

## Evolution of the Structure of Metabolic Networks

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For the past several decades biologists have mainly focused on studying evolution among species using DNA sequences or protein sequences. However, evolution of many complex biological systems cannot be uniquely determined by evolution of DNA sequences. The structure of biological networks such as metabolic networks, signal transduction networks, gene regulation networks and protein-protein interaction networks has more complex patterns of evolution than DNA sequences. It is structure of the networks that greatly influences function and dynamics in cells and introduce novel paradigm in biological research. To study evolution of biological networks allow us to measure evolution of complete biological processed and hence is of great importance in studies of function and evolution of biological systems.

Recent advances in genomic technologies have resulted in great exposition of information on biological networks, particularly metabolic networks. The structure of the metabolic networks as recorded in the databases is more complete than that of other biological networks. Therefore, we focus on evolution of the structure of metabolic networks.

The widely used methods for reconstruction of the evolutionary relationships of the metabolic networks are based on assessing the similarities among metabolic networks for different organisms. Many similarity measures are borrowed from terminology from sequence alignment. However, the previous approaches to evolution of metabolic networks have not revealed the pattern of evolution of their structure and showed how metabolic networks dynamically grow and increase their complexity. Although in the past decade general theory of networks has rapidly been developed the results of their applications to evolution of metabolic networks thus far are mixed. Purpose of this post is to report our findings of two principles underlying structural evolution of metabolic networks, which may lead to paradigm shift in evolutionary study of biological networks. One principle is that evolution of metabolic networks is by breaking symmetry. Symmetry is a universe phenomenon in complex systems and implies conservation laws of nature. Symmetry and complexity are general features of the nature. There is increasing recognition that the universal evolution is caused by symmetry break, generating diversity and increasing complexity and energy. Second principle is modular evolution. Symmetry break is often followed by addition of modules of functional unites that usually show local symmetry, improving function and generating diversity. We present algorithms for identifying local symmetry, followed by defining several quantities to measure symmetry. To gain deep understanding modular features of evolution of metabolic networks, we introduce a concept of irreducible graphs and develop algorithms for computing irreducible graphs. To investigate modular evolution and to uncover functional modules we develop algorithms for the geometric decomposition of the automorphism group of the metabolic network. To reconstruct evolutionary tree we develop a novel definition of distance between two networks which consider information of network structure. The developed new distance between networks will be applied to two types of metabolic networks: original metabolic networks and derived irreducible metabolic networks to reconstruct phylogenetic tree of the organism. The developed evolutionary theory was applied to reconstruction of evolutionary history of

glycolytic pathway of archaea.