— Keynote Address —

# Complex Systems Biology: Exploring Universal Statistical and Dynamical Features in Cellular Processes

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We intend to understand life as a 'complex system', by unveiling universal features underlying all biological systems. For this purpose, we take a constructive approach, by setting up a simple system both experimentally and theoretically, and answer general questions on a biological system. After surveying this standpoint, I discuss some of recent studies along this line, both in theory and experiment.

First, I discuss universal statistical laws of chemical abundances in a cell that sustains recursive production. From theoretical studies of simple cell models with catalytic reaction network, discovered are a power law in average gene expression and log-normal distribution of the abundances of each chemical by cells. Experimental verification of these statistical laws is also presented, while evolutionary origin of scale-free biochemical networks is explained as embedding of dynamics into network topology.

Second, to discuss relevance of this phenotypic fluctuations to evolution, we extend fluctuation-dissipation theorem in physics, to obtain universal relationship between phenotypic and genetic fluctuations. Proportionality between evolution speed and phenotypic fluctuation is derived, as is demonstrated experimentally.

The next problem we address concerns with search for some chemicals that suppress the above fluctuations. Taking a simple reaction network model, we show that molecules minority in number are preserved well by suppressing the fluctuations. These molecules control the behavior of a cell relatively strongly, and start to play the role of genetic information. Origin of heredity and evolvability are discussed, based on this minority controlled state.

Last, I Second, I discuss cell differentiation and developmental process from a viewpoint of coupled dynamical systems. Robustness in development and irreversible loss of multipotency from ES cell to stem cell and then to differentiated cells are highlighted as a universal feature of dynamical systems with internal degrees of freedom and interaction.

## References

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