Summary

1. Overview

This project will systematically explore the dynamical properties and evolutionary origins of the modular-hierarchical (MH) organization found in a broad range of living systems. MH structures consist of relatively autonomous modules that interact more strongly internally than with others, these can in turn be organized into even higher-level modules any number of times, producing a multi-level hierarchy of interactions that can span multiple spatiotemporal scales. MH architectures have been observed in diverse biological networks (e.g. genetic and metabolic) 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 develops the first steps towards a unifying theory of MH structures in living systems by studying idealized models and detailed models while interacting with a broad range of experimental and data-driven external collaborators. It will integrate and further current knowledge on MH systems, such as network growth algorithms that yield MH topologies or the emergence of modular structures under alternating fitness constraints. It will study new classes of network-based models; combining growth algorithms, Boolean or ODE-based node dynamics, and evolutionary algorithms to analyze MH systems and perform simple artificial-life simulations. It will also study diffusion based and active-matter based spatial MH structures to include physical features and develop intuition. Collaborators will provide insights from various specific biological systems and archetypical MH structures for theoretical analysis. These include groups that (1) engineer intracellular and extracellular interaction networks with different degrees of MH organization using synthetic biology, (2) analyze MH properties of metabolic biomass production networks, (3) study the symbiotic coupling of modular structures in certain squids and their microbiota, and (4) consider the role of MH structures in tumor development. These diverse systems will help unveil universal MH features while grounding to concrete examples the proposal's overarching questions: What dynamics are supported by MH structures? Do MH structures provide evolutionary advantages? How do MH structures emerge and evolve?

2. Intellectual Merit

The project integrates complex networks, evolutionary theory, non-equilibrium dynamics, and statistical physics approaches with the analysis of various experimental systems to elucidate the origins and consequences of MH structures in life. It aims to advance our fundamental understanding of MH systems, and thus of principles underlying structure and function in biology, by following an approach highly successful in physics: combining abstract models that capture universal features of classes of systems with detailed analyses of diverse experimental evidence to develop knowledge and produce predictions. The unveiling of fundamental MH properties will in turn provide novel perspectives for studying the biological systems considered.

The project will also further our understanding of nonequilibrium statistical physics by extending standard lattice- and mean-field-based analyses to biological MH structures. It will describe MH systems using spatial and network-based theory and models to explore their self-organization and adaptability.

3. Broader Impact

By clarifying the role of MH interactions in living systems, the project will enable the manipulation of complex biological systems to achieve desirable societal goals. For example, understanding how to incorporate MH structures when engineering novel biological functions could help produce new chemicals, fuels, and materials though biotechnology; recognizing MH networks within human or pathogen physiology could inform therapeutic measures to stabilize or destabilize their function; applying MH bio-inspired engineering solutions could help design and control robust and adaptable technological systems. External collaborators will help translate research products to applications in biotechnology, medicine, and robotics. Results will be actively disseminated among scientists, engineers, and the public. The project will develop an innovative, simple online game-based crowdsourcing experiment that will compare evolved and designed MH solutions and engage the public in current research while generating scientific results and tools for illustrating complexity and self-organization.