

### Networks of Networks in Biology Concepts, Tools and Applications

Biological systems are extremely complex and have emergent properties that cannot be explained or even predicted by studying their individual parts in isolation. The reductionist approach, although successful in the early days of molecular biology, underestimates this complexity. As the amount of available data grows, so it will become increasingly important to be able to analyse and integrate these large data sets. This book introduces novel approaches and solutions to the big data problem in biomedicine, and presents new techniques in the field of graph theory for handling and processing multi-type large data sets. By discussing cutting-edge problems and techniques, researchers from a wide range of fields will gain insights into how to exploit big, heterogeneous data in the life sciences through the concept of 'network of networks'.

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# Networks of Networks in Biology

Concepts, Tools and Applications

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## **CAMBRIDGE**UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom
One Liberty Plaza, 20th Floor, New York, NY 10006, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
314321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi 110025, India
79 Anson Road, #06–04/06, Singapore 079906

Cambridge University Press is part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning, and research at the highest international levels of excellence.

www.cambridge.org Information on this title: www.cambridge.org/9781108428873 DOI: 10.1017/9781108553711

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First published 2021

Printed in the United Kingdom by TJ Books Limited, Padstow Cornwall

A catalogue record for this publication is available from the British Library.

ISBN 978-1-108-42887-3 Hardback

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## **Preface**

Network Science is transforming research in different areas of living sciences, ranging from evolutionary biology to medicine. This book aims to introduce the most recent developments of Network Science and its biological applications. In particular, the architecture of biological systems will be characterized using both single networks (monoplexes) and networks of networks (multi-layer networks). Graph theory and social network analysis are classic subjects of mathematics and sociology that have been widely investigated in the twentieth century. However, only since the late 1990s, when several papers on the fundamental design principles of various kinds of large-scale networks were published, was Network Science established as a novel framework to analyse interacting systems, which led to the expansion of the research field of network analysis, with great impact in biology.

After 20 years, this field is still proliferating, and it has become increasingly clear that the challenge of integrating and modelling heterogeneity and complexity of living systems cannot be addressed by using a single-layer network (monoplex).

Instead, the complexity of living systems – such as the interactions between proteins and the microbiome – is captured by a multi-layer network approach. Multi-layer networks are formed by nodes and interactions of different natures, and connotations, forming different networks that interact with each other, creating a network of networks. The investigation of multi-layer networks is a very active research area in Network Science, which in the last ten years has led to the development of several methodologies to extract information for analysing large data sets and integrating the results from different experiments.

With contributions from key leaders, this book discusses topics in Network Science that are increasingly foundational for the quantitative understanding of living systems. Furthermore, it consolidates existing practical and theoretical knowledge of both monoplexes and multi-layer networks. The book balances application and theory to give a unified overview of this interdisciplinary science. It is intended to serve as an introductory text for graduate students and researchers in physics, biology, and biochemistry, and presents ideas and techniques from fields outside the reader's own area of specialization.

#### Aims of this Book

This book focuses on network-inspired approaches for the analysis and integration of the large data sets currently prevalent in life sciences. The principal aim of this work is to give a comprehensive overview of new techniques in the field of graph theory for handling and processing multi-type large data sets. By discussing state-of-the-art problems and techniques, this book offers researchers from a wide range of areas the unique opportunity to gain insights for exploiting the richness of life sciences data sets through the concept of 'networks of networks'. It presents a timely, multi-authored compendium representing a diverse set of backgrounds and methods developed in



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this area. Contributions have been selected and compiled to introduce the concept and cover different methods in a way that is accessible to people from diverse backgrounds. We hope that researchers from different areas of network analysis will learn new aspects and future directions of this emerging field.

#### How to Read this Book

In order to reach a broad spectrum of readers – biologists, biochemists, computer scientists, bioinformaticians – the book does not require a deep knowledge of computer science or biology. Instead, the reader will learn about graph theory, graph algorithms, and network analysis, as well as biology.

This book consists of five parts: Part I provides a brief overview of biological networks and graph theory; Part II includes chapters discussing network analysis; Part III presents chapters introducing multiplex and multi-layer networks and tools to extract relevant information from these networks of networks; Part 4 includes chapters presenting the application to real biological case studies and the initial insights gained in this relatively new field of research; finally, Part V provides concluding remarks and an outline of the future directions of the field. The book builds upon the introductory chapters and ends by addressing emerging trends in this growing, vibrant research area. Each chapter can be studied independently.