

## PREFACE

Over the last few years, biologists have accumulated at unprecedented pace huge datasets on systems at many different levels, ranging from molecules to populations. As these datasets typically consisted of a list of biological objects and of their interactions, they could naturally be captured by network representations. These uniform representations allowed any single domain of application to benefit from scientific breakthroughs originating in several disciplines, from graph theory to technological or social networks. This Book on Biological Networks testifies to the recent efficiency of this transversal approach, while anticipating that the advent of more sophisticated types of abundant data may inspire combinations of network methods with other approaches in an application-driven fashion.

### *Challenges*

In network models, the relevant components in a system are identified as nodes. The interactions between these components are represented as links between nodes. Following this abstraction step, it becomes possible to study the topological properties of the network thus obtained. The generality and uniformity of the network representation make it possible to compare systems of very different types. At present, pure and combined network-based approaches still present fascinating challenges with respect to topological properties, and to temporal and spatial development.

Transversal challenges (Fig. 1) include tackling networks with a high number of nodes, and partitioning them and recomposing their parts in a useful way. Partitioning a network into sub-networks is of interest only if the resulting sub-networks or modules are biologically relevant and display a characteristic dynamics, that they retain upon recomposition into the full picture. While partitioning into relevant modules has met with some success, it is noteworthy that network recomposition is still in its infancy. Recomposition is however a requisite for the full success of

the modular approach in fruitfully compacting representations and in building a knowledge of Nature's own design principles. Modularity has an evolutionary counterpart. In particular, it is quite possible that modularity contributes to the evolvability of organisms. In this respect, the relation between functional modules and evolutionary modules must be questioned.

Another important transversal challenge to network-based approaches (Fig. 1) consists in tackling heterogeneity, a central feature of most empirical networks. This implies the possibility of expressing an arbitrary number of link types among a single set of nodes (layered networks), or an arbitrary number of node types, or heterogeneities both in nodes and links. Besides heterogeneities of components and links, it will also be fruitful to deal with temporal heterogeneity, i.e. connections that individually vary over time, even though they remain privileged, specific interactions.

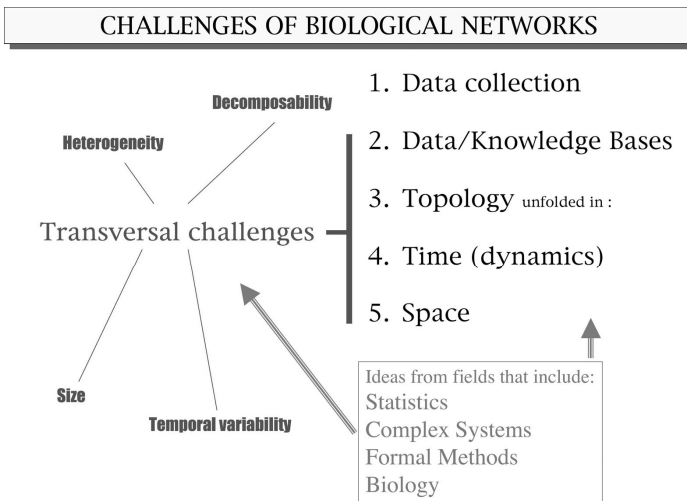


Figure 1. Challenges of biological networks.

In any realistic model, one would ideally like to unfold networks both in time (dynamics) and in space, to escape the static view that one often associates with network topological descriptions (Fig. 1). Among the shortcomings of current purely network-based approaches, most

conspicuous is the lack of a geometrical space where to place the biological objects in neighborhood situations with potentially important effects on the dynamics of their interactions, from cellular regulations to epidemics. Indeed, many studies in complex systems follow either a network-based or an agent-based approach. Seldom are these approaches used jointly. The reasons for disjoint use typically include the requirement for simplicity in the modeling process. However, these two approaches may rather be seen as complementary. Indeed, space and locality are at the heart of agent-based approaches. However, these models fall short of allowing for perennial relations between specific agents, such as those encountered among individuals, cells and even biomolecules. Network models allow such privileged interactions between specific agents. Thus, it would be useful to harness the network-based and the agent-based approaches together for more realistic modeling that would involve both the movement of agents in space and privileged interactions between specific agents.

Finally, the search for design principles afforded by network approaches to biology will logically lead to applying these principles to build new forms of synthetic Life, for engineering purposes as well as for a better understanding of natural Life.

## ***Outline***

Part 1 of the Book addresses transversal topics, thus covering generic issues and providing the mathematical setting. The Chapters in Part 1 each survey many types of networks with a common question, although they anchor their discussion in a few well-chosen case studies for the sake of understanding. The common questions are topology in Chapter 1 by Barabási and coworkers, modularity in Chapter 2 by Solé and coworkers, and reverse engineering in Chapter 3 by d'Alché-Buc.

Part 2 of the Book addresses vertical topics, thus covering in-depth various application domains at the molecular, cellular and population levels. Each such Chapter corresponds to one application domain, describing one type of network, from the interacting partners and discovery methods, to the overall structure, dynamics and modeling. At the molecular level, transcriptional networks are discussed in Chapter 4

by Képès, protein networks in Chapter 5 by Ideker and coworker, metabolic networks in Chapter 6 by Fell, and mixed molecular networks in Chapter 7 by Schächter. At the cellular level, neuronal networks are covered in Chapter 9 by Frégnac and coworkers, and immunological networks in Chapter 10 by Callard and Stark. At the population level, Chapter 11 by Bersier offers a historical perspective and a wide introduction to ecological studies, while Chapter 12 by Martinez and coworker provides detailed innovative views on food webs. Finally, epidemiological networks are discussed in Chapter 13 by Koopman.

A biological network cannot be fully understood unless the evolutionary dimension is considered. This is why counterparts on natural genesis or artificial generation of networks are provided when sufficient ground is available, notably for molecular networks in Chapter 8 by Bornberg-Bauer and coworkers, and to a lesser extent for ecological networks inside Chapter 11 by Bersier. Evolutionary considerations are not absent from the topical chapters though.

### ***Acknowledgements***

This Book is part of a nascent Series that World Scientific devotes to "Complex Systems and Inter-disciplinary Science". Without the exceptional dedication of Felix Reed-Tsochas from Oxford University, one of the Series Editor, this Book would have never seen the light of day. When Felix approached me with this idea, my response was immediately enthusiastic, as I had suffered in the past of the unavailability of a Book that would cover biological networks with both transversal spirit and in-depth insight, exactly what this Series was calling for. In preparing the Book project, his advices and encouragements have been particularly useful.

It has been a pleasure to interact with Authors originating from a variety of disciplines and countries, some I knew well, some I am still hoping to meet in person some day, all of them enthusiastic scientists. I have learnt a lot by reading their contributions, and I wish that the Reader will learn from these chapters and enjoy them as much as I did.

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François Képès