Models of Life

Dynamics and Regulation in Biological Systems

Reflecting the major advances that have been made in the field over the past decade, this book provides an overview of current models of biological systems. The focus is on simple quantitative models, highlighting their role in enhancing our understanding of the strategies of gene regulation and dynamics of information transfer along signaling pathways, as well as in unravelling the interplay between function and evolution.

The chapters are self-contained, each exploring key methods and principles for understanding quantitative aspects of life through the use of models. They focus, in particular, on connecting the dynamics of proteins and DNA with strategic decisions on the larger scale of a living cell, using *E. coli* and phage λ as key examples. Encompassing fields such as quantitative molecular biology, systems biology and biophysics, this book will be a valuable tool for students from both biological and physical science backgrounds.

End-of-chapter summary sections, along with questions placed throughout chapters, help to explain the key concepts to students. Solutions are available online at www.cambridge.org/sneppen.

KIM SNEPPEN is Professor of Physics at the Niels Bohr Institute and Director of the interdisciplinary Center for Models of Life (CMOL) at Copenhagen University, Denmark. Drawing on experience across several academic disciplines, his work explores the frontier between complex dynamic systems and living systems, and in his role at CMOL he promotes hands-on development of quantitative models of central biological processes. Sneppen is also co-author of *Physics in Molecular Biology* (Cambridge University Press, 2005).

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CAMBRIDGE
UNIVERSITY PRESS

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University Printing House, Cambridge CB2 8BS, United Kingdom

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/9781107061903

First published 2014

Printed in Spain by Grafos SA, Arte sobre papel

A catalog record for this publication is available from the British Library

Library of Congress Cataloging in Publication data
Sneppen, Kim, author.
Models of life : dynamics and regulation in biological systems / Kim Sneppen, Niels Bohr Institute and Center for Models of Life, Copenhagen University, Denmark.
pages cm

ISBN 978-1-107-06190-3 (Hardback)
1. Life sciences–Mathematical models. 2. Biology–Mathematical models.
I. Title.
QH323.5.S62 2014
570.1′51–dc23 2014003456

ISBN 978-1-107-06190-3 Hardback

Additional resources for this publication at www.cambridge.org/sneppen

Contents

Cambridge University Press
978-1-107-06190-3 - Models of Life: Dynamics and Regulation in Biological Systems
Kim Sneppen
Frontmatter
More information

Preface

This book is the result of outstanding collaborations with inspiring collegues and friends. A part of its content is based on an earlier book that I published with Giovanni Zocchi, with whom Mogens H. Jensen and I started the biological physics initiative at Copenhagen University. The major content of the book has been developed during the last decade, when I had the luck to be in charge of the Center for Models of Life at the Niels Bohr Institute. This center exists thanks to generous funding from the Danish National Research Council, who gave me the option to invite and employ inspiring collaborators.

Much of the content of this book is based on activities at the center. The book was also developed in parallel with our scientific endeavors and bachelor degree level courses on gene regulation, networks and complex systems for which I had the pleasure of lecturing. Accordingly, the big part of the book is devoted to classical models from molecular biology, spanning a wide spectrum of model systems and synthetic circuits as they unfold in classical model organisms like *Escherichia coli*.

I would hope that this book is useful for bachelor degree-level students in any quantitative discipline related to physics or biology. In fact, I believe the book also could be of inspiration for mathematically inclined high school and college students. If one just disregards the most boring and technical equations, the main messages should be conveyed by the frequent use of illustrations and provocative statements.

In general, the chapters of the book can be read without following any particular order, as they, to a large extent, provide alternative ways to work with quantitative aspects of life from the perspective of physics.

The focus of the book is quantitative, yet simple, models. A main criterion for selection is Occam's razor principle, where a model loses meaning as it gets too complicated. *Models of Life* is accordingly not aimed at giving a complete description of the studied systems. Rather it provides the reader with an understanding of interesting biology, facilitated by models developed within the criterion *that the quality of a model declines sharply with each added parameter*.

The proposed models will, occasionally, challenge this criterion, and in certain cases explore ways to hide the "parameter nightmare" with sampling over a large numbers of parameter sets. This will then leave the main messages to structural features of a model, like signs of feedbacks, or type of interaction that are essential to understand a given phenomenon.

Many friends and collegues have helped me both in scientic projects and inspiration. The most exceptional help was from Namiko Mitarai, who has been pivotal in many of the described models and finally took the effort to read and criticize the many mistakes I had in the nearly finished book. Major parts of the book are built on a beautiful and ongoing collaboration with Ian Dodd, who also taught me much of the biology I know today. Stanley Brown also deserves very special thanks as my mentor in biology, teaching me about the complexity of *E. coli*, and introducing me to the wonderfully quantitative scientists around the λ phage, including in particular Sankar Adhya, Donald Court, Barry Egan, Harvey Eisen, Max Gottesman, Keith Shearwin and Lynn Thomasen.

Important collaborators and tutors in biology also include Steen Pedersen and Genevive Thon from Copenhagen University, Kenn Gerdes from Newcastle University, Eric Masse from Sherbroke University and finally Szabolcs Semsey as our resident biologist in the center. Szabolcs also developed many models and helped with critical reading of the manuscript, pinpointing especially boring sections. I hope it has improved, and that the reader will find inspiration in most of the text.

All the PIs, post-docs and students that have resided at the center are also to be thanked, with very special thanks to Anne Alsing, Mikkel Avlund, Jacob Bock Axelsen, Sebastian Bernhardsson, Philip Gerlee, Jan Haerter, Silja Heilmann, Mogens Høgh Jensen, Sandeep Krishna, Ludvig Lizana, Joachim Matthiesen, Mille Micheelsen, Simone Pigolotti, Martin Rosvall and Ala Trusina, all of whom have been pivotal in the presented models. These models were also developed with physics friends from across the world, of whom, in particular, Per Bak, Stefan Bornholdt, Hiizu Nakanishi and Sergei Maslov contributed with central ideas and concepts.

I also thank the many students that took my courses through the years, of which my recent students Celie Feldager, Sirin Gangstad and Svend Steffensen took additional effort to give constructive comments to many of the currently used sections.

Finally I would like to express gratitude to my wife Simone and my children Albert, Eva, Thor and Ida, who had the patience to leave me in peace during the many evenings and weekends it took to write the book. In particular I am happy for discussions with my youngest son Albert, which, after careful reading of Darwin's original works, pinpointed many of the deep insights that this scientist developed on speciation and the enormous timescales of evolution.