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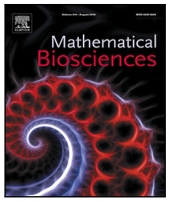

In Memory of Edmund John Crampin: Multi-scale and multi-physics phenomena in biology

This article collection of *Mathematical Biosciences* is dedicated to the memory of our dear friend and colleague, Professor Edmund John Crampin, who tragically passed away in 2021 at the young age of 47. Edmund was an exceptional scholar, a beloved mentor and colleague, and an accomplished cyclist and outdoors enthusiast. His contributions to the field of mathematical biology were numerous and impactful, and his loss is deeply felt by all who knew him. To honor his legacy, we have assembled a collection of 14 research articles that showcase the breadth and depth of mathematical biology, a field about which Edmund was passionate.

For us, this is not just a tribute to a brilliant scientist, but a deeply personal reflection on a life and career that touched us both profoundly. Edmund began his academic journey as a physicist, training at Imperial College London, where he won the University of London Granville Prize for Physics. He then came to Oxford to pursue a doctorate in pattern formation at the Centre for Mathematical Biology, where Philip Maini had the privilege of being his doctoral advisor. Santiago Schnell was also pursuing doctoral studies under the mentorship of Philip at the same time as Edmund, and they became close friends during this period. Even as a graduate student, Edmund's brilliance and passion for science were evident. He was always brimming with ideas, eager to discuss the latest research, and generous in sharing his insights with others. His thesis, which addressed a key problem with the classical Turing reaction–diffusion model for spatial pattern formation, namely its inability to generate patterns in a robust and reliable fashion, was a testament to his creativity and rigor. Edmund proposed the idea that domain growth could play a prominent role in pattern selection, and he was the first to rigorously formulate the Turing model on a growing domain. This work, which continues to be used by research groups worldwide, laid the foundation for his later research on the role of growth in biological pattern formation.

After completing his doctorate, Edmund shifted his focus to heart physiology, working with Denis Noble at Oxford. He was awarded a Junior Research Fellowship at Brasenose College and a Wellcome Trust Research Fellowship, during which he developed computational models of ion channels, signal transduction pathways, and gene regulation. In 2003, he moved to the Auckland Bioengineering Institute at the University of Auckland, where he led the Systems Biology research group and continued his work on computational modeling (see, Fig 1). It was during this time that Edmund met his wife, Annalisa, also an Auckland Bioengineering Institute alumna. They went on to have two children, Audrey and Peregrine, who were a source of immense joy and pride for Edmund.

In 2013, Edmund joined the University of Melbourne as the Rowden White Chair of Systems Biology and Director of the Systems Biology Laboratory. In this role, he brought together researchers from across the fields of mathematics, science and engineering to advance systems biology in all its aspects. He collaborated with engineers to develop thermodynamically based models and incorporate spatial effects, and with mathematicians to model modal gating in ion channels and cardiac calcium release. His interdisciplinary research was made possible by his encyclopedic knowledge of disparate fields and his inspirational leadership.

Edmund's research interests were wide-ranging, but he had a particular passion for understanding the complex processes that govern the behavior of biological systems. This passion is reflected in the articles presented in this special issue, which cover a diverse range of topics in mathematical biology.

Several articles focus on the application of mathematical modeling to understand biological processes at the cellular and subcellular levels. For example, Jewell et al. [1] generalize the analysis of pattern formation in a nonlocal model of cell–cell interactions from 1D to higher spatial dimensions. They use numerical simulations and linear stability analysis to demonstrate how the capacity for pattern formation changes with dimensionality, highlighting the importance of taking spatial dimension into account in biological modeling. Berkemeier and Page [2] investigate the dynamics of Notch–Delta signaling in the presence of long-range signaling via cellular protrusions. They use linear stability analysis and numerical simulations to explore the conditions for pattern formation and the emergence of multiple cell types. Cusseddu and Madzvamuse [3] investigate the role of bulk diffusion in cell polarization using a bulk-surface wave pinning model. They find that bulk diffusion is a key factor in determining the surface polarization response and that, for certain geometries, bulk heterogeneity can trigger polarization. Dowling et al. [4] develop a stochastic model of nanoparticle internalization that incorporates a suite of relevant biological phenomena, such as multistage internalization, cell division, asymmetric nanoparticle inheritance, and nanoparticle saturation. They derive analytic approximations of the nanoparticle dosage distribution under certain modeling assumptions and discuss the implications of their results for parameter estimation and model identifiability. Chung et al. [5] examine the role of IP3R activity in calcium signaling in cardiomyocytes, with implications for understanding cardiac function and disease. They develop a mathematical model of the dyad that incorporates the behavior of IP3Rs, in addition to RyRs, to reveal the

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Fig. 1. Santiago Schnell, Edmund Crampin, and Philip Maini take a break from the Auckland Bioengineering Institute Modelling Cellular Function Workshop to enjoy the scenic beauty of Waiheke Island, Auckland, New Zealand, in July 2003.

impact of IP3R activity on local Ca^{2+} handling and Ca^{2+} spark occurrence and properties. Musgrave et al. [6] investigate the properties of cross-bridge kinetics in cardiac muscle, using model linearization techniques to uncover the mechanisms underlying muscle contraction and the active complex modulus.

A workshop in honor of Edmund was held at the University of Melbourne in November 2022. Araujo et al. [7] provide a summary of the workshop and possible future directions in the field of mathematical biology.

Other articles in this issue explore broader questions in mathematical biology, such as the challenges and opportunities associated with modeling complex biological systems. Vittadello and Stumpf [8] provide an overview of open problems in mathematical biology, highlighting the need for new mathematical approaches to tackle the complexity of living systems. Gyllingberg et al. [9] offer a critique of current practices in mathematical modeling, advocating for a more pluralistic approach that embraces the diversity of biological phenomena. Simpson et al. [10] present a framework for parameter identifiability and model selection, addressing the challenge of choosing appropriate models for ecological population dynamics. Shahidi et al. [11] introduce a new methodology for converting SBML models to bond graphs, a powerful tool for analyzing the energetics of biological systems. Gawthrop and Pan [12] provide an overview of the bond graph approach to modeling biological systems, highlighting its ability to integrate diverse physical domains and capture the energy flow through complex networks. Germano et al. [13] present a novel 3D model of epithelial tissue that incorporates realistic deformations and cell turnover, providing insights into how tissues maintain their structure and function in dynamic homeostasis. Eilertsen et al. [14] revisit the quasi-steady-state assumption in the context of the irreversible Michaelis–Menten reaction mechanism, providing new insights into the necessary conditions under which this approximation is valid. By examining the anti-quasi-steady-state conditions, they identify parameter regions where the quasi-steady-state assumption fails and discuss the implications of these findings for parameter estimation and modeling in enzyme kinetics.

Edmund's legacy extends far beyond his research contributions. He was a gifted teacher and mentor, inspiring countless students and colleagues with his passion for science, his intellectual curiosity, and his unwavering support. But perhaps most importantly, Edmund was a true friend. He embodied the qualities that Erasmus so eloquently described in his letter dated 23 July 1519 to Ulrich von Hutten about Thomas More: a sincere and persistent devotee of friendship, accessible to all, accommodating, and constant. He was always ready with a joke, a kind word, or a listening ear. He found joy in the company of others, whether they were learned or unlearned, intelligent or simple. His was, in every sense of the word, a perfect example of true friendship. To echo Erasmus' words, "In company his extraordinary kindness and sweetness of temper are such as to cheer the dullest spirit, and alleviate the annoyance of the most trying circumstances" [15, line 100]. Edmund was not only a brilliant mind but also a gentleman, with a kind and generous soul, and his presence enriched the lives of all who knew him.

We believe that this article collection serves as a fitting tribute to Edmund Crampin's remarkable life and career. The articles presented here not only advance our understanding of specific biological processes but also highlight the power of mathematical modeling to address fundamental questions in biology. We hope that this collection of articles will inspire future research in this exciting and rapidly growing field, and that it will serve as a lasting reminder of Edmund's extraordinary contributions to science and to the lives of those he touched.

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Santiago Schnell *
Department of Biological Sciences and Department of Applied & Computational Mathematics & Statistics, University of Notre Dame, Notre Dame, 46556, IN, USA
E-mail address: santiago.schnell@nd.edu.

Philip K. Maini
Wolfson Centre for Mathematical Biology, Mathematical Institute, Andrew Wiles Building, University of Oxford, Radcliffe Observatory Quarter, Oxford, OX2 6GG, United Kingdom

* Corresponding editor.