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Editors

Mathematics Going Forward

Collected Mathematical Brushstrokes

 Springer

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Preface

Upon learning of Catriona Byrne's retirement from Springer's mathematics staff, we needed little convincing to suggest this commemorative volume. As the title suggests, the theme of this volume is the future of mathematics. This is meant in a broad sense: the contributions of the volume range from musings on the future of a particular field to problems for future research to new results closing one door and opening another. And for obvious reasons, this volume does not respect any of the rules of the series for multi-author volumes.

The contributing authors, 44 distinguished mathematicians, have embraced this challenge beautifully. Eighteen have presented a historical perspective of their field, in five cases complemented by problems and conjectures. Eleven have oriented reviews of their subject toward meaningful unsolved problems. There are also five articles on the history of mathematics, four papers presenting conjectures and nine original mathematical contributions.

The very diverse mathematical topics of this volume have been organized alphabetically into 12 parts. Each part is introduced by a teaser page highlighting some features of the articles, inspired by comments of the reviewers and LNM editors.

Most of the contributions begin with heartfelt tributes to Catriona Byrne. Over the past four decades, she has played a very important role in mathematics publishing. We dedicate this volume to her.

On behalf of the editorial board of the Lecture Notes in Mathematics,

Paris, France
Paris, France

Jean-Michel Morel
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Part IX

Mathematical Models

In his programmatic essay *Mathematical biology: Looking back and going forward*, Phillip Maini describes how “mathematical biology has grown over the past 50 years from a niche subject, pursued by a small number of visionary pioneers, to a core subdiscipline of mathematics that is becoming increasingly inter- and intra-disciplinary, and playing a key role in many areas within ecology, epidemiology and the life and medical sciences”. Citing Joel E. Cohen, he concludes that “Mathematics is biology’s next microscope, only better; Biology is mathematics’ next physics, only better”.

In *Kermack and McKendrick models on a two-scale network and connections to the Boltzmann equations* Stephan Luckhaus and Angela Stevens deliver casual notes about a famous epidemiological model, stressing the fact that it was inspired by Boltzmann, yet its study might bring back some new insight on Boltzmann’s equations. They explain a paradox: lockdown measures in a pandemic can actually have the opposite effect in a first phase.

Ivar Ekeland’s contribution *The Pygmalion syndrome, or how to fall in love with your model* is a philosophical dream about how mathematics could be used more critically in economic theory. It concludes with the statement of a theorem (Ekeland’s variational principle), epitomizing the author’s love of pure mathematics.

Morel’s title *Can we teach functions to an artificial intelligence by just showing it much “ground truth”* is self-explanatory and addresses one of the major pitfalls of artificial intelligence, which is currently identified with deep neural networks.

Mathematical Biology: Looking Back and Going Forward



Philip K. Maini

Personal Note

I would like to start by thanking Catriona Byrne for all the work she has done for mathematics. In particular, I am most grateful for the help and support that she, and Ute McCrory, gave me during my time as Editor for the Springer Lecture Notes in Mathematics Subseries, Biology.

1 What Is Mathematical Biology?

Mathematical biology is the name given to the study of biological phenomena through the use of mechanistic mathematical models. Here, the term “biology” includes ecology, epidemiology and medicine, and “mechanistic” is used to distinguish this field from purely statistical and data analysis approaches, such as bioinformatics. While the latter discover correlations between phenomena, the former is the study of *why* things happen. While such a mechanistic approach yields a deeper understanding of the science and is potentially more powerful than statistical/bioinformatics approaches, the latter are more tractable at present. But that is changing.

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2 How Has Mathematical Biology Changed?

Mathematical biology has always moved with the data. In the early days, data were largely very coarse-grained and at a macroscopic level—for example, simple visual observations such as the stripes on a zebra, or spatially-averaged temporal data, such as the number of people infected by a disease. Accordingly, models tended to be composed of coupled systems of discrete or ordinary/partial differential equations that would generate large scale dynamics, such as patterns resembling those observed on animal coats, or predictions of the temporal evolution of a disease through a population, to name but a few examples (see, for example [3, 7, 9, 12–16]). This allowed us to move to testing (and generating) hypotheses for systems which, due to their complexity, are not understandable by verbal reasoning alone. In many cases, the models were built with analytical tractability in mind, and results were generated that agreed, by visual inspection, with the data available. Of course, this is only the first step in model validation but further progress was usually hampered, partly due to limitations in biotechnology, but also to the fact that it was uncommon for theoreticians and experimentalists to work together.

The 1990s saw major advances in biotechnology, generating data at the gene level as well as across scales (cell and tissue level) and, together with increasing computational power, the sub-disciplines of bioinformatics and systems biology (including multiscale modelling) were born. While the former focussed on statistical approaches for correlation analysis, the latter continued the mechanistically-driven approach that is at the core of mathematical biology. Released from the constraints of analytical tractability, mathematical models became increasingly complex, not only in terms of the number and nonlinear complexity of equations, but also in the form models took. Thus, to bridge across scales, hybrid agent-based models were used, in which some variables are modelled discretely, others as continua. In this way, intracellular dynamics could feed into intercellular interactions, leading to macroscopic level behaviour (see, for example, [6]). While, in the case of epidemiology, multi-scale models allowed us to couple within-host infection dynamics with population level spread [11]. Other mathematical approaches also came into use, for example, Boolean algebra, topology, graph and network theory [2] to analyse large, complex interaction networks (for example, gene regulatory networks); stochastic modelling to account for the effects of noise and small numbers, when the continuum limit breaks down, came increasingly into focus [8].

These more complex models typically “outgrew” the experimental observations on which they were built in the sense that it was unusual to be able to fully, and accurately, parametrise them with data and then make testable experimental predictions.

3 Going Forward

We have now reached another critical step-change in the field of mathematical modelling, as ever-increasing amounts of dynamical data (time series, spatial dynamics) are now becoming available. For certain cases, sufficient data are available for machine learning (ML) and artificial intelligence (AI) approaches but, for other cases, data are too sparse and/or noisy. The challenges now are: can we use a mathematical biology approach to mechanistically understand the results from ML and AI [1, 4] and, in the cases where ML and AI cannot be used, how do we leverage sufficient information from the data, in terms of parameter estimation, identifiability etc? At the same time, it is being increasingly recognised by biologists that mathematics can be used to help, not only in identifying correlations, but in understanding mechanism. This is now leading to interdisciplinary research in which biological hypotheses are being translated into mathematical models, allowing us to generate predictions which are then tested experimentally, enabling us to refine our models and continue on the predict-test-refine-predict cycle. This leads to the challenge of which summary statistics are most informative for our modelling, requiring advances in statistics and in pure mathematics, such as topological data analysis.

Another major challenge in the field consists of bringing together mechanics [10] and biochemistry. These fields have, in the past, developed separately, but it is clear that in biology, these processes are intrinsically coupled through the phenomena of mechanotransduction, growth, geometry etc.

We all knew that biology was complicated but now we are on the verge of having the tools, both experimental and theoretical, necessary to dig deeper than ever before into acquiring a mechanistic understanding of this complexity. This will require bringing these tools together through research that is not only interdisciplinary, but also, intradisciplinary. For example, in mathematics, this means bringing together the sub-disciplines of mathematical modelling, applied analysis, stochastic analysis, numerical analysis and computation, network and graph theory, topology, algebra and statistics etc. This leads to a team science approach where the complexity of biology defines new problems that will require technical advances in these sub-disciplines, as well as finding creative and original ways of combining tools from across a large spectrum of mathematics to solve problems driven by the science. This, in turn, will lead to new biology. To borrow the title of Joel E. Cohen's 2004 paper [5] "Mathematics is biology's next microscope, only better; Biology is mathematics' next physics, only better".

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