

# Preface

In the past 30 years, progress in molecular and cellular biology has greatly benefited from the diversity of experimental methods. At the same time, the amount of data generated has been plethoric, posing real challenges for mathematics, theoretical physics, computer science and more areas. These challenges are extracting hidden features from large and high-dimensional data sets and generating fast multiscale simulations. To accomplish this program, various tools were further developed: fast stochastic simulations to simulate stochastic chemical reactions have been built on the Gillespie method. Other developments include the derivation of biophysical modelling or reducing the complexity of high-dimensional stochastic processes by projection into low-dimensional space, where the analysis is possible. Finally, deriving asymptotic formula has revived asymptotic analysis of partial differential equations, because they usually represent the new physical laws and clarify the role of singular parameters.

The convergence of these interests and techniques has engulfed mathematical biology into a new area at the intersection of statistical physics, applied mathematics, applied probability, computer science, biophysics and cell biology. This new field does not simply provide new tools to extract features from data or to simulate large amount of particles, but aims to contribute in quantifying and explaining the function of a cell or its subcellular components from the molecular organization (from nano- to micro- and higher scales).

Our young community has recently been challenged by producing modelling, analysis, effective and fast methods of computing, based on coarse-graining or analysis of the model equations. Examples of biological processes include diffusion in microdomains, calcium dynamics, gene regulation, chromatin organization and modification, signal transduction and molecular signalling, coagulation-fragmentation of proteins and cellular transport, but also synaptic formation and plasticity, cellular communication, neuronal network organization, early patterning during development and many more.

Molecular and cellular biology processes are inherently stochastic, which is the main driving force of many biological functions such as during ionic channels or synaptic transmission. Stochastic and rare events are at the basis of signal

transduction, but also facilitate phenotypic diversity of cellular populations and even drive mutation during evolution. At the scale of a single cell, stochasticity becomes relevant due to low copy numbers of biological molecules, such as mRNA or transcription factors, that take part in biochemical reactions driving cellular processes. When trying to describe such biological processes, the traditional mean-field or coarse-grained deterministic models are often inadequate, exactly because of these low copy numbers. But stochastic models are necessary to account for small particle numbers (intrinsic noise) and extrinsic noise sources. The complexity of these models depends crucially on whether the biochemical reactions are diffusion-limited or reaction-limited. In the latter case, processes are described by adopting the framework of Markov jumps and stochastic differential equations (chemical master and Fokker-Planck equations), while in the former it is possible to adopt the framework of stochastic reaction-diffusion models, including reaction-diffusion master equation, partial differential equations and particle-based Brownian dynamics simulations.

This book is divided into four main parts. The first describes stochastic and master chemical reactions with low copy numbers. The method involves dimensional reduction. The second concerns the theory and method of random simulations using stochastic processes for motion, but also chemical reactions. The third is dedicated to asymptotic analysis used to explore the parameter space. The fourth explores diffusion processes and stochastic modelling in cell biology. Several examples of cell biological systems are treated here such as the model of axonal growth and analysis of photoreponse with an emphasis in the multiscale chemical reactions for the signal transduction inside rod photoreceptors. At a cell population level, several stochastic models are introduced about the mitochondrial heterogeneity across network configurations and genetic heterogeneity within cells and between generations. Finally, using birth, death, immigration and local dispersal of individual's model, some empirical stochastic equations and observables are introduced to study spatial pattern organization.

The chapters are written for a large audience of mathematicians, physicists, computational biologists and computer scientists interested in studying stochastic and numerical methods and physical modelling for cellular processes. This collective effort originates from a 6-month programme that took place at the Newton Institute in Cambridge in 2016, organized by R. Erban, K. Zygalakis, S. Isaacson and myself about, "Stochastic Dynamical Systems in Biology: Numerical Methods and Applications" (<https://www.newton.ac.uk/event/sdb>). We thank the Newton Institute and its director John Tolland and the Simons Foundation for making this programme possible that resulted in the present book.

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David Holcman

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