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Analysis of Network Architecture

Universal Organizing Principles of Signaling Networks 🔈

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Abstract:

This talk will sketch the insights about the fundamental nature of complex biological and technological networks that can now be drawn from the convergence of three research themes. Molecular biology has provided a detailed description of much of the components of biological networks, and the organizational principles of these networks are becoming increasingly apparent. It is now clear that much of the complexity in biology is driven by its control systems, however poorly understood these remain. In addition, advanced technology is creating engineering examples of networks with complexity approaching that of biology. While the components are entirely different, there is striking convergence at the network level of the architecture and the role of protocols, control, and feedback in structuring complex system modularity. Finally, there is a new mathematical framework for the study of complex networks that suggests that this apparent network-level evolutionary convergence both within biology and between biology and technology is not accidental, and follows necessarily from the requirements that both biology and technology be efficient and robust. Through combinations of evolution and natural selection or engineering design, such systems exhibit highly symbiotic interactions of extremely heterogeneous components to create functional hierarchies, with massive use of control and feedback throughout.

Since the audience is largely biologists, this talk will draw on concrete examples from systems biology to illustrate common themes and challenges in developing a scalable scientific theory and software infrastructure for complex networks, and minimize the mathematical details. In the context of biology, the aim is to build on mathematics of systems engineering to create a coherent and complete theoretical infrastructure proceeding from experimental data to modeling, analysis, inference, and with tight feedback to experimentation and modeling throughout. Both data and modeling assertions and questions must be described in a common framework that is biologically natural, yet can be turned over to powerful algorithms for resolution. Is a model consistent with experimental data, which may come from extremely heterogeneous sources? If so, is it robust to additional perturbations that are plausible but untested? Are different models at multiple scales of resolution consistent? What is the most promising experiment to refute a model? Put in natural terms (which are typically stochastic, nonlinear, nonequilibrium, uncertain, hybrid and so on), such questions are conventionally viewed as computationally intractable, and biologists are forced to translate into unnatural terms in order to use available algorithms. This is undesirable and potentially unnecessary. A crucial insight is that both technological design and evolution favor high robustness to uncertain environments and components, yet allows severe fragility to novel perturbations, and this "robust yet fragile'" feature must be exploited explicitly in scalable algorithmic approaches.

The new modeling and inference framework under development need not handle arbitrary problems (presumably worst-case intractable) but only that subset of problems which are biologically and technologically meaningful. Organisms and successful technologies are highly

constrained in that they have not just developed and evolved, but necessarily done so in ways that are robust to uncertainties in their environment and their component parts. The many famous catastrophes in engineering systems can usually in retrospect be traced to explicit failures to properly invest in robust design. Robustness and efficiency create extremely severe constraints, not present in other sciences but essential in engineering, which emerge primarily at the network level in both biology and engineering. Robustness constraints play a central role in advanced technologies, but also a crucial if often hidden and implicit role in the informal processes that biologists use to reason about their experiments and are central in creating a scalable process of biological inference. A theoretical and software infrastructure that does not explicitly exploit the highly structured, evolved and/or designed, and "robust yet fragile" nature of such systems is hopelessly doomed to be overwhelmed by their sheer complexity. A key insight is that high computational complexity implies the existence of hidden fragilities in the original problem statements, models, or the data, that must be resolved either by refined modeling or new experiments. Put simply, "complexity implies fragility" and robust systems can be tractably modeled and understood, with the proper infrastructure.