Mathematical Medicine and Biology (2004) **21**, 73–74

Book Review

Modelling Neural Development
Edited by Arjen van Ooyen

xvi + 336 Pages, 96 Illustrations, The MIT Press, Cambridge, Massachusetts, 2003, ISBN 0-262-22066-0

Reviewed by MARKUS OWEN
Department of Mathematical Sciences, Loughborough University, Leicestershire LE11 3TU, UK

[Received on 20 January 2004]

This is the first book I am aware of that focuses on mathematical models for neural development. There has been a considerable amount of work done on the function of the adult nervous system, but not so much on how that system develops from neurulation (the formation of the neural tube from the neuroectoderm) to the development of cognition. In this book, fourteen chapters cover a wide range of topics from sub-cellular dynamics to the emergent and adaptive behaviour of large networks. It encompasses very early development of the nervous system, the migration of neural growth cones to form spatially extended networks, the subsequent self-organization into networks with appropriate connectivity, and the functional consequences of morphology and connectivity.

Chapter 1 covers gene transcription, boundary formation and the reading of chemical gradients, before discussing a detailed model for neurulation that couples automata and ODEs to incorporate cell adhesion, movement, division and signalling. In a similar vein, gene networks are the focus of Chapter 2, including an overview of complex biochemical models and Boolean networks. A detailed example illustrates how a network can 'learn' to produce the correct pattern of gene activation and neuronal specification. Chapters 3 and 4 focus on dendritic and axonal outgrowth and branching, considering lamellopodia formation via a calcium-induced spatial instability, lattice-based models, and evolution equations for axonal lengths. These models allow the investigation of different branching patterns in different cell types. Axon guidance via permissive or instructive signals (such as chemotactic cues) forms the basis for Chapter 5, which includes a review of the relevant signalling molecules, how they might define a co-ordinate system, and mechanisms of gradient detection. Electrical activity can influence neurite growth and retraction, and Chapter 6 discusses models for this process. The implications for network connectivity include the possibility of limit cycle behaviour and hysteresis. Chapter 7 concentrates on retinal mosaic formation, including cell fate determination, movement and death. Cell death as a mechanism for refining neuronal numbers and connectivity is explored further in Chapter 9. In contrast, Chapter 8 focuses on the modulation of ionic conductances in single neurons and at the network level. Because there is a long-term turnover of ion channels, their numbers are regulated, and this can be influenced

Mathematical Medicine and Biology 21(1), © The Institute of Mathematics and its Applications 2004; all rights reserved.

by electrical activity. Thus, Hodgkin–Huxley dynamics can be coupled to equations for the temporal evolution of ion channel densities. Interestingly, different patterns of conductivity can give the same type of electrical activity (e.g. tonic spiking, bursting). Chapter 10 covers models for the elimination of connections via competition for space, resources, or direct interactions. Many different types of model are discussed, as well as a connection with ecology and consumer resource systems. Topographic map formation forms the basis for Chapter 11. Examples include the map between the retina and cortex, and this mainly descriptive chapter describes some of the mechanisms for establishing such maps, including biochemical markers (such as Ephrins) and the maintenance of neighbour relationships. Chapter 12 covers models for the development of ocular dominance (the preferential response of a neuron to inputs from the right or left eye) and the similar phenomenon of orientation selection. Hebbian learning models evolve the strengths of synaptic connections in response to correlations between neuronal activity. Sets of discrete neurons are often considered, but mathematical analysis has been more commonly directed towards continuous spatial integrodifferential equations. Chapter 13 points out that neurons cannot really be considered as point processors, and hence the development and remodelling of sub-cellular structures has implications for memory and storage capacity. Finally, Chapter 14 presents some fundamental challenges and discusses the link between the cell and systems level, and how development relates to function.

Most chapters include a section on future modelling studies, and hence provide a rich source for relevant research problems. The degree of mathematical rigour varies somewhat, and I expect that there are many areas where a rigorous treatment of existing or modified models may appeal to readers of this journal. This book provides a good survey of mathematical and computational modelling activity in developmental neuroscience, and I recommend it to anyone interested in this area of research.