

Andreas Deutsch • Sabine Dormann

# Cellular Automaton Modeling of Biological Pattern Formation

Characterization, Examples, and Analysis

Second Edition

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 Birkhäuser

# Foreword to the Second Edition

The enormous advances over the past 10 years in molecular and cell biology (most notably imaging) have given us unprecedented data on behaviour at the single cell and tissue level. Consequently, more and more experimentalists and theoreticians are developing mathematical and computational models at this level and, with ever-enhancing computing power, these models are becoming increasingly diverse and sophisticated. There are now many different approaches to setting up models for spatio-temporal phenomena, ranging from the classical mathematical partial differential equation approach to the computationally very efficient cellular automaton models. To someone entering the field (and even to the expert) this diversity can be bewildering and confusing. Which approach should I use? Are various approaches related in some way?

In light of the above, this new edition of *Cellular Automaton Modeling of Biological Pattern Formation* could not be more timely. To reflect the vast amount of new research in this area over the past 10 years after the appearance of the first edition, the authors have produced a book that not only greatly expands chapters from the previous edition, but also includes new chapters on cell migration, tissue development, and tumour growth/invasion to reflect important applications of cellular automata. They have also updated the suggested research projects listed at the end of several chapters. In doing so, the authors have produced the most comprehensive text on modelling spatial patterning that I have seen. It brings together diverse modelling approaches (deterministic, stochastic, cell-based), explains each in detail, compares and contrasts them, and applies them to cutting-edge research in biology and medicine. Examples include single and collective cell migration, adhesive cell interactions, alignment and swarming, pigment pattern formation, tissue growth and development, Turing pattern formation, excitable systems, tumour invasion, and angiogenesis. The book elucidates key principles of cell interactions, as well as concepts such as self-organisation, stability, and bifurcation. It begins with

a thought-provoking and entertaining history of theories of pattern formation going back to the ancient Greeks and, through 14 chapters, brings the reader right up to date with the present thinking on biological patterning processes and disease dynamics. Notably, an accompanying cellular automaton simulator is now available for readers to perform their own simulations on many of the models covered in the text. QR codes are included within the figures for easy access to the simulator.

The book is accessible to theoreticians at all levels. The beginning graduate student will learn the basic theory behind the modelling method she/he wishes to adopt, while the experienced researcher will see where her/his approach sits in the wider context of models in this field. Many researchers are restricted by their background to the particular framework they use, and it may not be the most appropriate one for the problem at hand. This book, by putting in one place such a breadth of modelling approaches, and benefiting from the wealth of experience and insights acquired by the authors, who have worked in this field all their careers, will facilitate the choice of appropriate methodology. Therefore, not only does the book serve as an educational and training text, it will also advance research in significant ways as we continue to address the most important and challenging problems facing scientific researchers this century.

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# Foreword to the First Edition

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 characterisation 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 between 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 emerge 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 pattern, but cells which 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-organisation. Spatial patterns also arise via self-organisation 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 automaton 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 analysed. 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 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 multi-scale modelling in the life sciences, perhaps one of the most challenging and important tasks facing researchers this century.

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