Summary

1. Overview

This project will systematically explore the dynamical properties and evolutionary origins of the modular and hierarchical (MH) organization observed in a wide array of living systems. MH structures consist of relatively autonomous modules that interact more strongly internally than they do with other modules. These modules can often be subdivided into sub-modules, and these in turn into sub-sub-modules, etc., producing a multi-level hierarchy of structures. MH architectures have been observed in diverse biological interaction networks (e.g. genetic and metabolic networks) and emerge spontaneously in biologically-inspired models of evolving networks. Despite this apparent universality, the properties of MH structures and their role in living systems are still poorly understood.

The project will develop novel experimental and theoretical approaches that enable, for the first time, integrated investigations into the dynamics, robustness, adaptability and evolution of MH structures. The experimental platform will utilize tools from synthetic biology to engineer libraries of microbial ecosystems wherein genes and other intracellular and extracellular components are connected through defined interaction networks with different degrees of modular and hierarchical organization. The theoretical framework will develop both specific and generic models that formalize the link between experimental and abstract MH structures and allow model-based predictions. A ‘Network State Diffusion’ model will address physical coupling between intracellular modules via diffusion-mediated intercellular interactions. A new class of abstract network-based models will combine algorithms that generate MH topologies, Boolean and ODE-based rules for the dynamics of node states, and evolutionary algorithms to investigate the properties of MH structures and perform simple artificial-life simulations. Comparable MH structures will thus be examined using experiments, models, and theory to investigate the key questions: (1) what types of dynamics are supported by MH structures; (2) do MH structures improve fitness or confer other evolutionary advantages; and (3) how do MH structures emerge and evolve?

2. Intellectual Merit

The project integrates approaches from complex networks, non-equilibrium dynamics, statistical physics, and synthetic biology to investigate and elucidate the origins and roles of MH structures in living systems. It will produce new complementary experimental and theoretical approaches for characterizing and manipulating biological interaction networks while advancing the fundamental understanding of organizational principles underlying structure and function in living systems. It will extend network-based theory and models to describe physical and biological MH interactions and investigate their role in self-organization. It will provide a unifying perspective that relates the emergence, dynamics and evolution of complex MH biological structures to the study and design of robust and adaptable complex systems in general, thus building a bridge between physicists, engineers, biologists, and complex systems researchers.

3. Broader Impact

By elucidating the functions and roles of MH interaction networks in living systems, this project will enable researchers to better understand and manipulate complex biological systems to achieve desirable societal goals. For example, understanding how to incorporate MH structures when engineering novel biological functions could enable biotechnologies that achieve sustainable and cost-effective production of chemicals, fuels, and materials; recognizing MH networks within human or pathogen physiology could inform the design of therapeutics that stabilize or destabilize their function for medical applications; understanding the role of MH structures in ecosystems could improve environmental stewardship and conservation efforts; applying bio-inspired engineering solutions based on MH structures could help design and control robust and adaptable technological networks and robotic systems. A group of external collaborators will actively catalyze the translation of this project’s research products to applications in biotechnology, medicine, and robotics. Project results will be actively disseminated among scientists, engineers, and the public at large. In addition, an online game-based crowdsourcing experiment will engage the public in current research, generating new scientific results and tools for teaching complexity and self-organization in physical and biological systems.