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Scale-Free Networks in Contemporary Biology

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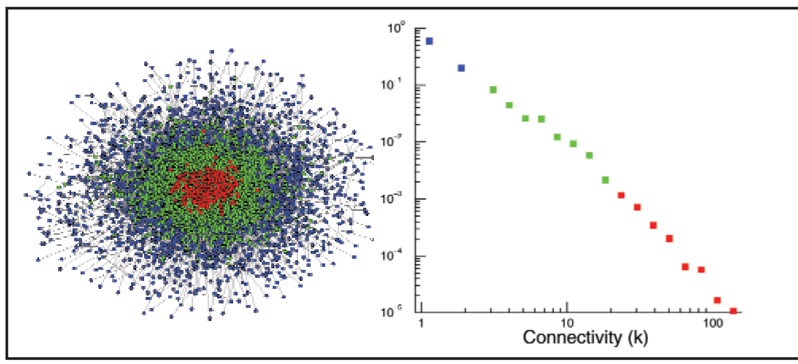
A standard dictionary definition of a network is "an interconnected or interrelated chain, group, or system." A cursory look at our surroundings shows that networks are ubiquitous. For instance, we can describe a single-celled organism as a highly complex web of multi-scale networks, ranging from the gene-regulatory system, to protein interactions, to metabolism. A chief challenge in modern biology is to develop a system-wide understanding of cellular function on the basis of genomic information. Network representations of complex biological systems have successfully served this purpose. Key characteristics of life, such as adaptation or robustness, can be translated into the interplay between network topology and dynamics. Recent discoveries of strong similarities in the architectural features of complex networks spanning the social, technological, and life sciences, have opened a new horizon in our understanding of the principles that govern and shape biological systems.[1]

Theoretical and experimental results have established that most biological systems are "scale-free," meaning that their connectivity distributions can be approximately described by a power-law function (see Figure). This "systems" feature has long been recognized in the context of economics (Pareto's law) and linguistics (Zipf's law). In biological networks such as signal transduction, transcriptional regulation and metabolism, the majority of the nodes (being either genes, transcription factors or metabolites) have only a few network connections, while a few nodes, the "hubs," have hundreds or even thousands of connections. We may interpret these hubs as ubiquitous metabolites, promiscuous enzymes, or versatile transcription factors.

A simple drawing of the wiring diagram demonstrates that biological networks are so compact that on average, any pair of molecules and chemical reaction events is connected in just a few steps. While scale-free networks are more vulnerable to intentional attacks targeting the hubs, they show a remarkable resilience to random failures, which are a common feature of evolutionary events. These discoveries may lead to an entirely new approach to pharmaceutical target identification, where the chance for development of drug resistance is significantly reduced.

Another significant feature of biological networks is their modularity: Similar to a computer program, it is possible to identify biological "subroutines" with a clearly defined function. However, biological functional units are highly interwoven on all levels, creating a hierarchical structure, suggesting that communication between the highly connected network regions is maintained by the hubs. This structural organization makes it possible for the systems to evolve using random mutations without disrupting the integrity of the whole system.

Trying to answer the old question of how living organisms achieve a robust state of being, the benefits of network approaches to biology become clear. Teasing apart the driving forces that have shaped these networks not only sheds light on evolutionary paths, but also provides guiding principles for current efforts in synthetic biology that aim to construct robustly operating biomimetic systems. □



The protein-interaction network (PIN) of Homo sapiens (from TheBiogrid 2.0.29), where proteins correspond to nodes, and a link indicates that two proteins physically bind. The low connectivity nodes (blue) coexist with nodes of intermediate (green) connectivity and hubs (red) with high connectivity. The connectivity distribution is scale-free.

DETAILS

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