



CDB SEMINAR

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16:30~18:00 Auditorium C1F

Noise, Regulation, and Cell-Cell Heterogeneity

Protein expression can be vastly inhomogeneous even among genetically identical bacterial cells. It is well established that the difference can be caused by noise or stochasticity in gene expression processes. There are also many positive and negative feedbacks in gene regulatory network that can be a source of the inhomogeneity. For example positive feedback can result in bistable gene expression, which can mediate epigenetic memory of gene expression level. Negative feedbacks can reduce noise, but given appropriate time delay it may cause temporal oscillation of the gene expression levels. When these dynamical behaviors are combined with noise, the cell-to-cell heterogeneity may be enhanced to form a structured population. In order to understand behavior of population of bacteria, we need to have better understanding of cell-to-cell heterogeneity.

In this talk, I first discuss burstiness in transcription caused by a competition between repressor and RNA polymerase binding [1]. Although promoter activity is often governed by a single limiting step, we argue here that the size of the noise strongly depends on whether this step is the initial equilibrium binding or one of the subsequent unidirectional steps. We show that nonequilibrium steps of transcription initiation systematically increase the cell-to-cell heterogeneity in bacterial populations. In particular, this allows also weak promoters to give substantial transcriptional noise.

I then move on to discuss possible spatial gene expression patterns caused by cell-to-cell heterogeneity in a growing colony [2]. We show that a simple genetic circuit composed of a positive-feedback loop and a negative-feedback loop can produce diverse expression patterns in colonies. We show that similar sets of gene expression patterns are observed in the simulation and the experiments. Because the combination of positive feedback and negative feedback is common in intracellular molecular networks, our results suggest that the protein content of cells is highly diversified in colonies.

[1] Mitarai, Namiko, Szabolcs Semsey, and Kim Sneppen. "Dynamic competition between transcription initiation and repression: Role of nonequilibrium steps in cell-to-cell heterogeneity." *Physical Review E* 92.2 (2015): 022710.

[2] Mitarai, Namiko, Mogens Høgh Jensen, and Szabolcs Semsey. "Coupled positive and negative feedbacks produce diverse gene expression patterns in colonies." *mBio* 6.2 (2015): e00059-15.

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