Petri Nets in Systems Biology Actions

Methodology and Applications

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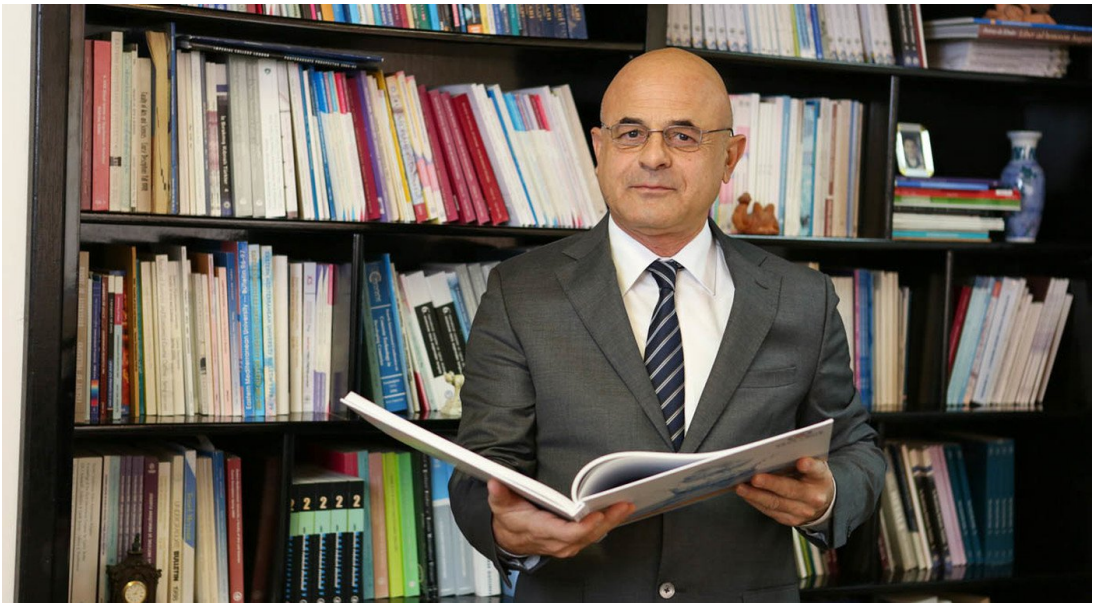

Foreword

Over the past two decades, modeling in systems biology has undergone a paradigm shift, from the selection of individual modeling tools to the adoption of comprehensive and context-appropriate modeling frameworks for representing biological systems. This evolution has been enabled, in part, by moving beyond traditional perspectives typically applied to the analysis of such systems. Among the emerging approaches, Petri nets have proven to be a mathematically rigorous and semantically expressive framework, particularly well suited to capturing the intricate dynamics of living systems.

In Petri Nets in Systems Biology: Methodology and Applications, Dr. Rza Bashirov offers a comprehensive and original contribution to this interdisciplinary field. His book is not merely a technical manual on Petri nets, nor is it a generalist overview of biological modeling. Rather, it is a rigorously constructed methodological treatise and application-driven study, aimed squarely at bridging the gap between formal modeling paradigms and practical biomedical research questions.

The first part of the book is foundational yet far from elementary. It develops a nuanced framework of Petri nets and their biologically motivated extensions — continuous, hybrid, stochastic, fuzzy, colored, and hierarchical nets—each presented with an eye toward biological realism. Unlike many introductory treatments, Bashirov does not limit himself to the textbook semantics of places, transitions, and tokens. Instead, he explores how these concepts encode reaction stoichiometry, molecular concentrations, and regulatory logic, supported by examples ranging from methane combustion to system of reversible enzymatic reactions.

What sets this work apart is the second part, where theory is put into practice across four highly focused case studies. The third chapter provides a simulation-based strategy for identifying optimal drug combinations in the treatment of spinal muscular atrophy. Rather than relying solely on in vivo experimentation or

static network analysis, in conducting simulations, Bashirov uses three distinct modeling frameworks: deterministic, purely stochastic, and fuzzy stochastic, and selects the paradigm that most appropriately reflects the intrinsic characteristics of the biological system under investigation. This strategy ensures that the resulting model serves as the most accurate approximation of the system's behavior. This approach not only highlights the potential for drug discovery based on in silico targets but also illustrates the versatility of Petri nets as predictive tools in therapeutic research and development.

In the fourth chapter, the focus shifts to β-globin disorders, notably β-thalassemia and sickle cell disease. Here, Bashirov constructs a hybrid Petri net model to simulate gene- and drug-based therapeutic interventions targeting the fetal-to-adult hemoglobin switching network. By applying fuzzy stochastic logic, the model captures both quantitative uncertainties and biological variability, providing a mechanistic rationale for the reactivation of γ-globin genes.

The fifth chapter ventures into oncology, where the dynamics of the p16-mediated signaling pathway, a critical regulator of cellular senescence, is modeled using fuzzy stochastic Petri nets. This is perhaps one of the book's most impressive contributions, as it brings together systems-level modeling, parameter uncertainty, and comparative dynamics to explore the differential behavior of cancer-related pathways under deterministic, stochastic, and hybrid assumptions.

The final chapter explores the use of Petri net analysis methods, such as P- and T-invariants, to reveal modular structures in Akt and MAPK signaling pathways, as well as their crosstalk, exemplifying the capacity of qualitative Petri nets to uncover architectural motifs and predict functional dependencies in complex networks.

Taken together, this book achieves what few works in the field manage to do: Build a unified methodological platform, offer rich and reproducible case studies, and provide biological insights that are both relevant and novel. It is clear that Bashirov is not simply an applied mathematician or a computer scientist with a strong biological background; he is a modeler in the truest interdisciplinary sense, capable of navigating between abstraction and biological specificity with precision.

For postgraduate students, this book is a rigorous entry point into computational systems biology. For researchers, it offers concrete methods for model development, validation, and application. For practitioners in drug discovery and therapeutic design, it offers a blueprint for how in silico modeling can de-risk and accelerate biological innovation.

In short, Petri Nets in Systems Biology is not just a contribution, it is a benchmark, and it will likely become a standard reference in the years to come for those working at the interface of systems biology, bioinformatics, and computational modeling.

Warsaw, July 2025 Professor Janusz Kacprzyk

Preface

Haruki Murakami once said that if you only read the books that everyone else is reading, you can only think what everyone else is thinking. This book was not written to be a bestseller; rather, its intention is to captivate postgraduate students and researchers intrigued by computer modeling in systems biology. It is my hope that this book will fill the gap between academia and industry regarding methods and models of computer science that will enable researchers to understand how to explore drug-gene-disease interaction networks to discover effective molecular targets in line with the disease modeling.

This book provides a methodology for the Petri net based modeling of biomedical networks as well as overview its recent applications in therapeutic target discovery. Situated at the intersection of emerging fields like Petri nets, bioinformatics, systems biology, target-based drug discovery, and biomedicine, the book consists of two main parts: a methodology part and an applications part.

The initial two chapters lay the groundwork by introducing Petri nets and their crucial analysis techniques for modeling biological systems. The subsequent chapters elucidate the methodological aspects of applying Petri nets and principles of process modeling. Following these foundational chapters are four case studies illustrating both quantitative and qualitative modeling of biomedical networks using Petri nets.

The third chapter presents a simulation-based prediction of optimal drug combinations for potentially effective treatment of spinal muscular atrophy, while the fourth chapter identifies the most prominent molecular targets that, when attacked can substantially alleviate severity of β-globin disorders like β-thalassemia and sickle cell disease. The fifth chapter focuses around the quantitative modeling of p16-mediated pathway, which holds a crucial role in regulating DNA damage and cellular senescence. Finally, the last chapter revolves around qualitative analysis with Petri nets to discover the modularity in signaling networks.

Famagusta, North Cyprus Rza Bashirov

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