Correlation of Gene Expression Noise During Cell Fate Transition

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Isogenic cells often exhibit different phenotypes under different circumstances, but the dynamic process of cell fate transition remains elusive. Here, by studying the correlation of gene expression noise of a ten-nodes gene regulatory network under different circumstances, we show that cell fate transition point corresponds to the bifurcation point of the gene regulatory network, where strong correlations of fluctuations among certain genes, which is defined as a core network, can be observed. Our preliminary results verify that correlation of fluctuations between genes might be used as an indicator of cell fate transition.

***Keywords* — Cell fate transition, Noise, Bifurcation, Correlation**

I. Introduction

Cell fate transition is widespread among unicellular and multicellular organisms[1-3]. Unicellular organism often change phenotype such as proliferation, quiescence or sporulation, in responding to sudden change of environment, such as starvation, UV-exposure. Cell differentiation is important for the development and maintaining hemostasis of multicellular organisms. Diseases, such as cancer, have long been regarded as an catastrophic transition after a long time of accumulation of mutations[4]. All these cell fates transition are governed by the underlying complex genetic regulatory networks. The ultimate goal in the research field of cell fate transition is to effectively control cell fates. Previous studies mostly focus on identifying the so called key regulators of this process. Yet little is known about the complex dynamic process. Recently, the dynamic systems view of cell fates has gained increasing attention, which regards cell fates as high dimensional attractors[5,6]. Cell fate transition in respond to external environment or clues is regarded as the qualitative change of the epigenetic landscape produced by the underlying gene regulatory network. Can we predict when cell fate transition happens? Is there any early signature that can be get from experimental measurements? Is there core network that responsible for the transition? How can we control cell fate transition effectively? To answer these questions we studied a ten-nodes random gene regulatory network under various circumstances.

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II. Results

Using ordinary differential equations, stochastic simulation, as well as analytical calculation, we show that when the gene regulatory network is tuned at bifurcation point, strong correlation of gene expression noise among certain genes can be observed.

We first study the behavior of toggle switch and binary cell fate decision motif when tuned at critical point. Using Langevin equation and Linear Noise Approximation method, we find both correlation of gene expression noise and variation of gene expression increasing rapidly when control parameter approaches the bifurcation point.

When the random ten-genes regulatory network is subjected to saddle-node bifurcation or pitchfork bifurcation, strong correlation of fluctuation among some genes can be observed. To mimic the real situation of cell fate transition, we gradually change the control parameter from one regime(monostable) to another(metastable). Under this circumstance, time series analysis of gene expression profiles shows that only when the control parameter changes slowly enough can strong correlation of fluctuations be observed. This result give some constraint that only when cell fate transition process is slow enough can early indicator of transition observed experimentally.

III. Conclusion

Gene regulatory network shows strong correlation of fluctuations when it is tuned at bifurcation point. Only when cell fate transition is slow enough can we find early indicator of transition from experimental measurements.

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