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### **Energy Landscape of Cellular Networks<sup>1</sup>**

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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 few studies of why the network should be robust and perform biological functions from global physical perspectives. In this work, we will explore the global properties of the network from physical perspectives. The aim of this work is to develop a conceptual framework and quantitative physical methods 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 and gene regulatory networks, from the experimentally measured or inferred inherent chemical reaction rates. The underlying dynamics of these networks can show bi-stable as well as oscillatory behavior. The global shapes of the energy landscapes of the underlying cellular networks we have studied are robust against perturbations of the kinetic rates and environmental disturbances through noise. We derived a quantitative criterion for robustness of the network function from the underlying landscape. It 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 may provide 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.

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