikawa.93@hosei.ac.jp`

Sundar R. Naganathan[1, 2, 3,]

Frank Jülicher[2]

Stephan W. Grill[1, 2, 3]

Controlling contractile instabilities in the actomyosin cortex

Cells and tissues represent active materials that generate stresses for driving morphogenesis. A fundamental challenge is to understand how spatiotemporal patterns arise in such active biological materials, driven by the interplay of active mechanical processes and regulation by signaling pathways. We study the mechanism of spatiotemporal pattern formation in the highly contractile actomyosin cortical layer, where transient accumulations of myosin motor proteins tend to form pulsatile networks to drive morphogenetic events. Using a novel image-based quantification technique (COmoving Mass Balance Imaging, COMBI) we determine the kinetic diagram of myosin activation by RhoA in the cell cortex of the polarizing one-cell stage *Caenorhabditis elegans* embryo. We find that the complete system of myosin activation by RhoA, active stress generation by myosin, and RhoA advection by actomyosin gel flow is unstable. Interestingly, a RhoA pacemaking oscillator controls the spatiotemporal myosin patterns that emerge beyond the instability. This endows the zygote with the ability to use a highly contractile and unstable system to drive polarizing flows. Taken together, these results highlight how introducing regulatory processes to active materials gives rise to novel pattern forming states.

S. Seirin Lee (Part I:Theory)
Department of Mathematical and Life Sciences, Hiroshima University
e-mail: `seirin@hiroshima-u.ac.jp`

Hiroshi Ichiai (Part II: Experiment)
PRESTO, JST
e-mail: `ochiai@hiroshima-u.ac.jp`

A challenging interdisciplinary approach to elucidate a mystery of remodeling process in nuclear architecture: Theory and Experiment

Nuclear architecture, which plays an important role in organizing the function of the nucleus, is composed of heterochromatin and euchromatin. Conventional nuclear architecture is found when the distribution of heterochromatin is enriched in the periphery of the nucleus. Conventional architecture is the primary structure in the majority of eukaryotic cells, and the rod cells of diurnal mammals contain this structure. In contrast, inverted nuclear architecture occurs when the heterochromatin is distributed in the center of the nucleus; this occurs in the rod cells of nocturnal mammals. Surprisingly, the inverted architecture found in the rod cells of the adult mouse is formed through reorganization of the conventional architecture during terminal differentiation. Although an experimental approach has shown the relationship between these two types of nuclear architecture at the molecular level, the mechanisms mediating the long-range reorganization processes remain unknown. Here, we suggest a new mathematical approach to understanding the dynamics of nuclear architecture, by which we found that the deformation of nucleus can play a critical role in the process of chromatin remodeling. With the interdisciplinary work, we succeeded in developing an *in vitro* experiment and found that the dynamical deformation of nucleus promotes the clustering of chromocenters. With the basis of theoretical observation, we prove that the deformation of nucleus is sufficient condition to induce the remodeling of chromatin architecture. This interdisciplinary work has been started from the theoretical hypothesis and we suggest a new framework of interdisciplinary research in life sciences.

Mini-Symposium

Sep 9, 14:00 – 15:30, Room B

The role of cost-benefit analysis in medicine

Organizer(s): Shingo Iwami
Department of Biology, Kyushu University, 744 Motooka Nishi-ku Fukuoka, 819-0395, Japan
e-mail: `siwami@kyushu-u.org`

To inform the audience of recent advances in our understanding of the cost-benefit analysis in biology, we discuss how mathematical modeling can help decision-making in various practical situations. The symposium is designed to be a fine example of how, using mathematics in the context of cost-benefit studies, we can extract unique and novel information that helps advance the knowledge in a number of subfields in biology (e.g. ecology, epidemiology, virology, etc.).

Time	**Title & Presenter**
14:00 – 14:25	**Health technology assessment and mathematical biology: A possibility for better economic evaluation** **Naoko Tomita** (*National Institute of Public Health, Japan*)
14:25 – 14:50	**Mathematica modeling vaccination against infectious diseases including dengue and influenza** **Eunha Shim** (*Soongsil University, Korea*)
14:50 – 15:15	**Characterization of cost-effectiveness of multidrug treatment - Case study on HCV treatment** **Shingo Iwami** (*Kyushu University, JST PRESTO & CREST, Japan*)
15:15 – 15:30	**Debate discussion** **Marko Jusup** (*Hokkaido University, Japan*) & **Shingo Iwami** (*Kyushu University, JST PRESTO & CREST, Japan*)

Naoko Tomita
National Institute of Public Health, Saitama, Japan
e-mail: `Naoko.Tomita@niph.go.jp`

Health Technology Assessment and Mathematical Biology: A Possibility for Better Economic Evaluation

Health Technology Assessment (HTA) is defined as a "systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies".[1] It consists of assessment by economic evaluation and appraisal to take into account economic, ethical, social and medical issues. Subjects of HTA include not only pharmaceuticals but also devices, procedures, vaccines and prevention.

In recent years, HTA has been adopted and has informed decision making in health care in several countries. From April 2016, a pilot introduction of HTA has started in Japan and five hepatitis C drugs and two cancer drugs are scheduled to be assessed.

This presentation will introduce the audience to HTA methodology and issues in HTA and consider the applicability of mathematical biology to HTA for better decision making in health care.

REFERENCES

[1]International Network of Agencies for Health Technology Assessment. http://www.inahta.org. Accessed 27 July 2016.

Eunha Shim
Department of Mathematics, Soongsil University, Seoul, South Korea
e-mail: `alicia@ssu.ac.kr`

Mathematica modeling vaccination against infectious diseases including dengue and influenza

Mathematical modeling of infectious diseases and the evolution of pathogens can contribute to the prediction of health policy effectiveness and best practices. Integrating mathematics, epidemiology, economics, and evolutionary biology, this interdisciplinary research generates predictions that could not be made by these disciplines alone, and has important impacts on these fields as well as for policy makers world-wide. For instance, dengue is one of the most problematic vector-borne diseases worldwide, and in December 2015 the first dengue vaccine was approved for use. In light of the recent approval of the dengue vaccine, we present its epidemiological and economic impact based on mathematical model of dengue vaccination. As such, health policies must be developed to maximize the benefit to the public and to balance health, social, and economic considerations. Achieving this aim requires combining molecular, individual, population, and national scales with evolutionary perspectives to understand the importance of trade-offs between disease control and the risk of pathogen replacement.

REFERENCES

[1] Shim, E., Brown, S.T., DePasse, J., Nowalk, M.P., Raviotta, J.M., Smith, K.J., Zimmerman, R.K. Cost effectiveness of influenza vaccine for U.S. children: live attenuated and inactivated influenza. Vaccine. In press
[2] Shim, E. Dengue dynamics and vaccine cost-effectiveness analysis in the Philippines. In submission.
[3] Shim, E. Cost-effectiveness of dengue vaccination in Mexico using a dynamic dengue transmission model. In submission

Shingo Iwami 1, 2
Department of Biology, Faculty of Sciences, Kyushu University, Fukuoka 812-8581, Japan. 1
PRESTO, JST, Saitama 332-0012, Japan. 8CREST, JST, Saitama 332-0012, Japan. 2
e-mail: `siwami@kyushu-u.org`

Characterization of cost-effectiveness of combination anti-HCV drugs

With the introduction of direct-acting antivirals (DAAs), treatment against hepatitis C virus (HCV) has been rapidly improving. To eradicate this worldwide infectious disease, the “best” multidrug treatment is demanded based on scientific evidence. However, there is no method available that systematically quantifies and compares the antiviral efficacy and drug-resistant profiles of drug combinations. Based on experimental anti-HCV profiles in an HCV cell culture system, we quantified the instantaneous inhibitory potential (IIP), which is the logarithm of the reduction in viral replication events [1], for both single and multiple drug combination treatments. From the calculated IIP of 15 anti- HCV drugs, we found that interferon-alpha (IFN-α) and a nucleoside polymerase inhibitor, sofosbuvir (SOF), had the largest potential to inhibit viral replication events. Profiling of 52 double-combination treatments indicated that the combinations based on a protease inhibitor, simeprevir (SMV), achieved high IIP. Our modeling also predicted the treatment amount of SOF in a SOF plus SMV combination could be reduced to 41% in comparison to the amount of SOF needed when combined with ledipasvir.

REFERENCES

[1] B. L. Jilek, M. Zarr, M. E. Sampah, S. A. Rabi, C. K. Bullen, J. Lai, L. Shen, R. F. Siliciano, A quantitative basis for antiretroviral therapy for HIV-1 infection. *Nat Med* 18, 446-451 (2012).

Mini-Symposium

Sep 9, 14:00 – 15:30, Room D

Real-time modeling approaches to vaccination and emerging infectious diseases

joint hosting symposium of The Toyota Physical and Chemical Research Institute, Specially Promoted Project

Organizer(s): **Kenji Mizumoto**
Hokkaido University
e-mail: `mizumotokenji@gmail.com`

Hiroshi Nishiura
Hokkaido University, Kita 15 Jo Nishi 7 Chome, Kita-ku, Sapporo-shi, Hokkaido 060-8638, Japan
e-mail: `nishiurah@med.hokudai.ac.jp`

It is increasingly recognized that real-time mathematical modeling plays a key role in clarifying the transmission dynamics of infectious diseases and estimating the effectiveness of interventions including immunization practice. This session aims to elaborate the formality of mathematical modeling of emerging infectious diseases and propagate the trend of real time modeling studies in the field of mathematical biology. A series of case studies on emerging infectious diseases including Middle East respiratory syndrome (MERS) and Zika virus infection are presented, along with modeling of vaccine preventable disease, especially vaccination against rubella is designed using a variety of mathematical models.

Time	**Title & Presenter**
14:00 – 14:18	**Estimating Seasonal Influenza-Associated Deaths in Japan** **Kenji Mizumoto** (*Hokkaido University*)
14:18 – 14:36	**Estimating risks of importation and local transmission of Zika virus infection** **Kyeongah Nah** (*Hokkaido University*)
14:36 – 14:54	**Optimizing vaccination program against rubella in Japan** **Ryo Kinoshita** (*Hokkaido University*)
14:54 – 15:12	**A Meta-Analysis of Risk and Risk Factors related mortality of Middle East Respiratory syndrome** **Ryota Matsuyama** (*Hokkaido University*)
15:12 – 15:30	**Spatiotemporal forecasting of rubella and its vaccination** **Masaya Saitoh** (*Institute of Statistical Mathematics*)

Kenji Mizumoto
Graduate School of Medicine, Hokkaido University
e-mail: mizumotokenji@gmail.com

Hiroshi Nishiura
Graduate School of Medicine, Hokkaido University

Estimating Seasonal Influenza-Associated Deaths in Japan

Influenza is highly contagious respiratory disease caused by influenza viruses. It can cause mild to severe illness, and sometimes it leads to death. In Japan, the number of deaths caused by seasonal influenza is estimated to reach to thousands in previous studies, and it is important to measure the disease burden of seasonal influenza, which is an indirect indicator of the lethality of an infection.

The purpose of present study is to examine the disease burden caused by influenza, mainly attributable to seasonal influenza, employing various robust models.

Statistical analysis:
Excess number of deaths were calculated by subtracting the expected from the observed data for each month included in the epidemic periods. CUMSUM method is used to calculate the annual excess number of deaths. Bayesian approach is used for parameter estimation
We set season is from September to August, and population size is modified accordingly.
Following methods are used:

1) Serfling least squares cyclical regression model:
2) Serfling-Poisson regression
3) Autoregressive integrated moving average (ARIMA) model
4) Rate-difference:

Dataset:
Two secondary datasets of census data and national surveillance reports, are analysed to quantify the disease burden.
Population size and monthly(weekly) deaths with codes from the international Classification of Diseases (ICD) for 2004-2014 were obtained from the Vital Statistics of Japan.
Monthly(weekly) number of influenza virus isolation/detection by virus type and subtype are obtained from the published report from National Institute of Infectious Diseases in Japan.

Result:
Here we report a preliminary estimate of the disease burden (e.g. mortality) we obtained using above modeling techniques.

REFERENCES

[1]Thompson WW et al. Estimates of US influenza-associated deaths made using four different methods. *Influenza Other Respi Viruses.* 2009 Jan;3(1):37-49..
[2] Park M, Wu P, Goldstein E, Kim WJ, Cowling BJ. Influenza-Associated Excess Mortality in South Korea. *Am J Prev Med.* 2016 Apr;50(4):e111-9.

Kyeongah Nah
Graduate School of Medicine, Hokkaido University, Sapporo, Japan
e-mail: `kynah@med.hokudai.ac.jp`

Yohei Yasuda
Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Kenji Mizumoto, Yuichiro Miyamatsu, Ryo Kinoshita, Hiroshi Nishiura
Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Estimating risks of importation and local transmission of Zika virus infection

An international spread of Zika virus (ZIKV) infection has attracted global attention. Potentially high importation risk of ZIKV in many temperate countries motivates us to explore the risks of importation and local transmission fueled by mildly infected travelers. Considering that the public health concerns over ZIKV infection stems from microcephaly, it is important to estimate the risk of local transmission that could involve pregnant women. In this study, we develop a statistical model that predicts the risk of local transmission of ZIKV in each country.

We collect arrival time of ZIKV importation (i.e., the time at which the first imported case was diagnosed) in each imported country from publicly available data sources. In addition to the importation data, we collected the list of countries with local transmission of ZIKV. Employing a survival analysis model in which the hazard is an inverse function of the effective distance as informed by the airline transportation network data, and using dengue and chikungunya virus transmission data, risks of importation and local transmission were estimated.

As a result, the predicted risk of local transmission was frequently seen in tropical and subtropical countries with dengue virus or Chikungunya virus epidemic experience, while the risk of importation was more scattered around the world. The diagnostic performance of risk model for local transmission was well supported by AUC value of 0.90. Whereas the risk of importation was well explained by the airline transportation network data, the risk of local transmission appeared to be best captured by additionally accounting for the presence of dengue and chikungunya viruses.

Ryo Kinoshita
Hokkaido University
e-mail: `kinoshitaryo@gmail.com`

Hiroshi Nishiura
Hokkaido University

Optimizing vaccination program against rubella in Japan

Vaccination program against rubella in Japan has become questioned after experiencing an epidemic in 2012-2014, involving more than 12,000 cases of rubella and yielding 45 congenital rubella syndrome (CRS) cases. While rubella is a vaccine-preventable disease, Japan has yet to be successful to implement an effective vaccination program to supplement against cohorts remaining susceptible to fully control the disease.

When rubella vaccination was first introduced in 1976, only women at childbearing age were targeted to prevent CRS. From 1995, both men and women were targeted to construct and maintain the herd immunity. After the shift in vaccination policy, the proportion seronegative has steadily declined, and susceptible birth events have been reduced. However, clusters of male adults born prior to the change in vaccination policy remained susceptible and has induced the recent epidemic. Moreover, the age at infection was elevated to 32.0 (17.0–42.0) years among men and 27.0 (7.0–37.0) years among women, which has allowed to increase the risk of infection of women at childbearing age allowing to increase CRS.

To intervene to prevent future epidemic of rubella in Japan, a convincing vaccination strategy must be considered. A mathematical model was constructed to optimize the vaccination considering the age dependent transmission dynamics. R_0 was calculated against the early exponential phase of the epidemic in 2012-14 to be 1.34. By accounting different scenarios of vaccination against different age groups, an optimal target of vaccination was defined to be against age group of 20s.

Ryota Matsuyama
Graduate School of Medicine, Hokkaido University
e-mail: `rmatsu0618@gmail.com`

Hiroshi Nishiura
Graduate School of Medicine, Hokkaido University

A Meta-Analysis of Risk and Risk Factors related mortality of Middle East Respiratory Syndrome

The Middle East respiratory syndrome corona virus (MERS-CoV) infection can cause a severe respiratory disease, with often fatal cases, and the risk and risk factors related mortality of the infection have been reported in many studies. However, those risk and risk factors sometimes differ among each studies or study types. A comprehensive understanding of risk and risk factors of MERS-CoV infection are needed.

The aim of the present study is to systematically understand results in each report including risk and risk factors of MERS-CoV by a meta-analysis.

Statistical analysis
To evaluate the risk of MERS-CoV infection, case fatality ratios (CFRs) in 25 studies were extracted or calculated. Combined value of 25 CFRs were calculated by weighted means of each CFR derived from variance of samples in each study. These analysis were also conducted among stratified study types that classified by study designs. In addition to CFRs, we also analyzed the risk factors of severity (sex and comorbidities) using odds ratio of each indexes.

In these analyses, heterogeneities among studies were also assessed by the Cochran's Q and $I2$ statistics.

Dataset:
Dataset from 25 eligible studies selected from 571 articles were used in the analyses. These studies include data from outbreaks of MERS-CoV in Saudi Arabia and Korea.

Results and Discussions

CFRs were ranged from 14.5% to 100% and the combined values among total studies was 39.1 %. CFR was high in ICU patients. Male and presence of comorbidities (diabetes mellitus, respiratory disease, hypertension, heart disease, renal disease) increased the odds of mortality. However, ICU patients possibly tend to become fatal without comorbidities. Risk factors of ICU admission should be clarified in future studies.

REFERENCES

[1]. Alsahafi AJ and Chen AC. The epidemiology of Middle East respiratory syndrome coronavirus in the Kingdom of Saudi Arabia, 2012–2015. *Int J Infect Dis*. 2016. 45:1-4.

[2]. Assiri A *et al*. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *Lancet Infect Dis*. 2013.13: 752–761.

Masaya M. Saito
The Institute of Statistical Mechanics
e-mail: `saitohm@ism.ac.jp`

Ryo Kinoshita
Graduate School of Medicine, Hokkaido University

Hiroshi Nishiura
Graduate School of Medicine, Hokkaido University

Progress report on modelling of rubella epidemic in Japan

In Japan, the proportion of rubella susceptible person's is currently near the threshold above which a major epidemic may occur. During 2012/13 the number of rubella cases in Japan was relatively large in recent years. The maximum number of weekly reported cases was 168 in Tokyo Prefecture and 268 in Osaka Prefecture while 1-2 or no cases are reported per week in usual years in each prefecture. This epidemic is almost limited to the metropolitan area while below ten cases per week were reported in 30 prefectures. Such a geographical contrast in reported cases reflects that the susceptibility is very close to the threshold of major outbreak. It is necessary to take into account a spillover of the disease via the person's movement and stochastic nature of transmission in order to reproduce such an infection trend. In the present study, it is shown that the 2012/13 epidemic is reproduced better by a stochastic meta-population model than a standard SIR model, under an appropriate model parameter.

REFERENCES

[1]. Colizza V, Barrat A, Barthe'lemy M, Vespignani A (2006) The modeling of global epidemics: Stochastic dynamics and predictability. Bulletin of Mathematical Biology 68: 473‐481.

[2]. Kinoshita R, Nishiura H (2016) Assessing herd immunity against rubella in japan: a retrospective seroepidemiological analysis of age-dependent transmission dynamics. BMJ Open 6: 1‐7.

Special Symposium

Sep 9, 14:00 – 15:30, Room E

Wanders will never cease: the current and future studies of the evolutionary ecology of dispersal

Organizer(s): **Ryosuke Iritani**
Kyushu University, Japan
e-mail: `lambtani@gmail.com`

Yuuya Tachiki
Kyoto University, Japan
e-mail: `tachiki@bio-math10.biology.kyushu-u.ac.jp`

Dispersal and migration influence arrays of ecological setups of organisms, from allelic distribution to community compositions. Dispersal is, at the same time, subject to diverse selective pressures, and thus an evolving trait by natural selection (e.g., kin competition, sib-mating avoidance, resource heterogeneity). Therefore, studies on evolutionary ecology of dispersal and migration have been of pivotal importance in population ecology. In the present symposium, we review our current understandings of dispersal and migration from evolutionary and ecological points. Specifically, we illustrate different theoretical approaches to model the evolution of dispersal and migration. Each speaker briefly reviews their recent projects, and highlight the future directions and steps to enhance the elaboration of studies of dispersal.

Time	**Title & Presenter**
14:00 – 14:05	**Introduction**
14:05 – 14:25	**Who escapes from whom: disease transmission among kin can drive the evolution of conditional dispersal in viscous host populations** **Ryosuke, Iritani** (*Kyushu University, Japan*)
14:25 – 14:45	**Evolution of dispersal in spatially and temporally heterogeneous environments** **Florence, Débarre** (*College de France, France*)
14:45 – 15:05	**The evolution of marine larval dispersal kernels in spatially structured habitats** **Allison, K. Shaw** (*University of Minnesota, US*)
15:05 – 15:25	**Evolutionary and ecological consequences of individual decisions, whether they stay or go, under environmental fluctuations** **Yuuya Tachiki** (*Kyoto University, Japan*)
15:25 – 15:30	**Discussion**

Ryosuke, Iritani
Department of Biology, Faculty of Sciences, Kyushu University
e-mail: `Lambtani@gmail.com`

Who escapes from whom: disease transmission among kin can drive the evolution of conditional dispersal in viscous host populations

In viscous populations, horizontal transmission of parasites can occur among closely related individuals, and sickness-dependent dispersal (individuals disperse conditionally according to their own disease status) might relax this menace. That is, infected individuals can lower the risk of transmission to siblings if they disperse, while uninfected individuals can escape from such a risk by dispersing. Empirical studies have indeed found evidence for both patterns of sickness-dependent dispersal. However, the costs and benefits of sickness-dependent dispersal have been poorly investigated so far. Here, I develop mathematical models to study the effect of transmission among kin on the evolution of sickness-dependent dispersal. The model reveals that at evolutionary endpoints, infected individuals are more dispersive, or uninfected individuals are more dispersive, and these two endpoints are bistable, i.e., evolution can lead to either outcome depending on the initial conditions. In particular, if horizontal transmission makes the genetic structuring for uninfected individuals more pronounced, then selection favours higher dispersal for uninfected individuals and lower dispersal for infected individuals. I discuss the mechanism accounting for such a concomitant effect of transmission avoidance in terms of altruism-spite interpretation of social evolution theory.

Florence, Débarre
Centre Interdisciplinaire de Recherche en Biologie (CIRB), Collège de France (Paris, FRA)
e-mail: `florence.debarre@normalesup.org`

Evolution of dispersal in spatially and temporally heterogeneous environments

Variations in environmental conditions, among locations and in time, have been suggested to affect the evolution of traits such as dispersal, habitat selection or local adaptation. Depending on whether environmental variations is averaged over a population in a single generation or in every single genotype over several generations, these variations select for generalist or specialist strategies, and may induce stabilizing or disruptive selection on studied traits. Here, we investigate the effect of the order of events in the life cycle on the evolution of dispersal in a spatially heterogeneous, temporally varying landscape. Our results show that the occurrence of intermediate singular strategies and disruptive selection are conditioned by the autocorrelation in patch state and the life cycle. With unconditional dispersal, “soft selection” and “hard selection” life cycles give different evolutionary outcomes. With informed dispersal, even the two “hard selection” life cycles disagree on evolutionary predictions. Our results highlight the importance of accounting for life cycle specificities when predicting the effects of the environment on evolutionarily selected trait values, as well as the need to check the robustness of evolutionary model conclusions against modifications of the life cycle.

Allison, K. Shaw,
Deparment of Ecology, Evolution, and Behavior, University of Minnesota (US)
e-mail: `ashaw@umn.edu`

Cassidy C. D'Aloia,
Dept. of Ecology & Evolutionary Biology, University of Toronto (CANADA)

and

Peter M. Buston
Department of Biology and Marine Program, Boston University (US).

The evolution of marine larval dispersal kernels in spatially structured habitats

Understanding the patterns, causes and consequences of dispersal is a major goal of ecology. However, most research on the causes of variation in dispersal in marine systems focuses on proximate causes (physical oceanography, larval behavior). Here, we investigate the ultimate, evolutionary causes of dispersal variation. Building on classic work by Hamilton and May, we develop a combination of analytic and simulation models for the evolution of larval dispersal kernels in spatially structured habitats. First, considering a world without bound, we find that the evolutionarily stable strategy (ESS), paradoxically, allocates most offspring to the longest dispersal distance class. Second, considering a world with bound resolves the first paradox, but creates its own paradox: the ESS strategy allocates next to nothing beyond the shortest dispersal distance class. Third, considering a patchy world with bound, we find a more realistic result: the ESS allocates most offspring to short distances classes, but still some to longer distance classes. Finally, we test our model predictions against an empirically derived dispersal kernel (the neon goby *Elacatinus lori*) from a real, spatially-structured habitat (the Belizean Barrier Reef System). The model's predictions are qualitatively similar to the empirical data: both data sets predict a high level of short-distance dispersal (< 2 km from source), and low levels of long-distance dispersal. This study provides a framework that can be used to model the evolution of dispersal kernels in other species and seascapes, which will provide new insights into variation in patterns of population connectivity.

Yuuya, Tachiki,
Institute for Virus Research, Kyoto University;
Department of Biology, Kyushu University.
e-mail: `tachiki@bio-math10.biology.kyushu-u.ac.jp`

and

Itsuro, Koizumi
Faculty of Environmental Earth Science, Hokkaido University.

Evolutionary and ecological consequences of individual decisions, whether they stay or go, under environmental fluctuations

Species sometimes choose one of alternative tactics in their life history. To explain this phenomenon, a threshold value for individual status is assumed, above and below which each individual should adopt either tactic to attain higher fitness. This framework is called the status dependent strategy and implicitly assumes the existence of an “absolute” value, so each individual chooses a tactic based only on its own status. However, it is also possible that animals assess their status based on surrounding individuals. This “relative” assessment considers that a threshold value can change depending on individual situations. Here, we incorporated Bayesian decision-making and adaptive dynamics frameworks to explore the conditions of each assessment to be an evolutionarily stable strategy (ESS). Our model demonstrates that absolute assessment is always an ESS under a stable environment, whereas relative assessment can be an ESS under stochastic environments; a mixed strategy was also selected as the intermediate [1]. Individuals’ responses to stochasticity are different between absolute and relative assessment. The proportions of alternative tactics fluctuate under stochasticity when animals adopt absolute assessment, while they are stabilized when animals adopt relative assessment. Our results underscore the need to better understand how individuals assess their own status to choose alternative tactics.

REFERENCES

[1] Tachiki, Y. and Koizumi, I. 2016. Absolute versus Relative Assessments of Individual Status in Status-Dependent Strategies in Stochastic Environments. *The American Naturalist.188.* 113-123.

Oral Session Abstract

Genki Ichinose
Department of Mathematical and Systems Engineering, Shizuoka University
e-mail: `ichinose.genki@shizuoka.ac.jp`

Takehiro Kurisaku
Department of Computer Science and Engineering, Toyohashi University of Technology

Effect of peer pressure on the evolutionary vaccination game

Preventing infectious disease like flu from spreading to large communities is one of the most important issues for humans. One effective strategy is voluntary vaccination, however, there is always the temptation for people refusing to be vaccinated because once herd immunity is achieved, infection risk is greatly reduced. Fu et al. and Cardillo et al. revealed that voluntary vaccination is effective despite the high cost in heterogeneous networks compared to homogeneous networks, because once hub nodes are vaccinated, the behavior immediately spreads to the whole population [1, 2]. In those networked models, when imitation of the strategy is conducted, only the payoff information of one particular neighbor is obvious. If people use broader information, what happens to the dynamics? Fukuda et al. investigated the effect of social status information in which each individual can use the information of the average payoff of its neighbors instead of the payoff of one randomly selected neighbor [3]. They showed that the effectiveness of the social status depends on both network structures and the cost of vaccination. In this paper, we study the effect of peer pressure on the vaccination behavior resulting in preventing infectious disease in networks. The evolutionary simulation results show that the peer pressure has both positive and negative effects on the vaccination behavior. Especially, in heterogeneous networks, if the vaccination cost is low the behavior is more promoted than the case without peer pressure. In contrast, if the cost is high, the behavior is reduced compared to the case without peer pressure. Moreover, the vaccination behavior is effective in heterogeneous networks more than in homogeneous networks. This implies that the peer pressure puts people at risk in homogeneous networks.

REFERENCES

[1] Fu, F., Rosenbloom, D. I., Wang, L. and Nowak, M. A., 2011. Imitation dynamics of vaccination behaviour on social networks, *Proc. R. Soc. B*, **278**: 42–49.

[2] Cardillo, A., Reyes-Suarez, C., Naranjo, F. and Gomez-Gardenes, J., 2013. Evolutionary vaccination dilemma in complex networks, *Phys. Rev. E* **88**: 032803.

[3] Fukuda, E., Kokubo, S., Tanimoto, J., Wang, Z., Hagishima, A. and Ikegaya, N., 2014. Risk assessment for infectious disease and its impact on voluntary vaccination behavior in social networks, *Chaos, Solitons & Fractals* **68**: 1–9.

Masayuki Kakehashi
Hiroshima University (Graduate School of Biomedical & Health Sciences), Hiroshima, Japan
e-mail: `kakehashi@hiroshima-u.ac.jp`

Shoko Kawano
Kurume University (School of Nursing), Kurume, Japan

An analysis on the effect of school closure against influenza: 'Back Monte Carlo' data approach

Taking advantage of infectious disease spread data collected in small sized groups such as school classes, using individually based stochastic model is considered to be appropriate. In spite that collected data are usually the numbers of cases (patients) on each time interval, the data required to estimate parameters in the model are those of persons just infected on each interval. To reconstruct infection data from case report data taking the effect of latent period into account, we proposed 'back Monte Carlo' calculation approach to analyze properly the effect of school closure.

Data used in our analysis were collected during September 2009 - March 2010 at schools in Oita in Japan. Totally 51,872 pupils or students in 134 schools (kindergartens, elementary schools, junior high schools and high schools) were reported their absence due to Pandemic flu by class and by day. Whether or not school or class closure was implemented was also reported.

In addition to the stochasticity due to latent period, there was an effect of reporting delay: i.e., the numbers of cases reported on Saturdays and Sundays were smaller than those on other week days in contrast to those on Mondays that were larger. This took place because some of the case reports were postponed to the next working day avoiding reporting on holidays. This was also observed on national holidays. We assumed constant rate of postponing report as 67% based on the observed data. We also assumed average duration of latent period was 3 days. Transmission were divided into three types: within class, within school and within whole school community. An addition of baseline level of transmission was also considered. Based on the assumptions described above, parameters in the model were estimated by maximum likelihood method where transmission were assumed not to happen in classes nor schools when on holidays or when class or school was under closure. Analyses were carried out for the data during September 1 - December 24 (115 days) when school vacations were not involved. Simulations based on the estimated parameters were also carried out.

In the analysis, transmission coefficients due to individual in the same class and due to those in the same school were separately and found the former was approximately 15 times larger than that of the latter. It was also found that the transmission coefficients due to individual in the same school was approximately 10 times larger than that in a different school.

We also examined the effect of successive days of school closure (the duration of each school closure), which was set 4 days according to relevant regulations. Among 2 - 5 days as the duration of each school closure, 3 days realized the best performance as a preventive measure.

‘Back Mont Carlo’ data approach was useful to estimate parameters involved in stochastic infectious disease spread model. The reason why 3 day school closure attained the best performance may be attributable to the fact that average latent period was assumed to be 3 days. In the evaluation of the effect of school closure, disadvantage of school closure must be incorporated in addition to benefit of school closure, i.e., the reduction of the number of cases, etc. It was then useful to calculate ‘the person-years of closure’ required to reduce one case. The results of simulation did not reproduce the rapid increase of cases in the last decade of October, which were considered to be attributed to specific episode not considered in the model. It was also considered useful to improve prediction that the spread of infection in whole community was considered.

REFERENCES

[1] Kawano, S. and Kakehashi, M., 2015. Substantial Impact of School Closure on the Transmission Dynamics during the Pandemic Flu H1N1-2009 in Oita, Japan. PLOS ONE, **10**: e0144839.

Takaaki Funo
Department of Biology, Kyushu University, Japan
e-mail: `funoseisu@gmail.com`

Shingo Iwami
Department of Biology, Kyushu University, Japan

Corrilation between malaria cases and rainfall

Malaria is a vector-borne disease transmitted by mosquitoes. In area of highly seasonal transmission, it is believed that asymptomatic patients persist over the course of the dry season and to reseed transmission when mosquito populations increase along with wetter conditions. In this study, we investigated how the Malthusian coefficient correlates with climate factors such as rainfall and temperature.

Yuji Sakai
Theoretical Biology Laboratory, RIKEN, Hirosawa, Wako, Saitama, 351-0198, Japan
interdisciplinary Theoretical Science iTHES, RIKEN, Hirosawa, Wako, Saitama, 351-0198, Japan
e-mail: `ysakai@riken.jp`

Masashi Tachikawa, Atsushi Mochizuki
Theoretical Biology Laboratory, RIKEN, Hirosawa, Wako, Saitama, 351-0198, Japan

Kazuya Kinoshita, Tatsuya Hirano
Chromosome Dynamics Laboratory, RIKEN, Hirosawa, Wako, Saitama, 351-0198, Japan

Chromosome condensation effects on the organization and segregation

The spatial organization of chromosomes in mitosis is a fundamental question of biology. Upon entry into mitosis, a mass of chromatin distributed in the interphase nucleus is converted into a discrete set of chromosomes with high condensed rod-shape structures.

The condensen protein complex is responsible for the chromosome condensation [1]. In the chromosome condensation, the condensin is associated with chromosomes, enriched on chromosome axes, and have distinct contributions to the chromosome organization.

It is experimentally considered that the condensin has two functions, making twisted loops in chromosome and attracting between near ones [1]. However since the chromosome condensation is very complex phenomena, it is not clear how the condensin functions contribute to the chromosome organization and the segregation.

In this study, we investigate effects of the condensin functions on the chromosome organization and the segregation by using coarse-grained molecular dynamics simulations. We model the chromosome as the rigid beads and the connecting springs, the condensin as the rigid beads. We model two condensin functions as follows. First, the one condensin bead attracts with the two chromosome beads and make a twisted loop structure in the chromosome. Second, the condensin beads attract with each other when they are in some distance.

By changing the strengths of the chromosome-condensin attraction and condensen-condensin attraction, we investigate the effects of the two condensin functions on the chromosome organization and the segregation. We show that these functions apparently affect on both the organization and the segregation. Particularly both the functions are necessary for both the organization of the rod-shape chromosomes and the segregation of the entangled chromosomes.

We also discuss the condensin spatial pattern formation. The condensing is enriched on chromosome axes, i.e., the condensin axis, in the chromosome condensation. Recently, the experiment shows that the condensin does not make the axis but makes many spot patters on the chromosome when the condensin subunit is knocked out [2]. We show that the spatial pattern changes can be reproduced by lack of the condensin looping function in our model.

REFERENCES

[1] Hirano, T., 2016, Condensin-Based Chromosome Organization from Bacteria to Vertebrates. *Cell*, **164**: 847-857.
[2] Kinoshita, K. and Hirano, T., 2016. Balancing Acts of Two HEAT Subunits of Condensin I Support Dynamic Assembly of Chromosome Axes. *Developmental Cell*, **33**: 94–106.

Hisao Honda
Kobe University Graduate School of Medicine, Kobe.
Center for Developmental Biology, RIKEN, Kobe.
e-mail: `hihonda@hyogo-dai.ac.jp`

Takaya Abe
Division of Bio-function Dynamics Imaging, RIKEN, Kobe.

Toshihiko Fujimori
National Institute for Basic Biology, Okazaki.
Division of Bio-function Dynamics Imaging, RIKEN, Kobe.

Mechanism of cardiac looping of the embryonic heart

We investigated a mechanism of heart looping using a mathematical model, the cell-based vertex dynamics for tissues. A simple straight tube consisted of polygonal cells could be deformed by various factors in the model. We considered two factors, left-right (LR) asymmetric expression of nodal cassette genes in the lateral plate mesoderms (LPM) and cell chirality that was recently recognized experimentally. Cells in the left side of tube were derived from the left LPM, and their growth was assumed to be rapid. In the computer simulation, the tube protruded one-side or bent, but did not loop. On the other hand, we assumed chiral behavior of cells. Most of cells divided along anterior-posterior (AP) axis of the heart. After cell division, two daughter cells assumed to rotate for small angle in counterclockwise direction (the chiral behavior). In the simulation the cells migrated on surface of the tube, but the tube did not loop. Finally, we performed the two assumptions (LR asymmetry of the tube and chiral rotation of the cells) simultaneously, the tube looped. We succeeded in recapitulation of the heart looping. The assumptions of difference of cell growth between the left and right sides of the tube, tendency of cell division along the AP axis and the counterclockwise rotation of daughter cells were substantiated by *in vitro* experiments of mouse embryos. In conclusion the cardiac looping was caused by asymmetry of LPM and chiral behavior of dividing cells.

Kenichi Nakazato
Theoretical Biology Lab, RIKEN
e-mail: `na@riken.jp`

Atsushi Mochizuki
Theoretical Biology Lab, RIKEN

Yuta Takase, Yoshiko Takahashi
Zoology Lab, Graduate school of science, Kyoto Univ.

Understanding Vascular Remodeling from the View of Continuum Mechanics

We are studying the vascular remodeling from immature vascular plexus to stable vascular network by combining experimental and mathematical methods. Experimentally, we found two types of endothelial cellular behavior. (1) Cells show migration in the tissue against the blood flow. (2) Cells show detachment from the tissue when blood flow is surpressed. Based on those observations, we developed mathematical framework to study macroscopic deformation of vascular organs from microscopic cell behaviors to determine responsible mechanisms for remodeling. Endothelial tissue should compensate for the density change brought by cellular behaviors in some way to keep its thickness constant. Assuming expansion and contraction of the tissue as the compensation, we construct mathematical model of remodeling. In our model, cellular behavior results in stress field on the tissue. Here, positive stress field generates expansion and negative one generates contraction. Analyzing the model, we show the direction of local deformation of the tissue is determined by two factors, the sign of stress field and the local curvatures of the tissue. In addition, we compared effect of two hypotheses on cellular behavior: increase of migration speed and decrease of ablation rate against the increase of speed of blood flow. As the results, we show (a) the directions of deformation are different between them and (b) migration has only minor effects compared to detachment to explain actual patterning.

In my talk, I will focus on another description of continuum, namely particle dynamics. Since the particle dynamics can be directly interpreted as cell center dynamics, we can capture the biological meanings of our model more intuitively.

Joe Yuichiro Wakano
Meiji Univeristy
e-mail: `joe@meiji.ac.jp`

Kenichi Aoki
Meiji University

William Gilpin, Marcus Feldman
Stanford University

Traveling waves of cultural invasion

Human range expansion has been studied based on genetic data (mainly modern human DNA + some ancient DNA of Neanderthals). It is estimated that the second wave of out-of-Africa by *Homo sapiens* took place roughly 50-100 kya, and they completely replaced the pre-existing hominids. On the other hand, *Homo sapiens* and Neanderthals are so closely related that the evidence of introgression is found [1,2]. In this study, we assume that the genetic difference between these species is negligible. We postulate that the relatively quick replacement is triggered not by genetic but by cultural differences. When a group with high cultural level (e.g., advanced stone-tools) appears, they might increase their population density and hence the spatial distribution of such high culture groups might spatially spread. Previous empirical [3] and theoretical [4,5,6] studies suggest the existence of positive feedback loop between cultural level and population size. There could exist two locally stable equilibria: "low" equilibrium consisting of low population density and low cultural level and "high" equilibrium consisting of high population density and high cultural level. Since previous models did not explicitly model spatial structure, theoretical predictions are made based on the basins of attractions of these equilibria in ODE systems. In this study, we propose spatially explicit reaction-diffusion model. We consider a traveling wave solution (TWS) connecting these equilibria, and obtain the condition under which "high" equilibrium expands its spatial distribution.

REFERENCES

[1] Viola B, Pääbo S (2013) What's new in Central Asia? Basic Issues in Archaeology, Anthropology and Ethnography of Eurasia: Festschrift on the Occasion of Anatoly Derevianko's 70th Birthday, eds Shunkov MV, Molodin V (SB RAS Press, Novosibirsk, Russia), pp 555–565.
[2] Prüfer K, et al. (2014) The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature* 505(7481):43–49.
[3] Henrich J (2004) Demography and cultural evolution: How adaptive cultural processes can produce maladaptive losses: The Tasmanian case. *Am Antiq* 69:197–214.
[4] Aoki K (2014) Modeling abrupt cultural regime shifts during the Palaeolithic and Stone Age. *Theor Popul Biol* 100:6–12.
[5] Ghirlanda S, Enquist M (2007) Cumulative culture and explosive demographic transitions. *Qual Quant* 41(4):591–600.
[6] Gilpin W, Feldman MW, Aoki K (2016) An ecocultural model predicts Neanderthal extinction through competition with modern humans. *Proc.Nat.Acad.Sci.USA* 100:6–12.

Riccardo Pansini
Kunming Institute of Zoology (CAS) and Yunnan University of Finance and Economics
e-mail: `r.pansini@gmail.com`

High cooperation levels in a PGG by Chinese subjects to mitigate climate change

Cooperation theories assume that interacting individuals can change their strategies under different expected payoffs, depending on the social situations. The willingness to invest into partners and to cooperate may therefore shift in China as opposed to Western countries partly as a result of cultural differences. An experiment was implemented to test the willingness of young Chinese subjects to mitigate the consequences of climate change in a country severely affected by air pollution. Following a design already implemented in Germany [1], we set up a Public Good game in which groups comprised of six students had to reach a minimum threshold of earned points to be able to invest the converted money into planting trees. Differently from the German model whose subjects did not manage to reach the threshold, the Chinese subjects were very successful at investing for this cause. These results are discussed in relation to a Social Value Orientation questionnaire we presented the subjects with to ascertain the social value profile of cooperators and non-cooperators.

REFERENCES

[1] Jacquet, J., Hagel, K., Hauert, C., Marotzke, J., Rohl, T. & Milinski, M. 2013. Intra- and intergenerational discounting in the climate game. *Nature Clim. Change*, **3**, 1025-1028, 10.1038/nclimate2024.

Cinthia Marie Tanaka
Department of Applied Mathematics, University of Sao Paulo, Brazil
e-mail: `cimarie@ime.usp.br`

Yoh Iwasa
Department of Biology, Kyushu University, Japan

Persistence of local dialect in the face of a national standard language: a mathematical study

Many languages had gone extinct or were put in the endangered list of languages in the last century, with the number of languages decreasing at a faster rate than mammals and birds species. Since late 1990s, mathematical models have been proposed to study the language change dynamics and language survival dynamics [1][4]. In particular, Abrams and Strogratz [1] proposed a simple model for the competition of two languages and concluded that when there are no bilinguals in the population, one of the two languages will eventually become extinct.

Dialects can be defined as different speech systems of the same language which are mutually intelligible [2]. The rise of a dialect as a national language is relatively common, and it has happened in history many times, e.g. Tokyo dialect (Japanese), Paris dialect (French) and Athens dialect (Greek). The standardization process of a language may cause other dialects to be perceived as a lower-class or rural speech. This endangers the survival of different dialects; in the case of Japan, there was a fear that dialects would disappear after the language unification [3]. However, the persistence of dialects, as the Piedmontese dialect (Italy) or the Kansai dialect (Japan), proves that dialects dynamics are more complicated than initially thought.

Here we propose a deterministic model to investigate the dynamics of the survival of a local dialect (B) when competing against a national language (A). We assume individuals may be able to use different dialects, in response to different situations. For example, in public situations, e.g. in a formal workplace, they may use the national language, while in private situations, e.g. in family or close friend meetings, they may use a local dialect.

We consider the choice of a dialect (for private situations) is guided by, mainly, two forces: (i) pride of the local language (negatively affects probability of changing dialect π); and (ii) willingness to speak the same dialect (conformity parameter, ξ) inside a private group.

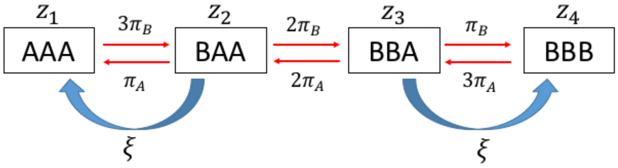


Figure 1. Dialect change dynamics for different groups. Conformity parameter ξ affects the change from mixed groups, where A and B dialects are both spoken, to homogeneous groups (all A or all B). Pride of the language A negatively affects the probability of changing to language B (π_B), and vice-versa.

Our preliminary results show that the conformity parameter has no influence in the final outcome if the private group has only two individuals (married couple). In particular, in this case, the stable frequency of speakers of the standard language A is given by $\pi_A/(\pi_A+\pi_B)$. However, this result does not hold when we increase the number of individuals per group. This may indicate that the number of individuals matters when it comes to the fate of a dialect.

REFERENCES

[1] Abrams, D. M., & Strogatz, S. H., 2003. Linguistics: Modelling the dynamics of language death. *Nature*, **424**(6951): 900.

[2] Crystal, D., 2000. *Language Death*. Cambridge University Press.

[3] Inoue, F., 1993. The significance of new dialects. *Dialectologia et Geolinguistica*, **1**: 3-27.

[4] Nowak, M. A., & Krakauer, D. C., 1999. The evolution of language. *Proceedings of the National Academy of Sciences*, **96**(14): 8028-8033.

Hiromi SENO
Research Center for Pure and Applied Mathematics
Department of Computer and Mathematical Sciences
Graduate School of Information Sciences
Tohoku University
Aramaki-Aza-Aoba 6-3-09, Aoba-ku, Sendai 980-8579
JAPAN
e-mail: `seno@math.is.tohoku.ac.jp`

Mathematical Modeling of Metapopulation Dynamics: Revisiting Its Meaning

The following 2-state metapopoulation dynamics model is well known as Levins model [2,3]:

$$\frac{dE}{dt} = e_{\mathrm{P}}P - cPE$$

$$\frac{dP}{dt} = cPE - e_{\mathrm{P}}P$$

In a patchy habitat, E and P mean the frequency (or the probability of existence) of patches with 'vacant' state and that with 'occupied' state, respectively. Since E and P satisfy the condition that $E + P = 1$ independently of time, this model can be described in a mathematically equivalent form by the following single ordinary differential equation as known well:

$$\frac{dP}{dt} = cP(1-P) - e_{\mathrm{P}}P$$

The parameter e_{P} means the coefficient for the occurrence of transition from the state 'occupied' to 'vacant' which is due to the extinction of population in the 'occupied' patch, and c means the coefficient for the transition of vacant patch to the 'occupied' state due to the successful settlement of some immigrants from the 'occupied' patches.

Interesting and valued point of mathematical modeling by Levins [2, 3] is its treatment of dynamics in terms of 'state' transition of each patch without considering the temporal variation of population size itself in each patch [1]. However, the frequency of migration, that is, the strength of migration effect on the state transition is significant in the modeling since it takes the effect of immigrants into account for the cause of state transition, and the strength of migration effect necessarily depends on the size of migrating population. Therefore it requires a rational combination of patch states and population size for the modeling by the idea of Levins [2, 3] to aggregate the population dynamics in a patchy habitat into a dynamics of patch state transition.

In the work [4], we will discuss a mathematical modeling, focusing on how the strength of migration could be involved in it to construct a metapopulation dynamics model, with the same idea with Levins'. Although the similar problem has been discussed in some previous papers, we will independently consider the mathematical modeling of Levins' idea, and try to discuss the problem about the rationality of its modeling typical with the mass-action terms.

REFERENCES

[1] Hanski, I. and M. Gilpin, M., 1991. Metapopulation dynamics: Brief history and conceptual domain. *Biol. J. Linnean Soc.*, **42**: 3–16.
[2] Levins, R., 1969. Some demographic and genetic consequences of environmental heterogeneity for biological control. *Bull. Entomol. Soc. Am.*, **15**: 237–240.
[3] Levins, R., 1970. Extinction. In M. Gerstenhaber (ed.), *Some Mathematical Problems in Biology, Lectures on Mathematics in the Life Sciences*, Vol. 2, pp. 75–107, American Mathematical Society, Providence, Rhode Island.
[4] Seno, H., 2016. Mathematical modeling of metapopulation dynamics: Revisiting its meaning. *Math. Model. Nat. Phenom.*, **(in press)**.

Kei Tokita
Department of Complex Systems Science, Graduate School of Information Science, Nagoya University
e-mail: `tokita@nagoya-u.jp`

Species abundance patterns of a food web model

In community ecology, the relation between diversity, stability and species abundance patterns (SAP) has been discussed as one of the ``unanswered questions in ecology in the last century'' [1]. In special, theoretical understanding of SAP for a system in a single trophic level has been greatly progressed in this century, based on Hubbell's neutral theory [2, 3]. Meanwhile, for more complex systems occurring on multiple trophic levels and including non-neutral species with various types of interspecies interactions among them, a pioneering work by May [4], which triggered a controversial debate on the relation between diversity and stability [5], has demonstrated efficacy of a linear analysis and the theory of random matrices.

Beyond the linear model, statistical mechanics have been employed for analyzing nonlinear models and have provided global and quantitative information for diversity, stability and SAP [6-10]. Recently, we presented that sparse interactions essentially change SAP and it reveals multiple peaks that have been discovered in several field researches [11, 12]. Our analyses also give the first theoretical prediction that the sparse (specialist-specialist) interactions stabilize the system and realize all-species coexistence at finite intraspecific competition that was never predicted in a model with all-to-all interactions.

In my talk, statistical mechanics of SAP for a food web model is presented. Based on the classical theory of Edward Kerner for the antisymmetirc Lotka-Volterra equations [13, 14], we analytically obtained species abundance distributions such as a lognormal distribution and the Fisher’s logseries in a limit of the “eco-temperature” parameter value. We also discuss the corresponding species-area curve.

REFERENCES

[1] May, R.M., 1999. Unanswered questions in ecology. *Phil. Trans. R. Soc. London*, **B 264**: 1951-1959.
[2] Hubbell, S.P., 2001. The United Neutral Theory of Biodiversity and Biogeography. Princeton University Press.
[3] Etienne, R.S. and Alonso, D., 2007. Neutral community theory: how stochasticity and dispersal limitation can explain species coexistence. *J. Stat. Phys.* **128**: 485-510.
[4] May, R.M., 1972. Will a large complex system be stable? *Nature* **238**: 413-414.
[5] McCann, K.S., 2000. The diversity-stability debate. *Nature* **405**:228-233.
[6] Tokita, K., 2004. Species abundance patterns in complex evolutionary dynamics. *Phys. Rev. Lett.* **93**: 178102.
[7] Galla, T., 2006. Random replicators with asymmetric couplings, *J. Phys. A: Math. Gen.* **39**: 3853-3869.
[8] Yoshino, Y., Galla, T. and Tokita, K., 2007. Statistical mechanics and stability of a model eco-system. *J. Stat. Mech.*: P09003.
[9] Yoshino, Y., Galla, T. and Tokita, K., 2008. Rank abundance relations in evolutionary dynamics of random replicators. *Phys. Rev. E*, **78**: 031924.
[10] Tokita, K., 2015. Analytical theory of species abundance distributions of a random community model. *Popul. Ecol.*, **57**: 53-62.
[11] Obuchi, T., Kabashima, Y. and Tokita, K. 2016. Multiple peaks of species abundance distributions induced by sparse interactions. *Phys. Rev. E*, in print. [http://arxiv.org/abs/1605.09106]
[12] Obuchi, T., Kabashima, Y. and Tokita, K. 2016. Relative species abundance of replicator dynamics with sparse interactions. *J. Stat. Mech.*, submitted. [https://arxiv.org/abs/1605.09490]
[13] Kerner, E. H. 1957. A statistical mechanics of interacting biological species. *Bull. Math. Biophys.* **19**: 121-146.
[14] Kerner, E. H. 1974. Why are there so many species? *Bull. Math. Biol.* **36**:477-488.

Ryo Oizumi
Ministry of Health, Labour and Welfare
e-mail: `oizumi@ms.u-tokyo.ac.jp`

Twofold stochasticity in structured population models

Organisms are faced with twofold stochasticity that are internal and external stochasticity. The fomer belongs to scale of individuals and generates heterogeneity in life schedules. The latter affects population scale as environmental stochasticity [1]. The internal stochasticity brings about diversity of strategies in individual life history which is represented stochastic processes [2]. On the other hand, a paper argued that the external stochasticity conditionally reduces the population growth rate in the long term perspective [3]. The paper vilified the argument by use of an innovative perturbation method which is referred to as Tuljapurkar's approximation. The method clarifies the relationship between effects of external stochasticity on life history and population dynamics in matrix population models. In this study, by adapting Tuljapurkar's approximation to a matrix model containing twofold stochasticity, we reveal that the relationship between internal and external stochasticity in life histories.

REFERENCES

[1] Oizumi, R., and Takada, T. 2013. Optimal life schedule with stochastic growth in age-size structured models: Theory and an application. *Journal of Theoretical Biology*, **323**: 76–89.
[2] Oizumi, R., 2014. Unification theory of optimal life histories and linear demographic models in internal stochasticity. *PLOS ONE*, 9 (6) **e98746**.
[1] Tuljapurkar, S., 1982. Population dynamics in variable environment III Evolutionary dynamics of r-selection. *Theoretical population Biology*, **21**: 141–165.

Takashi Shimada
Department of Applied Physics, Graduate School of Engineering, The University of Tokyo 1
e-mail: `shimada@ap.t.u-tokyo.ac.jp`

Fumiko Ogushi
Advanced Institute for Material Research, Tohoku University 2
e-mail: `fumiko.ogushi.e3@tohoku.ac.jp`

Robustness of evolving open systems with mutual interactions

An important and universal feature of ecosystems, and also other many real complex systems such as biological, social, economic, and engineering systems, is that those are open: in those systems, constituting elements are not fixed and the complexity emerges (at least persist) under successive introductions of new elements. Those systems sometimes grow, but also sometimes collapse. A fundamental question that why and when, in general, we can have such open and complex systems is still not fully understood.

We have revisited this classical problem using a very simple graph-dynamics model in which the interaction between species are modeled by directed and weighted links. This model gives either continuous growth or stagnation in system size, depending on the model's unique parameter: the average number of weighted links per node $\boldsymbol{m}$. Systems can grow only if the connection is moderately sparse, i.e. $4 < \boldsymbol{m} < 19$. This transition is found to originate from an essential balance of two effects: although having more interactions makes each node robust, it also increases the impact of the loss of a node [1, 2]. This novel relation might be a one scenario for solving the diversity-stability paradox [3]. The non-trivial distribution function of the lifetime of species is also reproduced in this model [3].

An important feature we should consider next on applying this theory to dynamical systems such as population dynamics models of ecological systems is that interaction often should have considerably high chance to be bidirectional [5]. Therefore we here consider the system with bidirectional interactions. In the talk, we will report how the phase portrait of the system’s growing nature is changed by the introduction of bidirectional interactions. The model with a mix of unidirectional and bidirectional interactions will be also discussed.

REFERENCES

[1] T. Shimada, in *Mathematical Approaches to Biological Systems: networks, Oscillations and Collective Motions* (Springer, 2015) p. 95-117.
[2] T. Shimada, Scientific Reports Vol. 4, 4082 (2014).
[3] M. R. Gardner and W. R. Ashby, Nature 228 784 (1970).
[4] Y. Murase, T. Shimada, & N. Ito, New J. of Physics 12, 063021 (2010).
[5] T. Shimada, Y. Murase, & N. Ito, Proceedings of the International Conference on Social Modeling and Simulation, plus Econophysics Colloquium 2014, p. 99-109 (2015).

Akane Hara
Kyushu University
e-mail: `hara.akane32a@gmail.com`

Yoh Iwasa
Kyushu University

When is the allergen immunotherapy effective?

Allergen immunotherapy is one of the methods to treat Japanese cedar pollen allergy (JCPA). In the immunotherapy of JCPA, patients have a small amount of pollen every week over several years, which might suppress severe allergic symptoms when they are exposed to a large amount of environmental pollen later [1]. In the mechanism of this therapy, Regulatory T cells (Treg cells) play an important role [2]. Treg cells suppress overreaction of immune system and help avoiding allergic responses [3]. Since it takes several years to be effective, it is important to choose participants who are likely to benefit from this therapy.

We develop a simple mathematical model and identify the conditions for success of allergen immunotherapy. In the model, two differential equations (1) and (2) describe the dynamics of type-2-helper-T-cells (Th2) and regulatory-T-cells (Treg). H and R represents the number of Th2 and Treg cells, respectively, and $A(t)$ stands for the amount of pollen the participant takes in. Both of them are differentiated from naive T-cells stimulated by pollen (Fig.1). During therapy period of several years, the patient receives a small dose every week, and then he or she becomes exposed to a large amount of environmental pollen. We assume that Treg cells live much longer than Th2 cells, which makes Treg cells accumulate over the therapy period. Accumulation of Treg cells leads the therapy to be effective. We define that the therapy is successful if all the following three conditions are satisfied: (1) without therapy the patient develops allergic symptoms upon exposure to the environmental pollen, (2) with therapy the patient does not develop allergic symptoms upon exposure, and (3) the patient does not develop allergic symptoms caused by the therapy itself.

$$\frac{dR}{dt} = b \cdot A(t) \cdot (1-c) - d_r \cdot R \qquad (1)$$

$$\frac{dH}{dt} = \frac{b \cdot A(t) \cdot c}{1 + m(R+n)} - d_h \cdot H \qquad (2)$$

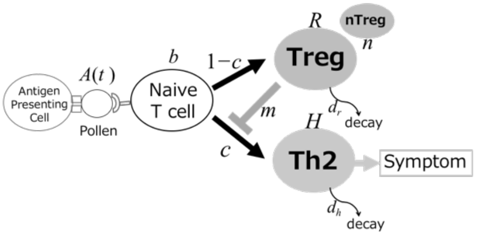


Fig. 1 Scheme of the model

As a result of analysis of the model, we find the conditions of each parameter for successful therapy. For example, Treg cells should have a long life span, and many naïve T cells should be stimulated and differentiated per unit amount of pollen. We also find that the therapy with dose linearly increasing time, rather than constant dose, is more able to reduce allergic symptoms caused by the therapy itself. We can extend this model to other kind of allergy, such as food allergy.

REFERENCES

[1] Okubo, K., Gotoh, M., 2009. Sublingual immunotherapy for Japanese cedar pollinosis. *Allergol Int,* **58**, 149-54.
[2] Radulovic, S., Jacobson, M. R., Durham, S. R., Nouri-Aria, K. T., 2008. Grass pollen immunotherapy induces Foxp3-expressing CD4+ CD25+ cells in the nasal mucosa. *J Allergy Clin Immunol* **121**, 1467-72, 1472.e1.
[3] Sakaguchi, S., Yamaguchi, T., Nomura, T., Ono, M., 2008. Regulatory T cells and immune tolerance. *Cell* **133**, 775-787.

Yoshiki Koizumi
School of Medicine, College of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Ishikawa, Japan
e-mail: `koizumi.yoshi@gmail.com`

Mathematical modeling of drug administration schedule in HCV infection

In the era of direct-acting antiviral agents (DAAs), hepatitis C virus (HCV) infection can be cured by combining several DAAs. Although DAAs have achieved the success of drug combination therapy against HCV infection, the cost of drug treatments has increased and imposed a financial burden on the patients. In Japan, for instance, the price of a drug combination of sofosbuvir and ledipasvir, the first-line DAAs treatment on HCV genotype 1, is about 54,000 yen per pill and more than 4,500,000 yen per standard 12-week treatment. Such the heavy financial burden may increase the national medical expenses and threaten the national health insurance system. To save the high cost of DAAs treatment, one possible solution is to reduce the treatment duration with optimizing a drug regimen for a rapid eradication of HCV. Using the previous mathematical model[1,2] of viral dynamics and PK/PD, here we try to compare the treatment duration between double and triple drug combinations, and discuss the optimized drug regimen from the financial aspect of DAAs treatments.

REFERENCES

[1] Adiwijaya, B. S., et al. "A viral dynamic model for treatment regimens with direct-acting antivirals for chronic hepatitis C infection." *PLoS Comput Biol*, 8.1 (2012): e1002339.
[2] Ke, R., et al. "Rational design and adaptive management of combination therapies for Hepatitis C virus infection." *PLoS Comput Biol*, 11.6 (2015): e1004040.

Tatsuya Kurusu
Department of Biology, Faculty of Sciences, Kyushu University, Fukuoka 812-8581, Japan.
e-mail: `b.c.kurupon11rm16@gmail.com`

Koichi Watashi
Department of Virology II, National Institute of Infectious Diseases, Tokyo 162-8640, Japan

Shingo Iwami [1,2]
Department of Biology, Faculty of Sciences, Kyushu University, Fukuoka 812-8581, Japan. 1 PRESTO, JST, Saitama 332-0012, Japan. 8CREST, JST, Saitama 332-0012, Japan. 2

Modeling Hepatitis B Virus entry

Hepatitis B virus (HBV) is one of the major factors of hepatic disease, and there is few specific medicine. For antiviral drugs, virus entry is important target, but there is no quantitative model describing the viral entry. With the model, we can estimate how percentage virus replication decrease when virus entry is inhibited, so we propose a novel mathematical model for HBV entry. In this study, we analyzed HBV experimental dataset, and estimated viral cell-attachment and detachment rate, cell-entry rate and nuclear-entry rate. Using this parameter, we simulated our mathematical model and predict the kinetics of HBV entry. In addition, we would like to discuss about the relationship between the entry inhibitive ratio and the decrease of cccDNA, the factor of replication.

REFERENCES

[1] Watashi, K., Urban, S., Li, W., Wakita, T., 2014. NTCP and Beyond: Opening the Door to Unveil Hepatitis B Virus Entry. *International Journal of Molecular Sciences*, **67**: 2892–2905.
[2] Seeger, C., Locarnini, S., 2015. The Hepatitis and Delta Viruses. New York, Cold Spring Harbor Laboratory Press.

Haru Negami

Gen Kurosawa
Theoretical Biology Laboratory, RIKEN, Wako 351-0198, Japan
Core Research for Evolutional Science and Technology, JST
e-mail: `g.kurosawa@riken.jp`

Theoretical studies on temperature and biological clocks

Biological phenomena are often sensitive to temperature. For example, cell growth gets faster at higher temperature. In contrast, the period of daily rhythms is robust to temperature. This phenomenon is peculiar because the system level property (period) is insensitive to temperature while the elements of the system (biochemical reactions) are sensitive to temperature. The phenomenon is called "temperature compensation", and the mechanism has been elusive for more than 60 years. Thanks to molecular biology studies, we now know genes and proteins essential for daily rhythms. In our study, we aim to uncover the mechanism for the robustness of daily rhythms to temperature by combining computational modeling and quantitative experiments

Regulation of gene expression is essential for the autonomous daily rhythms in mouse, *Drosophila*, and *Arabidopsis*. On the other hand, the autonomous rhythm in *Cyanobacteria* can be reconstituted in *vitro* using three key proteins and ATP [1]. While temperature compensation is observed at both mouse and *Cyanobacteria*, the mechanism for temperature compensation might be different between the two species. To address this possibility, we used published mathematical models for mammalian [2] and *Cyanobacterial* [3] daily rhythms. Under the assumption that all reactions should accelerate with temperature, we numerically analyzed the condition for the robust period in the two models. Unexpectedly, we found that geometrical mean of amplitudes should be larger at higher temperature to generate the robust period to temperature in both mammalian [2] and *Cyanobacterial* [3] models, suggesting that the mechanism for temperature compensation might be shared between mammals and *Cyanobacteria*. From the numerical results, we predict that amplitudes of state variables should be larger at higher temperature in temperature compensated systems.

To test the theoretical prediction, we measured expression of genes essential for mammalian daily rhythm at different temperature in mammalian cultured cells. We found that amplitudes of gene-expressions tend to be larger at higher temperature in the cells, consistent with the prediction. Moreover, we re-visited the time-series of yeast respiration rhythms [4] whose 4hr period is also temperature compensated. We confirmed that amplitude of the respiration rhythm increases with temperature.

By combining computational modeling and quantitative experiments in mammalian cultured cells, we conclude that amplitudes of oscillations should be larger at higher temperature to generate the robust period to temperature. This study has been conducted in the collaboration with Atsuko Fujioka (Kindai), Satoshi Koinuma (Kindai), Tu Benjamin (UT Southwestern), Atsushi Mochizuki (RIKEN), and Yasufumi Shigeyoshi (Kindai).

REFERENCES

[1] Nakajima, M., Imai, K., Ito, H., Nishiwaki, T., Murayama, Y., Iwasaki, H., Oyama, T., and Kondo, T., 2005 Reconstitution of circadian oscillation of cyanobacterial KaiC phosphorylation in vitro. *Science*, **308**: 414.
[2] Kim, J.K. and Forger, D.B., 2012 A mechanism for robust circadian timekeeping via stoichiometric balance. *Molecular Systems Biology,* **8**: 630.
[3] Kurosawa, G., Aihara, K., and Iwasa, Y., 2006 A model for the circadian rhythm of cyanobacteria that maintains oscillation without gene expression. *Biophysical Journal*, **91**: 2015.
[4] Chen, Z. and McKnight, S.L., 2007 A conserved DNA damage response pathway responsible for coupling the cell division cycle to the circadian and metabolic cycles. *Cell Cycle*, **6**, 2906.

Koichiro Uriu
Graduate School of Natural Science and Technology, Kanazawa University, Kanazawa, Japan
e-mail: `uriu@staff.kanazawa-u.ac.jp`

Tei Hajime
Graduate School of Natural Science and Technology, Kanazawa University, Kanazawa, Japan

Genetic Oscillations by Positive and Negative Feedback Loops Interlocked at Competitive Binding Sites

Positive and negative feedback loops are often present in regulatory networks for genetic oscillations. Motivated by the mammalian circadian clock and synthetic genetic oscillators, we study genetic oscillations caused by positive and negative feedback loops interlocked at competitive binding sites.

In the mammalian circadian clock, a key clock gene *Bmal1* is regulated by a repressor *Rev-erb* and an activator *Ror*. *Bmal1* activates both of them, forming interlocked feedback loops. The activator and repressor compete for the same binding sites in the *Bmal1* promoter region. Moreover, their time scales and peak phases are predicted to be very close in the central clock tissue, intensifying competition. Thus, it remains unclear how the positive and negative feedback loops interlocked at competitive binding sites regulate oscillations of *Bmal1* expression. To address this question we develop a theoretical model describing the time evolution of these three components as a system of delay differential equations. We find an optimal ratio of dissociation constants of the activator and the repressor for the binding sites to enhance the amplitude of *Bmal1* oscillations. The optimal ratio allows them to switch occupancy in the binding sites over time. In addition, numerical simulations indicate that sharp switch like oscillation of the repressor and small amplitude oscillation of the activator are required for the amplification of *Bmal1* oscillation.

Secondly, it has been shown that interlocked positive and negative feedback loops can produce synthetic genetic oscillations even in the absence of long time delays in the negative feedback loop. To generate oscillation, however, the time scale of the activator needs to be faster than that of the repressor. Non-competitive binding sites for the activator and repressor have been used previously, but whether they are suitable to generate oscillations remains to be revealed. We show that competitive binding sites are more likely to generate oscillation than the non-competitive binding sites when the time scales of the activator and repressor are not well separated.

Taken together, our results suggest that the dynamics of the activator and repressor needs to be tightly linked with their binding sites for effective use of the interlocked positive and negative feedback loops for robust genetic oscillations.

Shingo Gibo
Theoretical Biology Laboratory, RIKEN
e-mail: `shingo.gibo@riken.jp`

Gen Kurosawa
Theoretical Biology Laboratory, RIKEN

Toward understanding the mechanism of the regulation for circadian clocks by RNA methylation

Methylation of mRNA stabilizes or destabilizes its mRNA. Considerable attention has been paid to regulation of RNA methylation because RNA methylation possibly links metabolic to gene regulatory systems. Recently, RNA methylation inhibition was found to elongate circadian period by as-yet-unidentified mechanism in vitro and in vivo [1]. Revealing this phenomenon helps understand the interaction between metabolic and gene regulatory systems. In this study, we theoretically investigate the mechanism of period-alteration by RNA methylation.

According to experimental results [1], a methylation inhibitor (DAA) stabilizes mRNAs of many (not all) circadian related genes. Thus, we analyzed a published realistic model for mammalian circadian clock [2] by incorporating the changes in kinetics under RNA methylation inhibitor. We estimated the changes in mRNA under a methylation inhibitor using experimental data, and confirmed that calculated circadian period should elongate under RNA methylation inhibitor, consistent with experimental data.

RNA methylation possibly changes other reaction rates in gene regulatory system. To predict which reaction processes can be activated by methylation, we analyzed period sensitivity of realistic model [2]. We found that when fast reaction rate elongates the circadian period, the inhibitor abundance tends to increase, possibly slowing down the transcription process.

To understand these results, we simplified the realistic model into 4 variables model, which keeps multiple protein modification processes. Using Fourier analysis [3, 4], we derived the exact period formula of our simplified model. The period formula states that fast reaction rate tends to shorten the period. It also states that fast reaction rate can lengthen period only when amplitudes of inhibitor changes. By using our simplified model, we can understand the result of realistic model. The present approach opens the way for understanding how variation in kinetics parameters changes oscillatory period.

REFERENCES

[1] Fustin, JM. Doi, M., Yamaguchi, Y., Hida, H., Nishimura, S., Yoshida, M., Isagawa, T., Morioka, MS., Kakeya, H., Manabe, I., and Okamura, H., 2013. RNA-Methylation-Dependent RNA Processing Controls the Speed of the Circadian Clock. *Cell*, **155**: 793–806.

[2] Zhou, M., Kim, JK., Eng, GWL., Forger, DB., and Virshup, DM., 2015. A Period2 Phosphoswitch Regulates and Temperature Compensates Circadian Period. *Molecular Cell*, **60**: 77-88.

[3] Panter, PF., 1965. Modulation, Noise, and Spectral Analysis, Applied to Information Transmission (McGraw-Hill, New York) p viii.

[4] Forger, DB., 2011. Signal processing in cellular clocks, *PNAS*, **108**: 4281-4285.

Prabhat Shankar
Lab for Physical Biology, Riken QBiC, Kobe, Japan
e-mail: `pshankar@cdb.riken.jp`

Tatsuo Shibata
Lab for Physical Biology, Riken QBiC, Kobe, Japan

Hitoshi Niwa
Department of Pluripotent Stem Cell Biology, Kumamoto University, Kumamoto, Japan

Inference of Gene Regulatory from Experimental Data

Many important functions of a cell are governed by gene regulatory networks, where a set of genes activate of repress the functions of other genes, working in synchrony to regulate some function. Recent developments in experimental methods have enabled collection of gene expression profile data from a number of gene simultaneously. But the gene expression data by itself is not sufficient to uncover the regulatory principles, and need the help of mathematical models and analysis for deeper insight. Such a network model leads into understanding of the regulatory principles underlying the function. Number of approaches have been proposed in this direction recently [1]. In this work, we present an algorithm to infer a gene regulatory network in terms of a deterministic Boolean Network, obtained from a stationary gene expression data. This algorithm is based on the principle of consistency, that is, identical inputs must have identical outputs. Using time evolution, the number of candidate networks satisfying the gene expression data can further be reduced.

Using our algorithm, we analyzed a set of gene expression data obtained from the mouse pluripotent ES cells, and inferred the regulatory interactions underlying beneath. The approach uncovered hitherto unknown interactions. We hope our simple and intuitive approach can be applied to many other cellular systems as well.

REFERENCES

[1] Dunn, S-J., et al. Defining an essential transcription factor program for naive pluripotency. *Science* 344.6188 (2014): 1156-1160.

Hisashi Ohtsuki
SOKENDAI, Hayama, Japan
e-mail: `ohtsuki_hisashi@soken.ac.jp`

Kalle Parvinen
University of Turku, Turku, Finland
IIASA, Laxenburg, Austria

Joe Yuichiro Wakano
Meiji University, Tokyo, Japan

Does spatiality hinder evolutionary branching?

Convergent stable evolutionarily singular points are classified into two types. One is an evolutionarily stable point where no mutants can invade. The other is an evolutionary branching point where nearby mutants can invade and thus the population splits into two morphs. A recent study has shown a general condition for evolutionary branching in a spatially structured population in terms of fitness derivatives[1], yet it was too general to obtain insights into practical questions, such as “whether spatiality hinders evolutionary branching” or “whether there exists a case where spatiality promotes evolutionary branching”.

In this study, we have adopted Wright’s island model with non-overlapping generations as our model framework and studied fecundity selection there. In particular, we have assumed that social interactions within an island affect one’s fecundity, f. We have then derived conditions for evolutionary branching in terms of first-order and second-order fecundity derivatives, as well as of island size, migration rate, and the survival probability in migration.

Our results show that evolutionary branching is always hindered when either the migration rate or the survival probability in migration is close to zero. We also provide two simple necessary conditions for the inhibition of evolutionary branching by spatial structure. These results are consistent with the previous finding that evolutionary branching is hindered in a deme-structured population[2]. We can construct, however, a 3-person game example where evolutionary branching does not occur in a well-mixed population but it does in Wright’s island model with an intermediate migration rate. Overall, our results help us intuitively understand the effect of spatial structure on conditions for evolutionary branching.

REFERENCES

[1] Ajar, É., 2003. Analysis of disruptive selection in subdivided populations. *BMC Evol. Biol.*, **3(22)**: 1–12.
[2] Wakano, J.Y., Lehmann, L., 2014. Evolutionary branching in deme-structured populations. *J. Theor. Biol.*, **351**: 83–95.

Ryo Yamaguchi
Department of Biology, Kyushu University
e-mail: `ryamaguchi@bio-math10.biology.kyushu-u.ac.jp`

Yoh Iwasa
Department of Biology, Kyushu University

A tipping point in speciation with gene flow

More than two loci are involved in reproductive isolation in most cases of putative recent speciation. We study the speciation between two geographically isolated populations connected by infrequent migration, in which incompatibility is controlled by quantitative loci. Incompatibility genetic distance is defined as the fraction of compatibility controlling loci different between individuals. Complete reproductive isolation is established when the distance reaches a threshold level in spite of occasional migration and subsequent hybridization that reduce it.

Here we study how the time to speciation depends on the manner the magnitude of incompatibility increases with the genetic distance. Both the increases of the genetic distance due to the accumulation of separate mutations and the decrease due to rare migration and subsequent hybridization include stochasticity.

Results are: (1) The time to speciation is short if the migration rate is smaller than the mutation rate, or if intermediate levels of genetic distance cause mild incompatibility, making migrants less effective in reducing genetic distance. (2) Genetic distance may fluctuate around a positive quasi- equilibrium level for a long time, and suddenly show a quick passage to speciation when it goes beyond a “tipping point.” (3) Speciation becomes very slow if incompatibility is effective for individuals differing only one locus. These findings provide testable predictions that reproductive traits controlled by specific incompatibility accumulation forms can facilitate the speciation process.

REFERENCES

[1] Yamaguchi, R. and Y. Iwasa. 2013. First passage time to allopatric speciation. A contribution to a special issue of ‘Modelling biological evolution: recent progress, current challenges and future direction" Interface Focus 2013 **3**, 20130026. **doi:** 10.1098/rsfs.2013.0026
[2] Yamaguchi, R. and Y. Iwasa. Smallness of the number of incompatibility loci can facilitate parapatric speciation. Journal of Theoretical Biology (in press)

Yuma Sakai

Norio Yamamura
Culture and Information Science, Doshisha University, Kyoto, Japan
e-mail: `nyamamur@mail.doshisha.ac.jp`

Population Dynamics and Optimal Management of 4 Species (Grass, Shrub, Sheep and Goat) in Nomadism

It is an urgent subject to make rich life of people without deterioration of environment. I describe population dynamics of grass, shrub, sheep and goat in nomadism, and examine the optimal selling rates of sheep and goat in order to attain a high economical gain with a rich biomass of grass.

In the dynamics, grass and shrub grow as Logistic equations that are grazed by sheep and goat, and human sell animals at constant rates with proportion of their biomass. Assuming parameter conditions that sheep prefer grass and goats prefer shrub [1], only one equilibrium among the following six equilibria is globally stable, depending on values of two selling rates: (1) four species, (2) three species other than goat, (3) three species other than sheep, (4) sheep and shrub, (5) goat and grass, and (6) grass and shrub. Indirect effects are observed such that raising sheep selling rate induces reduction of grass through increase in shrub and goat, although direct effect should increase grass.

On the stable equilibria, I obtained optimal selling rates by environmentally-optimized model, economically-optimized model, and both-optimized model. In the environmentally-optimized model, high selling rates without no animals give an optimum as I maximized the sum of grass and shrub biomass. In the economically-optimized model, intermediate selling rates give an optimum where four species coexist when prices of sheep and goat per biomass do not much differ as I maximized selling proceed. In the both-optimized model, higher selling rates with less animals give an optimum than in the economically-maximized model as I maximized the sum of selling proceed and plant biomass. Finally, I examined how the optimal solution changes corresponding to changes in environmental awareness, trend of economy, and global climate.

REFERENCES

[1] Fujita, N., Amarrtuvshin, N. and Ariunbold, E., 2013. Vegetation interaction for the better understanding of a Mongolian ecosystem network. In: The Mongolian ecosystem network (Yamamura, N., Fujita, N. and Maekawa, A. eds.), Springer, pp.157-184.

Shigeo YACHI
Center for Ecological Research, Kyoto University
e-mail: `yachi@ecology.kyoto-u.ac.jp`

Dynamics of community-based ecosystem management: the role of context-dependent ecosystem services

In this paper, I present a dynamic model of a community-based ecosystem restoration process catalyzed via ecosystem services which stakeholders of the community can evaluate in their own contexts of interests. It has long been worried that biodiversity and ecosystem services on earth have been degraded intensively by human activities. IPBES (Intergovernmental Panel on Biodiversity and Ecosystem Services), for example, has started to improve this situation by promoting collaborative framework between researchers and diverse stakeholders including governments, local governments, enterprises, NGOs and communities through publishing scientific assessment reports on biodiversity and ecosystem services, and developing tools for communication and capacity building between stakeholders such as models and scenarios.

Among the difficulties to overcome between stakeholders in large-scale management issues is the mismatch with the pressing issues of the concerned stakeholders. In the context of ecosystem restoration, management at the watershed scale is regarded as effective; however, as the management scale becomes larger, the diversity of stakeholders increases and so the mismatch on what is the pressing issue. One of the representative mismatches of urgent issues typically observed in local communities in Japan expresses as ecosystem restorations at the watershed scale vs. restoration or revitalization of communities of smaller scales in the watershed, which are to be driven to extinction by depopulation and aging. Ecosystem restoration would fail if there is keen mismatch with the pressing issue of the concerned stakeholders. Here, community-based ecosystem management which focuses on the role of ecosystem services evaluated in the stakeholders' context is suggested as a candidate to resolve this mismatch (K. WAKITA). The essential mechanism lies in the emergence of multiple functions or multiple services of an ecosystem which can work as effective services in the context of community restoration as the ecosystem restoration proceeds.

A dynamic model was constructed to evaluate the role of community-context dependent ecosystem services, by introducing supply of multiple ecosystem services evaluated in the context of ecosystem restoration context and community restoration context. Frequencies of multiple preferences of stakeholders corresponding to ecosystem services, too, are formulated as variables which changes dynamically as ecosystem restoration proceeds and, in turn, affect the improvement of ecosystem restoration. By combining these two kinds of variables, an ecosystem restoration process is formulated. I will report under what conditions community-based ecosystem restoration would overcome the mismatch of issues between stakeholders.

Yuki Kubo
Graduate School of Sistems Life Sciences, Kyushu University
e-mail: `yukikubo@kyudai.jp`

Joung-Hun Lee
Institute of Decision Science for Sustainable Society, Kyushu University

Takahiro Fujiwara
Institute of Decision Science for Sustainable Society, Kyushu University

Yoh Iwasa
Department of Biology, Faculty of Science, Kyushu University

Management of tropical forests with agroforestry and profit sharing

Illegal logging is a very serious problem for plantation management in tropics [1]. Here we study the profit-sharing and agroforestry as management strategies [2-4].

Owner chooses the age of trees to cut, and the workers choose their monitoring effort to prevent illegal logging.

We derived two recursive formulas for the values of a site with trees of age t to the owner and to the workers. After the trees were removed, either by cutting, physical disturbances, or illegal logging, the owner hires workers to replant young trees. While trees are young, the land is also used as agriculture. In addition, the owner may share a fraction of profit obtained by selling logs with the workers. Illegal logging may be prevented by hiring forest guards or by monitoring effort of the workers.

Results are: (1) As the fixed cost of harvesting increases, the foresters delay the tree harvesting age. (2) If the discount rate is high, the foresters may use the land for continual agriculture by cutting trees at their young ages. (3) Under the presence of illegal logging pressure, the owner may find it profitable to share the income with the workers to solicit their monitoring efforts. We discuss policy implications of these results.

REFERENCES

[1] Tacconi, L., 2012. Illegal logging: law enforcement, livelihoods and the timber trade. Earthscan.
[2] Fujiwara, T., Awang, S.A., Widayanti, W.T., Septiana, R.M., Bariatul, H., Rahmat, M., Suyanto, A. and Sato, N., 2011. Overcoming vulnerability of privately owned small-scale forest through collective management unit establishment: a case study of Gunung Kidul district, Yogyakarta in Indonesia. International Journal of Social Forestry, 4(2), pp.95-120.
[3] Nawir, A.A., Santoso, L. and Mudhofar, I., 2003. *Towards mutually-beneficial company-community partnerships in timber plantation: lessons learnt from Indonesia* (No. CIFOR Working Paper no. 26, pp. xvi-77p). CIFOR, Bogor, Indonesia.
[4] Peluso, N.L., 1992. Rich forests, poor people: Resource control and resistance in Java. Univ of California Press.

Mayuko Nakamaru
Department of Innovation Science, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo, 152-8552, Japan
e-mail: `nakamaru.m.aa@m.titech.ac.jp`

Hayato Shimura
Department of Value and Decision Science, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo, 152-8552, Japan

Yoko Kitakaji
Research Center for Future Design, Kochi University of Technology, Eikokuji Campus: 2-22 Eikokuji, Kochi City, Kochi 780-8515, Japan

Susumu Ohnuma
Department of Behavioral Science, Hokkaido University, North 10 West 7, Kita-ku, Sapporo, Hokkaido, 060-0810, Japan

The evolution of cooperation in the division of labor: Industrial waste illegal dumping as an example

Cooperation is a foundation of our society. The evolution of cooperation is an unsolved research topic and has been investigated from the viewpoint of not only evolution but also other research areas such as social sciences. We are on an equal footing and cooperation among peers is essential in some social situations. Many previous researches have focused on the evolution of cooperation among peers. While, we are on a different footing, different players play different social roles such as leaders and subordinates in a group and hierarchy in some organizations, and then players playing different social roles cooperate to achieve their goal. In this talk, we focus on cooperation in the division of labor.

The industrial waste treatment process is an example of the division of labor and consists of five types of industry: generators (or W_1), the 1st waste haulers (or W_2), the intermediate treatment facilities (or W_3), the 2nd waste haulers (or W_4) and the landfill sites (or W_5) [1]. The player of W_i can choose two strategies: legal treatment or illegal dumping ($i = 1-5$). In legal treatment, the player of W_i pays a cost to have the player of W_{i+1} treat the waste ($i = 1-4$). In illegal dumping, the player of W_i does not pay any cost ($i = 1-5$). However, the illegal dumping damages the environment, and all players suffer from the damage or have to pay for the environmental restoration. This situation is equivalent to social dilemma and the studies about the evolution of cooperation can be applied into this situation. The previous studies about the evolution of cooperation show that cooperators punishing defectors promotes the evolution of cooperation. In reality, the administrative organ introduces two punishment systems to solve the illegal dumping problem: the actor responsibility system and the producer responsibility system. In the actor responsibility system, if players who choose illegal dumping are discovered, they are penalized a fine. However, it is hard to discover those who choose illegal dumping, and this system may not work. While, in the producer responsibility system, the generator is penalized a fine if the generator cannot hand the manifest to the local administrative organ as the players of W_i ($i = 1-5$) who choose illegal dumping do not hand the manifest to the generator. We investigate whether the producer responsibility system can restrain the illegal dumping more than the actor responsibility system.

We analyzed the replicator dynamics when (i) there are two types of industry, generators and the landfill sites, and (ii) there are three types of industry, generators, intermediate treatment facilities, and landfill sites. Then we found that (1) the three-industry model explains the present situation of illegal dumping more than the two-industry model, and (2) both the actor responsibility system and the producer responsibility system promote the evolution of cooperation in the division of labor more than the system without penalty. While, the actor responsibility system promotes the evolution of illegal dumping more than the producer responsibility system.

REFERENCES

[1] Kitakaji, Y. and Ohnuma, S., 2014, Demonstrating that monitoring and punishing increase non-cooperative behavior in a social dilemma game. The Japanese Journal of Psychology, **85**:9-19. (In Japanese)

Akira Sasaki
Department of Evolutionary Studies of Biosystems, The Graduate University for Advanced Studies, Hayama, Kanagawa, 240-0193, JAPAN
e-mail: `sasaki_akira@soken.ac.jp`

A Bayesian updating model for the antigenic escapes of influenza virus subtypes

Human influenza viruses are known to escape continuously from host immune defense by accumulating mutations on hemagglutinin. A recent multivariate statistic technique has extracted their surprisingly simple evolutionary trajectories on a low dimensional projected trait spaces. Here I propose a simple Bayesian update model to reproduce such evolutionary trends.

The antigen space is assumed to be two dimensional. The evolutionary dynamics is made up of the series of the following 3 processes in each year: (1) an epidemic of a particular strain, (2) the change in fitness landscape (the probability that a mutant can establish itself in host population) on antigen space according to the buildup of herd immunity against the epidemic strain, (3) a mutant that will cause epidemic in the next year is chosen randomly according the its probability of being generated by the parental strain, multiplied by its fitness determined by the past past infection history in the host population.

This model generates nearly linear trends in the series of epidemic strains placed on antigen space with a randomly chosen direction. The angles made by consecutive axes of annual antigenic changes are narrowly distributed around 0, and the distance between epidemic strains has a peaky distribution around the characteristic width of cross-immunity. An extension that allows more than two epidemic strains sampled in each year, and its relation to occasional turns in trajectories are discussed.

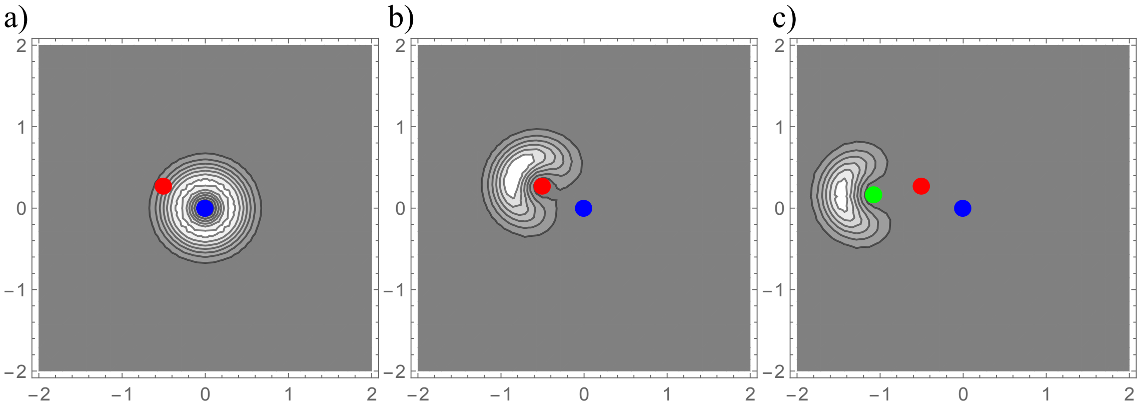


Figure 1. The time sequence of epidemic strains on two-dimensional antigen space. a) The epidemic strain in year *t* (blue point) newly introduced in host population, and the likelihood for the position of the next epidemic strain (contours -- the lighter the gray scale, the greater the probability is). Red point is the strain actually sampled with this probability distribution. b) The likelihood after two epidemic strains (blue in year *t*, and red in year *t*+1) has a skewed, hammer-head like landscape. c) The chosen epidemic strain of the year *t*+2 (green point) and the likelihood for the year *t*+3.

Kazunori Sato
Shizuoka University
e-mail: `sato@sys.eng.shizuoka.ac.jp`

Lattice model of foot-and-mouth disease revisited

Ringa and Bauch (2014)[1] analyze the lattice model of foot-and-mouth disease (FMD), in which farm-to-farm disease spatially transmits, using pair approximation. Their SEIRV (susceptible-exposed-infectious-recovered-vaccinated) model includes both ring and prophylactic vaccinations, and they consider the effects of these vaccinations depending on duration of vaccine immunity and disease re-introduction rate. Then they clarify the differences in dynamics between FMD-free countries and FMD-endemic ones, and argue the necessity of these kinds of mathematical models to examine the case of FMD-endemic countries.

Generally speaking in epidemics, the basic reproduction number R_0 is a key estimator by which we can expect whether the disease outbreak occurs or not. We can find several previous studies of R_0 for some infectious disease models on lattice space (e.g. Bauch 2005[2]; Keeling 1999[3] Trapman 2007[4]) and then we should carefully choose the method of calculation to estimate the value of R_0. Ringa and Bauch (2014)[1] obtained R_0 for their FMD model based on the procedure by Bauch (2005)[2]. Even for the case without both ring and prophylactic vaccinations, the parameter dependence of their R_0 much differs from R_0 by corresponding completely mixing model (or no spatial-structured model). Then I will examine the reason why that difference takes place. In addition I would like to compare R_0 by usual approach with their R_0 and consider the effect of spatial structure of the model on R_0. Finally, I will propose an appropriate R_0 for the modeling of FMD.

REFERENCES

[1] Ringa, N. and Bauch, C.T., 2014. Dynamics and control of foot-and-mouth disease in endemic countries: A pair approximation model. *Journal of Theoretical Biology*, **357**: 150–159.
[2] Bauch, C.T., 2005. The spread of infectious diseases in spatially structured populations: an invasory pair approximation. *Mathematical Biosciences*, **198**: 217–237.
[3] Keeling, M.J., 1999. The effects of local spatial structure on epidemiological invasions. *Proceedings of the Royal Society* B, **266**: 859-867.
[4] Trapman, P., 2007. Reproduction numbers for epidemics on networks using pair approximation. *Mathematical Biosciences*, **210**: 464–489.

Noriyuki Suzuki
College of Science and Engineering, Aoyama Gakuin University, Kanagawa 252-5258, Japan.
e-mail: `c5616003@aoyama.jp`

Shinji Nakaoka
Graduate School of Medicine, The University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 133-0033, Japan.
e-mail: `shinzy.nakaoka@gmail.com`

Yasuhiro Takeuchi
College of Science and Engineering, Aoyama Gakuin University, Kanagawa 252-5258, Japan.
e-mail: `takeuchi@gem.aoyama.ac.jp`

HIV infection dynamics with pyroptosis of target cells

In ethical reasons, it is impossible to perform experimental operations to humans when a person is infected with human immune-deficient virus (HIV). In such a situation, mathematical modeling and simulation is powerful and useful approach to investigate mechanisms underlying the cause of disease. In [1], it is reported that pyroptosis may play a promoting role in HIV infection cycle, leading to a vicious cycle in HIV infection. Although pyroptosis is a type of cell death which induce secretion of pro-inflammatory cytokines such as IL1-beta to inform immune cells to be recruited and initiate pro-inflammatory response, recruitment of CD4 positive T cells via pytoptosis is suggested to be important in HIV infection. In order to take into account for the effect of cell recruitment via pyroptosis, we construct a mathematical model for HIV infection which describes cell recruitment and HIV infection. A simplified one-dimensional mathematical model is derived from our original model to understand clearly how pyroptosis mediates HIV infection. In our mathematical analysis, typical time scale to develop to acquire immune-deficiency (AIDS), defined as the declined CD4 positive T cell counts below 200 per micro-liter, can be explained by our simplified mathematical model.

REFERENCES

[1] Gilad Doitsh *et al*, Cell death by pyroptosis drives CD4 T-cell depletion in HIV-1 infection, Nature **505**, 509–514.

Tsuyoshi Mizuguchi
Department of Mathematical Sciences, Osaka Prefecture University, Sakai, Osaka, Japan
e-mail: `gutchi@ms.osakafu-u.ac.jp`

Makoto Yomosa
Department of Mathematical Sciences, Osaka Prefecture University, Sakai, Osaka, Japan

Yoshinori Hayakawa
Center for Information Technology in Education, Tohoku University, Sendai, Miyagi, Japan

Gábor Vásárhelyi
Department of Biological Physics, Eötvös Univeristy, Budapest, Hungary

Máté Nagy
Department of Collective Behaviour, Max Planck Institute for Ornithology, Konstantz, Germany

Spatial and temporal structure of flying bird flocks

Collective behavior of animals such as flock of birds, school of fish, swarm of insects and crowds of humans fascinate people for a long time. There are rather “regular” behaviors such as V-shape formed by larger birds while the swarm of insects seems to be irregular. One key concept to characterize these regularities is their relative positions with respect to their moving direction, which are important to describe the internal structure of the flock[1].

The development of measurement devices makes it possible to extract three-dimensional position data of distant objects like flying birds. And collective motions of birds in flocks are studied based on real data using these devices such as GPS or digital camera[2-5]. We focus on flocks of hooded gull (*Larus ridibundus*) which fly around and along Yamatogawa River in Osaka, Japan[6]. Behaviors of birds in flocks are analyzed with time series of their velocities and relative positions, which are three-dimensionally reconstructed from pictures taken by a portable stereo camera system. We define "bird coordinates" based on the averaged motion of each individual. The distribution of lateral component of relative position has two peaks around zero, which suggests that individuals avoid the position just behind others by an interaction between them. The time series of oscillating velocity component caused by a flapping motion are also analyzed.

Analysis of pigeon flocks obtained by GPS system is also introduced[7]. By focusing on the free flight state their internal structure of the flocks are analyzed and are compared with those of hooded gull flocks.

REFERENCES

[1] Bajec, I. L. & Heppner, F. H., 2009. Organized flight in birds. *Animal Behaviour*, **78**: 777-789.
[2] Ballerini, M., et al., 2008. Interaction ruling animal collective behavior depends on topological rather than metric distance: Evidence from a field study. *PNAS*, **105**:1232-1237.
[3] Nagy, M., et al, 2010. Hierarchical group dynamics in pigeon flocks. *Nature*, **464**: 890-894.
[4] Portugal, S. J., et al. 2014. Upswash exploitation and downwash avoidance by flap phasing in ibis formation flight. *Nature*, **505**: 399-404.
[5] Hayakawa, Y., 2010. Spatiotemporal dynamics of skeins of wild geese. *Europhysics Letters*, **89**:48004.
[6] Yomosa, M., Mizuguchi, T. and Hayakawa, Y., 2013. Spatio-temporal structure of hooded gull flocks. *PLoS ONE*, **8**: e81754.
[7] Yomosa, M., et al., 2015. Coordinated behavior in pigeon flocks. *PLoS ONE*, **10**: e0140558.

Yumino Hayase
Hiroshima Universit
e-mail: `yumino@hiroshima-u.ac.jp`

Shota Fujii
Hiroshima University

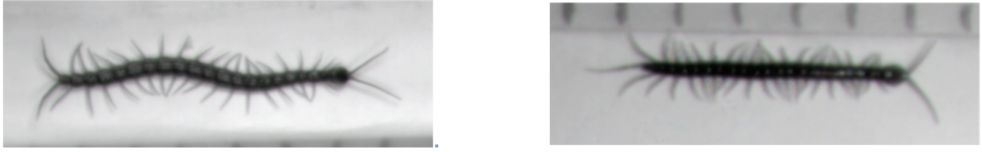
Ryo Kobayashi
Hiroshima University

An active undulation of centipede locomotion

A centipede can move very fast with a velocity more than 200mm/s although his body length is only a few centimeters. It is obvious that a centipede does not control each leg independently, but a central control rule of legs is still unknown. From observations of centipedes, we found that some species use its body undulation and others do not. For example, we compare centipede “Scolopendra subspinipes mutilans”(Fig. a) with centipede “Scolopcryptos rubiginosus”(Fig, b). Both belong to the same order “Scolopendramorpha” and their physical sizes are almost the same. “Scolopendra subspinipes mutilans” uses the body undulation, but “Scolopcryptos rubiginosus” does not. The difference is not only the body undulation, but also the locomotory wave. At a low velocity of about 30mm/s, both take on the retrograde wave. At a high velocity, while “Scolopendra subspinipes mutilans” takes still the retrograde wave, “Scolopcryptos rubiginosus” changes the locomotory wave to direct wave. From this observation, we assume that “Scolopendra subspinipes mutilans” converts a transversal oscillation into a longitudinal motion.

We propose a simple mathematical model with an active body undulation. We discuss the relation between the body undulation and the wave direction. The efficiency of the locomotion with/without undulation is also discussed.

Figure



(a) Scolopendra subspinipes mutilans

(b) Scolopendra subspinipes multians

Nariya Uchida
Department of Physcis, Tohoku University
e-mail: `uchida@cmpt.phys.tohoku.ac.jp`

Collective dynamics of bacteria at interfaces

Collective dynamics of swimming bacteria attached to solid walls are investigated by numerical simulations. A monolayer of bacteria (bacteria carpet) exhibits collective reorientation as the flagellar activity is tuned by sodium concentration, which resembles a second-order phase transition [1,2]. We propose a simple model incorporating the three-dimensional rotational degrees of freedom of the flagella, hook elasticity, and hydrodynamic interaction between flagella. Densely packed bacteria chains exhibit collective waving due to steric repulsion. The waving behavior is reproduced by a model based on semi-flexible and self-propelling chains with excluded volume interaction.

REFERENCES

[1] Y.-T. Hsiao, J.-H. Wang, K.-T. Wu, J. Tsai, C.-H. Chang, and W.-Y. Woon, 2014. Collective flow dynamics across a bacterial carpet: Understanding the forces. *Appl. Phys. Lett.*, 105: 203702-1–203702-5. [2] Y.-T. Hsiao, K.-T. Wu, N. Uchida, and W.-Y. Woon, 2016. Impurity-tuned non-equilibrium phase transition in a bacterial carpet. *Appl. Phys. Lett.*, 108: 183701-1–183701-5.

Takahiro Kamioka
Department of Biology, Faculty of Science, Kyushu University
e-mail: `t.kamioka.530@gmail.com`

Yoh Iwasa
Department of Biology, Faculty of Science, Kyushu University

Evolution of density dependence and juvenile hormone regulation in wing polymorphic insects

The wing-polymorphic insects show two wing types within species. The experienced density affects the wing determination [1]. Physiologically, the level of juvenile hormone is responsible in this process [1]. However, the action of the density is different among species or local population [1,2,3]. To observe the factor of this various result, we studied the evolution of density-dependent dispersal and juvenile hormone (JH) regulation in wing-polymorphic insects.

The population dynamics is shown in Fig. 1. Assumptions are: An asexual species with larval and adult stages live in many patches. Larval growth rate depends on the amount of renewable resources within a patch, which are consumed by the larvae. Dispersal type adults migrate out of the natal patch just before reproductive stage; which reproductive type adults in contrast have a large fertility but no dispersal ability. The fraction of dispersal type may change with the density experienced in larval stages. Genotypes differ in the way in which the fraction of dispersal type responds to the density experienced in the larval stages. The carrying capacity of the resources fluctuates between high and low values.

Density-dependent dispersal evolved if the environmental fluctuation was large. Some dispersal type adults were produced if the density was above a threshold, with the rate increases with the density. In contrast, no dispersal type appeared if the environmental fluctuation was small.

The rate of production of dispersal type increased with the density more rapidly in more severely fluctuating environment. The growth rate of larva and the recovery of resource also affect the production of dispersal type at high density.

We also examined the evolution in a situation in which the JH level to produce has a fixed variance and the mean responding to the density experienced by the larvae, in which wing type is determined by whether the JH level is higher than a threshold (Fig. 2). In more severely fluctuating environment, the density-dependent degradation of JH evolved to be faster and the variance of JH level evolved to be smaller, both leading to an enhanced fraction of dispersal type adults.

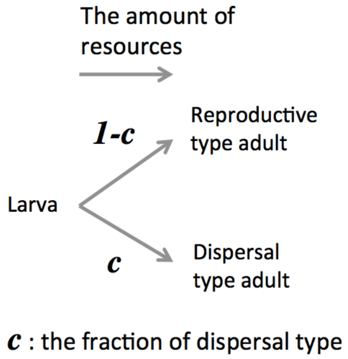


Fig. 1 Scheme of the model

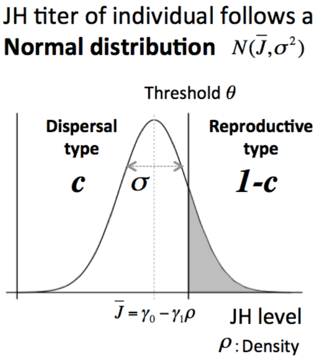


Fig. 2 Wing determination by JH

REFERENCES

[1] Zera and Denno, 1997. *Annual review of entomology*, **42**: 207–230.
[2] Iwanaga and Tojo, 1985. *Entomologia experimentalis et applicata*, **38**: 101–108.
[3] Denno, 1991. *The American Naturalist*, **138**: 1513–1541.

Masato S. Abe
National Institute of Informatics, JST ERATO Kawarabayashi Large Graph Project, Tokyo, Japan
e-mail: `masatoabee@gmail.com`

Shin-ichiro Nakayama
National Research Institute of Fisheries Science, Kanagawa, Japan

Haruna Fujioka
Graduate School of Arts and Sciences, The University of Tokyo, Tokyo, Japan

Masakazu Shimada
Graduate School of Arts and Sciences, The University of Tokyo, Tokyo, Japan

Detecting interaction patterns in ant society by cross-embedding method

Collective behavior is ubiquitous in living systems ranging from cells to animal groups, and can lead to rapid and accurate responses to environments or efficient division of labor at group level. Especially, it has shown that social insects such as ants and bees often exhibit sophisticated collective behavior including searching foods through pheromone trails, quorum sensing, and so on. Although it is crucial to understand how collective behavior in social insects can emerge from interactions between individuals, it is less understood due to difficulty in obtaining and analyzing data. Here, to investigate who influences whom and untangle collective dynamics, we automatically obtained the trajectory of movements in ant individuals (*Diacamma* sp.) by image analysis, and detected interactions and their strength between individuals using time-series analysis based on state space reconstruction and cross-embedding [1, 2]. We show that the interaction patterns driving collective dynamics depends on the behavioral castes (i.e., nurses and foragers), and discuss how the collective dynamics emerges from interactions in ant society.

REFERENCES

[1] Sugihara, G., May, R., Ye, H., Hsieh, C. H., Deyle, E., Fogarty, M., & Munch, S., 2012. Detecting causality in complex ecosystems. *Science*, **338**(6106), 496-500.

[2] Deyle, E. R., May, R. M., Munch, S. B., & Sugihara, G., 2016. Tracking and forecasting ecosystem interactions in real time. *Proc. R. Soc. B,* **283**, 20152258.

Wataru Nakahashi
SOKENDAI, Hayama, Japan
e-mail: `w.nakahashi@gmail.com`

Hisashi Ohtsuki
SOKENDAI, Hayama, Japan

Cost and benefit of emotional contagion in group-living animals

Many animals including humans show emotional contagion, the phenomenon that a strong emotion of an individual (demonstrator) triggers similar emotions and behaviors in other individuals (observers). This may cause consistent group behaviors of many animals. Although we have already investigated conditions for emotional contagion to be adaptive in a two-player (a demonstrator and an observer) situation [1], it remains unclear whether emotional contagion is adaptive in a large group. As group size increases, two probabilities may increase, the probability that someone recognizes a change in the situation to behave correctly (e.g., finds a predator to escape) and that someone misrecognizes the situation to behave wrongly. Therefore, we may suppose that individuals with emotional contagion may receive both cost and benefit from the increasing group size. Taking this into account, we theoretically study the effect of group size on the evolution of emotional contagion in group-living animals.

REFERENCES

[1] Nakahashi, W. and Ohtsuki, H., 2015. When is emotional contagion adaptive? *Journal of Theoretical Biology*, **380**: 480–488.

Emmi Schlicht
Peter Santema
Bart Kempenaers
Department of Behavioural Ecology and Evolutionary Genetics,
Max Planck Institute for Ornithology, Seewiesen, Germany

Robert Schlicht
Department of Forest Sciences,
Technische Universität Dresden, Tharandt, Germany
e-mail: `robert.schlicht@tu-dresden.de`

Evidence for conditional cooperation in biparental care systems?

In species with biparental care, the joint benefit from care by each parent makes it possible to free ride on the partner's investment. As an evolutionary solution to this conflict over care, Johnstone et al. [1] propose conditional cooperation, where parents show a tendency to take turns in feeding their young. Using a simple Markov process based model they show for data from a great tit (*Parus major*) population that parents indeed reduce their feeding rates after feeding and before the partner feeds next. Additionally, by randomizing intervisit times, they show that this effect is not merely due to the adoption of constant rates between feeding events.

We here argue [2] that fundamental assumptions of this model are violated in many biologically relevant settings, and that alternating feeding patterns result from many simple realistic processes. By slightly modifying the randomization, we demonstrate that patterns such as those observed occur without any form of conditional cooperation when feeding rates are affected by both time of absence and changing external conditions, as is biologically plausible. We therefore believe the conclusion of conditional cooperation is premature.

In this talk I first introduce the original model, then present our alternative randomization procedure and its conclusions, and finally discuss the response to our analysis by Johnstone et al. [3].

REFERENCES

[1] Johnstone, R.A., Manica, A., Fayet, A.L., Stoddard, M.C., Rodriguez-Gironés, M.A., Hinde, C.A., 2014. Reciprocity and conditional cooperation between great tit parents. *Behavioral Ecology*, **25**: 216–222.
[2] Schlicht, E., Santema, P., Schlicht, R., Kempenaers, B., 2016. Evidence for conditional cooperation in biparental care systems? A comment on Johnstone et al. *Behavioral Ecology*, **27**: e2–e5.
[3] Johnstone, R.A., Manica, A., Fayet, A.L., Stoddard, M.C., Rodriguez-Gironés, M.A., Hinde, C.A., 2016. Evidence for conditional cooperation: a response to Schlicht et al. *Behavioral Ecology*, **27**: e6–e7.

Shinsuke Satoi
Kyushu Univ.
e-mail: `ssatoi257n@gmail.com`

Yoh Iwasa
Kyushu Univ.

Theoretical study of chemical mimicking strategy in ants

Mimicry is widely observed strategy for avoiding attacks by other animals and preying on other animals efficiently. There is a strategy of mimicry simulating chemical trait and this strategy is called chemical mimicry. One typical example of chemical mimicry is parasites of ants. Their strategy is classified in two types: simulating host's chemical trait (mimic) and reducing the total amount of body chemicals (cryptic) [1]. Since newly emerged workers of ants lack chemicals, host ants cannot distinguish cryptic parasites from callow workers. Mimic parasites are more common than cryptic parasites.

Here, we report theoretical study for the evolution of mimicking strategies, especially focusing on the evolution of these two strategies. We consider multi-dimensional space indicating mixtures of chemicals. Assumptions: Ants of a nest accept an individual if its ratio of chemical traits is close to their own and if the absolute amount of chemical traits is smaller than their own. For any colony of a parasite, there exist conspecific colonies with similar chemical composition. We define the fitness of a parasite as a combination of the benefit of being accepted by the host and the risk of accepting those parasites from other colonies. Results: Crypsis is advantageous if the strength of intraspecific competition is week. Mimicry evolves if the recognition accuracy of host is high and the competition with other colonies is intense. We discuss the chemical strategies of ant parasites.

REFERENCE

[1] Kilner, R. M. and N. E. Langmore (2011). "Cuckoos versus hosts in insects and birds: adaptations, counter-adaptations and outcomes." Biol Rev Camb Philos Soc **86**(4): 836-852.

Makoto Douge
Kyushu University
e-mail: `makotodouge@gmail.com`

You Iwasa
Kyushu University

Advantage of sex due to sibling diversity in an environment fluctuating over space and time

Many hypotheses for the maintenance of sex have been presented after Maynard Smith proposed a concept of "two-fold cost of sex". However the general answer has not been found yet. There is a potent following idea. In an environment with intense sib-competition, phenotypic diversity among sexual siblings might favor sexual reproduction over asexual reproduction. Maynard Smith studied it by computer simulation called sib-competition model. From the simulation result he concluded that in a certain condition sexual had advantage. However if there was an environmental correlation the advantage disappeared.

We investigated the model and knew that the diversity of sexual was not reflected well. Then we revised the model in which the diversity was more reflected. In the revised model, the sexual had more advantage irrespective of there is an environmental correlation or not. Suppose, N is the number of siblings of a mother, the simplest idea is that the sexual has N-fold advantage and asexual has 2-fold advantage due to the 2-fold cost of sex. However the simulation showed more complicated result, not so simple, and we found some factors for the difference. However we could show that the relative fitness of sexual is basically $N/2$.

From the simulation result and analysis, we think that the sib-competition has important roll for the evolutionally maintenance of sex.

Daisuke Shikayama
Graduate School of Integrated Science and Technology Department of Engineering Mathematical and System Engineering course, Shizuoka University, Japan
e-mail: `tennsitann@gmail.com`

Kazunori Sato
Graduate School of Integrated Science and Technology Department of Engineering Mathematical and System Engineering course, Shizuoka University, Japan

Improvement of the overestimation for invasion speed in higher birth-rate population

Population invasion speed and critical birth-rate for successful invasion in lattice space are calculated by pair-edge approximation that estimate the wave front position by using pair approximation.[1] That approximation is imperfect in two-dimensional lattice space and gives the method of calculation by considering lattice space as height-3 stripes. We calculated invasion speed in higher lattice space applying the approximation and confirmed that both invasion speed and critical birth rate become farther from simulation value than 3-line calculation. In this research, we aim to improve the way of calculation and gain better approximation for critical value and invasion speed above it.

Ellner et al. (1998)[1] use Growing Phase Approximation (they assume that density of front is zero, GPA) and Look Both Ways approximation (they assume that density of front is half of internal density, LBW). However, their approximations strongly reply on a newly introduced parameter, which rather seems to be an artifact Then we consider all the possible states of front and use their occurrence probabilities for the invasion calculation. Using this method, in height-3 stripe lattice space, we got higher critical birth-rate than both GPA and LBW, so approximation got worse, but for the range above critical birth-rate, we got lower and better invasion speed than both GPA and LBW. In height-5 stripe lattice space, we got lower critical birth-rate than 3-line space and lower and worse invasion speed than GPA.

Considering all the possible states on the front, we can see that approximation value somewhat got worse, but this method of calculation enables us to gain invasion speed that has good approximation value without artificially assuming front shape as GPA or LBW.

REFERENCES

[1] Ellner, S.P., Sasaki, A., Haraguchi, Y. and Matsuda, H., 1998. Speed of invasion in lattice population models: pair-edge approximation. *J. Math. Biol*, **36**: 469–484.

Takuji Oba
Graduate School of Informatics, Kyoto University
e-mail: `takuji_oba@acs.i.kyoto-u.ac.jp`

Jun Kigami
Graduate School of Informatics, Kyoto University

When does invasion implies substitution?

Suppose that a monomorphic population, called the resident, with a trait A is in a stationary state under stable environment. When small number of mutants with a new trait B will emerge, plausible outcomes of the resulting competition are typically the following (a), (b) and (c):
(a) eventually the original resident will win the battle and the population will return monomorphic with the trait A,

(b) eventually the mutants will drive out the original resident and the population will become monomorphic with the trait B,

(c) original resident and the mutants will coexist with certain ratio, i.e. the population will become dimorphic with traits A and B.

Under a suitable mathematical model associated with adaptive dynamics(See [1] and [2] for example), we study general sufficient conditions for (a) and (b). More precisely we consider a model of competition of two traits and show sufficient conditions for (a) and (b). If our two traits' model is a restriction of a three traits' model, our result corresponds to the condition for “invasion implies substitution” proven by Dercole and Rinaldi[3]. On the other hand, in the case when the two traits' model is not derived from a three traits' model, we obtain a class of simple examples where the “invasion implies substitution” condition is satisfied but the situation (c) occurs, i.e. the population will become dimorphic with two different traits.

REFERENCES

[1] Metz, J.A.J., Geritz, S.A.H., Meszéna, G., Jacobs, F.J.A. and van Heerwaarden, J.S., 1996. Adaptive dynamics, a geometrical study of the consequences of nearly faithful reproduction. *IIASA Working Paper WP-95-099*, **1**: 183– 231.
[2] Geritz, S.A.H., Kisdi, E., Meszéna, G. and Metz, J.A.J., 1998. Evolutionarily singular strategies and the adaptive growth and branching of the evolutionary tree. *Evolutionary Ecology*, **12**: 35–57.
[3] Dercole, F. and Rinaldi, S., 2008. Analysis of evolutionary processes. Princeton Series in Theoretical and Computational Biology.

Shota Nishijima
National Research Institute of Fisheries Science
Yokohama, Japan
e-mail: `nishijimash@gmail.com`

Hiroyuki Matsuda
Yokohama National University
Yokohama, Japan

Eco-evolutionary dynamics of a plant-pollinator system under climate change

It is challenging but important to predict the impacts of climate change on organisms with consideration for species interactions and adaptive evolution. Pollination provides an ecosystem service, but climate change is one of the causes of the declines in pollinators such as bumblebees. A previous study has shown that a bumblebee population has shortened their tongue in order to adapt to resource scarcity due to climate change, causing functional mismatch between the pollinators and deep flowers [1]. However, the underlying mechanism and eco-evolutionary consequences of the plant-pollinator interaction remain poorly understood.

In this study, we develop and analyze a mathematical model to understand and predict eco-evolutionary dynamics of the plant-pollinator system under climate change. In the model, a bumblebee population consumes two prey items (deep and shallow flowers) according to optimal foraging theory. We assume that the length of bumblebee controls the handling times for these prey items and can evolve so as to increase the fitness of bumblebee. We also assume that foraging by the bumblebee elevates plant growth and climate change increases the mortality rates of plants with deep flowers.

As a result, the bumblebee shortens its tongue under moderate climate change and, thereby, becomes a generalist from a specialist to short flowers, because climate change decreases the resource availability of shallow flowers. This prediction is consistent with empirical observation [1]. Severe climate change makes the length of bumblebee's tongue further shorter, increasing shallow flower density. Therefore, the bumblebee can become specialist to shallow flowers, leading to sudden extinction of deep flowers because they do not ever receive benefit from the bumblebee pollinator. When the adaptive evolution is absent, such extinction does not occur, indicating adaptive dynamics increase extinction risk of plants in this pollinator system. However, the extinction can be avoided when shallow flowers are moderately sensitive to climate change, because shallow flowers are unlikely to increase. This suggests that a negative impact of climate change on a species can rescue another species through interspecific interactions and adaptive dynamics. To conserve deep flower species in this system, inhibiting pollinator evolution and population management of shallow flowers are important as adaptation strategy to climate change.

REFERENCES

[1] Miller-Struttmann, N. E., Geib, J. C. Franklin, J. D. Kevan, P. G. Holdo, R. M. Ebert-May, D. Lynn, A. M. Kettenbach, J. A. Hedrick, E. and Galen, C. 2015. Functional mismatch in a bumble bee pollination mutualism under climate change. *Science* **349**:1541–1544.

Mizuho Nagata
College of Science and Engineering, Aoyama Gakuin University, Kanagawa 252-5258, Japan.
e-mail: `minmi.unya@gmail.com`

Yasuhiro Takeuchi
College of Science and Engineering, Aoyama Gakuin University, Kanagawa 252-5258, Japan.
e-mail: `takeuchi@gem.aoyama.ac.jp`

Shinji Nakaoka
Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo 133-0033,Japan.
e-mail: `shinzy.nakaoka@gmail.com`

Mathematical model of T and NK cell therapy against cancer

Different types of immune response can be induced in response to cancer associated antigen expressed MHC class I molecules. While high expression level of MHC class I molecules on the surface of cancer cells are required to activate CD8 T cells, NK cells specifically detect a type of cancer cells expressing low level of MHC class I (missing-self hypothesis). To incorporate different expression levels of MHC class I molecules, we construct a mathematical model which describes dynamics of immune response against cancer by introducing two different types of cancer in terms of the expression level of MHC class I. Cancer is assumed to be classified to high or low MHC class I expression. Different types of immune responses (implicitly assumed CD8 T cells and NK cells) eliminate corresponding cancer phenotype. By stability analysis and numerical simulations of our mathematical model, a key parameter was found which covers major qualitatively different behaviors of cancer-immune dynamics. Biological implications derived from our mathematical analysis and numerical computation results will be discussed.

REFERENCES

[1] Mizuho Nagata, Yutaro Furuta, Yasuhiro Takeuchi, and Shinji Nakaoka, Dynamical behavior of combinational immune boost against tumor, *Japan Journal of Industrial and Applied Mathematics* 32 (2015) 759–770.
[2] Naoki Nakada, Mizuho Nagata, Yasuhiro Takeuchi and Shinji Nakaoka, Mathematical modeling and analysis of combinational immune boost for tumor elimination, *AIP Conference Proceedings* 1723 (2016) 020002.

Shoya Iwanami
Graduate School of Systems Life Sciences, Kyushu University, Fukuoka 819-0395, Japan
e-mail: `iwanamishoya@gmail.com`

Ryo Yamamoto
Institute for Stem Cell Biology and Regenerative Medicine, Stanford University, Stanford, CA 94305, USA

Shingo Iwami
Department of Biology, Faculty of Sciences, Kyushu University, Fukuoka 819-0395 Japan

Hiroshi Haeno
Department of Biology, Faculty of Sciences, Kyushu University, Fukuoka 819-0395 Japan

Mathematical model of hematopoietic system with myeloid-restricted progenitors with long-term repopulating activity

Hematopoietic system is maintained by hematopoietic stem cells (HSCs) with dual abilities of long-term self-renewal and differentiation to all types of blood cells. Recently, using a single-cell transplantation system and mice expressing a fluorescent protein, myeloid-restricted progenitors with long-term repopulating activity (MyRPs) were found. Moreover, by using paired daughter cell assay, MyRPs were directly differentiated from HSCs. Because of the non-step division from HSCs, myeloid cells were repopulated faster than lymphoid cells after transplantation.

In this study, we investigated hematopoietic system incorporating the novel insight that there existed a cell type that exclusively differentiated to myeloid lineages. There were five populations in the model: (i) long-term HSCs, (ii) short-term HSCs, (iii) MkRPs; one of MyRPs which are directly differentiated from LT-HSCs, (iv) myeloid cells, and (v) lymphoid cells. Myeloid cells were produced after transplantation of a single HSC via short-term HSCs or MkRPs, while lymphoid cells were produced via only short-term HSCs. This is the first study of investigating hematopoiesis with MkRPs. From the analysis of the model, we successfully reproduced the experimental observation that myeloid cells were repopulated faster than lymphoid cells after transplantation of a single HSC. Moreover, we estimated differentiation rates, self-renewal rates and death rates of all cell types that fitted the published data. Finally, MkRPs are important to reproduce platelets in emergency such as transplantaion.

REFERENCES

[1] Yamamoto, R., et al. 2013. Clonal analysis unveils self-renewing lineage-restricted progenitors generated directly from hematopoietic stem cells. *Cell* 154(5): 1112-1126.

Min Yu
College of Science and Engineering, Aoyama Gakuin University, Sagamihara 252-5258, Japan
e-mail: `yumin8618@gmail.com`

Yueping Dong[2], **Yasuhiro Takeuchi**[1]
Graduate school of Medicine, The University of Tokyo, Tokyo 113-0033, Japan 2
College of Science and Engineering, Aoyama Gakuin University, Sagamihara 252-5258, Japan 1

Dual role of delay effect in a tumor immune system

In this paper, a previous tumor immune interaction model is simplified by considering a relatively weak immune activation, which can still keep the essential dynamics properties. Since the immune activation process is not instantaneous, we incorporate one delay effect for the activation of the effector cells by helper T cells into the model. Furthermore, we investigate the stability and instability region of the tumor-presence equilibrium state of the delay-induced system with respect to two parameters, the activation rate of effector cells by helper T cells and the helper T cells stimulation rate by the presence of identified tumor antigens. We show the dual role of this delay that can induce stability switches exhibiting destabilization as well as stabilization of the tumor-presence equilibrium. Besides, our results show that the appropriate immune activation time plays a significant role in control of tumor growth.

REFERENCES

[1] J. Arciero, T. Jackson and D. Kirscher, 2004. A mathematical model of tumor-immune evasion and siRNA treatment. Discrete Contin. Dyn. Syst., Ser. B 4: 39–58.
[2] Y. Dong, H. Gang, R. Miyazaki and Y. Takeuchi, 2015. Dynamics in a tumor immune system with time delays, Appl. Math. Comput. 25: 99–113.

Sachi Yamaguchi
Department of Information Systems Creation, Kanagawa University
e-mail: `sachi.dwarfmale@gmail.com`

Time required for sex change in teleost fishes: hormonal dynamics shaped by selection

Sex change is observed in many species of teleost fishes. The evolution of sex change has been explained by size advantage hypothesis, which postulates that each individual chooses the more profitable sex given its body size and social condition. In haremic species, when the dominant (harem) male disappears, the largest female changes to male. When social condition changes, transition of sex takes for several days to a few months. In some species, the length of the time required for sex change is similar between two directions (male-to-female, and female-to-male); in other species, male-to-female transition takes clearly longer time than female-to-male transition. To understand the difference in the length of time for sex change in two directions, I propose a simple mathematical model for the hormone-enzyme dynamics. Aromatase (P450arom) catalyzes the synthesis of estradiol (female hormone) from testosterone (male hormone). I assume that the change of the social condition for the individual affects the rates of production and degradation of P450arom. I then consider the evolution of parameters in the dynamics. The optimal parameter values are those that minimize the total fitness cost, defined as the sum of the fitness losses by the delay as a functional male and as a functional female, and the cost for the acceleration of the degradation of P450arom in changing from female to male. The model predicts that, in haremic species, as the number of females in a harem increases, the sex changer promotes the faster degradation of P450arom, realizing a faster female-to-male transition than the transition in the opposite direction. In contrast, in monogamous species, or when the number of females is small, faster degradation of P450arom when changing to male is not beneficial, resulting in about equal length of the time for sex change in two different directions.

REFERENCES

[1] Yamaguchi, S., 2016. Time required for sex change in teleost fishes: hormonal dynamics shaped by selection. *Journal of Theoretical Biology* (in press).

Kouki Uchinomiya
RIKEN, iTHES
e-mail: kouki.uchinomiya@riken.jp

Modeling optimal resource allocation in plant-fungi mutualism

Mycorrhizal fungi colonize roots of terrestrial plant. The relationship of plant and fungi becomes mutualism by trading resource. The host plant produces carbohydrate by photosynthesis and allocates it to the fungi. The fungi can get soil nutrition more efficiently than plant. Mycorrhizal fungi supply soil nutrition to its host plant. In nature, one plant has many mycorrhizal fungi. Some studies show growth of plant is better when there are many mycorrhizal fungi (e.g. Gustafson and Casper, 2006). In this study, I discuss resource allocation when one plant has one fungus and one plant has multiple fungi.

I assume plant can get only carbon and fungi can get only phosphorus. Plant and fungi allocate acquired resource to the partner for maximizing their biomass at the end of mutualistic relationship. I express dynamics of carbon and phosphorus in plant and fungus by differential equations.

According to Pontryagin's maximum principle and conditions of singular control (Bryson&Ho, 1975), allocation fraction is affected by resource acquisition ability and resource allocation efficiency when there are only one plant and one fungus. In addition, when one plant has two fungi, total phosphorus supplied by fungi become larger than the case one plant has only one fungus. On the other hand, total carbon supply to the fungi decreases.

REFERENCES

[1] Gustafson, D. J., & Casper, B. B., 2006, Differential host plant performance as a function of soil arbuscular mycorrhizal fungal communities: experimentally manipulating co-occurring Glomus species. *Plant Ecology*, **183**(2), 257-263.
[2] Bryson, A. E., & Ho, Y., 1975, Applied optimal control: optimization, estimation and control. CRC Press

Ross D. Booton
University of Sheffield, UK
e-mail: `r.booton@sheffield.ac.uk`

Ryo Yamaguchi
Kyushu University

Yoh Iwasa
Kyushu University

The Role of Cannibalism in Determining Insect Voltinism Patterns

Pupa-eating cannibalism occurs naturally in several subfamilies of Lepidoptera. Within the subfamily Papilionidae, *Byasa alcinous* is a multivoltine species of Red-bodied Swallowtail butterfly found in East Asia which diapauses over the winter, and whose larvae cannibalise eggs and pupae. We investigate the effects on population dynamics of increasing the cannibalistic attack rate of *B. alcinous* larvae in changing environmental conditions. We do this by theoretically formulating the change in weight functions of a generalised system of univoltine and bivoltine larvae over two generations in the spring and summer months. We predict that a declining resource over summer can force the population to become entirely univoltine, unless the second generation bivoltine larvae increase their cannibalistic attack rate, and consume the diapausing pupae. The model shows that under extreme environmental conditions, the persistence of univoltine larvae is favoured when faced with the threat of extinction. The model also predicts conditions for coexistence of both univoltine and bivoltine larvae, and the degree to which they can both coexist, which decreases as the resource in the second generation increases. This work provides the grounding for future theoretical and experimental consideration on the role of cannibalism in the onset of diapause in a multivoltine insect setting.

Toru Osaki
Shizuoka University Graduate School at Science and Technology Graduate School, Hamamatsu City Nakaku Johoku 3-5-1,Japan
e-mail: `osaki311@icloud.com`

Kazunori Sato
Shizuoka University Graduate School at Science and Technology Graduate School, Hamamatsu City Nakaku Johoku 3-5-1,Japan

Spatial pattern and its stability formed by algal blooms

Algae, in order to protect themselves from predators, is known to have the morphological changes. The shape change is considered to be one of the most important protective strategies to avoid predation from grazing zooplankton. For example, algae aggregation makes herbivorous zooplankton difficult to predate.

The morphological changes between the colonial algae and unicellular algae depend the density of the herbivorous zooplankton . If the density of herbivorous zooplankton is low, change from the colonial algae to the unicellular algae occurs. On the other hand, if the density of herbivorous zooplankton is high, a large proportion of the changes to the colonial algae from unicellular algae is observed.

As pioneering researches, Vos et al. (2004)[2] and Serizawa et al. (2008)[1], which improved Vos et al. (2004)[2], are known.Furthermore, in the model including the diffusion into Serizawa et al. (2008)[1], it has been shown to produce a complex spatial pattern from around the unstable equilibrium point.

In this study, it focuses on the morphological change between the colonial algae and the unicellular algae, induced by predators of herbivorous zooplankton, to consider the spatial pattern and its stability, which is formed by the algae bloom. In particular, with respect to some of the models, including the previous researches, changing the parameters and initial conditions, we would like to consider what kind of spatial patterns to appear.

REFERENCES

[1]Serizawa et al , 2008. Mathematical modeling of colony formation in algal blooms:phenotypic plasticity in cyanobacteria. *Ecol Res***23**:841–850.
[2]Vos et al,2004.Inducible defences and the paradox of enrichment.*OIKOS***105**:471-480.

Hiroshi Ueno

Yoshihiro Morishita
Laboratory for Developmental Morphogeometry, RIKEN, Quantitative Biology Center, Japan
e-mail: `yoshihiro.morishita@riken.jp`

Ken-ichi Hironaka
Laboratory for Developmental Morphogeometry, RIKEN, Quantitative Biology Center, Japan
The Japan Society for the Promotion of Science, Japan

Sang-Woo Lee
Laboratory for Developmental Morphogeometry, RIKEN, Quantitative Biology Center, Japan

Takashi Jin
Laboratory for Nano-Bio Probes, RIKEN Quantitative Biology Center, Japan

Daisuke Ohtsuka
Laboratory for Developmental Morphogeometry, RIKEN, Quantitative Biology Center, Japan

Reconstructing 3D deformation dynamics for curved epithelial sheet morphogenesis from positional data of sparsely-labelled cells

Quantifying global tissue deformation patterns is essential for understanding how organ-specific morphology is generated during development and regeneration. However, due to imaging difficulties and complex morphology, little is known about deformation dynamics for most vertebrate organs such as the brain and heart. To better understand these dynamics, we propose a method to precisely reconstruct global deformation patterns for 3D morphogenesis of curved epithelial sheets using positional data from labeled cells representing only 1-10% of the entire tissue with limited resolution. By combining differential-geometrical and Bayesian frameworks, the method is applicable to any morphology described with arbitrary coordinates, and ensures the feasibility of analyzing many vertebrate organs. Application to data from chick optic vesicle formation demonstrated that our method provides not only a quantitative description of tissue deformation dynamics but also predictions of the mechanisms that determine organ-specific morphology, which could form the basis for the multi-scale understanding of organ morphogenesis.

REFERENCES

[1] Y. Morishita, K. Hironaka, S.-W. Lee, T. Jin, and D. Ohtsuka, “Reconstructing 3D deformation dynamics for curved epithelial sheet morphogenesis from positional data of sparsely-labelled cells” (under review)
[2] Morishita, Y. Kuroiwa, A. and Suzuki, T. "Quantitative analysis oftissue deformation dynamics reveals three characteristic growth modes and globally-aligned anisotropic tissue deformation during chick limb development", Development, 142: 1672-1683 (2015)
[3] Morishita, Y. and Suzuki, T. Bayesian inference of whole-organ deformation dynamics from limited space-time point data, Journal of Theoretical Biology, 357: 74-85,(2014)

Masashi Tachikawa

Takashi Okada
Theoretical Biology Laboratory, RIKEN, Wako 351-0198, Japan
e-mail: `takashi.okada@riken.jp`

Atsushi Mochizuki
Theoretical Biology Laboratory, RIKEN, Wako 351-0198, Japan
CREST, JST 4-1-8 Honcho, Kawaguchi 332-0012, Japan
e-mail: `mochi@riken.jp`

Law of Localization in Chemical Reaction Networks

In living cells, many biochemical reactions connect to one another and form complex networks, like the carbon metabolism pathway. One experimental approach to study such network systems is sensitivity analysis where the amount or activity of the enzymes is perturbed and responses (concentrations of chemicals and fluxes) are measured. However, due to the complexity of the systems, it has been unclear how the network structures influence the responses of the systems. In this study, we introduce a mathematical method, named structural sensitivity analysis, to determine responses of chemical reaction systems to the perturbation of the enzyme amount/activity based only on information of network topology. We found that (1) qualitative responses at steady state are determined from network structure only. We also found that (2) nonzero responses of chemicals exhibit two characteristic features, localization and hierarchy. Finally, we found (3) a general theorem that directly connects network topology and response patterns, which we call the *law of localization*. These results also imply that network topology is an origin of biological adaptation and robustness. We also apply our method to several hypothetical and real life chemical reaction networks, including the metabolic network of the E. coli metabolic network.

REFERENCES

[1] Mochizuki A. & Fiedler B. J. Theor. Biol. (2015) 367, 189-202.
[2] Okada T. & Mochizuki A. (2016) Phys. Rev. Lett. 117, 048101.

Poster Session Abstract

Kazumasa Kaneko
Department of Electrical Engineering and Information Systems, The University of Tokyo
e-mail: `kaneko@sat.t.u-tokyo.ac.jp`

Ryo Yokota
Institute of Industrial Science, The University of Tokyo

Taishin Akiyama
Institute of Medical Science, The University of Tokyo

Tetsuya J. Kobayashi
Institute of Industrial Science, The University of Tokyo

Modeling and inferring dynamics of T cell population in thymus

A development of T cell, a type of immune cells, in the thymus is a dynamic process that generates the repertoire of T cell population. During the maturation of T cells, they interact with thymic epithelial cells (TECs) and TECs positively and negatively select functional and nonself-reactive T cells respectively. Although the chemical reactions that constitute the positive and negative selection has been revealed, the dynamic aspects of the selection and differentiation of T cells is not fully understood [1]. While T cell population and its generation in thymus is homeostatically maintained normally, various external perturbations such as stress and drug lead to its failure [2,3]. Mathematical modeling is indispensable to understand the dynamics of the thymic functionality and to infer the mechanism of the disorder.

In this study, we construct a mathematical model on the recovery dynamics of CD4-CD8- double negative, CD4+CD8+ double positive T cells after X-ray irradiation by employing experimental data on joint dynamics of T cell and TEC populations. The inferred model suggests that cortical TECs controls division and differentiation rates of double negative T cells and shows positive/negative correlation between medullary/cortical TECs and the stable population size of the double positive T cells. We also analyze the possibility on cell division of CD4+CD8+ double positive T cells. An extended model to include CD4-CD8+/CD4+CD8- single positive T cells may also be discussed.

REFERENCES

[1] Akiyama, T., Tateishi, R., Akiyama, N., Yoshinaga, R., & Kobayashi, T. J. 2015. Positive and negative regulatory mechanisms for fine-tuning cellularity and functions of medullary thymic epithelial cells. *Frontiers in Immunology*, *6*(SEP).

[2] Billiard, F., Kirshner, J. R., Tait, M., Danave, A., Taheri, S., Zhang, W., … Skokos, D. (2011). Ongoing Dll4-Notch signaling is required for T-cell homeostasis in the adult thymus. *European Journal of Immunology*, 41(8), 2207–2216.

[3] Gruver, A. L., & Sempowski, G. D. (2008). Cytokines, leptin, and stress-induced thymic atrophy. *Journal of Leukocyte Biology*, 84(4), 915–923.

Naoki Nakada
e-mail: c5615017@aoyama.jp
College of Science and Engineering, Aoyama Gakuin University,
Kanagawa, 252-5258, Japan.

Shinji Nakaoka
e-mail: shinzy.nakaoka@gmail.com
Graduate School of Medicine, The University of Tokyo, Hongo 7-3-1,
Bunkyo-ku , Tokyo, 133-0033, Japan.

Yasuhiro Takeuchi
e-mail: takeuchi@gem.aoyama.ac.jp
College of Science and Engineering, Aoyama Gakuin University,
Kanagawa, 252-5258, Japan.

Mathematical modeling and analysis of cancer immunotherapy: exploring the effect of cytokine mediated communication among T and NK cells

Treatment of cancer is broadly classified as surgical, radiotherapy, and chemotherapy. Immunotherapy is an emerging type of cancer therapy which attracts attention in late years because of its therapeutic potential and less burden of side effects. Immune cell transfer therapy boosts immune cells taken from a body, and then activates cells *ex vivo*, and finally returns the activated cells to a body.

The populations of natural killer (NK) cell and T cell are known as candidates of cancer immune-therapy. Two types of cell attack cancer in a different manner according to the expression level of MHC class I molecules which are expressed on the surface of cancer cells. NK cell is a member of innate immunity which attacks cancer cells exhibiting low MHC class I expression (missing-self hypothesis). On the other hand, CD8 positive T cells specifically recognize cancer associated antigen directly, or presented by antigen presenting cells as MHC class I complex. Hence CD8 positive T cells kill high MHC class I expressing cancer cells. To investigate dynamical behaviors of cancer killing by two different immune cell types, we construct a mathematical model that describes mutual interactions among NK cells, T cell via produced interferon gamma.

Mathematical analysis and numerical simulations are performed to investigate dynamical behavior of immune response against cancer. We specifically focus on the role of interferon gamma as a mediator of mutual activation of two different cell types. Our computational results imply the possibility of cancer elimination which is mediated by the establishment of mutual activation among NK and CD8 T cells. Biological implications based on our mathematical and computational results will be discussed.

REFERENCES

[1] Mizuho Nagata, Yutaro Furuta, Yasuhiro Takeuchi, and Shinji Nakaoka, Dynamical behavior of combinational immune boost against tumor, *Japan Journal of Industrial and Applied Mathematics* **32** (2015) 759–770.
[2] Naoki Nakada, Mizuho Nagata, Yasuhiro Takeuchi and Shinji Nakaoka, Mathematical modeling and analysis of combinational immune boost for tumor elimination, *AIP Conference Proceedings* 1723 (2016) 020002.

Shinji Nakaoka
Graduate School of Medicine, The University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo, 133-0033, Japan
e-mail: `shinzy.nakaoka@gmail.com`

Development of a computational grammar for immune cell processes

Immune response against foreign antigen is dynamics and mediated by a considerable number of immune cell types [1]. Both inflammatory and regulatory cell types are associated with antigen clearance. Cytokines are extracellular proteins which mediate cellular communication among immune cell types. Some cytokines such as IL-6 and IL-10 are pleiotropic as they promote and suppress immune cell activities. On the other hand, some cytokines are known to be redundant: IL-4 and IL-13 share a common biological function as to promote allergic immune response.

One of challenging tasks in the field of computational immunology is to correctly describe a context dependent manner of interactions among immune cell types mediated by cytokine communications. Although case specific description of cytokine function on immune cell activation and suppression has been massively found, a computationally available framework to describe immune cell dynamics has been poorly investigated.

The aim of this study provides a description of immune cell dynamics based on transcriptional gene regulatory networks associated with cytokine production. In this talk, I would like to present recent research progress on construction of computational grammar to describe immune cell dynamics.

REFERENCES

[1] Gérard Eberl, A., 2016. Immunity by equilibrium. *Nature Reviews Immunology*, **doi:10.1038/nri.2016.75**.

Seiya Nishikawa
Department of Electrical Engineering & Bioscience, Waseda University, Tokyo, Japan
e-mail: `seiya.nskw@gmail.com`

Shoko Baba
Graduate School of Biostudies, Kyoto University, Kyoto, Japan

Shizue Ohsawa
Graduate School of Biostudies, Kyoto University, Kyoto, Japan

Tatsushi Igaki
Graduate School of Biostudies, Kyoto University, Kyoto, Japan

Atsuko Takamatsu
Department of Electrical Engineering & Bioscience, Waseda University, Tokyo, Japan

Fate after ‘cell competition’ depending on initial states in tumor-suppressor system

Coordinated cell population forms multicellular organisms. In tissue of multicellular organisms, interaction among different cell-species would play important roles for normal organ development and maintaining organs themselves. A phenomenon called ‘cell competition’ discovered in *Drosophila* system [1] is considered to be one of the candidates for such the interaction. ‘Cell competition’ is defined as follows: cells with higher fitness (called “winner”) eliminate cells with lower fitness (called “loser”) by inducing cell death among the loser cells [2]. The elimination occurs only at their interface between the two types of cells.

Interestingly, it is reported that an experimental system consisting of tumor-suppressing-function-defecting mutant, *Rab5*, shows initial-state dependent fates [3]. Although the mutant cells possess strong growth competence, they can be “loser” once introduced in a normal tissue, when the mutant population is small. In contrast, *Rab5* cells survive and form tumor when the initial population is larger than a certain value.

To elucidate fate after ‘cell competition’, namely, a condition determining whether the *Rab5* cells are exterminated or survive, we performed both-side analysis with a mathematical model and an experimental system. We constructed a mathematical model for ‘cell competition’ based on Lotka-Volterra competition equation, by introducing the predator-prey interaction at interface [4]. As experimental approach, *Rab5* cells were induced in *Drosophila* imaginal wing disc by using heat shock method in which the initial number of *Rab5* cells and the time can be controlled.

As a result of analyzing our mathematical model, we obtained the condition in which the fate after ‘cell competition’ is depends on initial states of numbers of mutant cells and normal cells. After a number of combinations in initial states tested in the experiment, we verified that the phase portrait and vector field depicted using the mathematical model can roughly explain the experimental observations. To refine the mathematical model, we are trying to introduce a phenomenon observed in the experimental system [3] that mutant cell death induced by ‘cell competition’ has context-dependent effect on controlling proliferation.

REFERENCES

[1] Morata, G. and Ripoll, P., 1975. Differential mitotic rates and patterns of growth in compartments in the *Drosophila* wing. *Dev. Biol.,* **42**: 211–221.

[2] Baker, N, E., 2011. Cell competition. *Curr. Biol.*, **21**: R11–R15.

[3] Ballesteros-Arias, L., Saavedra, V. and Morata, G., 2014 Cell competition may function either as tumour-suppressing or as tumour-stimulating factor in *Drosophila*. *Oncogene*, **33**: 4377–4384.

[4] Nishikawa, S., Takamatsu, A., Ohsawa, S. and Igaki, T., 2016. Mathematical model for cell competition: Predator–prey interactions at the interface between two groups of cells in monolayer tissue. *J. Theor. Biol*, **404**: 40–50.

Kentaro Inoue
Laboratory for Integrated Cellular Systems, RIKEN Center for Integrative Medical Sciences,
Yokohama, Japan
e-mail: kentaro.inoue.hv@riken.jp

Hisaaki Shinohara
Laboratory for Integrated Cellular Systems, RIKEN Center for Integrative Medical Sciences

Gouhei Tanaka
Institute of Industrial Science, The University of Tokyo

Kazuyuki Aihara
Institute of Industrial Science, The University of Tokyo

Mariko Okada-Hatakeyama
Laboratory for Integrated Cellular Systems, RIKEN Center for Integrative Medical Sciences
Laboratory of Cell Systems, Institute for Protein Research, Osaka University

Mathematical model for NF-κB signal transduction system

A mathematical model of molecular networks can explain molecular mechanism of a complex biological system and also predict dynamical behaviors of individual molecules in cells. Signal transduction can transmit extracellular information to intracellular transcription factors (TFs). The activation of TFs can induce gene expression and lead to cell differentiation, proliferation and apoptosis. Nuclear factor-kappa B (NF-κB) is a transcriptional factor and relates to a variety of cellular functions, such as immune response. Dynamic behaviors of NF-κB activity after cell stimulation show damping oscillation [1] and switch-like response [2] necessary for target gene induction. To reveal the molecular mechanism of the NF-κB activity dynamics, we constructed and analyzed a mathematical model which can recapitulate both the oscillation and switch-like response.

The model consists of 47 differential equations with 190 kinetic parameters and contains multiple positive and negative feedback loops. Simulation of the model reproduced experimental results. We performed sensitivity analysis and identified sensitive components in the model critical for oscillation and switch-like response of NF-κB. In addition, we constructed a core model regarding those components. The core model explained one of the roles of the switch-like activation on the oscillation.

The model proposed here is the first model which can recapitulate both oscillation and switch-like response of NF-κB, and provides valuable insights for understanding the regulatory mechanisms of NF-κB signaling.

REFERENCES

[1] A. Hoffmann, A. Levchenko, M. L. Scott, D. Baltimore, 2002. The IkappaB-NF-kappaB signaling module: temporal control and selective gene activation. *Science* 298, 1241-1245.
[2] H. Shinohara et al., 2014. Positive feedback within a kinase signaling complex functions as a switch mechanism for NF-kappaB activation. *Science* 344, 760-764.

Masashi Kamo
Advanced Industrial Science and Technology, Research Institute of Science for Safety and Sustainability, Tsukuba, Ibaraki, Japan
e-mail: `masashi-kamo@aist.go.jp`

Hiroyuki Yokomizo
National Institute for Environmental Studies, Center for Health and Environmental Risk Research

Explanation of non-additive effects in mixtures of similar mode of action chemicals

The risk assessments of chemical substances are often carried out to evaluate the risk by single substance. Even though risk by single substances is negligibly small, there is an anxiety that total risk by many chemical substances cannot be neglected if exposed all together. Recently, there is an increased interest for a risk assessment of combined effect by multiple chemicals.

Researches for combined effects have a long history. They have started in the pharmacology to predict combined effects of drug efficacies. Loewe's concentration addition (CA) in 1926 [1] and Billis' independent action (IA) in 1936 are the two major models [2]. Bliss considered that effects by drugs are random events and tried to predict a total effect by multiple of effects by single drug. Whereas, Loewe tried to predict a total effect by a sum of concentrations of each drug. When combined effects of drug are predicted by the CA, the effect is termed additive. When the combined effects are not additive, it is considered that there is a synergism, or an antagonism among drugs. The synergism is the effects to pursue in pharmaceuticals but to avoid in the risk assessment of chemical.

The CA is somehow a heuristic model and it cannot offer answers to questions such as what an applicability domain of the model is. There are a couple of belief such as (1) the CA yields accurate prediction for chemicals having the same or similar modes of action, (2) if slopes of dose-response curve of each chemical are the same, CA is applied to predict toxic effect of chemical mixture, and (3) due to a non-additive effects (synergism/antagonism), CA may not predicts an accurate toxicity when number of chemicals in mixture is small; however, prediction becomes accurate as number of chemicals in mixture are large because synergism and antagonism are canceled out (the funnel hypothesis [3]). In this paper, we use a simple model of enzyme catalysis to investigate if these beliefs are true or not [4].

We found that the belief (1) is partially true. The CA is true for chemicals having exactly the same modes of action, but the synergism or antagonism appear for chemicals having the similar modes of action. The belief (2) is also not always true. Chemicals having the same slope in dose-response curve may lead to the synergism or antagonism when they are mixed. The funnel hypothesis in the third belief is true, but the reasoning for the accuracy for the CA prediction is wrong. Additivity in the chemical mixture appears not by the cancelation of synergism and antagonism, but appears by the linear approximation of the multiple terms of concentration in the model. In toxicity tests with many chemicals in mixture, concentrations of each chemical are held low (otherwise all die immediately). For chemicals leading to non-additive effects, deviation from the CA prediction rises by multiple terms of concentrations. When the concentration of chemicals are low, such non-linear terms can be neglected, and the effects can be approximated by the CA in which the toxicity is predicted by a sum of concentrations. The number of chemicals is not the key in Funnel Hypothesis, but the low concentrations of chemical are.

In the risk management chemical mixture, it is often criticized that the use of the CA is dangerous because the model cannot predict the non-additive effects. According to our results, use of the CA are nots so dangerous because environmental concentrations of chemicals are low in many cases.

REFERENCES

[1] Loewe, S., Muischnek, H. (1926) Effect of combinations: mathematical basis of the problem. *Arch. Exp. Pathol. Pharmakol.* 114, 313–326.

[2] Bliss, C.I. (1939) The toxicity of poisons applied jointly. Ann. Appl. Biol. 26, 585–615

[3] Warne, M.S., Hawker, D.W. (1995) The number of components in a mixture determines whether synergistic and antagonistic or additive toxicity predominate: the funnel hypothesis. *Ecotoxicol. Environ. Saf.* **1**:23-8.

[2] Kamo, M,. Yokomizo, H. (2015) Explanation of non-additive effects in mixtures of similar mode of action chemicals. *Toxicology*, **1**: 1–10.

Isao Kawaguchi
Center for Radiation Protection Knowledge,
National Institute of Radiological Sciences,
National Institutes for Quantum and Radiological Science and Technology
e-mail: `kawaguchi.isao@qst.go.jp`

Tetsuya Sakashita
Department of Radiation-Applied Biology Research,
Takasaki Advanced Radiation Research Institute,
National Institutes for Quantum and Radiological Science and Technology

Mathematical model approach to understand abscopal effect with radiotherapy

Since Roentogen's discovery of X-rays, the medical use of the radiation has been increased and applicable scope of radiation was extended not only to diagnosis but also to treatment. Especially, effectiveness of localized irradiation to cancer has been recognized and application of the radiotherapy to cancer treatment is extended. By progression of radiotherapy, indirect effect of the localized radiotherapy referred as "abscopal effect" was reported from around the 1970's, where the non-irradiated tumors were shrunk by irradiation to primary tumor. According to review by UNSCEAR[1], it was suggested that immune reaction induced by radiation exposure could be related to abscopal effect. In addition, an effect of the tumor immunity in late years attracts attention, and interest increases for the use of abscopal effect by the combination with the radiation therapy. On the other hand, there were also known that relations between immunity and tumor progression are very complicated, so that it is still unknown how abscopal effect stably is induced by localized irradiation treatment.

In this study, a mathematical model for the abscopal effect by radiotherapy to the primary tumor was developed and analyzed to find the condition for abscopal effect induced stably. We assumed cell death is induced by radiation exposure for the primary tumor, and tumor antigen is produced from irradiated tumor cells. And immune response to the tumor antigen is induced and activated immune cells are diffused to other tumor cites which metastasized. It is also assumed that the tumor cells evolve in the direction escaping from immune reaction with time.

From the analysis of the model, it was found that it was difficult to decrease a metastasized tumor successfully only by abscopal effect with the radiation therapy. In addition, it was suggested that the tumor size could be decrease by the combination with the immune therapy.

REFERENCES

[1] United Nations Scientific Committee on the Effects of Atomic Radiation, UNSCEAR 2006 Report to the General Assembly, with scientific annexes Volume II: Scientific Annexes, 2009.

Masahiko Higashi
Nagoya University, Nagoya, Japan
e-mail: `higashi@alife.cs.is.nagoya-u.ac.jp`

Reiji Suzuki
Nagoya University, Nagoya, Japan

Takaya Arita
Nagoya University, Nagoya, Japan

A Coevolution Model of Individual and Social Learning in a Rugged Fitness Landscape

The role and importance of social learning have been investigated by many researchers, because it is observed in many animals and it is expected to play a significant role in cultural phenomena. We explore the coevolution between individual learning and social learning in a rugged fitness landscape, as a realistic condition in which they can interact with each other. This rugged fitness landscape was designed by Suzuki and Arita [1], and they revealed how learning facilitates the evolution in the fitness landscape. Our purpose is to investigate how social learning affects evolution and how it interacts with individual learning. We constructed an agent-based evolutionary model in which each individual can accommodate its plastic phenotypes using both individual learning based on trial-and-error and social learning based on imitation of phenotypes from the most adaptive individual. We found that social learning has two important roles to enhance individual fitness through the two-step evolution process of the Baldwin effect (i.e., the evolution of learning ability and the subsequent occurrence of the genetic assimilation of acquired traits). First, social learning can spread and keep the adaptive phenotypes that are acquired by individual learning in the population (Fig. 1). Second, such an effect of social learning allows individuals to explore a wide range of fitness landscape (Fig. 2). The first role of social learning affects each of two steps of Baldwin effect, and the second role of social learning affects first step of Baldwin effect. Therefore, the 2 steps of the Baldwin effect will be reformulated as follows. 1) the first and second roles of social learning accelerate the first step of Baldwin effect. 2) the first role of social learning enables individuals to acquire adaptive phenotypes culturally, so the second step of Baldwin effect is compensated by cultural inheritance.

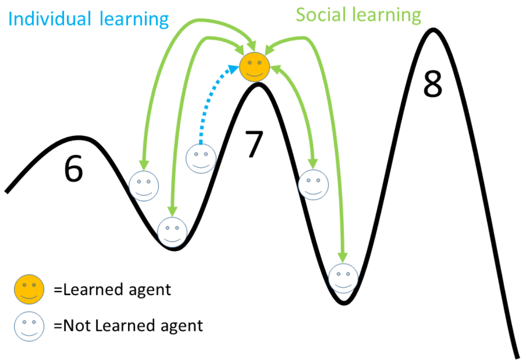


Fig. 1 The 1st role of social learning: spread of adaptive phenotypes.

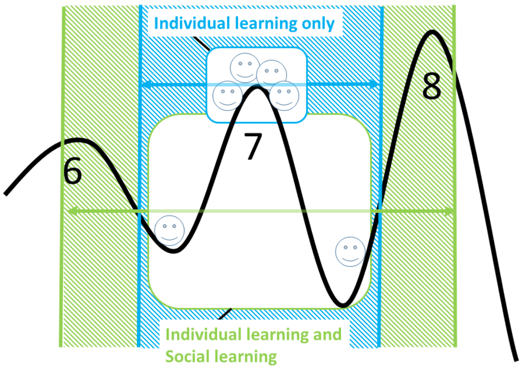


Fig. 2 The 2nd role of social learning: expansion of search area.

REFERENCES

[1] Suzuki, R. and Arita, T., 2007. Repeated occurrences of the Baldwin effect can guide evolution on rugged fitness landscapes. *In Proceedings of the First IEEE Symposium on Artificial Life (IEEE-Alife'07)*, pp. 8-14.

Mariko Ito
Department of Evolutionary Studies of Biosystems, The Graduate University for Advanced Studies (Sokendai), Hayama, Kanagawa Japan
e-mail: `ito_mariko@soken.ac.jp`

Hisashi Ohtsuki
Department of Evolutionary Studies of Biosystems, The Graduate University for Advanced Studies (Sokendai), Hayama, Kanagawa Japan

Akira Sasaki
Department of Evolutionary Studies of Biosystems, The Graduate University for Advanced Studies (Sokendai), Hayama, Kanagawa Japan

Emergence of opinion leaders in reference networks

An opinion of an individual is often influenced by those of other members of the society. We describe this situation by a network model with nodes representing individuals and edges representing information flow as is assumed in many studies of opinion formation [1][2]. In such networks, individuals who have a large number of reference links are greatly influential to others, so we call them opinion leaders. Here we ask how opinion leaders emerge in an evolving network where each agent rewires one's reference links adaptively, and what role they will play in the evolved network.

To answer these questions, we constructed a network model where, in each iteration round, each agent makes a decision sequentially on a given problem with the majority vote among oneself and his or her neighbors' opinions, and rewires his or her links according to the performance of the linked individuals. Since each agent makes decision with majority vote, his or her probability to find a correct answer by oneself, which we call his/her "ability", is different from his or her actual probability of finding a correct answer by referring to others, which we call "performance". The rewiring rule is as follows; each individual monitors his or her neighbors' performance and breaks the link if the neighbor's performance becomes worth than a preset threshold. We also assume that individuals vary in their ability.

Our analysis shows the following results. (1) The threshold for breaking a link, which stands for how strictly agents assess their neighbors, strongly affects whether or not opinion leaders emerge, or, more strictly, whether or not the distribution for the number of followers becomes significantly different from binomial distribution under random connection. When opinion leaders emerge in the model, (2) the mean number of followers each individual has increases more than linearly with his or her ability, and (3) the average performance of agents becomes higher but shows more temporal fluctuation than when each individual makes a decision independently. Furthermore, as long as the threshold value for rewiring links is greater than 0.5, which is the minimum ability an individual may have, the lower the threshold we set, the higher the mean performance each agent will have. Some of these results can be explained by considering a random walk of the monitoring value of the neighbor's performance and its first hitting time to the threshold: for example, the effect of a threshold on the emergence of opinion leaders, and the mean number of followers that an agent with a given ability can attract.

REFERENCES

[1] C. Castellano, S. Fortunato, V. Loreto, 2009. Statistical physics of social dynamics, *Rev. Mod. Phys.* 81, 591.
[2] T. Gross, B. Blasius, Adaptive coevolutionary networks: a review, 2008. *J. R. Soc. Interface 5*, 259-271.

Mitsuhiro Nakamura
Department of Evolutionary Studies of Biosystems,
SOKENDAI (The Graduate University for Advanced Studies),
Hayama, Kanagawa 240-0193, Japan
e-mail: `nakamuramh@soken.ac.jp`

Ai Kawamori
Department of Data Sciences,
The Institute of Statistical Mathematics,
10-3 Midori-cho, Tachikawa, Tokyo 190-8562, Japan

Learning processes and matching behavior in domestic chicks' foraging

Environmental harshness in food resources varies in nature, thus foraging animals should adapt their cognitive ability to environment in different levels [1]. Learning mechanism is in particular important among several aspects of animal cognition. However, how they adapt their learning strategies to environment is unclear. Rescorla–Wagner (RW) and Roth–Erev (RE) learning rules are classical reinforcement learning models that explain animals' choice behavior regarding their implicit estimation of resource amounts, namely values, of different patches. RW-rule learning maximizes the expected value, whereas RE-rule learning does not. However, RE-rule learning has been often observed in nature and laboratory experiments. What kind of environmental condition makes animals maximize their fitness? Performing a Bayesian model-fit analysis to behavioral data of domestic chicks in laboratory tests affected by environmental change, we show that chicks use RW-rule learning in high risk environments. In low risk environments, they show diverse behavioral patterns; thus, it is not easy to identify which learning rule they adopt. Nonetheless, we found that in low risk environments, chicks show a generalized matching law, implying that they select a choice that has provided resources at past. RE-rule learning satisfies such property.

REFERENCES

[1] Shettleworth, S. J., 1998. *Cognition, Evolution, and Behavior*. Oxford, NY: Oxford University Press.
[2] Rescorla, R.A., Wagner, A.R., 1972. A theory of Pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. *Classical Conditioning II*, 64–99.
[3] Roth, A., Erev, I., 1995. Learning in extensive-form games: experimental data and simple dynamic models in the intermediate term. *Games and Economic Behavior* **8**, 164–212.

Junepi Okuno
Dept. of Elec. Eng. & Biosci.Waseda University, Tokyo, Japan
e-mail: wsd.j.o@asagi.waseda.jp

Atsuko Takamatsu
Dept. of Elec. Eng. & Biosci.Waseda University, Tokyo, Japan

Foraging strategy using multi-tentacles in plasmodial slime mold

Decision making during foraging is important problem for every organism even for brainless primitive organisms. Plasmodium of true slime mold, *Physarum policephalum* is a giant multinucleated unicellular organism. The plasmodium extrudes the portion of the body as tentacles to explore food in environment. Latty and Beekman found trade-off between decision speed and accuracy, and trade-off between harmful light stimulation and food reward in foraging decision in plasmodiums, where the decisions are that of final states [1,2]. In fact, the plasmodium can explore multiple food simultaneously by using multiple tentacles. Therefore, we focus on the process of decision making with the multi-tentacles.

In our observation, three food blocks were placed in contact with tentacles extending in three directions (Fig.1*a*). It was observed, after 3-12 hours cultivation, that the tentacles extend over the food blocks alternatively (Fig.1*b*).

The relationship between nutrient concentration of food sites and extending speed of the tentacles (activity), capturing time of the food sites, or the resident period was quantified. The results of analysis suggest that priorities during foraging decision depend on activity of tentacles when nutrient concentrations are equal. In contrast, when the concentrations are different, the priorities depend on complex factors of the concentration and the activity.

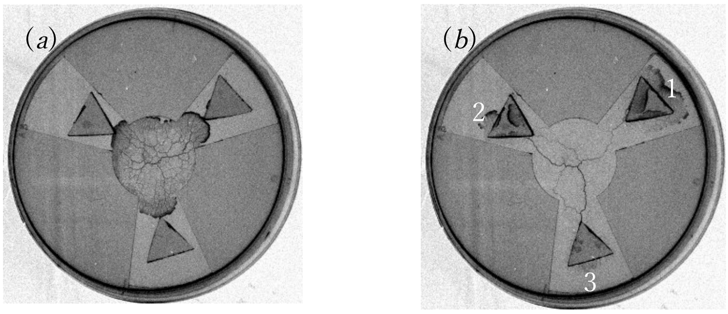


Fig.1: Experimental set-up. (*a*) A plasmodium extrudes three tentacles contacting with each food block. (*b*) A plasmodium forages three food sites (The food sites 1-3 contain extraction of 10, 5, 3w/v% ground oat flakes).

REFERENCES

[1] Latty, Tanya, and Madeleine Beekman., 2010. "Food quality and the risk of light exposure affect patch-choice decisions in the slime mold Physarum polycephalum." *Ecology*, **91.1**: 22-27.

[2] Latty, Tanya, and Madeleine Beekman., 2011. "Speed–accuracy trade-offs during foraging decisions in the acellular slime mould Physarum polycephalum." *Proceedings of the Royal Society of London B: Biological Sciences*, **278.1705**: 539-545.

Chikoo OOSAWA
Department of Bioscience and Bioinformatics, Kyushu Institute of Technology,
680-4 Kawazu Iizuka Fukuoka JAPAN 820-8502
e-mail: `chikoo@bio.kyutech.ac.jp`

Yamato HAMADA
Dept. of Biosci. Bioinfor. Kyushu Institute of Technology

Gathering animals by escaping

Introduction:

Simple models for relationship between sheep and sheepdogs have developed to capture major factors behind collective behavior of sheep. Even with the simple model can provide show gathering behavior of sheep without using famous Boids model [1]. We also find that effective conditions of moving sheepdogs for gathering sheep.

Model:

In our model, two-dimensional squared lattice sheep farm with fence (zero-flux boundary conditions) is considered. Each site is empty or occupied by one animal: a sheep or sheepdog. A large number of the sheep can only escape from the nearest sheepdog as far as possible [2]. On the other hand a small number of sheepdogs are controllable: (1) running along the fence, (2) running in circle, (3) chasing the nearest sheep, (4) running at random (no chase).

To evaluate differences of sheepdog behaviors, 2~8 sheepdogs are placed along the fence and sheep are distributed at random and gathering efficiency is defined by density of sheep in the central region of farm.

Results and discussions:

Most of conditions show that the density increases with time, demonstrating that even simple model can generate collective behavior of sheep. In general the higher efficiency of gathering sheep are shown with larger number of sheepdogs as well as the more regular behaviors of sheepdogs can provide the higher efficiency.

REFERENCES

[1] C.W.Reynolds, Flock,Herds, and Schools: A Distributed Behavioral Model ,1987, *Computer Graphics*, **21**(4):25.
[2] A. Kimura, T. Ohhira, 2010. Group chase and escape, New Journal of Phyiscs, **12**:053013.

Hemma Philamore
Kyoto University, University of Bristol, Bristol Robotics Laboratory.
e-mail: `hemma.philamore@bristol.ac.uk`

Tomohiro Hayakawa
Kyoto University

Bo Hyeon Kim
Kyoto University

Jonathan Rossiter
University of Bristol, Bristol Robotics Laboratory.

Ioannis Ieropoulos
University of the West of England, Bristol BioEnergy Centre

Fumitoshi Matsuno
Kyoto University

Trophallaxis for Swarms of Energy-Scavenging Artificial Organisms.

One of the greatest challenges in robotics is to achieve operation with the degree of autonomy we observe in natural organisms. For complete autonomy, in addition to actuation and computation, a robot must be capable of independent energy self sufficiency. Robots that supplement their power demand by conversion or direct use of environmentally scavenged sources of energy have shown great potential for energy autonomous operation [1]. However, the stochastic conditions that typify most real world environments mean that it is often challenging for a single energy-scavenging robot to maintain its energy needs. In the case of robots with limited power generation or on-board energy storage capabilities, periods of starvation can be a threat to survival [2]. This applies to small, simple agents that typify a swarm of ubiquitous robots [3] and those which take their energy from relatively low power sources such as microbial fuel cell technology [4]. Properties that demonstrate system robustness when operating in real environments, such as increased power generation with prolonged environmental exposure [5], inherent fault tolerance [6], and bio-remediative effects, may be compromised due to the low energy capabilities of individual robots.

Here we demonstrate the use of a bio-inspired decentralised control strategy using a swarm of simulated robots, tasked with cleaning up a biodegradable environmental pollutant, which simultaneously serves as their sole source of energy. The simulated robots ingest the pollutant and convert it to electrical energy using on-board artificial stomachs. Trophallaxis; inter-agent feeding inspired by the behaviour of social organisms including ants, bats and bees, is employed for group energy distribution and communication. Communication and sensing are minimised to conserve stored agent energy. Additionally, relay-chain formation is employed as a means to connect distal swarm members to the food supply. Increased robot aggregation at the food supply is shown in response to the use of social mechanisms; trophallaxis and relay chain formation in combination. Notably using only trophallaxis results in the longest swarm survival time. In contrast, use of relay chains alone is detrimental to overall performance. We expect the outcomes of this study to have impact in the adoption of swarm robots for real world applications and radically new designs for future robots.

REFERENCES

[1] Mars Exploration Rover Landings Press Kit. *Technical Report January*, NASA, 2004.

[2] McFarland D and Spier E, Basic Cycles Utility and Opportunism in Self-Sufficient Robots. *Robotics and Autonomous Systems*, pages 179-190, 1997.

[3] Kim B.H, Fukushima H, and Matsuno F. Cooperative Transportation of a Disk Object by Multiple Robots without Communication. In *SWARM 2015: The First International Symposium on Swarm Behavior and Bio-Inspired Robotics*, pages 94–95, 2015.

[4] Ieropoulos I, Greenman J, Melhuish C, and Horsfield I. EcoBot-III : a robot with guts. In *Proceedings of the Alife 7 Conference*, pages 733-740, 2010.

[5] Tender L, Microbial Fuel Cells for Powering Navy Devices, *Naval Research LaboratoryWashington, DC*, 2014.

[6] Winfield AFT, Nembrini J, Safety in Numbers: Fault Tolerance in Robot Swarms, *International Journal of Modelling Identification and Control,* **1**:30-37 (2006)

Motohide Seki
Kyushu University, Fukuoka, Japan
e-mail: `seki.evol@gmail.com`

Optimality and evolutionary stability of life histories with stages for cultural transmission of information

Social leaning, by which a leaner acquires pieces of information held by an exemplar regardless whether the information is adaptive or harmful, is essentially a free-riding behaviour; it can evolve when it poses less learning cost than individual learning does. Game-theoretic approaches are required to predict evolutionary consequences of individual and social learning.

It has been shown that social learning rarely contributes to the total amount of information carried by the whole population. Specifically, a coexisting state of individual and social learners can be evolutionarily stable depending on the environment, where the total amount of information carried by the mixed population is exactly the same as that carried by the population purely consisting of individual learners [1]. This finding was counterintuitive because we often attribute the ecological success of human species based on high technology to our innate ability of social learning.

It is believed that one of a few exceptional cases in which social learning improves the level of collective knowledge is cross-generational transmission of cumulative information. A previous study considered the case that infant individuals acquire information held by random post-reproductive individuals from the parental generation (i.e. oblique transmission) [2]. It predicted that life history including such an infant period evolves when efficiency of the cross-generational information transmission is sufficiently high. Though the study included the cost for having and extending the infant period, it did not explicitly consider cost for post-reproductive period during which an individual plays a role of exemplar.

The present model examines the effect of benefit and cost for living after reproduction on the life history evolution. It also focuses on the difference between oblique and vertical transmission of information. The results suggest that a post-reproductive period longer than the infant period, which is observed in human species, may be a complex outcome of cultural transmission and the improved efficiency of parental care due to the cumulative information.

REFERENCES

[1] Rogers, A., 1988. Does biology constrain culture? *American Anthropologist*, **90**: 819–831.
[2] Lehmann, L. et al., 2013. On optimal learning schedules and the marginal value of cumulative cultural evolution. *Evolution*, **67**: 1435–1445.

Shohei Utsunomiya
Dept. of Elec., Eng. & Biosci., Waseda University, Japan
e-mail: `shohei.utsunomiya.ant@gmail.com`

Atsuko Takamatsu
Dept. of Elec., Eng. & Biosci., Waseda University, Japan

Diversity of behavioral preference on cooperative transport in ants reduces obstacle passing time

Cooperative transport is known as an action, in which two or more individuals move a single item from a location to another (Fig.1) [1]. The advantages are, as reported in previous studies, that group of individuals can drag heavier items and move faster than a single does [2, 3]. It was observed that some ants try to drag the item from the opposite site against the nest, which seems to disturb the effective transport toward the nest. We focus on the behavior of the disturbing ants, and its advantage in the group during passing through obstacles.

We found two characteristics through a quantitative analysis of experimental observation: First, increase in number of ants participating the transport reduces the obstacle passing time. Second, individual ants do not always move straightforwardly toward their nest and some go toward unexpected directions during their solo transportation. From these experimental results, we hypothesize that diversity of behavioral preference in ants could optimize something during cooperative transportation of an item. To verify it, we performed numerical simulation using a mechanical model.

In the model, the diversity of behavioral preference is assumed to be directional preference during item transportation to the nest. The simulation result revealed that the behavioral diversity reduces the obstacle passing time.

Fig.1: Cooperative transport in ants.

REFERENCES

[1] Czaczkes, T. J. and Ratnieks, F. L. W., 2013. Cooperative transport in ants (Hymenoptera: Formicidae) and elsewhere. *Myrmecol News*, **18**: 1-11.

[2] Czaczkes, T. J., Nouvellet, P. and Ratnieks, F. L. W., 2011. Cooperative food transport in the Neotropical ant, *Pheidole oxyops*. *Insectes Sociaux*, **58**: 153-161.

[3] Hölldobler, B., Stanton, R. C. and Markl, H., 1978. Recruitment and food-retrieving behavior in *Novomessor* (Formicidae, Hymenoptera). *Behavioral Ecology and Sociobiology*, **4**: 163-181.

Fumiko Ogushi
Advanced Institute for Material Research, Tohoku University
e-mail: `fumiko.ogushi.e3@tohoku.ac.jp`

Takashi Shimada
Department of Applied Physics, Graduate School of Engineering, The University of Tokyo

A mean-field analysis of the simple model of evolving open systems

A graph dynamical model of evolving open systems (EOS) with uni-directional interactions gives a novel transition in the robustness. The system keeps growing in the case that a newly incoming species has a moderate number of initial interactions $\boldsymbol{m}$ ($4 < \boldsymbol{m} < 19$, diverging phase). In the cases that the newly introduced species have sparser or denser interactions, the system remains in a finite size ($\boldsymbol{m} \leq 4$ or $\boldsymbol{m} \geq 19$, finite phase). In addition, the structure of the interaction network of the emergent system has no strong correlation. It suggests that the emergent system is composed of simple tree structures without any loop structures. On a basis of such mean-field treatment, the total number of extinctions of resident species per introduction of a new species is found to be a function of the product of the extinction probability of a species at single link-change event and the average out-degree of the species, $\boldsymbol{m/2}$. A further simplified theoretical process suggests that the extinction probability should monotonically decreases with $\boldsymbol{m}$ but slower than $\boldsymbol{1/m}$. This means that increasing of $\boldsymbol{m}$ makes each node stronger but makes the whole system fragile, predicting the transition from the diverging phase to the finite phase.

However, the transition point estimated from this simple theoretical process $\boldsymbol{m_c=13}$ is considerably apart from the real transition point (i.e. 18.5). This difference in the point of transition can stem either or both from the neglected structure of the emergent systems and/or the inaccurate estimation of the mean-field extinction probability. Therefore, in this study, we investigate the validity of the mean-field approach in detail, with improving the estimation of extinction probabilities using the information of emergent systems. The transition point estimated from the mean-field treatment with the empirically calculated extinction probabilities is found to agree with the true transition point. This result suggests that the error in the transition point we had in the previous study is due to the not accurate estimation of true mean-field extinction probabilities. And the correlation in the interaction network of the emergent system does not play a major role to the determination of the transition point.

REFERENCES

[1] T. Shimada, Scientific Reports, **4** (2014) 4082.
[2] T. Shimada, in Mathematical Approaches to Biological Systems (Springer, 2015), p.95-117.
[3] T. Shimada and F. Ogushi, to appear in J. of Physics Conference Series

Shota Shibasaki
Graduate School of Arts and Sciences, the University of Tokyo, Komaba 3-8-1, Meguro-ku, Tokyo 153-8902, Japan
e-mail: `shibasaki.sh@gmail.com`

Yuka Shirokawa
Graduate School of Arts and Sciences, the University of Tokyo, Komaba 3-8-1, Meguro-ku, Tokyo 153-8902, Japan

Masakazu Shimada
Graduate School of Arts and Sciences, the University of Tokyo, Komaba 3-8-1, Meguro-ku, Tokyo 153-8902, Japan

The evolutionary game in sexual reproduction of the social amoeba

The evolution of cooperation is one of the most important problems in biology because of its vulnerability to cheating. *Dictyostelium discoideum*, or the social amoeba, is used as a model organism to solve this problem. The social amoeba lives as free-living cells in most of the time, but it has also two dormant phases in starvation; one is the fruiting body and the other is the macrocyst. Although each dormant phases is hypothesized to be kin cooperation, it is unclear how these cooperative systems are maintained where the genetic diversity has been reported [1]. Here, we suggest the coexistence with fruiting bodies makes macrocyst formation stable.

In fruiting body formation, ten thousands of cells are attracted by the chemoattractant, cyclic AMP (cAMP). After the aggregation, the cells form the fruiting body, which is regarded as cooperation because nonviable stalk cells help the dispersal of spore cells. In chimeric fruiting bodies, cheater strains whose cell-type ratio is weighted toward spore cells are reported [2]. Many studies have focused on why fruiting body formation has been maintained though cheaters exist in nature [3].

On the other hand, the social amoeba also cooperates in during sexual reproduction called macrocyst formation. In darkness, some cells become gametes but the others stay vegetative cells [4]. After the gamete fusion, the zygotes secrete cAMP and collect the surrounding vegetative cells. Then, the zygotes cannibalize the cells, which leads to macrocyst formation. If these cannibalized cells have high relatedness with the zygotes, this sexual cannibalism is regarded as kin cooperation. However, there has been no empirical study, to our knowledge, why such a cooperative cannibalism has been maintained in the social amoeba.

In this study, we formed a mathematical model to test the hypothesis that the coexistence with fruiting bodies enabled macrocysts to be maintained. This hypothesis reflects the fact that both macrocysts and fruiting bodies use the common chemoattractant, cAMP. In the model, we assume there exist residents of each mating types and a mutant in either of the mating types. We investigate whether the mutant can invade the population in following two cases. When fruiting bodies are excluded from the model, it shows macrocyst formation is not maintained. Including fruiting bodies, however, the model predicts one strategy with macrocyst formation is not invaded by any other strategy; *i.e.* macrocyst formation is the evolutionarily stable strategy (ESS). Moreover, our experiment showed the coexistence of macrocysts with fruiting bodies at the same time. Therefore, it is suggested that macrocyst formation has been maintained due to the coexistence with fruiting bodies.

REFERENCES

[1] Fortunato, A., Strassmann, J. E., Santorelli L. and Queller, D. C. 2003. Co-occurrence in nature of different clones of the social amoeba, *Dictyostelium discoideum. Mol. Eco.*, **12**: 1031-1038.
[2] Strassmann, J. E., Zhu, Y. and Queller, D. 2000. Altruism and social cheating in the social amoeba *Dictyostelium discoideum.Nature*, **408**: 695-697.
[3]Li, S. I. and Purugganan, M. D. 2011. The cooperative amoeba: *Dictyostelium* as a model for social evolution. *Trends Genet.*. **27**: 48-54.
[4] McConachie, D. R. and O'Day, D. H. 1986. The immediate induction of extensive cell fusion by Ca2+ addition in Dictyostelium discoideum. *Biochem. Cell Biol.*, **64**: 1281-1287.

Masanori Tsuchiya
Graduate School of Information Science, Nagoya University, Nagoya 464-8601, Japan
e-mail: `tsuchiya@alife.cs.is.nagoya-u.ac.jp`

Reiji Suzuki
Graduate School of Information Science, Nagoya University, Nagoya 464-8601, Japan

Takaya Arita
Graduate School of Information Science, Nagoya University, Nagoya 464-8601, Japan

An agent-based evolutionary model for diversification of phenotypic plasticity and personality in resource partitioning

Organisms have plasticity and personality in their phenotypes. Phenotypic plasticity is the ability of an organism to change its phenotype in response to changes in the environment. Personality is individual differences in behavior that are consistent over time or contexts. The evolutionary significance of the inter- and intra- specific diversity in plasticity and personality has been discussed recently [1, 2, 3]. Wolf et al. showed that, in the hawk-dove game, the presence of responsive individuals can trigger a coevolutionary process which gives rise to populations in which responsive individuals coexist with unresponsive individuals who show high levels of adaptive consistency in their behavior [2]. Suzuki et al. constructed a coevolutionary model of behavioral plasticity in which several different species participate in a partitioning of their shared niches, and evolve their behavioral plasticity to avoid an overlap of their niche use. They showed that the two different types of asymmetric distributions of phenotypic plasticity among species emerge depending on the settings of the degree of congestion of the shared niches [3].

Our purpose is to further consider the evolutionary significance of such inter- and intra- specific diversity in behavioral plasticity and personality in the context of resource sharing. As a first approach, we constructed an agent-based evolutionary model of behavioral plasticity and personality in a single species [4]. The whole population is composed of groups in which there are some individuals sharing several niches. Each individual in the group chooses one of niches at each time step, obtains the fitness contribution if the focal individual has dominated a niche. With a genetically determined probability (i.e., plasticity), each individual has a chance to change the niche to use in the next time step by choosing one of the other currently unused niches if the current niche use of the focal individual overlapped with the use of others. Otherwise, in the case of the non-plastic behavior, the focal individual chooses consistently a genetically determined niche (i.e., personality) irrespective of the use of others. The results showed that diversity in the behavioral plasticity and personality emerged when the number of niches was slightly smaller than the number of individuals in a group. That is, individuals with high and low plasticity coexisted and they also had different personality due to the balances between benefit and cost of overlap avoidance behaviors.

We further extended this model to be able to adjust the numbers of species and the ratio of inter- to intra- specific interactions. In preliminary experiments under the condition of the evolution of phenotypic plasticity only (i.e., an individual keeps its own choice of niche in the case of non-plastic behavior), we observed that the intra-specific and unstable differentiation of phenotypic plasticity emerged when there were the necessary and sufficient number of niches and intra-specific interactions occur often in groups. On the other hand, the inter-specific differentiation of the phenotypic plasticity emerged, which is similar to the results in [3], when inter-specific interactions occur frequently. We also observed that both inter- and intra- specific diversity of phenotypic plasticity sometimes emerged when the ratio of inter- to intra-specific interactions was intermediate.

REFERENCES

[1] Dingemanse, N. J. and Wolf, M., 2013. Between-individual differences in behavioural plasticity within populations: causes and consequences, *Animal Behavior*, **85**, 1031-1039.

[2] Wolf, M., Van Doorn, G. S. and Weissing, F. J., 2011. On the coevolution of social responsiveness and behavioural consistency, *Proceedings of the Royal Society B*, **278**, 440-448.

[3] Suzuki, R. and Arita, T., 2014. Emergence of a dynamic resource partitioning based on the coevolution of phenotypic plasticity in sympatric species, *Journal of Theoretical Biology*, **352**, 51-59.

[4] Tsuchiya, M., Suzuki, R. and Arita, T., 2016. An evolutionary model for diversification of phenotypic plasticity and personality in resource partitioning (written in Japanese), *Proceedings of the78th National Convention of the Information Processing Society of Japan*, *Vol. 1, pp.* 293-294.

Yu Uchiumi
Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Kanagawa 240-0193, Japan
e-mail: `uchiumi_yu@soken.ac.jp`

Hisashi Ohtsuki
Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Kanagawa 240-0193, Japan

Akira Sasaki
Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Kanagawa 240-0193, Japan

Evolution of vertical transmission of symbionts by reducing the rate of cell division

Chloroplasts and mitochondria evolved from free-living bacteria via intracellular symbiosis. Through the evolutionary transition from symbionts to organelles, symbionts has become transmitted vertically and remained persistently in a host cell. In intracellular symbiosis, such as the relationship between protists and algae, vertical transmission is ensured by synchronized cell divisions of symbionts and hosts. If symbiont division is faster or slower than the host, symbionts accumulate in or are lost from their host cell. In particular, excessive accumulation makes symbionts a burden to their host and will induce host cell death. Indeed, the regulation of symbiont division rate is well observed in various symbiotic systems, for example in the symbiosis between ciliates (*Paramecium bursaria*) and green algae (*Chlorella* spp.)[1].

There are two hypotheses for the maintenance of synchronized cell divisions. The first hypothesis is that a host suppresses excessive cell divisions of symbionts. The second hypothesis is that a symbiont restrains its own cell division for the synchronization. The latter may seem paradoxical because symbionts' growth rate may increase by virtue of symbiotic interaction, and it is actually unclear whether symbionts self-restrain their own division evolutionarily.

Therefore, we theoretically explored the condition for the evolution of self-restraints in symbiont cell division. We analyzed a mathematical model, in which symbiont dynamics within a host cell is explicitly taken into account. We assumed that excessive accumulation of symbionts in a host cell leads to the host death and its burst. We also assumed that the host may acquire free-living symbionts, and, once in host cell, symbionts can be inherited randomly in daughter cells during host cell division. These assumptions lead the tradeoff between horizontal and vertical transmission as in many protist-algae symbiotic systems. If the division rate is higher in symbiont than in host, symbionts tend to accumulate in a host cell, leading to the host burst and their release into the environment. As a result, such symbionts tend to be transmitted horizontally and lose the opportunity of vertical transmission. Additionally, we also assumed that both host's and symbiont's symbiotic benefits are to reduce their death rates.

An analysis of our model reveals that a low cell division rate evolves if symbiotic benefit is large in both host and symbiont. This is because a larger symbiotic benefit given to hosts makes infected hosts advantageous over uninfected ones, leading to lower density of uninfected hosts, with which released symbionts from dead host become difficult to find next hosts. In contrast, sybmiont cell division rate evolves to a large value or increase without limit if either symbiont's or host's benefit is not sufficiently large. Thus, our results suggest that if symbiotic benefit is large both in host and symbiont, synchronized cell division can result from symbionts' self-restraint of their own division even if host's suppression of symbiont's division is absent.

We also examined the case where host, rather than symbiont, regulates the division rate of symbionts, and found that the evolutionarily stable cell division rate is different (and is smaller) than when it is self-regulated by symbionts, suggesting unresolved evolutionary conflict in either evolutionary equilibrium.

REFERENCES

[1] Kadono, T., Kawano, T., Hosoya, H., & Kosaka, T., 2004. Flow cytometric studies of the host-regulated cell cycle in algae symbiotic with green paramecium. *Protoplasma* **223**: 133-141.

Takahiro Yamagishi
Center for Ecological Research, Kyoto University, Japan
e-mail: `yamagishi@ecology.kyoto-u.ac.jp`

Ross Booton
School of Mathematics and Statistics, The University of Sheffield

Atsushi Yamauchi
Center for Ecological Research, Kyoto University, Japan

Joint Evolution of cytoplasmic male sterility and selfing rate in plant

It has been reported in some plants species that their populations consist of hermaphrodite individuals and female individuals. This type of sexual system is called gynodioecy. There are cases where cytoplasmic factor cause male sterility and change plant population from hermaphrodite into gynodioecy. This phenomenon is also known as cytoplasmic male sterility (CMS) [1]. In self-compatible species, hermaphrodite individuals can reproduce by both outbreeding and selfing, whereas female individual reproduce outbreeding only. That's why a selfing rare has influence on the evolution of gynodioecy [2]. On the contrary, sexual system, or sex ratio, would affect the evolution of selfing rate. In order to investigate joint evolution of the gynodioecy and selfing, we analyzed the evolutionary process by using mathematical model.

We considered that sexual system is determined by two types of mitochondria. The wild type mitochondria do not disturb the original hermaphrodite, although mutant mitochondrial prevent pollen production, resulting in feminization. Each individual possesses either mitochondria that inherit from their mother. On the other hand, a selfing rate is governed by quantitative gene on nuclear genome in the considered diploid organism. Our analysis has two steps. First, we assumed selfing rate as fixed value for a while, and found equilibrium frequency of CMS as previous studies did [2, 3]. Subsequently, It can be discussed whether the nuclear mutant allele which bring higher or lower selfing rate can invade the population or not. This two-step way allows us to analyze evolutionary process of gynodioecy and selfing.

Our analysis suggests that higher selfing rate can evolve as anti-CMS strategy of plants. In gynodioecious population, higher selfing rate is easy to be selected, and it suppress increase in CMS. The evolutionary branching about selfing rate is also expected, and demonstrated by individual based model. These are unique results, which have not been found in previous studies with fixed selfing rate, and this joint evolution is worthy to study in more detail.

REFERENCES

[1] Jacobs, M. S., & Wade, M. J. (2003). A synthetic review of the theory of gynodioecy. The American Naturalist, 161(6), 837-851.
[2] Dornier, A., & Dufay, M. (2013). How Selfing, inbreeding depression, and pollen limitation impact nuclear-cytoplasmic gynodioecy: a model. Evolution, 67(9), 2674-2687.
[3] Dufay, M., Touzet, P., Maurice, S., & Cuguen, J. (2007). Modelling the maintenance of male-fertile cytoplasm in a gynodioecious population. Heredity, 99(3), 349-356.

NOBUYUKI ISHIZUKA
e-mail: `ousiryu@gmail.com`
College of Science and Engineering, Aoyama Gakuin University, Kanagawa 252-5258, Japan.

Shinji Nakaoka
e-mail: `shinzy.nakaoka@gmail.com`
Graduate School of Medicine, The University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo,133-0033, Japan.

Yasuhiro Takeuchi
e-mail: `takeuchi@gem.aoyama.ac.jp`
College of Science and Engineering, Aoyama Gakuin University, Kanagawa 252-5258, Japan.

Analysis of Lymph tissues network model of HIV infection dynamics

HIV infection is known to be difficult to eradicate from a body of an infected person. One of major reason of HIV persistence is existence of reservoir cells that maintain HIV virions despite sufficient level of multiple types of drug injection. Moreover, reservoir cells are believed to stay in tissue. Importantly, lymph nodes are the main place of reservoir cells to stay. Since lymph nodes constitute a network structure, it is important to understand how network structure can mediate HIV persistence.

Here we report our progress on analyzing a mathematical model when all the migrations between N lymph nodes have equal immigration rate m. The objective of this talk is to derive explicit form of disease free equilibrium of our network model. To obtain an insight, we start with using symbolic calculation package *Sympy* to perform symbolic computation for disease free equilibrium of our model for $N = 2, 3, 4$. Based on the result, we conjecture an explicit form of the disease free equilibrium. Finally, based on the conjecture derived from symbolic computation, we have succeeded in obtaining explicit values of the disease free equilibrium for general N. We will show another progress on numerical simulation of HIV infection dynamics in lymph node network.

REFERENCES

[1] Shinji Nakaoka, Shingo Iwami, and Kei Sato, Dynamics of HIV infection in lymphoid tissue network, *Journal of Mathematical Biology,* 72:909–938 (2016) (DOI:10.1007/s00285-015-0940-x).

Yusuke Ito
Department of Biology, Kyushu University, Japan e-mail: uks3tkwbft@gmail.com

Azaria Remion
U941, INSERM, France

Alexandra Tauzin
U941, INSERM, France

Yoh Iwasa
Department of Biology, Kyushu University, Japan

Fabrizio Mammano
U941, INSERM, France

Shingo Iwami
Department of Biology, Kyushu University, Japan

Estimating the number of HIV-1 to infect target cells in nonrandom co-infection

Co-infection is a simultaneous infection event by multiple viruses and largely causes the diversity of HIV-1 through recombination. One interesting recent finding is "nonrandom HIV-1 co-infection", in which co-infection of HIV-1 occurs more frequently than it would be random, reported by Q. Dang et al., 2004[1]. "Heterogeneity of susceptibility of target cell" but not any other viral factors is thought to be a potential factor for this phenomenon[1,2].

In this study, we developed the mathematical model for nonrandom co-infection including "heterogeneity of susceptibility of target cell" and analyzed co-infection experiments. Our results show that the number of infection events per target cell based on different amount of inoculated HIV-1 is 1.02 to 1.62, and are consistent with previous experimental one[3]. Furthermore, using the parameters, we revealed that up to 40% of infected cells are co-infected, which indicates co-infection is likely to promote the HIV-1 diversity through recombination. Taken together, our experimental-mathematical approach quantitatively revealed that the frequency of co-infection events in infected cells is surprisingly high and co-infection can be a major factor to drive the diversity of HIV-1.

REFERENCES

[1] Dang, Q. et al, Nonrandom HIV-1 infection and double infection via direct and cell- mediated pathways, *Proc. Natl. Acad. Sci. USA*, **101**, (2004), 632-637.

[2] Chen J. et al, Mechanisms of Nonrandom Human Immunodeficiency Virus Type 1 Infection and Double Infection: Preference in Virus Entry Is Important but Is Not the Sole Factor, *J. Virol*, **79**, (2005), 4140-4149.

[3] Portillo. A. D et al Multiploid Inheritance of HIV-1 during Cell-to-Cell Infection, *J. Virol*, **85** (2011), 7169–7176

[4] Robertson D. L et al, Recombination in HIV-1, Nature, **374**, (1995), 124-126.

[5] Remion A.et al,Kinetics of the establishment of HIV-1 viral interference and comprehensive analysis of the contribution of viral genes, *Virology*, **487**, (2015), 59-67.

Nao Yamamoto
Hokkaido University
e-mail: `nao.m.yamamoto@gmail.com`

How Does Correlation between Condom Use and Partner Type Influence the Transmission Dynamics of STI?

Background:
No systematic review of prospective studies has been reported on the relationship between condom use and partner type or the number of sexual partners. It is pressing to clarify how this relationship has an impact on epidemic dynamics.

Objectives:
To examine under what kind of sexual relationships individuals are more likely to use condoms and to clarify its population impact on the dynamics of sexually transmitted infections using a mathematical model.

Methods:
A systematic review and meta-analysis of published studies are performed, analyzing literature that epidemiologically examined the relationship between condom use and sexual partnership. Subsequently, we compute the reproduction number accounting for the number of partners and incorporating the condom coverage, which is different dependent on the partnership (single or multiple). Finally, we evaluated the effect of reducing multiple partnerships on R0 varying condom coverage of the people with multiple partnerships.

Results:
A greater number of people used condoms during sexual intercourse outside of an ongoing relationship than with a steady partner. Furthermore, people with multiple partners use condoms more frequently than people with a single partner. Through the computational simulation, we have ascertained that as people with multiple partnerships increase, effective reproduction numbers increase in conjunction, which implies that multiple partnerships accelerate the HIV epidemic. However the association can change depending on the relative condom use of multiple partnerships, which implies we cannot conclude that multiple partnerships are the only cause of the epidemic.

Conclusions:
In spite of the high frequency of sexual contact that people with multiple partnerships have, the HIV epidemic may be primarily maintained by individuals with single partnerships due to low condom coverage. The intervention should be implemented towards peoples with single and multiple partnerships.

Kenta Yashima
The Graduate University for Advanced Studies (Sokendai), Kanagawa, Japan
e-mail: `yashima_kenta@soken.ac.jp`

Akira Sasaki
The Graduate University for Advanced Studies (Sokendai), Kanagawa, Japan

Network centrality measure based on sensitivity analysis of the basic reproductive ratio

Identification of epidemiologically high-risk communities in a metapopulation network is required for effective and efficient intervention strategies. The network centrality measure, which quantifies the relative importance of each community, is commonly utilized for this purpose. As the condition for the invasion of disease is given from the basic reproductive ratio R0, we have introduced a novel centrality measure based on the sensitivity analysis of this R0 and shown its capability of revealing the characteristics that has been overlooked by the conventional centrality measures. The epidemic dynamics over the commute network of the Tokyo metropolitan area is theoretically analyzed by using this centrality measure. We found that, the impact of countermeasures at the largest station (Shinjuku station) is more than 1,000 times stronger compare to that at the second largest station (Tokyo station), even though the population sizes are only around 1.5 times larger. Other population has even minor effect, but its relative importance in countermeasures is again most strongly determined by the existence and the number of commuters to the largest station (Shinjuku). It is well known that the hubs are the most influential nodes, however, our analysis shows that only the largest among the network plays an extraordinary role. Lastly, we also found that, the location that is important for the prevention of disease invasion does not necessarily match the location that is important for reducing the number of infected.

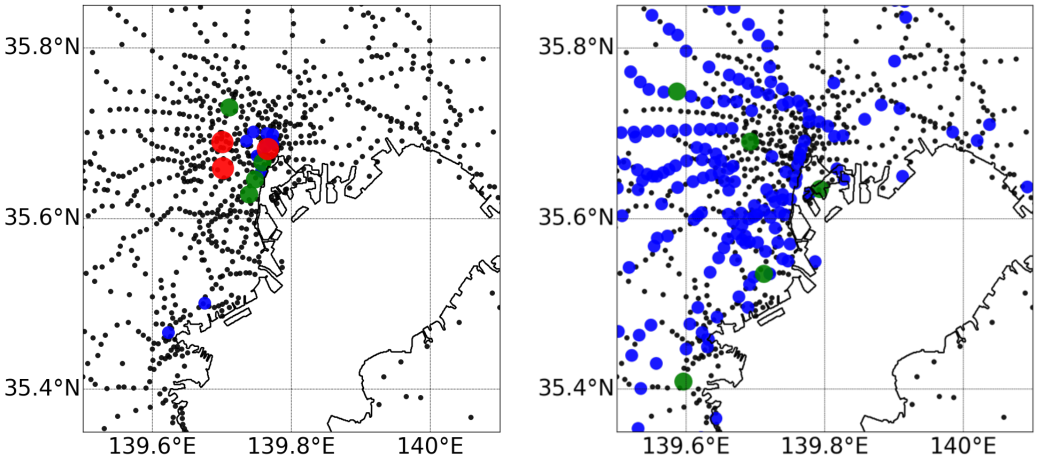


Figure: Final size of epidemic (the proportion of hosts that are eventually infected) at each local station (left: daytime, right: nighttime).

●: 0.00~0.25, ●: 0.25~0.50, ●: 0.50~0.75, ●: 0.75~1.00

Shiori Abe
Department of Information and Computer Science, Nara Women's University
e-mail: `abe-shiori1201@ics.nara-wu.ac.jp`

Fugo Takasu
Department of Information and Computer Science, Nara Women's University

Population viability analysis of the Japanese rock ptarmigan

The Japanese rock ptarmigan (*Lagopus muta japonica*) is endangered species that breeds in limited alpine zones in Japan. Total population size was estimated around 3,000 in 1980. But the population has decreased in number and the present estimation is about 1,700. To conserve the Japanese rock ptarmigan, several protective measures have been undertaken such as guarding fledgling by human attendants and artifitial incubation of eggs in order to increase the survivability of young.

In this study, we work on population viability analysis of the Japanese population based on breeding parameters estimated by field studies in the past. Suzuki at al. 2013 [1] has carried out PVA of the Japanese rock ptarmigan and concluded that the local population in Mt. Norikura is stable and the risk of local extinction is low based on breeding parameters collected by 2011. In this study, we include breeding parameters collected after 2011 [2].

We first evaluate sensitivity and elasticity of the eventual population growth rate λ on breeding parameters using matrix model [3]. We then study stochastic population dynamics using an individual-based approach in which each individual is assigned a set of properties (age, sex, holding a breeding territory or not, etc.) and reproduces and survives one year stochastically according to the breeding parameters (age-dependent annual survival probability, and clutch size, etc.)

The model analysis show that 1) increasing survival rates of young is effective to raise λ, and 2) the risk of local extinction is higher when we consider recent breeding parameters.

Based on the model analyses, we discuss effective protective measure to conserve the Japanese rock ptarmigan population.

REFERENCES

[1] Suzuki, A., Kobayahi, A., Nakamura, H., Takasu, F, 2013. Population viability analysis of the Japanese rock ptarmigan. *Wildlife Biology*, **19**: 339–346.

[2] Kobayahi, A., Nakamura, H. and Takada, M, 2014. Life history and population dynamics of the Japanese rock ptarmigan in alpine belt. *Toho University*. *(In Japanese).*

[3] Caswell, H, 2001. Matrix population models. 2nd edition. *Sinauer Associates, Inc. Publishers, Sunderland, Massachusetts, USA, 722pp.*

Miki Hamada
Graduate School of Human and Sciences, Nara Women's University
e-mail: `u1284018@gmail.com`

Fugo Takasu
Department of information and Computer Science, Nara Women's University

Spatial SIS model as a point pattern dynamics

The SIS model is one of the classical models of mathematical epidemiology [1]. The model describes the dynamics of susceptible S and infections I under the assumption that S and I are well mixed and infection occurs by the law of mass action. This deterministic model has been served as a conceptual model to study the dynamics of disease that confers no immunity. However, this model completely ignores spatial distribution of S and I. In order to explore disease spread over a space, we need to somehow extend the model to be spatial.

In this study, we extend the SIS model as a point pattern dynamics [2]. Each individual is represented by a point in two dimensional space and its status can change from S to I to S according to the following rules. Infection (S to I) occurs with the infection rate as a function of the distance from a focal S to I's. Recovery (I to S) occurs with a constant recovery rate. We simulate stochastic point pattern dynamics as an individual-based model and study the dynamics of the number of S and I and spatial distribution. A point pattern can be quantified by focusing on the number of points (1st order structure) and the number of pairs displaced by a certain distance (2nd order structure), etc. We derive deterministic dynamics of the singlet probabilities (an arbitrary chosen point is in status S and I) and the pair probabilities (an arbitrary chosen pair is in status S-S, S-I, I-S, I-I). We explore to what extent this deterministic description can explain simulation results.

REFERENCES

[1] Matt J. Keeling and Pejman Rohani. 2008. *"Modeling infectious diseases in humans and animals."* Princeton.

[2] Law Richard, David J. Murrell, and Ulf Dieckmann. 2003. "Population growth in space and time: spatial logistic equations." *Ecology*, **84.1**: 252–262.

Yusuke Ikegawa
Ryukyu Sankei Co., Ltd., Maji 123, Naha, Okinawa, 902-0072, Japan
e-mail: `y.ikegawa224@gmail.com`

Effects of spatial and temporal homogeneity of releases of sterile insects on control of pests with limited dispersal ability

Sterile insect technique (SIT) is a genetic pest control method by periodically releasing mass-reared sterile insect and thereby impeding successful reproduction of fertile pests [1]. In Okinawa Prefecture, the SIT project against West Indian sweet potato weevil, *Euscepes postfasciatus* (Fairmaire), which is an important agricultural pest of sweet potato, *Ipomoea batatas* (L.), have been initiated after success in that against some species of fruit flies. However, *E. postfasciatus* is flightless and usually shows much lower mobility than the fruit flies. It might lead to spatial segregated distributions of the wild and sterile weevils, for instance due to spatially biased releases of the latter, and consequently inhibit eradication of the former. Recently, considering a trade-off between the number of released sterile insects per release and the number of patches where the insects were released, a metapopulation model predicted that the spatially biased releases of the sterile insect could inhibit success in the SIT [2]. However, no studies proposed effective measures to improve the negative effect.

In this study, I consider that managers can vary the number of released sterile insects toward each of patches at every release so that the spatial bias for the previous release is counterbalanced (hereafter called 'temporal balancing'), as a measure to improve the negative effect of the spatially biased releases. Extending a non-spatial SIT model [3], I constructed a simple two-patch Ricker model comprised of the pest and sterile insect moving between the two habitats. I examined effectiveness of the temporal balancing on eradication of the pest in the two habitats, by numerically simulating the model with some release strategies (the number of released sterile insects, release intervals, and spatial evenness of the releases). Demographic parameter values were derived from some previous empirical works on *E. postfasciatus*.

I confirmed that the spatially biased releases inhibited successful eradication of the pest in both the two habitats as shown in previous models, and revealed that the negative effect of the spatially biased releases was dramatically improved by the temporal balancing. This was because the pests lost the spatial refuge arisen from the spatially biased releases, due to the temporal balancing of the releases. However, shortening releases intervals was necessary for efficient pest control, because the sterile insect monotonically decreased during no-release terms and the pest could temporally enjoy lower reproductive interference from the sterile insect.

In this model, the failure in the SIT is primarily mediated by too low mobility of the target insect. If I assume that the mobility of the target insect becomes sufficiently high, regional eradication of the pest is achieved, irrespective of the spatial evenness of the releases. It indicates that the spatially even release of the sterile insect is much more crucial for eradication of the pest with low mobility (e.g., *E. postfasciatus*) than for that with high mobility (e.g., some species of fruit flies), and that this is the reason why the temporally balancing spatial distribution of the sterile insect is a reasonable measure to control less mobile *E. postfasciatus*.

REFERENCES

[1] Knippling, E.F., 1955. Possibilities of insect control or eradication through the use of sexually sterile males. *J. Econom. Entomol.* **48**: 459-462.

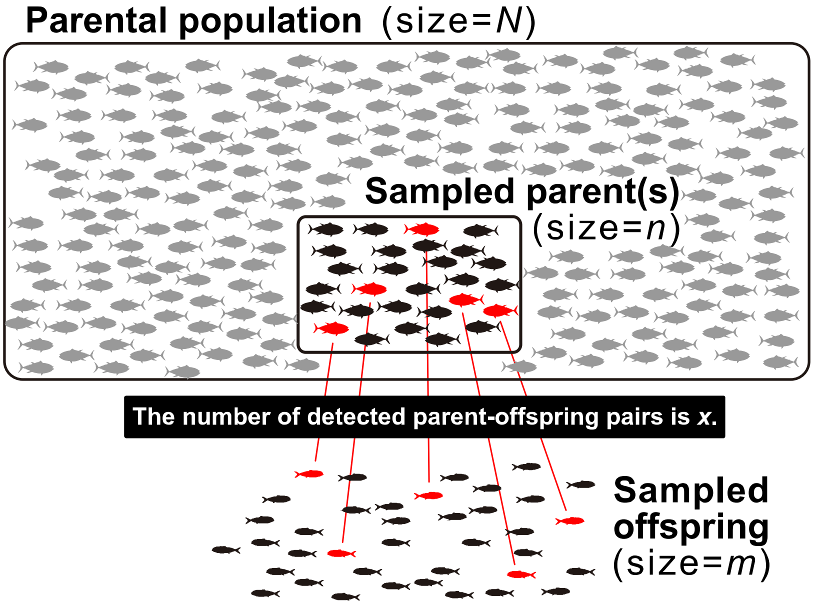
[2] Evans, T.P.O., Bishop, S.R., 2014. A spatial model with pulsed releases to compare strategies for the sterile insect technique applied to the mosquito *Aedes aegypti*. *Math. Biosci.* **254**: 6-27.

[3] White, S.M., Rohani, P., Sait, S.M., 2010. Modelling pulsed releases for sterile insect techniques: fitness costs of sterile and transgenic males and the effects on mosquito dynamics. *J. Appl. Ecol.* **47**: 1329-1339.

Takahiro Irie
Atmosphere and Ocean Research Institute, The University of Tokyo
e-mail: `irie@aori.u-tokyo.ac.jp`

A hierarchical Bayesian estimation of wild population size From the neutral genetic information

In conservation biology and fishery science, there is a strong need to improve the estimating techniques for wild population sizes of marine organisms. Current estimation methods have problems with both accuracy and precision, because of heavily relying on fishery-derived data, collected in a non-random manner. A new technique based on the neutral genetic information of randomly sampled individuals across generations is expected to be the next generation alternative. This procedure is referred to as the Close-Kin approach, in which the numbers of parent-offspring pairs (POPs) and half-sibling pairs (HSPs) are assumed to be the metrics of population size. These kinships are quantified by comparing neutral allele frequencies (e.g., those at SNPs) by means of the RAD-sequencing. However, no statistical procedure has been established yet to estimate population size from kinship information. Accordingly, the present study proposes a hierarchical Bayesian model to compute the posterior distribution of wild population size from the numbers of parental and offspring samples, POPs, and HSPs. This task begins with formulating the probability mass function (pmf) describing the stochastic behavior of POPs and HSPs, in which the parameters are population size ($\mathbf{N}$), parental sample size ($\mathbf{n}$), and offspring sample size ($\mathbf{m}$). The author tentatively termed this pmf as the modified multivariate Hypergeometric (MMHG) distribution. The parameters $\mathbf{N}$, $\mathbf{n}$, and $\mathbf{m}$ are given as vectors because of being stratified with the parental reproductive success (= the number of surviving offspring from the focal parent). For the same reason, both POPs and HSPs are matrices rather than scalars. The model also considers the parental reproductive success follows the negative binomial (NB) distribution with two parameters. These NB-parameters affect the values of parametric vectors $\mathbf{N}$, $\mathbf{n}$, and $\mathbf{m}$, which is the reason why this model has a hierarchical structure. In theory, the joint posterior distribution of population size (N) and two NB-parameters can be generated by evaluating MCMC using the Metropolis–Hastings algorithm, under the given parental sample size, offspring sample size, POPs, and HSPs. However, this method suffers from a technical difficulty, in which computational steps rapidly increases with increasing sample sizes, because the multidimensional convolution based on repeated integer partitioning is required when calculating the probability from the MMHG distribution. In this paper, I will propose some technical ideas to avoid the computational complexity due to combinatorial explosion.



Kenta Suzuki
Center for Environmental Biology and Ecosystem Studies, National Institute for Environmental Studies
e-mail: `suzuki.kenta@nies.go.jp`

Katuhiko Yoshida
Center for Environmental Biology and Ecosystem Studies, National Institute for Environmental Studies

Resilience of hydrothermal vent communities: a metacommunity framework

Hydrothermal vent communities have a patchy spatial distribution that is well-suited to a metacommunity framework. To evaluate the effect of disturbance on local community structure caused by resource mining, we developed a spatially explicit, multi-species competition model, implementing the distribution of hydrothermal vents in Okinawa trough and the connectivity between these local habitats. Using this model, we performed numerical experiments to understand the resilience of local communities in the metacommunity context. It was difficult for a community to recover its original state when it is distant from other communities. More interestingly, in some cases when a disturbed community could not recover its original state, other non-disturbed communities were "infected" with the alternative community structure without any disturbance. The result suggests that when evaluating the effect of resource mining, one should not only consider the recoverability of community at the focal location, but also its effect on other communities that are not directly disturbed.

Takenori Takada
Hokkaido University, Japan
e-mail: `takada@ees.hokudai.ac.jp`

Population statistics of random matrices

Projection matrix models have been often employed as an effective tool to quantify the population dynamics of both trees and herbs. Elasticity analysis is the most frequently-used analytical method, and Franco and Silvertown published a famous paper, where they mapped elasticity vectors of survival, growth and fecundity for 102 plant species in triangle simplex and found that they are located in specific regions depending on groups of plants with different life history and growth forms.

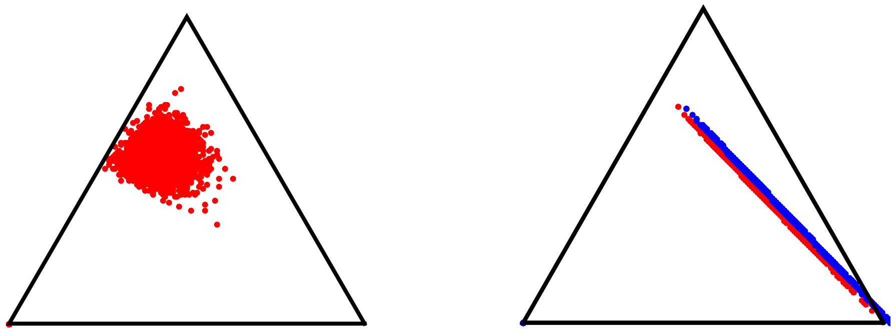
To understand and clarify why they are located in specific regions, we constructed four types of random matrices. 4 by 4 random matrices is compose of two parts: fecundity and transition probabilities from a stage to another. The distribution of fecundities is a Poisson distribution with the average p. The transition probabilities range from zero to one, whose row sums are less than 1. The elasticities for survival, growth and fecundities are calculated using 3000 random matrices and the elasticity vectors are plotted in the triangle map. Four types of matrices are as follows: (1) random matrices with no zero-element, (2) random matrices with no zero-element and the survival probabilities increase as individuals grow, (3) random matrices which have non-zero elements only on diagonal and sub-diagonal positions, (4) random matrices which have non-zero elements only on diagonal and sub-diagonal positions and the survival probabilities increase as individuals grow. The results are: (a) distribution of elasticity vectors moves to upper-left region of the triangle map as the average of fecundity increases (Fig. 1a). (b) In the third and fourth types of random matrices, the distribution is located on a line whose slope is equal to 46 degrees (Fig.1b). The slope can be proved by the following formula:

$$\tan\theta = \frac{(n-1)\sqrt{3}}{(n+1)}$$

when $n = 4$, where n is the size of projection matrix. The angle, θ, ranges from 30 to 60 degrees with n= 2 to infinity. (3) There is no elasticity vectors in the bottom half of the triangle map.

Fig.1 The triangle map of elasticity vectors of survival, growth and fecundity.

(a) For random matrices with no zero-element. (b) When individuals don't grow rapidly



Takahiro Hiraga
Department of Mathematical and Life Sciences, Hiroshima University
e-mail: m164154@hiroshima-u.ac.jp

Ryo Kobayashi
Department of Mathematical and Life Sciences, Hiroshima University

Mathematical study of the rising movement and its support from the chair

Japan is facing to the serious situation of declining birthrate and a growing proportion of elderly people. It is expected that the number of people who need nursing care drastically increase in near future. Thus it is important to reduce the physical load of care workers, and caring robots are developed for the purpose.

We propose a mathematical model of standing up motion and its support by preparing a imaginary doll named “Tachiagari-san” which consists of body, thighs, lower leg and foot connected by waist, knee and uncle joints. Firstly, we construct a healthy people’s model using the standing up data of one of the authors. Time sequence of the torque at each joint was calculated by ODE. After that, we restricted the maximum torque at the selected joint, which causes falling down of the doll. It is a model of a person who requires nursing care. Then we apply the support power to the point of the chest in three different ways. Support of Type 1 is pulling the supporting point from the same direction at all time. Support of Type 2 is pulling the supporting point from the fixed point. Support of Type 3 is pulling the supporting point so as to follow the healthy people’s model. Comparing these 3 types by appropriate criteria, it turned out that Type 3 was the best.

I simulated the standing up motion and supporting. I made a standing up simulation doll named “Tachiagari-san” consists of body, thighs, lower leg, and foot. It has waist, knee, and uncle joints. I made the “healthy people model.” It is my standing up data. After that, I weakened its torque, so it fells in the standing up motion. And I apply the support power for it. I researched the way to the 3 types support. Type 1 is pulling same direction at all time. Type 2 is pulling from the fixed point. Type 3 is pulling the user to healthy people model. Type 3 is the best support of the 3. Type 3 support applies a force that is proportional to the distance between the location of the chest and the location of the chest of the healthy people model.

In the support of Type 3, the supporting force is proportional to the displacement vector between the supporting point of the doll and the corresponding point of the healthy people’s model. It seems to be better to take larger constant of proportion. However, too large constant not only causes an uncomfortable feeling to the users, but also makes a cared person not to use their own muscles, which is an essential problem. In contrast, too small constant fails in supporting itself. The constant of proportion was searched by simulations, in which the less the machine uses energy the better constant is under the restriction of successful rising up. We obtained the best constant of proportion in various situations.

Shigehide Iwata
Tokyo University of Marine Science and Technology
e-mail: `siwata0@kaiyodai.ac.jp`

The catch control by the allocation of number boat

Marine species, especially fish lives with migration among some area. To correspond the spatial pattern of fish, fisherman moves to fish ground to maximize catch. This means the allocation of effort. The allocation of effort is important issue in two meanings; one is to increase a benefit for fisherman, the other one is taking care of stock (to take care of special area i.e. marine protected area, MPA or by the miss judge of the fisherman). Both points are trade-off. Recently, electronic searching system were developed. Ross et. al., [1] were assessed the efficiency of multiple electrofishing scenarios by comparing various strategies for the spatial and temporal allocation of sampling effort so as to improve a coastal fish community survey. This situation is same as fisherman. Therefore, the stock may not sustain if catch amount increase or there is no management. So, the optimal strategy of the allocation of boat (effort) for fishing is theoretically considered in the talk.

The optimal strategy of the fish boat, catch and fish amount, we suggest the model incorporating these factors. We consider a simple model which is constructed by two fishing ground and one port. Total fish boat is constant in the port. These one takes two states, one is operating fishery, and the other is absent among total boat. Of course, operating fish boat can be separate the boat going to one fishing ground or others.

For an analysis, we consider several situations on the fish stock dynamics, in other words, to assume the several types of movement, and population dynamics. Under the situation, we virtually operate fish boat allocation. Furthermore, all boat has same fishing ability, so the effort is proportional to the fish boat. Finally, we discuss the balance of allocation of fish boat based on several types of fish.

REFERENCES

[1] J. E. Ross, C. M. Mayer, J. T. Tyson & E. J. Weimer, 2016. Comparison of Electrofishing Techniques and Effort Allocation across Diel Time Periods, Seasons, Sites, and Habitat in the Ohio Coastal Waters of Western Lake Erie. *North American Journal of Fisheries Management*, **36**: 85–95.

Kodai Sato
Dept. of Elec., Eng. & Biosci., Waseda University, Tokyo, Japan
e-mail: `kodaisato1@gmail.com`

Shin Watanabe
Dept. of Elec., Eng. & Biosci., Waseda University, Tokyo, Japan

Atsuko Takamatsu
Dept. of Elec., Eng. & Biosci., Waseda University, Tokyo, Japan

Zone planning for emergency evacuation using *physarum* algorithm

Natural disasters, e.g. the Greatest East Japan Earthquake, sometimes bring a large number of casualties. Effective emergency evacuation planning is very important to save such people. In this poster, a zone planning method for emergency evacuation is proposed using a bio-inspired algorithm of *physarum* [1]. The easiest method for zone planning is that using Voronoi diagram. It is known as a method for partitioning of a plane into regions each of which includes a specific point as a shelter. In this method, distance between any points inside the specific regions and the shelter is minimized. However, this method takes no account of actual routes on the road network. The *physarum* algorithm mimics adaptive network formation observed in plasmodium of *phsarum* [1]. The algorithm can be applied to multi-objective optimization problem on networks.

Zone planning for emergency evacuation was calculated using *physarum* algorithm (PA). The results are evaluated using two performance functions related to cost and congestion degree [2], comparing with the results calculated by network Voronoi diagrams (ND) [3].

Congestion degree calculated by PA increases according to a control parameter μ, which represents an adaptive process of tubular structures in the road network, while the value by ND is always large than those by PA ($1.2 \leq \mu \leq 2.2$). In contrast, cost calculated by PA degreases monotonically, while the value by ND is in the middle of those in PA. The network performances calculated using PA are optimized multi-objectively under certain range of parameter μ.

REFERENCES

[1] Tero, Atsushi, Ryo Kobayashi, and Toshiyuki Nakagaki. "A mathematical model for adaptive transport network in path finding by true slime mold." Journal of theoretical biology 244.4 (2007): 553-564.
[2] Watanabe, Shin, et al. "Traffic optimization in railroad networks using an algorithm mimicking an amoeba-like organism, Physarum plasmodium."Biosystems 105.3 (2011): 225-232.
[3] Okabe, Atsuyuki, et al. "Generalized network Voronoi diagrams: Concepts, computational methods, and applications." International Journal of Geographical Information Science 22.9 (2008): 965-994.

Takuya Sekiguchi
National Institute of Informatics
e-mail: `sekiguchi_takuya@nii.ac.jp`

Kohei Tamura
Tohoku University

Naoki Masuda
University of Bristol

How population clusters predict the population growth in Japan

Population trends are often measured and discussed on the basis of administratively defined subdivisions of countries. However, residential mobility and the birth rate can be affected by the socioeconomic and geographic factors, which are independent of administratively defined borders. In the present study, we extract population clusters, applying the city clustering algorithm [1, 2] to Population Census of Japan, and analyze the population growth in each cluster during the period from 2000 to 2010. Our statistical analyses show that the population density, the male-to-female ratio, and the shape of the cluster have significant effects on the population growth within the cluster. We also report how those factors affect the changes in the shape of the cluster.

REFERENCES

[1] Rozenfeld, H. D., Rybski, D., Andrade, J. S., Batty, M., Stanley, H. E., & Makse, H. A. (2008). Laws of population growth. *Proceedings of the National Academy of Sciences of the United States of America*, **105**(48), 18702-18707.
[2] Rozenfeld, H. D., Rybski, D., Gabaix, X., & Makse, H. A. (2011). The area and population of cities: New insights from a different perspective on cities. *American Economic Review*, **101**(5), 2205-2225.

Mayumi Seto
Faculty of Sciences, Nara Women's University, Nara, Japan
e-mail: `seto@ice.nara-wu.ac.jp`

Koichiro Uriu
Graduate School of Natural Science and Technology, Kanazawa University, Ishikawa, Japan

Isao Kawaguchi
Research Center for Radiation Protection, National Institute of Radiological Sciences, Chiba, Japan

Hiroyuki Yokomizo
Center for Health and Environmental Risk Research, National Institute for Environmental Studies, Ibaraki, Japan

Cost-benefit analysis of food safety management: The case of radioactive contaminant

Public concerns about food risks have increased due to repeating food safety incidents (e.g., bovine spongiform encephalopathy (BSE), microbial and chemical contaminations) in the past few decades. Early hazard identification and prompt safety regulation on sale and consumption of contaminated food are important for the protection of consumers' health. Strict food safety regulations can reduce consumers' health risk, whereas food safety policy attempting to achieve zero risk may increase economic costs involved with prolonged regulations.

In this study we propose a theoretical approach to analyze consumers' benefit by avoiding food risk and producers' cost by restriction on food export, both of which are associated with food restriction period. The food restriction period is controlled by the probability of food samples passing a safety test, which depends on both food safety regulation policy (e.g., the number of samples, the condition for removal of food restriction) and the dynamics of contaminants [1]. Consumers' risk and benefit are estimated from the amount of dose that is avoided until the restriction is removed. Meanwhile, producers' cost is evaluated from the economic losses due to product bans during the food restriction period.

We applied our approach to the case of radioactive contamination (especially ^{134}Cs and ^{137}Cs contamination) on food caused by the nuclear accident at the Fukushima Daiichi nuclear power plant on March 11, 2011, and following food safety management adopted by the Japanese Ministry of Health, Labour and Welfare. The results suggested that the rapid decrease of radioactive cesium in the most common foods could keep the potential dose exposure per consumer lower than the permissible dose limit, which is consistent with the previous studies (e.g., [2]). Although the consumers' benefit tends to be bounded, the producers' cost is accumulated throughout the food restriction period, which emphasis the importance of considering both cost and benefit of food safety regulation when adopting a food safety policy.

REFERENCES

[1] Seto, M. and Uriu, K., 2015 Organizer, 2016. Sample Size Allocation for Food Item Radiation Monitoring and Safety Inspection. Risk Anal. 35, 409–422.
[2] Harada, K. H., Fujii, Y., Adachi, A., Tsukidate, A., Asai, F., Koizumi, A., 2012. Dietary intake of radiocesium in adult residents in Fukushima prefecture and neighboring regions after the Fukushima nuclear power plant accident: 24-h food-duplicate survey in December 2011. *Environ. Sci. Technol.*, **47**(6): 2520–2526.

Hironori Fujita
National Institute for Basic Biology, Okazaki, Aichi 444-0867 Japan
e-mail: `hfujita@nibb.ac.jp`

Masayoshi Kawaguchi
National Institute for Basic Biology, Okazaki, Aichi 444-0867 Japan

Keiko U. Torii
Howard Hughes Medical Institute, University of Washington, Seattle, WA 98195 USA

Pattern density control in Turing systems

The self-organization of stable patterns is critical in the field of developmental biology and has been explained by the Turing mechanism, in which the interactions among diffusible molecules translate into stable patterns. However, such stable patterns induced by the Turing mechanism are difficult to be predicted from model dynamics. Thus, these patterns are usually investigated using numerical simulations. In this study, we found that the pattern density (proportion of area with a high concentration of dynamics molecules) is correlated with the relative equilibrium position between the upper and lower constraints. Based on this finding, we established a theoretical method that can predict pattern density according to model dynamics and successfully applied this method to a representative case of animal skin color patterning. This relationship between pattern density and equilibrium position is detected in various Turing systems, including linear and nonlinear dynamics, activator–inhibitor-type dynamics, and substrate–depletion-type dynamics. Our method may be widely applicable to self-organized patterns induced by the framework of local activation and long-range inhibition. Thus, this application would be a powerful and reliable tool for elucidating developmental mechanisms in biological systems.

REFERENCES

[1] Shoji, H., Iwasa, Y., Kondo, S., 2003. Stripes, spots, or reversed spots in two-dimensional Turing systems. *J. Theor. Biol*. **224**: 339-350.
[1] Miyazawa, S., Okamoto, M., Kondo, S., 2010. Blending of animal colour patterns by hybridization. *Nat. Commun*. **1**: 66.

Ryosuke_Kohno
Graduate School of Life and Medical Sciences, Doshisha University, 1-3 Tatara Miyakodani, Kyotanabe, Kyoto, Japan

Yoshiki_Kamiya
Graduate School of Life and Medical Sciences, Doshisha University, 1-3 Tatara Miyakodani, Kyotanabe, Kyoto, Japan

Hiroshi_Kawakami
Faculty of Engineering, University of Tokushima, 2-1 Minamijohsanjima-cho, Tokushima, Japan

Masatomo_Matsushima
Faculty of Life and Medical Sciences, Doshisha University, 1-3 Tatara Miyakodani, Kyotanabe, Kyoto, Japan
e-mail: `mamatsus@mail.doshisha.ac.jp`

Classifying of synchronization pattern in oscillator circuits with optical signal

In this presentation, We introduce the synchronization phenomenon patterns of the square wave oscillator. These oscillators were introduced SEKIKAWA et al., 2011[1].

They are controlled by an optical signal. There are three kinds of oscillator circuits. Two kinds of their circits are designed by arranging the position of a electornic element (phototransistor), and another circit are designed without a phototransistor. Phototransistor plays a role to sense light of the LED. Therefore, these oscillator circits are called “Electric fireflies’’ or “LED fireflies’’.

This time, we inform new discovery. When three oscillator circits are coupled circularly, Blinking of the lights of the LED turn around. Example, clockwise or counterclockwise. This phenomenon does not last long. After having done about ten laps, blinking of the lights become the different mode. This mode is that reversing synchronization by two circits (forward synchronization) and another circit. This phenomenon has multiple stability.

We consider that this phenomenon resembles the transmission circits of the brain. And so, we call these circits “Optical network’’. Analysis of the multiple stability is necessary for the control of the optical network. But, the multiple stability is too complicated, and it is difficult to analyze it by a true circit.

We model these oscillators circits in substitution for a true circit. We use “MapleSim’’ for modeling. We introduce analysis by MapleSim.

REFERENCES

[1] Munehisa SEKIKAWA, Keiko KIMOTO, Takashi KOHNO, Hiroshi KAWAKAMI, and Kazuyuki AIHARA, 2011. Synchronization phenomena in square-wave oscillators with optical coupling. *IEICE Technical Report*, **CAS2011-45,NLP2011-72**: 73–78.

Naoto Shingu
Kyushu University
e-mail: `kiani127x525y@gmail.com`

Akiko Nakamasu
Kyushu University
e-mail: `nakamasu@anat1.med.kyushu-u.ac.jp`

Takashi Miura
Kyushu University
e-mail: `miura_t@anat1.med.kyushu-u.ac.jp`

Mathematical analysis for aging effects of endothelial cells on their self-organized pattern size

Vascular networks spread around the body and deliver nutrients and oxygen to various tissues. Vascular endothelial cells cover the lumen of blood vessels and have the capacity to make self-organized patterns. When HUVECs are cultured on Matrigel, a kind of extracellular matrix, they generate the net-like pattern autonomously.

With this culture system, we found that their pattern size varies depending on the passage numbers of component cells, suggesting ageing of cells affect the pattern size. Consistent with this observation, it has been reported that vascular endothelial cell specific ARIA (apoptosis regulator through modulating IAP expression) gene, inhibitor of apoptosis, is increased in the aged cells [1]. Gene knock down experiments shows that the ARIA functions to reduce apoptosis then accelerated chemotactic cell migration and tube formation (i.e. the reduction of the pattern size) [1],[2].

In this work, we mathematically analyze these two effects (apoptosis and chemotaxis) on pattern size. We used well-known Keller-Segel model that was reaction-diffusion system with a chemotaxis term to the analysis of this system. To consider the effects of apoptosis and chemotaxis, at first we performed linear stability analysis to obtain the fastest growing wavenumber. Then the Monte Carlo methods were used to reveal the qualitative change of the most-unstable wavelength as particular parameters (related to apoptosis and chemotaxis) were increased. For qualitative understanding of effects of the parameters, geometrical analysis using null clines was also performed. We plot null clines of two components against the wave number k. It was predicted that the wavelength became approximately most unstable when the difference of the slopes of two null clines was maximum. The wavelength derived from dispersion relation was compared to that obtained by null clines.

REFERENCES

[1] Ikeda, K., *et al.*, 20011. Apoptosis regulator through modulating IAP expression (ARIA) controls the PI3K/Akt pathway in endothelial and endothelial progenitor cells. *PNAS*, **108**: 9472–9477.
[2] Koide, K., *et al.*, 2009.Identification of ARIA regulating endothelial apoptosis and angiogenesis by mofulating proteasomal degradation of clap-1 and clap-2. *PNAS*, **106**: 8227–8283.

Hiroto Shoji
Kyoto Prefectural University of Medicine
e-mail: `shoji@koto.kpu-m.ac.jp`

Physical Analysis of Branching Patterns of Sinusoidal Networks in Hepatic Lobule

The liver is one of the most important organs and is capable of regenerating itself [1]. The sinusoid is defined as a small blood vessel and the bile canaliculi is a thin tube that collects bile secreted from hepatocytes; these two tubes are arranged along cords of hepatocytes, without crossing each other. Since morphology changes of branching networks cannot be fully understood in two dimensions, three-dimensional (3D) analysis is needed for mathematical understanding of morphology. Confocal microscope images are useful for observing 3D structures; however, it is necessary to explicitly describe the vessel structures using 3D images of sinusoidal endothelial cells. For this purpose, we proposed a new approach for image segmentation based on the Turing reaction-diffusion model, in which temporal and spatial patters are self-organized. Turing conditions provided reliable tools for describing the 3D structures. Using the proposed method, the sinusoidal patterns of rat fed a high-fat/high-cholesterol diet were examined; these rat exhibited pathological features similar to those of human patients with nonalcoholic steatohepatitis related to metabolic syndrome. The findings showed that the parameter in diffusion terms differed significantly among the experimental groups [2]. Moreover, we also discuss the relationship between structures and functions of the biological branching system of sinusoid. To quantify the structural properties of the branching systems and the physical properties of fluid dynamics on the systems, a branching network model introduced [3].

REFERENCES

[1] Sheila, S. and Dooley, J., 2002. *Diseases of the liver and billary systems*. Willey-Blackwell.
[2] Shoji, H. and Yamada, K., A reaction-diffusin algorithm for segmentation of three-dimensional sinusoidal networks in rats fed a high-fat and high-cholesteril diet. *(submitted)*.
[3] Shoji, H., Sakuma, S., Hontani, H., Akahoshi, K. and Kudoh, A., 2016. Three-dimensional periodic network patterns of micro structures in rat liver from a view of fractal analysis. *RIMS Kokyuroku*, **1994**: 94–100.

Takaaki Yonekura
Botanical Gardens, Graduate School of Science, The University of Tokyo
Hakusan 3-7-1, Bunkyo, Tokyo 112-0001, Japan
e-mail: `yonekura@ns.bg.s.u-tokyo.ac.jp`

Munetaka Sugiyama
Botanical Gardens, Graduate School of Science, The University of Tokyo

Analysis of orixate phyllotactic pattern with expanded Douady and Couder's model

Phyllotaxis is the arrangement of leaves around a stem. Research on phyllotaxic pattern generation has a long history, and already in the early days, morphological studies attributed phyllotactic patterning to the nature that a new leaf primordium is formed in the largest gap between existing primordia, and as far away as possible from them on the periphery of the shoot apical meristem (SAM), which later led to the hypothesis that the position of primordium formation is determined under the influence of the inhibitory effect by the preceding primordia. Many mathematical models have been constructed based on this hypothesis and succeeded in the generation of several major types of phyllotactic patterns. Of these, here we focus on the simple and powerful models proposed by Douady and Couder (DC models); DC model I and DC model II [1, 2].

DC model I assumes periodical formation of leaf primordia one by one at the position on the SAM periphery where the sum of inhibitory effects from preceding primordia is smallest, and thus it is specialized for alternate phyllotaxis. DC model II assumes that a leaf primordium develops on the SAM periphery when and where the sum of inhibitory effects falls below a given threshold, and it allows whorled phyllotaxis as well as alternate phyllotaxis. In both models, the inhibitory power of each existing primordium is fixed to be constant, and the inhibitory effect is supposed to decline with the distance from the primordium.

Computer simulations with DC models revealed that most of common phyllotactic patterns, such as distichous, spiral (with divergence angles close to the golden angle), decussate, and tricussate patterns, are generated by the models according to parameter settings. There are, however, still some phyllotactic patterns that cannot be produced by DC models, an interesting example of which is orixate phyllotaxis.

Orixate phyllotaxis is a specific type of alternate phyllotaxis named from *Orixa japonica*, and is characterized by repetition of a sequence of different divergence angles; 180˚, 90˚, 180˚, and 270˚. Although species that show orixate phyllotaxis are rare, they are found in several distant taxa, suggesting that orixate phyllotaxis occurred independently in each taxon. It is therefore likely that orixate phyllotaxis is generated by a common regulatory mechanism of leaf primordium formation under some particular condition rather than by an orixate-unique mechanism. If this is true, mathematical models that fully account for spatial regulation of leaf primordium formation should be able to produce not only major phyllotactic patterns but also orixate phyllotaxis.

In the present study, we expanded DC models by introducing primordial age-dependent changes of the inhibitory power, and examined them for the abilities of generation of orixate phyllotaxis. The expanded versions of both DC models I and II returned orixate phyllotaxis in computer simulation with definite ranges of parameters. Morphometrically, the orixate phyllotactic pattern produced by computer simulation using expanded DC model II fitted well with the actual orixate patterns observed in the winter buds of *Orixa japonica*.

REFERENCES

[1] S. Douady and Y. Couder, 1996. Phyllotaxis as a dynamical self organizing process part I: the spiral modes resulting from time-periodic iterations. *Journal of Theoretical Biology*, **178**: 255–274.

[2] S. Douady and Y. Couder, 1996. Phyllotaxis as a dynamical self organizing process part II: the spontaneous formation of a periodicity and the coexistence of spiral and whorled patterns. *Journal of Theoretical Biology*, **178**: 275–294.

Yoshinori Hayakawa
Theoretical Biology Laboratory, RIKEN
e-mail: `y.hayakawa@riken.jp`

Masashi Tachikawa
Theoretical Biology Laboratory, RIKEN

Atsushi Mochizuki
Theoretical Biology Laboratory, RIKEN

Mathematical study of gene expression and morphogenesis coupling that realizes flat leaf formation

Most of the land plants generally have dorsoventrally flat leaves, maximizing the surface area of both upper (adaxial) side and lower (abaxial) side. The former is specialized for light capturing for photosynthesis and the latter is specialized for gas exchange. From findings of molecular genetics, it has been considered that the coupled dynamics between tissue morphogenesis and gene regulation for cell identity is responsible for making flat leaves. The hypothesis claims that a flat leaf is generated under two assumptions, i) regulations between two groups of genes specifying adaxial and abaxial sides are mutually recessive, ii) cell divisions are induced at the limited region in the leaf margin where expressions of two groups are overlapped. We examined the plausibility and possibility of this hypothesis from the dynamical point of view. We studied a mathematical model where two processes are coupled, tissue morphogenesis induced by cell division and deformation, and dynamics of gene regulations. We used vertex dynamics for modeling of the cell-based morphogenesis. For the second process of gene expression, we used an ODE for the dynamics of activity of each gene in each cell under the assumption that gene activities are uniform inside of each cell. From the analysis of the model we found that the classically believed hypothesis is not sufficient to generate flat leaves with high probability. We examined several different modifications and revision of the model. Then we found that a simple additional rule of polarized cell division facilitates flat leaf formation. The result of our analysis gives prediction of possible mechanism, which can be easily verified in experiments.

Kazuya Horibe[1]
e-mail: `kazuya-horibe@ist.osaka-u.ac.jp`
Ken-ichi Hironaka[2,3,4]
Katsuyoshi Matsushita[2]
Koichi Fujimoto[2]

[1]Graduate School of Information Science and Technology, Osaka University
1-4, Yamadaoka, Suita-shi, 565-0871, Japam
[2]Graduate School of Science, Osaka University
1-1, Machikaneyama-cho, Toyonaka-shi, 560-0043, Japan
[3]JSPS Research Fellow(PD)
Kojimachi Business Center Building, 5-3-1 Kojimachi, Chiyoda-ku, Tokyo, 102-0083, Japan
[4] RIKEN Center for Developmental Biology
2-2-3 Minatojima-minamimachi, Chuou-ku, Kobe, 650-0047, Japan

Curvature-driven splitting of a planar traveling wave

Although reaction-diffusion equations provide the variety of traveling waves dynamics such as collision and annihilation mainly on a flat surface[1], little is known about the role of curved surface. Here we numerically show the sequence of dynamics, i.e., bending, collision, annihilation and splitting of a traveling wave, can be driven by a curved surface represented by the two dimensional Gaussian function. When a planar traveling wave of Fitzhugh-Nagumo reaction-diffusion equation[2] passed through the bell-shaped surface, its traveling direction varied depending on the local curvature; The wave first bended backwardly into a wedge shape outlining the bell shape. Next, parts of wave passing on the both sides of the bell shape rotated into opposite directions and then collided head-on. Finally, these collision parts annihilated each other whereas the other parts split into two parts, i.e., a ring wave surrounding the bell shape traveling to the peak and a planar wave traveling behind the bell shape to same direction as the initial condition. The sequence to wave splitting occurred above a threshold ratio of the height and width of the bell shape. The wave split utilizing the curvature information could function as a signal processing on convoluted surface such as amoeboid cells[3] and brain cortex[4].

REFERENCES

[1] S.Ei, M.Mimura, M, Nagayama, *Physica D*, **165** (2002): 176-198
[2] R. Fitzhugh, *Biophys. J.,* **1** (1961): 445–466
[3] D. Taniguchi et al., *PNAS*, **110** (2013): 5016-5021
[4] E. Santos, M. Schöll, R. Sánchez-Porras et al., *Neuroimage*, **99** (2014): 244–255

Osamu Iizuka
Kyushu University School of Medicine, Fukuoka, Japan
e-mail: `1MD14002G@s.kyushu-u.ac.jp`

Akiyoshi Uemura
Graduate school of Medicine, Nagoya City University

Takashi Miura
Kyushu University Graduate School of Medical sciences, Fukuoka, Japan

Mechanism of Scaling law formation in developing retina vasculature

During retina development, the endothelial cells migrate from optic disk on part of preexisting fine astrocyte mesh to form initial network structure [1]. Later blood flow is established, results in remodeling of initial vascular network. In adult retina vasculature, certain scaling law was observed by box count method [2]. In the present study, we tried to understand how the scaling law is established during development.

At first, we measured the number and size distribution of islands surrounded by capillary meshwork. The log-log plot showed single peak sandwiched by two linear relationships in larger and smaller scale. We try to understand these characteristics separately.

(1) Existence of peak can be reproduced by assuming repulsive cell-cell interaction. Single peak represents there is a mechanism to generate structure of similar size. We tried to understand this characteristic by voronoi division. We considered astrocyte meshwork structures as voronoi polygon generated by repulsion by Muller glia cells [3], and investigated features of voronoi polygon. In this process, we derived the size distribution of 1D voronoi division and predicted the size distribution of multidimentional voronoi division. By using this prediction formula, we found that astrocyte meshwork structures are considered as voronoi division.

(2) Larger scale relationship can be interpreted by the formation of avascular zones around arteries. Large islands are mainly distributed in avascular zone in which some of the meshwork is removed stochastically around the arteries. We model this phenomenon by a size distribution of one dimensional rectangular mesh whose boundary are randomly removed. Simple analysis showed that the size distribution should be linear on log-linear plot.

(3) Smaller scale relationship comes from formation of random connection between endothelial cells.

REFERENCES

[1] A. Uemura, M. Ogawa, M. Hirashima, T. Fujiwara, S. Koyama, H. Takagi, Y. Honda, S. J. Wiegand, G. D. Yancopoulos, and S.-I. Nishikawa, “Recombinant angiopoietin-1 restores higher-order architecture of growing blood vessels in mice in the absence of mural cells,” *Journal of Clinical Investigation*, vol. 110, no. 11, pp. 1619–1628, Dec. 2002.

[2] P. Ball, *Flow*. Oxford University Press, 2011.

[3] A. Reichenbach and A. Bringmann, “New functions of Müller cells,” *Glia*, vol. 61, no. 5, pp. 651–678, Feb. 2013.

Sang-Woo Lee
RIKEN QBiC, Kobe, Japan
e-mail: `ledman97@gmail.com`

Yoshihiro Morishita
RIKEN QBiC, Kobe, Japan

Neutral cell competition and tissue growth efficiency

Cell competition was originally reported as the competition between two cell populations with different genetic backgrounds. On the other hand, recent studies reported that non-negligible number of cells are extruded from developing tissues even in a genetically-identical cell population [1-4]. Not only in such experimental studies, in mechanical simulations for epithelial tissue, cell extrusion is observed even when mechanical/growth parameters are identical for all cells. In this manner, the extrusion of a portion of cells from tissues itself is not necessarily due to the difference in genetic background, and not programmed a priori. In that sense, the extrusion from a genetically homogeneous tissue may be referred as a result of "neutral" cell competition (NCC). In contrast to NCC, the competition between the cell populations with different genetic background which is caused through specific signaling pathways may be called "regulatory" cell competition (RCC). We here studied mechanisms of NCC because we can approach it from a pure mechanical viewpoint independently of specific chemical signaling and gene regulation that are not fully understood.

In this study, we first introduce two kinds of fitness, cellular and tissue-level ones. Regarding each cell population with a certain growth/mechanical trait as "species", the time derivative of its logarithmic growth curve defines a fitness measure of the species. On the other hand, when different cell populations with different traits are mixed, the growth rates of each population and the whole tissue are different in general. Then tissue-level fitness is defined as the average of cellular fitness between species weighted by the frequency of each species. Importantly, in the mixed situation, both cellular and tissue-level fitness varies over time as a result of the change in the frequency distribution of species constituting the focal tissue through competition between them.

After defining the fitness, by numerical simulations of vertex dynamics model, we examined the dependence of cell extrusion rate or cellular fitness on mechanical/growth parameters of cells in the cases of pure population. We found that the dependence was summarized in how those parameters affect geometrical and stress heterogeneity in tissues. By using the results, we proposed possible feedback mechanisms depending on cellular stress state, which reduces the energetic loss due to cell extrusion.

Furthermore, we examined what happens through competition in a population where cells with different mechanical traits are mixed. When daughter cell epigenetically inherited its parent's trait, the trait distribution within the tissue drastically changed with the tissue growth and, as a result, the fitness at the tissue-level increased, clearly showing that the NCC can improve tissue growth efficiency through the selection of cell mechanical traits, i.e., intra-tissue "evolution". Further, through the selection, cellular phenotype was homogenized, which is considered to be another possible role of NCC. From a more theoretical side, we proposed another differential equation model of competition dynamics that permits to approximately calculate the time evolution of tissue-level fitness and trait distribution. The model is useful in predicting what happens when the tissue size is much larger, e.g., reached at fully-developed size with 10^6 cells, because direct simulations of cell-based mechanical model require immense amount of computation time.

REFERENCES

[1] Marinari, E. et al., 2012. Live-cell delamination counterbalances epithelial growth to limit tissue overcrowding. *Nature*, **484**: 542-545.
[2] Eisenhoffer, G.T. et al., 2012. Crowding induces live cell extrusion to maintain homeostatic cell numbers in epithelia. *Nature*, **484**: 546-549.
[3] Etournay, R. et al., 2015. Interplay of cell dynamics and epithelial tension during morphogenesis of the Drosophila pupal wing. *eLife*, **4**: e07090.
[4] Guirao, B. et al., 2015. Unified quantitative characterization of epithelial tissue development. *eLife*, **4**: e08519.

Fumito Mori
Theoretical Biology Laboratory, Riken, Wako, Japan
e-mail: `fumito.mori@riken.jp`

Atsushi Mochizuki
Theoretical Biology Laboratory, Riken, Wako, Japan

Origin of cell diversity: Analysis of fixed points in Boolean networks

In cell differentiation, identity of cell is determined by a gene expression pattern, where a subset of genes is constantly active. Therefore, dynamics of gene activities based on regulatory network are expected to have ability to generate at least as many gene expression patterns as the number of cell types. To clarify the mechanism providing a sufficient number of gene expression patterns is important for discussing origin of diversity of cell types. Boolean network model [1] has been employed to describe gene regulatory dynamics, where a fixed point in the state space corresponds to a gene expression pattern for cell identity. Interestingly, the average number of fixed points in randomly constructed Boolean network is just one [2]. Thus, real gene regulatory systems would have special characteristics, which may be expected to be effective network structure of regulations and effective regulatory functions for generating various gene expression patterns.

In this study, we investigate how the average number of fixed points in Boolean network is dependent on network structure and also biased choice of Boolean functions. Here, a network consists of a set of genes and directed links representing existence of gene regulations. We fix network and assign a Boolean function consistent with the network structure to every gene at random. Under the condition, we prove that the average number of fixed points is independent of network structure and exactly one.

Next, we introduce biases in choice of functions to examine influence of them to the average number of fixed points. We pick up one or several genes and apply bias to the choice of Boolean functions only for these genes while the other genes have no bias. It is proven that the average number of fixed points is also one unless the subgraph consisting of genes biased and links between them has a cycle in the regulatory network. Moreover, we demonstrate that positive and negative feedback respectively increases and decreases the average number of fixed points. Consequently, real regulatory networks would have positive feedbacks appropriately.

REFERENCES

[1] Robeva Raina, and Terrell Hodge, eds. *Mathematical concepts and methods in modern biology: using modern discrete models*. Academic Press, 2013.
[2] Mochizuki, Atsushi. "An analytical study of the number of steady states in gene regulatory networks." *Journal of Theoretical Biology* 236.3 (2005): 291-310.

Shigeru Moriyama
Department of Developmental Biology, Shimane University Faculty of Medicine, Shimane, 693-8501, Japan
e-mail: `moriya12@vega.ocn.ne.jp`

Junko Kuramoto
Department of Developmental Biology, Shimane University Faculty of Medicine, Shimane, 693-8501, Japan

Hiroki Otani
Department of Developmental Biology, Shimane University Faculty of Medicine, Shimane, 693-8501, Japan

Mathematical representation and analysis of the number of cells in the intestinal epithelium of mouse embryos

We have been trying to represent developmental phenomena in mathematical models, and conducted the present study on the intestinal epithelium.

We measured the number of total cells in the intestinal epithelium of mouse embryos by stereology at embryonic day (E) 11.5, 13.5, 15.5, and analyzed the data using Excel and Image J software.

We examined whether the exponential growth model of cultured cells in culture media is applicable for the growth of the cells in the intestinal epithelium *in vivo*, and showed that the proliferation of cells in the intestinal epithelium *in vivo* is represented by an exponential function curve.

We also confirmed that the growth of epithelial cells using an Excel built-in formula, and estimated the epithelial cell numbers for the other embryonic days every 0.5 day.

Whereas sections of the intestine are elliptic, we hypothesized that the genuine intestinal tract is a cylinder. We measured the minor axis of the ellipses of the epithelial-mesenchymal boundary, built an approximation formula, and using the formula we predicted the minor axis of the other parts of the intestinal tract.

We also measured the length of the inner circumference of the epithelium and observed that it changes in a similar manner with the minor axis of the ellipse. We calculated the tilting angle of the ellipse of each cross-section against the cylinder, and corrected the length of the inner circumference.

We showed that epithelial outside diameter and the inner circumference of E15.5 changed in a stepwise manner along the long axis of the intestinal tract.

REFERENCES

[1] 巌佐庸，数理生物学入門 1998, 2-7.

[2] 倉本純子，2015. マウス胎仔の腸管上皮における細胞数の計測，島根大学大学院医学系研究科修士論文， 2015, 3.

[3] Matsumoto A., Hashimoto K., Yoshioka T., Otani H., 2002. Occlusion and subsequent re-canalization in early duodenal development of human embryos: integrated organogenesis and histogenesis through a possible epithelial-mesenchymal interaction. *Anatomy and Embryology*, **205**: 53-65.

[4] 森山茂，2016. マウス胎仔の腸管上皮における細胞数と発生過程の数理表現と解析，島根大学大学院医学系研究科修士論文，2016, 3.

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Yuto Naroda
Kyushu University Faculty of Medicine
e-mail: `nrdyt0117@yahoo.co.jp`

Kenji Yoshimura
Department of Neurology, Osaka City General Hospital

Yoshinaga Kajimoto
Department of Neurosurgery, Osaka Medical College

Tomohisa Ohmura
Department of Neurosurgery, Osaka Medical College

Takashi Miura
Kyushu University Graduate School of Medical Sciences

Mathematical analysis of fractality of skull sutures

Skull suture has been regarded as typical example of fractal structure in biology. Theoretical models based on Eden front [1] or Diffusion-Limited Aggregation (DLA) [2] had been proposed. We have previously shown that the maintenance of suture tissue width and formation of interdigitation in skull suture can be reproduced by reaction-diffusion framework [3]. Simple reaction-diffusion model can only produce structure with single characteristic length. To generate a fractal structure in this framework, we introduced a time-dependent parameter in the model. By this effect, the model generates larger structure at first, and it gradually adds smaller structures to preexisting larger structures.

To examine whether this mechanism is actually working *in vivo*, we observed time course of human skull suture development by 3DCT. Contrary to our expectation, small and large structures appeared simultaneously during suture development. These data are more consistent with Eden and DLA type mechanisms. Therefore, we need to modify the model to generate fractal structure from the early phase of pattern formation.

We are now trying to incorporate Eden like effect in biologically plausible context. At first we developed an intuitive explanation why random growth of interface can generate fractal pattern using simplified Eden model. Next, we formulated a model with biologically plausible assumption in which mesenchyme cells differentiate into bones *in situ*, and their differentiation capacity is stochastic. Numerical simulation of the model generated fractal structure, and we found that simplified version of the model is equivalent to simplified Eden model.

REFERENCES

[1] Y. Oota, T. Nagamine, K. Ono, and S. Miyazima, “A Two-Dimensional Model for Sagittal Suture of Cranium,” *Forma*, vol. 19, pp. 197–205, 2004.

[2] C. P. E. Zollikofer and J. D. Weissmann, “A bidirectional interface growth model for cranial interosseous suture morphogenesis,” *J Anat*, vol. 219, no. 2, pp. 100–114, May 2011.

[3] T. Miura, C. A. Perlyn, M. Kinboshi, N. Ogihara, M. Kobayashi-Miura, G. M. Morriss-Kay, and K. Shiota, “Mechanism of skull suture maintenance and interdigitation,” *J Anat*, vol. 215, no. 6, pp. 642–655, Dec. 2009.

Toshiki Oguma
School of Medicine, Kyushu University
e-mail: `t.oguma.111@s.kyushu-u.ac.jp`

Tomoharu Shinoda
Graduate school of Medicine, Nagoya University

Shuntaro Ogura
Graduate school of Medicine, Nagoya City University

Akiyoshi Uemura
Graduate school of Medicine, Nagoya City University

Takaki Miyata
Graduate school of Medicine, Nagoya University

Takashi Miura
Graduate school of Medicine, Kyushu University

The effect of cell dynamics on Delta-Notch pattern formation during retinal angiogenesis

Delta-Notch interactions have an important role for development and maintenance of vascular pattern in angiogenesis. Delta and Notch are membrane proteins, the former is ligand and the latter is receptor. Lateral inhibition by Delta and Notch results in spatially alternate pattern in 1D [1]. The expression pattern of Dll4 in retinal vasculature falls into three categories: alternate, sporadic and homogeneous [2]. Arteries show alternate pattern and veins show homogeneous pattern. Expression of Dll4 contribute to prevent oversprouting [3].

We examined the effect of endothelial cell movement [4] and proliferation [5] on Delta-Notch pattern formation during retinal angiogenesis. We experimentally observed cell dynamics in retina organ culture, and the results show random endothelial cell movements and cell divisions in a region-specific manner. Based on these experimental results, we formulated a minimal model of Delta-Notch interaction and cell dynamics that is analytically manageable. In the model, we regarded random cell movement as a flip of two the neighboring cells and cell division as duplication of a cell. We reproduced the three patterns observed in *vivo* by numerical calculations and analytically derived the instability condition. These results are consistent with experimental results and suggest that local differences of mobility and cell proliferation critically affect Delta-Notch patterns in endothelial cells.

REFERENCES

[1] Collier, J. R., Monk, N. A. M., Maini, P. K., & Lewis, J. H. (1996). Pattern Formation by Lateral Inhibition with Feedback: a Mathematical Model of Delta-Notch Intercellular Signalling. *Journal of Theoretical Biology*, *183*(4), 429–446. http://doi.org/10.1006/jtbi.1996.0233

[2] Claxton, S., & Fruttiger, M. (2004). Periodic Delta-like 4 expression in developing retinal arteries. Gene Expression Patterns. GEP, 5(1), 123–7. http://doi.org/10.1016/j.modgep.2004.05.004

[3] Kim, J., Oh, W. J., Gaiano, N., Yoshida, Y., & Gu, C. (2011). Semaphorin 3E-plexin-d1 signaling regulates VEGF function in developmental angiogenesis via a feedback mechanism. Genes and Development, 25(13), 1399–1411. http://doi.org/10.1101/gad.2042011

[4] Arima, S., Nishiyama, K., Ko, T., Arima, Y., Hakozaki, Y., Sugihara, K., … Kurihara, H. (2011). Angiogenic morphogenesis driven by dynamic and heterogeneous collective endothelial cell movement. Development (Cambridge, England), 138(21), 4763–76. http://doi.org/10.1242/dev.068023

[5] Uemura, A., Ogawa, M., Hirashima, M., Fujiwara, T., Koyama, S., Takagi, H., et al. (2002). Recombinant angiopoietin-1 restores higher-order architecture of growing blood vessels in mice in the absence of mural cells. *Journal of Clinical Investigation*, *110*(11), 1619–1628. http://doi.org/10.1172/JCI200215621

Daiki Sasaki
Department of anatomy and cell biology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka, Japan
e-mail: `s-daiki@anat1.med.kyushu-u.ac.jp`

Takashi Miura
Department of anatomy and cell biology, Graduate School of Medical Sciences, Kyushu University

A mathematical model for meshwork formation of endothelial cells in fibrin gel

Vasculogenesis is the process that the first primitive vascular plexus is made from endothelial progenitor cells in the embryo. *In vitro* experimental system of vasculogenesis is extensively studied. In this culture system, Human Umbilical Vein Endothelial Cells (HUVECs) are cultivated *on* Matrigel. Within 24 hours, these cells form meshwork structure that resembles capillary plexus. To make a mathematical model for vasculogenesis, Murray et al. used a deformation of the extracellular matrix [1]. Serini et al. use chemotaxis model based on vascular endothelial growth factor (VEGF) [2].

In this study, we focused on the pattern formation of HUVECs embedded in the fibrin gel. The cells also produce meshwork spontaneously. This system was considered to be particularly useful since it develops perfusable capillary meshwork. However, the deformation of substrate and the gradient of VEGF in fibrin gel is not observed as in the Matrigel system described above. In fibrin system, cells themselves do not move but make protrusions actively to connect to the adjacent cell.

Time-lapse observation revealed

1. Cells do not move, but make protrusions actively.
2. Protrusions repeat extension and collapse.
3. Whenever the protrusion collides with the surface of the adjacent cell, connection is established.
4. Formation of the protrusion is not affected by the neighboring cells.
5. Collapse speed is higher than extension speed.
6. Two neighboring cells have higher probability to connect when they are closer.

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Based on these findings, we constructed a mathematical model for the extension of a protrusion, using discrete-time stochastic process. A protrusion extends at a rate *c* per unit time, and it connects to a neighboring cell when it collides with the surface of the adjacent cell. The protrusion collapses at probability *p* per unit time, and the length becomes *0* instantaneously. We assume the time for meshwork formation as *t*, the distance between the cell membranes as *l*. Then, the connection probability function *P(t, l)* is expressed as following recurrence equation

$$P(t+1,l) = P(t,l) + \{1 - P(t - \frac{l}{c}, l)\}p(1-p)^{\frac{l}{c}}.$$

We obtained an analytical solution of *P(t, l)* by taking continuous limit of the recurrence equation and the boundary conditions (When *t < l/c, P(t, l) = 0*, When *t = l/c, P(t, l) = (1-x)^(l/c)*) as follows:

$$\begin{cases} P(t,l) = \sum_{k=1}^{[\frac{ct}{l}]}\{\frac{(-p)^{k-1}}{k!c^n}(1-p)^{\frac{l}{c}k}(ct-kl)^{k-1}(kc-klp+cpt)\}([\frac{ct}{l}] > 0) \\ P(t,l) = 0([\frac{ct}{l}] = 0). \end{cases}$$

Using the solution, we can evaluate connection probability of two cells in two dimensions. Numerical simulation of connection formation of randomly dispersed cells reproduces morphology of observed endothelial meshwork.

REFERENCES

[1] Manoussaki, D., Lubkin, S. R., Vernon, R. B. & Murray, J. D., 1996. A mechanical model for the formation of vascular networks in vitro. Acta Biotheor. **44**: 271–82.
[2] Serini, G. et al., 2003. Modeling the early stages of vascular network assembly. EMBO J. **22**: 1771–9.
[3] Miura, T. & Tanaka, R., 2009. In vitro Vasculogenesis Models Revisited - Measurement of VEGF Diffusion in Matrigel. Math. Model. Nat. Phenom. **4**: 118–130.

Hisako Takigawa-Imamura
Anatomy and Cell Biology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
e-mail: `hisaima@med.kyushu-u.ac.jp`

Takashi Miura
Anatomy and Cell Biology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Emergence of hierarchical structure of lung: a model and observation of cellular response to FGF

We investigated how the hierarchical branch formation is regulated during lung developmental process. It has been considered that the high sensitivity of cells to the distribution of FGF within the developing lung is the principle mechanism guiding shape change. We experimentally examined the cellular responses to FGF10 in lung epithelium. It was demonstrated that uptake of FGF10 by epithelial explants of the pseudoglandular stage lung in Matrigel was sensitive over a wide range of FGF10 concentrations. It was also shown that MAP kinase activity downstream of FGF10 was affected by the epithelial explant size and shape as well as the FGF10 concentration. The cellular responses of lung epithelium showed higher dependency on the FGF10 concentration in embryonic day 13.5 (E13.5) than E14.5. To assess how these cellular responses result in shape formation of the lung epithelium, we constructed a mathematical model in which an epithelial tip splits depending on the proliferative and chemotactic activities. It was revealed that higher contrast in the activities resulted in the longer segment length of branches, which is reminiscent of the actual lung pattern where segment lengths are longer in earlier branches.

Masaki Sekiguchi
Tokyo Metropolitan Ogikubo High School, Tokyo, Japan
e-mail: `emafarms@gmail.com`

Emiko Ishiwata
Tokyo University of Science, Tokyo, Japan
e-mail: `ishiwata@rs.tus.ac.jp`

Yukihiko Nakata
Shimane University, Shimane, Japan
e-mail: `ynakata@riko.shimane-u.ac.jp`

Effect of time delay for an ultra-discretized logistic equation

Ultra-discretization is proposed as a special procedure to obtain a discrete system. There are various ultra-discrete models related to the cellular automaton and traffic flow, but few examples of the application of ultra-discretization in mathematical epidemiology.

In this presentation we introduce two ultra-discrete models derived from logistic type differential equations and discuss dynamical properties regarding global attractivity as in [2, 3] and periodicity of the solution. Here logistic equations appear from epidemiological models with waning immunity, such as SIS and SIRS models. It is shown that our ultra-discrete model capture the qualitative dynamics of a delayed SIS epidemic model by Cooke [1]. Potential use of the ultra-discrete model to analyze the periodic oscillation is also discussed.

REFERENCES

[1] Cooke, K. L., 1979. Stability analysis for a vector disease model. *Rocky Mt. J. Math.,* **7**: 253–263.

[2] Kocic, V. L. and Ladas, G., 1993. Global behavior of nonlinear difference equations of higher order with application. Kluwer Academic Publishers.

[3] Ruan, S., 2006. Delay differential equations in single species dynamics. Delay Differential Equations and Applications. Springer, 477-517.

Yohei Saito
Institute of Industrial Science, University of Tokyo, 4-6-1, Komaba, Meguro-ku, Tokyo 153-8505 Japan
e-mail: `yoheis@sat.t.u-tokyo.ac.jp`

Yuki Sughiyama
Institute of Industrial Science, University of Tokyo, 4-6-1, Komaba, Meguro-ku, Tokyo 153-8505 Japan

Kunihiko Kaneko
Department of Basic Science, University of Tokyo, 3-8-1, Komaba, Meguro-ku, Tokyo 153-8505 Japan

Tetsuya J. Kobayashi
Institute of Industrial Science, University of Tokyo, 4-6-1, Komaba, Meguro-ku, Tokyo 153-8505 Japan

Discreteness-induced transition in multi-body reaction systems

Finiteness of system size may cause qualitative change in dynamics and small-system size effect attracts much attention in various fields of study, e.g., systems biology (stochastic chemical reactions), ecology (population dynamics), game theory, and social networks (agent dynamics). Increase in multiplicative noise-intensity owing to smaller system size can induce qualitative transition of stationary distribution, which has been known as noise-induced transition and has been investigated well since 1970s [1]. Although finite system size not only increases noise intensity but also emphasizes the state space discreteness, the role of discreteness of state space has rarely been studied [2].

In this work [3], we propose a simple 1- and 3-body reaction system as a toy model which exhibits pure discreteness-induced transition and obtain a sufficient condition under which the discreteness induced transition arises. Furthermore, we find that the critical size of discreteness-induced transition can become quadratically large, if multi-body reactions are allowed.

REFERENCES

[1] W. Horsthemke and R. Lefever, *Noise-Induced Transitions in Physics, Chemistry, and Biology* (Springer, 2006).
[2] Y. Togashi and K. Kaneko, Phys. Rev. Lett. **86**, 2459 (2001).
[3] Y. Saito, Y. Sughiyama, K. Kaneko, and T. J. Kobayashi, arXiv:1605.06273.

Yuki Sughiyama
Institute of Industrial Science, The University of Tokyo
e-mail: yuki.sughiyama@gmail.com

Tetsuya J. Kobayashi
Institute of Industrial Science, The University of Tokyo

Steady State Thermodynamics in Population Dynamics

Prediction and control of a population of growing cells are relevant for understanding evolution of microorganisms and for designing effective drug treatment to pathogenic and cancer cells. Methods of statistical physics can contribute to resolving these problems because of a mathematical similarity between statistical physics and population dynamics. The long term expansion rate of population size (population growth) is an important observable in the population dynamics. In a fixed environment, the population growth converges to a stationary growth rate, and can be evaluated mathematically by the largest eigenvalue of the time-evolution operator of the population dynamics by using the Perron-Frobenius theorem. In contrast, in a changing environment, the evaluation of the population growth is a more difficult problem because the higher eigenvalues non-negligibly contribute to the population growth due to disturbance of the convergence by the changing environment. In this study, to extract and evaluate the contribution of the higher eigenvalues from the population growth, we employ the framework of steady state thermodynamics (SST), which is used in nonequilibrium statistical physics.

SST was established for understanding a “thermodynamics” of transitions between nonequilibrium steady states (NESS). The core of this theory is a decomposition of total heat during environmental change into housekeeping and excess parts. The housekeeping heat represents the sum of the stationary heat dissipations in each NESS, and the excess heat is the heat generated due to the change of environment. By using this decomposition, Clausius inequality is formulated for the excess heat.

In this talk, by using the SST framework, we decompose the population growth into two parts, the sum of the stationary growth for each environmental condition (i.e. the contribution of the largest eigenvalues) and the excess growth, which is generated by the switching of environment (i.e. the contribution of the higher eigenvalues). Focusing on the excess growth, we obtain a Clausius inequality for population dynamics, which gives the upper bound of the excess growth. The equality is achieved in quasistatic changes. We also clarify that this bound can be evaluated by ``lineage fitness”, which is an experimentally observable quantity.

REFERENCES

[1] Y. Sughiyama and T. J. Kobayashi, arXiv:1509.06448 (2015).
[2] T. J. Kobayashi and Y. Sughiyama, Phys. Rev. Lett. **115**, 238102 (2015).
[3] Y. Sughiyama, T. J. Kobayashi, K. Tsumura and K. Aihara, Phys. Rev. E **91**, 032120 (2015).

Participant List

Akane Hara	7A3-O5-1
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Alexey Martyushev	8D1-S10-2
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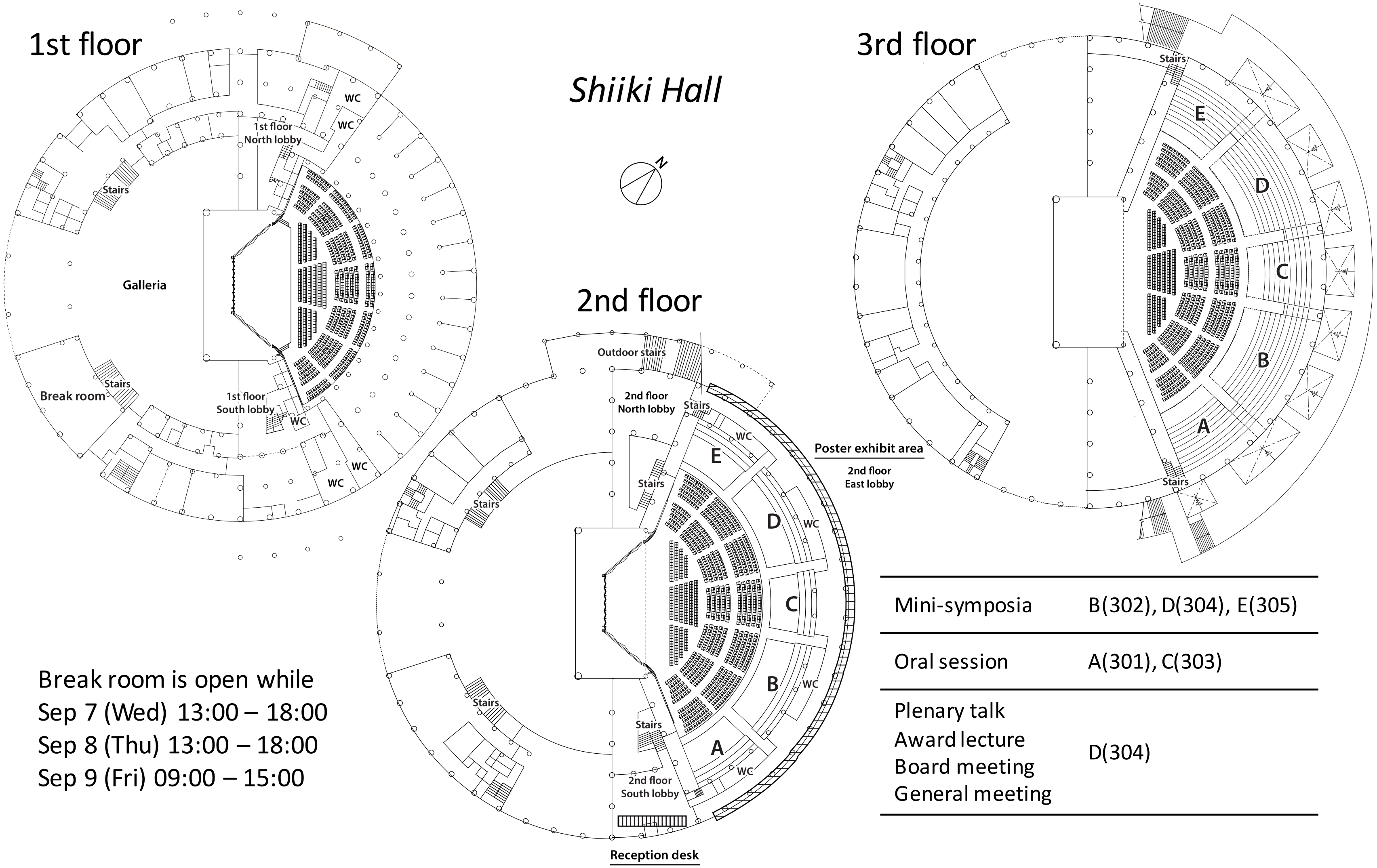

Break room is open while
Sep 7 (Wed) 13:00 – 18:00
Sep 8 (Thu) 13:00 – 18:00
Sep 9 (Fri) 09:00 – 15:00

Mini-symposia	B(302), D(304), E(305)
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