Spontaneous Adaptation of a Cell by Time Scale Interference

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***Short Abstract* — Cells exhibit adaptive behavior to a variety of environmental conditions. Hereby we propose a general dynamical-systems mechanism for spontaneous adaptive responses [1]. We consider a cellular process consisting of gene transcription and protein synthesis and degradation. In normal condition, the former has a slower time scale, and protein reactions faster, while in a bad environmental condition, the time scale of protein process is slowed down, so that gene and protein's time scales interfere, so that gene expression pattern switches, to change cellular state. If the selected state is adaptive, the time scales are again separated and the adaptive state is maintained. Hence spontaneous adaptation generally follows.**

***Keywords* — Gene regulatory networks, Protein interaction networks, Cell growth, Adaptation, Time scale.**

I. Cell Model

Cells, in general, exhibit adaptation to many environmental conditions. Is this adaptation always controlled by specifically designed signal networks or is there common mechanism for "spontaneous" adaptation? By studying a cell model that consists of gene transcription and protein interaction networks allowing for cell growth, we find a general mechanism for spontaneous adaptive response. Here we consider a cell model consisting of a gene regulatory network and a protein interaction network. Interaction with environment is included as a diffusion process of resource from the medium.

A. Gene Regulatory Networks

Cells have N_g genes; with the expression of the i-th gene represented as g_i. A gene is regulated by proteins that work either as activator and inhibitor. Gene regulatory process is described by Hill equation as below, where C_g gives the time scale for the gene transcription process.

$$\frac{dg_i}{dt} = C_g \left\{ \frac{p_{A(i)}^{\alpha}}{k_g^{\alpha} + p_{A(i)}^{\alpha} + p_{I(i)}^{\alpha}} - g_i \right\}$$

B. Protein Interaction Networks and Cell Growth

Cells have N_p proteins; i-th protein is represented as p_i. All proteins have interaction with other proteins. Each reaction process is governed by Michaelis-Menten kinetics. Each reaction is catalyzed by one gene expression, chosen randomly. Resource chemical is taken from the environment, through diffusion, leading to a cell volume growth, which in turn causes dilution of each protein concentration:

$$\frac{dp_i}{dt} = \delta p_i + D\sigma_i \left(p_i^{\mathrm{Ext}} - p_i \right) - S p_i$$

$$\delta p_i = \sum_j \frac{g_{E(i,j)} p_i}{k_p + p_i} - \sum_j \frac{g_{E(j,i)} p_j}{k_p + p_j}$$

$$S = \sum_j D\sigma_j \left(p_j^{\mathrm{Ext}} - p_j \right)$$

II. Results

We studied the model numerically by taking a network having multiple fixed points in gene expression dynamics. Here cell growth speed S depends on each fixed point. By perturbing each fixed point, we have found that the transition from lower to higher growth state occurs more frequently than the other way around. This adaptive response is widely observed independently of the choice of the network, as long as the time constant C_g is smaller than unity.

Analyses of the model extract the following general mechanism for the adaptive response. If the growth speed is sufficiently high, the gene transcription process has a slower time scale than the protein dynamics, as C_g is smaller than 1. When the growth speed is low for the corresponding gene expression, however, the protein time scale is slowed down, so that the two time-scales interfere, with which gene expression pattern is switched from the original fixed point by perturbation. By the switch, if the growth speed, i.e., the protein time scale is fast again, the separation of time scales is recovered so that the switched fixed point is stable. Hence there appears a biased transition to an adaptive state in general.

The proposed mechanism is based solely on the time scale difference between two coupled systems, and is general so that it is applied not only to adaptation but also to cooperation of multi-cellular organism, and learning problem in neural systems.

References

[1] E. Hoshino and K. Kaneko, in preparation.

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