Analyzing Network Data in Biology and Medicine
An Interdisciplinary Textbook for Biological, Medical, and Computational Scientists

The increased and widespread availability of large network data resources in recent years has resulted in a growing need for effective methods for their analysis. The challenge is to detect patterns that provide a better understanding of the data. However, this is not a straightforward task because of the size of the datasets and the computer power required for the analysis. The solution is to devise methods for approximately answering the questions posed and these methods will vary depending on the datasets under scrutiny. This cutting-edge text introduces biological concepts and biotechnologies producing the data, graph and network theory, cluster analysis and machine learning, before discussing the thought processes and creativity involved in the analysis of large-scale biological and medical datasets, using a wide range of real-life examples. Bringing together leading experts, this text provides an ideal introduction to and insight into the interdisciplinary field of network data analysis in biomedicine.

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An Interdisciplinary Textbook for Biological, Medical, and Computational Scientists

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To my loving family: Cvita, Bogdan, Nina, Sofia, and Laurentino.
And to my best friend, Vesna.
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Preface

We are witnessing tremendous changes in the world around us. Technological advances are impacting our lives and increasing our ability to measure things. They are yielding an astounding harvest of data about all aspects of life that form large systems of diverse interconnected entities. We are beginning to utilize the data systems to improve our understanding of the world and find solutions to some of the foremost challenges.

One such challenge is to better understand biological phenomena and apply the newly acquired understanding to improve medical treatments and outcomes. Even at the level of a cell, we are far from fully understanding the processes that we measure by genomic, epigenomic, transcriptomic, proteomic, metabolomic, metagenomic, and other “omic” data. All these different data types measure different aspects of the functioning of a cell. As these observational data grow, it is increasingly harder to analyze them and understand what they are telling us about the cell, not only due to their sizes, but also their complexities. It is not only the biology that we need to understand, which is being measured, but also the ways to abstract these complex data systems by using mathematical models that make the data amenable to computational analyses. In addition, we need to comprehend the computational challenges coming from the theory of computing, which teach us about the problems that we can efficiently and exactly solve by using computers, and about those that we cannot. Furthermore, we need to put all this biology, mathematics, and computing jointly in use by the medical sciences if we are to contribute to personalizing treatments and improving our health.

This textbook provides a resource for training upper level undergraduate students, graduate students, and researchers in this multidisciplinary area. The goal is to enable them to understand these complex issues and undertake independent research in this exciting, emerging field. The textbook presents the material in a way understandable to researchers of diverse backgrounds. Exercises are provided at the end of each chapter to put the learned material into practice. The solutions to exercises are also provided for lecturers on www.cambridge.org/bionetworks.

The textbook material is carefully chosen to start from basics and lead to more advanced concepts in a succession of chapters that build on the previous ones. The book first introduces the complex genomic and epigenomic data related to diseases and risk prediction along with the main machine learning, bioinformatics and other methods used in this domain (Chapters 1 and 2). Then it introduces the widely adopted mathematical models of graphs (networks) and the basic theory needed to understand the tools constructed for analyzing complex omics network data (Chapter 3). A very important and widely studied omics network is that of physical interactions between proteins in a cell. Hence, the biotechnologies producing these data are surveyed in Chapter 4, the quality of the data is discussed and major public databases containing the data are introduced. An introduction into methods for advanced analyses of these data is given in Chapter 5.

The textbook proceeds with the basics of machine learning commonly used to analyze network data. First, it introduces a key methodology of unsupervised
learning, cluster analysis (Chapter 6) and the applications of it in this interdisciplinary area. Then it proceeds with the basics of machine learning for data integration (Chapter 7) and advanced topics in machine learning for biomarker discovery (Chapter 8).

Just as aligning genetic sequences has revolutionized our biological and medical understanding, aligning molecular networks is expected to have similar groundbreaking impacts. This important topic is addressed and network alignment methods introduced in Chapter 9. The field of network medicine is introduced in Chapter 10. Methodology for elucidating genotype-to-phenotype relationships via analyses of human tissue-specific interactomes is presented in Chapter 11. Another important interconnected network is that of neurons in our brain. The basics of network neuroscience are presented in Chapter 12. Finally, a description of how the material presented in the textbook can be put to practice by using a major software package for analyzing network data, Cytoscape, and a major protein interaction database, STRING, are presented in the last two chapters.

I hope you will find this textbook a good resource for getting you started with doing research in this exciting and inspiring multidisciplinary area. I wish you enjoyable learning!

Nataša Pržulj