Estimating cell lineage: Theory and application to actual organisms

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Cell lineage of a multicellular organism has been analyzed by introducing a genetic or chemical marker that is inherited from a cell to its daughter cells and is detectable even after several cell divisions. To construct a complete cell lineage, all the cells at different developmental stages need to be identified, and then the intracellular marker must be introduced to each cell. I have studied a new method of estimating cell lineage based on distributions of intercellular markers observed at a single stage, which are introduced randomly at earlier stages. In this talk, I show the application of this method to actual organisms, and the usefulness of the method as a tool of developmental biology. Assumptions are: (1) cell lineage is invariant between embryos; (2) a small number of cells are marked in each experiment; and (3) the total number of replicate experiments is sufficiently large. Then we identify the most likely cell lineage pattern (or tree topology) as the one that requires the least marker insertions to be compatible with the observed distributions of cell markers. If the number of cells is large, we can use clustering method in which a pair of cells with the highest correlation in marker labelling are merged sequentially. I tried to reconstruct a part of cell lineage of nematode, C. elegans by using the data obtained from random marker-introduction. The lineage of C. elegans has been studied from direct observation of living worms. We focus on the cell lineage of intestine made from 20 cells, where each cell is easy to observe. The mechanism of random marker-introduction is realized by the extrachromosomal gene in the nematode cell. The circular gene is slightly unstable and may be lost occasionally from each cell during somatic cell division. By including a reporter gene, GFP (green fluorescent protein) gene into the array, we obtain the data of distribution of marked cells at an observation stage just by observing the lack of the fluorescence. The estimated lineage is just same as previously obtained one.