From the evolution of metabolic pathways to the emergence of complex properties.

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Abstract

The formation of complex systems and their properties is an intriguing field of research in biology with many unresolved questions. The knowledge that can be gained from it is not only beneficial for the understanding and optimization of existing systems but also for constructing many kinds of novel artificial systems. We are investigating the emergence of complex properties in biological systems by studying the evolution of metabolic pathways and observing the structure and dynamic behavior of metabolic networks. Therefore, we have implemented a multi-level computational model for simulating the evolution of catalyzed reaction-networks, complemented by a versatile metabolic pathway analysis tool that allows us to extract static and dynamic properties of the networks. With the use of meaningful measures for system-level properties we hope to turn our observations of network properties into hypotheses about system-level properties such as robustness and modularity.

Metabolic Pathway Analysis

Metabolic pathway analysis is the calculation and analysis of the pathway distribution of a steady-state metabolic network to gain insights about its structure, functionality and properties [1]. The calculation starts with the formation of the stoichiometric matrix presentation of the network and delivers the extreme pathways spanning the entire steady-state flux space, as the final result.

Evolution of metabolic Pathways

Our model of ribozyme-catalyzed metabolism consists of protocellular entities, containing a genome, a set of catalytic reactions, an algebraic chemistry and molecules that can be involved in chemical reactions and exchange mass with the environment. The molecules are abstracted as vertex- and edge-labeled graphs and chemical reactions are realized as Graph rewrite rules. The graph-based model is supported by an artificial fitness landscape that captures the fitness of the system. The genome codes for a set of catalytic reaction which are applied on the molecules in the protocol. Using the reaction rates, we determine the molecule concentrations. All molecules above a certain concentration threshold are combined further in the next network generation step. New chemical reactions may be introduced through alterations (mutations) in the protocol’s genome.

Network Properties

By examining the network structure with conventional network measures as well as measures suited for metabolic reaction networks, we intend to gain insights about the properties of the investigated networks. Since we also have different stages in the evolution of this networks available, we can even make hypotheses on the emergence of these properties. Here we focus on measures for the robustness of the networks.

Results

On the one hand, with our model we can make statements about the evolution of metabolic pathways and its elements. On the other hand, we observe the development of certain properties of the networks. We find that enzymes which were introduced in the system at later stages usually are much more specific than their counterparts. Another observation is the formation of so-called hub metabolites in the course of the simulations. This leads to scale free and robust networks as described in the discussion of the node degree distribution.

The robustness measures (see Network Properties, R1,…, Rn) all increase steadily throughout evolution, converging to values close to 1. These results indicate that the overall function of the network is maintained almost perfectly for knockout (enzymes) or deletions (metabolites) of single components. Furthermore, the discussion of the minimal knockout set size distribution shows that also for specific target functions the network becomes more and more robust against single and multiple knockouts.

Outlook

In future work, we will test the existing measures and hypotheses with more extensive simulation runs and experiment with some realistic scenarios to make statements about real-world metabolic pathways. We also intend to extend the study of the robustness of our networks through barrier trees of the set of extreme pathways. Further we want to introduce measures for modularity of networks, inspired by the notion of biological organizations and autocatalytic sets. With the use of visualization tools specifically adapted to metabolic networks, we hope to be able to explore the structure and dynamics of our networks on a different levels to gain new insights.

Finally, an extensive comparison of our results on the network property measures with those for real-world of different type is desirable for validating our conclusions and possibly further insights.