Energy Landscape and Robustness of Cellular Networks

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Cellular Networks are in general quite robust and perform their biological functions against the environmental perturbations. Progresses have been made from experimental global screenings, topological and engineering studies. However, there are so far very few studies of why the network should be robust and perform biological functions from global physical perspectives. In this work, we explored the global properties of the network from physical point of view.

The aim of this work is to provide a conceptual framework and a physical tool to study the global nature of the cellular network. The main conclusion of this presentation is that we uncovered the underlying energy landscape for several small cellular networks such as MAPK signal transduction network, budding yeast cell cycle network and gene regulatory networks. From the experimentally measured or inferred inherent chemical reaction rates, we discovered that the energy landscape of the MAPK signal transduction and budding yeast cell cycle networks are funneled towards the global minimum. The gene regulatory networks, however, typically have several funnels or basins of attractions for the underlying energy landscape.

The global shapes of the energy landscapes of the underlying cellular networks we have studied are quite robust against perturbations of the kinetic rates and environmental disturbances through noise. We derived a quantitative criterion for robustness of the network function. The robustness against changes is reflected by the steepness of the funnel for MAPK as well as yeast cell cycle network and the barrier height between the basins of attractions for gene regulatory networks. This provides a natural explanation of the robustness and stability of the network for performing biological functions. We believe the robust landscape is a global universal property for cellular networks.

We believe the robust landscape is a quantitative realization of Darwinian principle of natural selection at the cellular network level. It provides a novel algorithm for optimizing the network connections, which is crucial for the cellular network design and synthetic biology. Our approach is general and can be applied to other cellular networks.