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Book review

Arjen van Ooyen, Modelling Neural Development, The MIT, Cambridge, Massachusetts, 2003, ISBN 0-262-22066-0, xvi + 336 pp., 96 illustrations

Computational and mathematical modeling in neuroscience has focused so far mainly on information processing in the adult nervous system. This book is one of the first that stresses mathematical models for neural development.

The book editor, Arjen van Ooyen, now at the Center for Neurogenomics and Cognitive Research of the Vrije Universiteit Amsterdam, has brought together a community of authors who share the conviction that just as formal models are needed to understand the functioning of the nervous system, they are also needed to obtain an understanding of its development.

The 14 chapters of the book follow loosely the time course of neural development, from basic processes of morphogenesis at the molecular and cellular level, to neural developmental processes underlying the development of cognitive functions. The authors demonstrate how computational models are used to study mechanisms of gene expression, neuronal morphogenesis, the formation of maps and columns and the emergence of networks potentially capable of generating complex cognitive states.

Chapter 1 presents models for the control of gene transcription during development, formation of boundaries among cellular areas and the reading of chemical gradients. Gene networks are the focus of Chapter 2, including a detailed example that illustrates how a recurrent neural network can be trained to produce the correct pattern of gene activation and neuronal specification. These chapters also provide links to Turing's classical reaction–diffusion approach, Lindenmayer systems and Boolean networks. Chapters 3–5 deal with the important issues of how neurons get their distinguishing shape, how neurites arise and differentiate into dendrites and an axon. In particular, models of dendritic and axonal outgrowth and branching are presented in Chapters 3 and 4, considering lamellopodia formation via a calcium-induced spatial instability, dendritic growth as stochastic process, and evolution equations for neurite outgrowth. These models allow the investigation of different branching patterns in different cell types. The guidance of axonal processes by external signals is the topic of Chapter 5. Also included is a review of the relevant signalling molecules, how they might define a coordinate system, and the detection of gradients of target-derived diffusible factors by growth cones, an active area of experimental in vitro studies.

The next triple of Chapters (6–8) is concerned with issues related to network formation and activity-dependent processes. Chapter 6 presents a computational model of neurite outgrowth, which incorporates the influence of neural activity on the spatial extent of the outgrowth and on the degree of interconnectivity. Interestingly, the model is capable of reproducing several

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key phenomena such as a transient developmental phase of high connectivity, the presence of multiple stable states at different connectivity levels, and the emergence of neuritic fields of different size for excitatory and inhibitory cells. Chapter 7 presents two models of retinal mosaic formation, including cell fate determination, movement and death. In a general context, cell death as a mechanism for refining neuronal numbers and connectivity is further discussed in Chapter 9.

Chapter 8 focuses on the problem how neurons generate and maintain their specific and characteristic electrophysiological properties, by expressing channels and receptors that give rise to voltage-dependent and synaptic conductances. A series of models is described in which the properties of neurons and synapses are dynamically regulated by patterns of neuronal electrical activity. Thus, Hodgkin–Huxley channel dynamics were coupled to equations for the temporal evolution of ion channel densities. It is shown that different conductance patterns can give rise to the same type of electrical activity (tonic spiking, bursting).

In Chapter 10, a concise overview of classical models in the area of nerve connection refinement via competition is given. The types of competition include those for space, resources, or direct interactions. Various models for the neuromuscular and the visual system are reviewed, and parallels with population biology are sketched. A new model is discussed in more detail, connecting competitive interactions with the basal effects of neurotrophins, a class of extracellular molecules involved in controlling the shape and density of neuronal pathways.

Formation of topographic maps is discussed in Chapter 11. This issue has attracted much attention and led to various modeling efforts in recent times. A comprehensive review of the main hypotheses about map formation is provided in this chapter, followed by a discussion of topical models incorporating a variety of cellular and molecular data. Examples include the map between the retina and the cortex. Chapter 12 reviews the variety of models for the development of ocular dominance (the preference for stimuli of a neuron from visual cortex to inputs from one of the two eyes) and orientation selectivity (preference for stimuli of a particular orientation). Almost all of the models share the following framework: a two-layer feedforward net (lateral geniculate nucleus–cortex), spatially correlated activity patterns in the input layer, and Hebbian modification of synaptic strengths. The models differ with respect to learning rules and initial conditions.

In Chapter 13, physiological and anatomical evidence and computational models are presented suggesting that the morphology of the axo-dendritic ‘interface’ of single neurons actually matters in determining their function. Two phenomena are particularly important: (1) dendritic trees may show a significant degree of compartmentalization of their electrical signals, and (2) there is evidence for lifelong continuous structural remodeling of the dendrites. The combination of these effects may have implications for memory and storage capacity of neural tissue. Obviously, this view of the neuron is incompatible with the concept of a point processor, as used in the field of artificial neural network modeling.

Finally, Chapter 14 is dedicated to developmental cognitive neuroscience, an research area with the explicit aim of integrating cognitive (i.e., computational) and neural perspectives on brain development. This more descriptive chapter touches on computational learning theory, measures of structural (anatomical) and cognitive (representational) complexity and the problem of how they might be related.

Most chapters include sections on future modeling and experimental studies, and hence make available a stock of relevant research problems. In conclusion, the book provides a valuable overview on mathematical and computational approaches in developmental neuroscience, and I expect that everyone interested in this field should read it with profit.

Andreas Schierwagen
University of Leipzig,
Institute of Computer Science,
Intelligent Systems Department,
Neuronal and Cognitive Modeling Branch,
Augustusplatz 10–11,
D-04109 Leipzig,
Germany
E-mail address: schierwa@informatik.uni-leipzig.de

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