Modeling and Simulation in Science, Engineering and Technology

Andreas Deutsch
Sabine Dormann

Cellular Automaton Modeling of Biological Pattern Formation

Characterization, Applications, and Analysis

Foreword by Philip K. Maini

Birkhäuser
Boston • Basel • Berlin

Andreas Deutsch
Dresden University of Technology
Center for High Performance Computing
D-01062 Dresden
Germany

Sabine Dormann
University of Osnabrück
Department of Mathematics
D-49069 Osnabrück
Germany

AMS Subject Classifications: 00A72, 0001, 0002, 9208, 92B05, 92B20

Library of Congress Cataloging-in-Publication Data
Deutsch, Andreas, 1960-
Cellular automaton modeling of biological pattern formation : characterization, applications, and analysis / Andreas Deutsch, Sabine Dormann.
p. cm — (Modeling and simulation in science, engineering & technology)
Includes bibliographical references and index.
ISBN 0-8176-4281-1 (alk. paper)
1. Pattern formation (Biology) 2. Cellular automata–Mathematical models. I. Dormann, Sabine. II. Title. III. Series.

QH491.D42 2004
571.3–dc22 20030638990
CIP

ISBN 0-8176-4281-1 Printed on acid-free paper.

Printed in the United States of America. (TXQ/MV)

9 8 7 6 5 4 3 2 1 SPIN 10855758

Birkhäuser is a part of *Springer Science+Business Media*
www.birkhauser.com

To our parents

Foreword

The recent dramatic advances in biotechnology have led to an explosion of data in the life sciences at the molecular level as well as more detailed observation and characterization at the cellular and tissue levels. It is now absolutely clear that one needs a theoretical framework in which to place this data to gain from it as much information as possible. Mathematical and computational modelling approaches are the obvious way to do this. Heeding lessons from the physical sciences, one might expect that all areas in the life sciences would be actively pursuing quantitative methods to consolidate the vast bodies of data that exist and to integrate rapidly accumulating new information. Remarkably, with a few notable exceptions, quite the contrary situation exists. However, things are now beginning to change and there is the sense that we are at the beginning of an exciting new era of research in which the novel problems posed by biologists will challenge the mathematicians and computer scientists, who, in turn, will use their tools to inform the experimentalists, who will verify model predictions. Only through such a tight interaction among disciplines will we have the opportunity to solve many of the major problems in the life sciences.

One such problem, central to developmental biology, is the understanding of how various processes interact to produce spatio-temporal patterns in the embryo. From an apparently almost homogeneous mass of dividing cells in the very early stages of development emerges the vast and sometimes spectacular array of patterns and structures observed in animals. The mechanisms underlying the coordination required for cells to produce patterns on a spatial scale much larger than a single cell are still largely a mystery, despite a huge amount of experimental and theoretical research. There is positional information inherent in oocytes, which must guide patterns, but cells that are completely dissociated and randomly mixed can recombine to form periodic spatial structures. This leads to the intriguing possibility that at least some aspects of spatio-temporal patterning in the embryo arise from the process of self-organization. Spatial patterns also arise via self-organization in other populations of individuals, such as the swarming behaviour of bacteria, and in chemical systems, so that it is a widespread phenomenon.

Modelling in this area takes many forms, depending on the spatio-temporal scale and detail one wishes (or is able) to capture. At one extreme are coupled systems of

ordinary differential equations, in which one assumes that the system is well stirred so that all spatial information is lost and all individuals (for example, molecules) are assumed to have identical states. At the other extreme are cellular automata models, in which each element may represent an individual (or a collection of individuals) with assigned characteristics (for example, age) that can vary from one individual to the next. This approach allows for population behaviour to evolve in response to individual-level interactions. In hybrid cellular automata, one can model intracellular phenomena by ordinary differential equations, while global signalling may be modelled by partial differential equations. In this way, one can begin to address the crucial issue of modelling at different scales. There are many modelling levels between these extremes and each one has its own strengths and weaknesses.

Andreas Deutsch and Sabine Dormann bring to bear on this subject a depth and breadth of experience that few can match. In this book they present many different modelling approaches and show the appropriate conditions under which each can be used. After an introduction to pattern formation in general, this book develops the cellular automaton approach and shows how, under certain conditions, one can take the continuum limit, leading to the classical partial differential equation models. Along the way, many interesting pattern formation applications are presented. Simple rules are suggested for various elementary cellular interactions and it is demonstrated how spatio-temporal pattern formation in corresponding automaton models can be analyzed. In addition, suggestions for future research projects are included. It is also shown that the model framework developed can be used more generally to tackle problems in other areas, such as tumour growth, one of the most rapidly growing areas in mathematical biology at the present time. The accompanying website (www.biomodeling.info) allows the reader to perform online simulations of some of the models presented.

This book, aimed at undergraduates and graduate students as well as experienced researchers in mathematical biology, is very timely and ranges from the classical approaches right up to present-day research applications. For the experimentalist, the book may serve as an introduction to mathematical modelling topics, while the theoretician will particularly profit from the description of key problems in the context of biological pattern formation. The book provides the perfect background for researchers wishing to pursue the goal of multiscale modelling in the life sciences, perhaps one of the most challenging and important tasks facing researchers this century.

Philip K. Maini
Centre for Mathematical Biology
Oxford, GB
January 2004

Contents

List of Figures

List of Notation

CA	cellular automaton
LGCA	lattice-gas cellular automaton/automata 67

Greek symbols

$\beta \in \mathbb{N}_0$	number of rest (zero-velocity) channels 72
$\Gamma(q)$	Boltzmann propagator 95
δ	length of temporal unit 107
ϵ	length of spatial unit 107
$\boldsymbol{\eta}(r) = (\eta_i(r))_{i=1}^{\tilde{b}} \in \{0,1\}^{\tilde{b}}$	node configuration in a LGCA 72
$\boldsymbol{\eta}_{\mathcal{N}(r)}$	local configuration in a LGCA 72
Λ_M	spectrum of the matrix M 91
μ	spectral radius 91
$\mu(q)$	spectral radius according to wave number q 96
$\nu = \lvert\mathcal{N}_b^I\rvert$, $\nu_o = \lvert\mathcal{N}_{bo}^I\rvert$	number of neighbors in the interaction neighborhood 70
$\rho(r,k) \in [0,1]$	local particle density of node r at time k 86
$\rho(k) \in [0,1]$	total particle density in the lattice at time k 86
$\varrho(r,k) \in [0,\tilde{b}]$	local mass of node r at time k 86
$\varrho(k) \in [0,\tilde{b}]$	total mass in the lattice at time k 86

$\sigma \in \{1, \ldots, \varsigma\}$	single component in a model with ς components 69
$\Psi_a(\boldsymbol{\eta}(r,k)) \in \{0,1\}$	indicator function 139

Further symbols

$\lvert \cdot \rvert$	cardinality of a set
$[y]$	integer closest to $y \in \mathbb{R}^+$
$\lceil y \rceil$	smallest integer greater than or equal to $y \in \mathbb{R}^+$ 222
$\boldsymbol{y}^T$	transpose of the vector $\boldsymbol{y}$
$A_j \in \mathcal{A}_{\tilde{b}}$	permutation matrix 116
b	coordination number; number of nearest neighbors on the lattice $\mathcal{L}$ 68
$\tilde{b} = b + \beta$	total number of channels at each node 72
$c_i \in \mathcal{N}_b, i = 1, \ldots, b$	nearest neighborhood connections of the lattice $\mathcal{L}$ 68
$\mathcal{C}_i\left(\boldsymbol{\eta}_{\mathcal{N}(r)}(k)\right) \in \{-1, 0, 1\}$	change in occupation numbers 78
$\tilde{\mathcal{C}}_i\left(\boldsymbol{f}_{\mathcal{N}(r)}(k)\right) \in [0,1]$	change of the average number of particles 88
$\boldsymbol{D}\left(\boldsymbol{\eta}_{\mathcal{N}(r)}\right)$	director field 164
$\mathcal{E} = \{z^1, \ldots, z^{\lvert\mathcal{E}\rvert}\}$	(finite) set of elementary states 71
$\boldsymbol{f}(r) = (f_i(r))_{i=1}^{\tilde{b}} \in [0,1]^{\tilde{b}}$	vector of single particle distribution functions; average occupation numbers 86
$\boldsymbol{f}^s(k)$	vector of spatially averaged occupation numbers 220
$\boldsymbol{F}(q) = (F_i(q))_{i=1}^{\tilde{b}}$	Fourier-transformed value 94
$\mathtt{I}$	(general) interaction operator 77
$\boldsymbol{J}(\boldsymbol{\eta}(r))$	flux of particles at node r 164
$k = 0, 1, 2, \ldots$	time step 75
$\mathcal{L} \subset \mathbb{R}^d$	d-dimensional regular lattice 67
$L_i, i = 1, \ldots, d$	number of cells in space direction i 68
$\mathtt{M}$	shuffling (mixing) operator 115

$\mathrm{n}(r) \in \{0, \ldots, \tilde{b}\}$	total number of particles present at node r	72
$\mathcal{N}_b$	neighborhood template	68
$\mathcal{N}_b^I$	interaction neighborhood template	70
$\mathcal{N}_{bo}^I$	outer interaction neighborhood template	70
$\mathtt{P}$	propagation operator	77
$q \in \{0, \ldots, L\}$	(discrete) wave number	93
q^s	wave number observed in simulation	220
$q_* \in Q^c$	dominant critical wave number	96
Q^c	set of critical wave numbers	96
Q^+, Q^-	subsets of critical wave numbers	96
$r \in \mathcal{L}$	spatial coordinate, cell, node, site	67
(r, c_i)	channel with direction c_i at node r	72
$\mathtt{R}$	reactive interaction operator ("Turing" model)	212
$\mathcal{R} : \mathcal{E}^v \to \mathcal{E}$	cellular automaton rule	73
$s(r) \in \mathcal{E}$ $s : \mathcal{L} \to \mathcal{E}$	state value at node r	71
$\boldsymbol{s} = (s(r_i))_{r_i \in \mathcal{L}} \in \mathcal{S}$	global configuration	71
$\boldsymbol{s}_\mathcal{M} = (s(r_i))_{r_i \in \mathcal{M}}$, $\mathcal{M} \subset \mathcal{L}$	local configuration	72
$\mathcal{S} = \mathcal{E}^{\lvert\mathcal{L}\rvert}$	state space	72
$W : \mathcal{E}^v \to [0, 1]$	time-independent transition probability	74
X_σ	particle of "species" σ	78

Cellular Automaton Modeling of Biological Pattern Formation