

# Preface

Membrane Computing was introduced in 2000 [1], as a research topic in Natural Computing. It soon became a very active research area and just three years after the publication of this seminal paper, the Institute for Scientific Information (ISI) identified the paper as being *fast breaking* in the field of Computer Science [2]. Since then the field has flourished giving birth to many research topics, triggering connections with many other research areas and producing interesting applications. The models introduced are called membrane (or P) systems. Many theoretical aspects related to computability, complexity and decidability have been investigated for various classes of membrane systems—accounts of these developments have been reported in [3–6]. Membrane systems have been employed for solving various problems in Computer Science, Graphics, Linguistics, Robotics, and other fields [7]. A recently published comprehensive handbook [8] provides a thorough overview of the main theoretical developments, it points to the main links between membrane systems and other computational models and describes some of the most important applications in this field and some of the tools developed throughout the years.

In parallel to investigations of the key research questions related to Membrane Computing and their applications, there have been studies related to the use of the Membrane Computing paradigm in modelling biological systems. These applications represent not only significant contributions to modelling various processes and phenomena in Biology, but they also point out interesting and challenging problems in studying the complexity and emergent properties of such systems. Some of the contributions related to these applications have been collected in a special issue of BioSystems [9], but there is no monograph dedicated to such issues, and this is a clear gap in the literature of membrane systems. The present monograph aims to fill this gap.

The authors invited to write chapters for this volume have already published papers on a broad spectrum of problems related to Biology, from modelling and simulations, to system analysis and identification, and to the development of methods and tools necessary in supporting these investigations. There have been reported studies on modelling oscillating and catalytic chemical reactions [10], diffusing processes with geometrically constrained molecules [11] or occurring in a signal transduction pathway [12]. Stable oscillatory states in budding yeast [13], biochemical signalling pathways [14] and Fas pathways [15] have been considered.

Classes of probabilistic membrane systems have been introduced for studying populations and ecosystems [16] and metabolic P systems, a special class of deterministic systems, have been utilised in solving complex problems in biotic systems [17, 18]. Membrane systems have been used to model and simulate the behaviour of logical gates [19] and register machines [10] in a synthetic biology setting. Slightly more general models, like agent-based approaches, have been utilised for studying three-dimensional multiscale phenomena in human epidermis [20]. The definition of formal languages for specifying complex molecular interactions in biological systems [21], verification tools for non-deterministic [22] and stochastic systems [23], and the development of complex platforms for specification, analysis and simulation of systems and synthetic biology problems [24] have been considered. Appropriate sets of methods and tools [17, 18] have been developed and efficient implementations of classes of membrane systems for complex simulations [25] have been produced.

The chapters contained in this monograph give a clear image of the depth and breadth of the applications of membrane systems for the study of various biological processes and phenomena.

- In [Chap. 1](#), *Infobiotics Workbench: A P Systems-Based Tool for Systems and Synthetic Biology*, a comprehensive overview of an integrate software platform, the Infobiotics Workbench, and of its usage in specifying, simulation, verification and parameter optimisation of models operating at the cellular and intercellular levels is provided.
- In [Chap. 2](#), *Statistical Model Checking of Membrane Systems with Peripheral Proteins: Quantifying the Role of Estrogen in Cellular Mitosis and DNA Damage*, a methodology and a software platform for integrating a membrane system simulator with a statistical model checker are described. These are used for studying the dosage of antagonist that minimises the uncontrolled replication of abnormal cells.
- In [Chap. 3](#), *Molecular Diffusion and Compartmentalisation in Signal Transduction Pathways: An Application of Membrane Systems to the Study of Bacterial Chemotaxis*, intracellular diffusion processes are studied. A class of membrane systems, called  $\tau$ -DPP, is used in analysing both single volume pathways and multivolume diffusion interactions.
- In [Chap. 4](#), *Membrane Systems-Based Models for Specifying Dynamical Population Systems*, a class of probabilistic systems for studying population dynamics of ecosystems is presented. The theory behind the simulation of such models is presented, a software platform allowing the specification, simulation on different platforms, including CUDA, and analysis of such systems is described and a complex case study analysed.
- In [Chap. 5](#), *Membrane Systems and Tools Combining Dynamical Structures with Reaction Kinetics for Applications in Chronobiology*, three relevant studies in chronobiology are addressed, proving their convergent results. These case studies are specified and analysed with a software package, called SRSim, allowing spatial interaction rules and a powerful visualisation engine.

- In [Chap. 6](#), *Biochemical Networks Discrete Modelling Inspired by Membrane Systems*, a new version of Gillespie algorithm is presented. Comparisons between this model and others based on differential equations and Gillespie method are performed on a number of case studies.
- In [Chap. 7](#), *MP Modelling for Systems Biology: Two Case Studies*, a class of deterministic membrane systems, namely metabolic P (MP) systems, is described. The modelling capabilities of such models, expanding from metabolic systems to more general dynamical systems, and the power of a regression algorithm allowing the identification of MP models from the time series associated with observations are studied.
- In [Chap. 8](#), *Modelling and Analysis of E.coli Respiratory Chain*, a more general modelling approach, based on agent systems, and a method to derive a class of membrane systems specifications, called kernel P systems are presented. This process, which allows the formal verification of such specifications by using model checking methods, is illustrated by a prototype model of *E.coli* respiratory chain.

The entire description of all the examples discussed in this monograph together with simulation results and tools utilised are provided as auxiliary materials by the authors. Each chapter contains a link to webpages describing the case study(ies) presented.

The book is addressed to researchers interested in applications of discrete models in Biology, the interplay between membrane systems and other approaches and methods in specifying and analysing complex systems and revealing their behaviour. The readers are encouraged to use and assess the models described in the book chapters and the tools provided. Comments and suggestions for improving the functionality of the models and the usability of the tools are welcome.

This book is dedicated to Gheorghe Păun, the initiator and the main driving force behind the research in Membrane Computing. We thank Gheorghe for his continuous support, contagious enthusiasm and for being an example and source of inspiration.

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