

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

Non-adiabatic Dynamics of Gene Regulatory Network

By

Cong Chen

Gene regulatory network is a mathematical model of gene expression and regulation in cell environment. The concept of network comes from network in math and computer science. In gene network each node is a gene that has different expression level and links between nodes represent direct regulation (activation or repression). Gene network is stochastic with intrinsic noise from biochemical reactions involved and extrinsic noise from environment. It is non-equilibrium with frequent matter/energy exchange and active entropy production. One crucial character of gene network is the involvement of multiple timescales: timescale of protein synthesis/degradation and timescale of regulation processes. Conventional studies are concentrated at adiabatic limit where regulation processes are much more frequent than protein synthesis/degradation and adiabatic approximation is valid. We explore non-adiabatic dynamics of gene network by develop a mapping from N -dimensional protein concentration space to $2N$ extended space using similarity to quantum mechanics and path integral. We applied our theory to self activator which is the simplest network motif. Our theory is able to explain steady states at different adiabaticity and demonstrates non-equilibrium properties like eddy current. We also studied relationship between cancer heterogeneity and non-adiabatic dynamics of core cancer network. In non-adiabatic regime, the steady states of cancer network shows alternation of phenotypic states, weaker stability, optimal transition rate and diversity of transition paths. This suggests possible source of cancer heterogeneity from non-adiabatic dynamics of core cancer network.

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