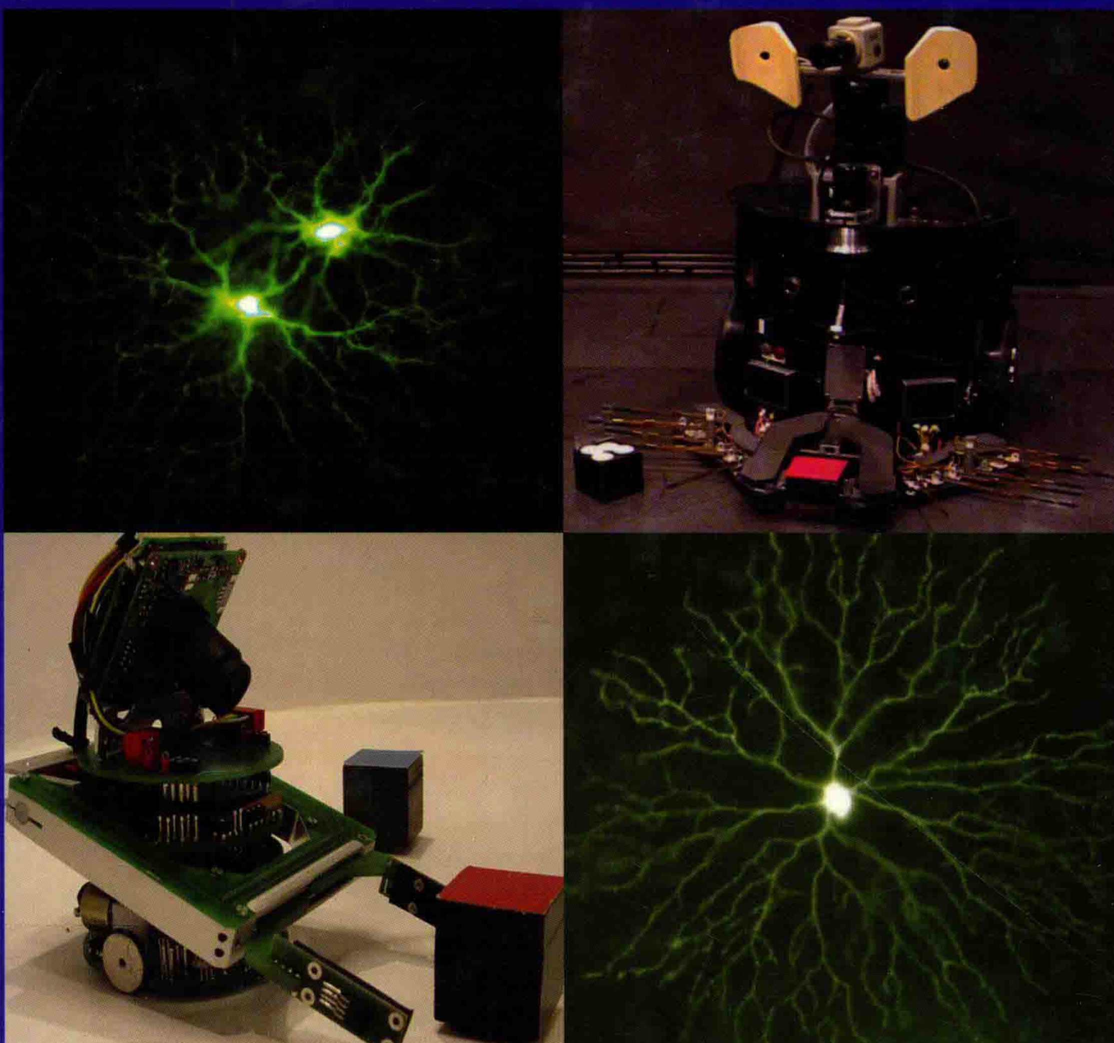
Second Edition

MODELING IN THE NEUROSCIENCES

From Biological Systems to Neuromimetic Robotics



EDITED BY

G. N. Reeke, R. R. Poznanski, K. A. Lindsay, J. R. Rosenberg, and O. Sporns

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Preface to the Second Edition

The Second Edition of *Modeling in the Neurosciences* appears on the fifth anniversary of the publication of the first edition. Inspired by the wealth of new work since that date, we were determined to bring the book up to date, to discuss the most important new developments in neuronal and neuronal systems modeling, including use of robotics to test brain models.

The goal of the book is to probe beyond the realm of current research protocols toward the uncharted seas of synthetic neural modeling. The book is intended to help the reader move beyond model ingredients that have been widely accepted for their simplicity or appeal from the standpoint of mathematical tractability (e.g., bidirectional synaptic transfer, updates to synaptic weights based on nonlocal information, or mean-field theories of rate-coded point neurons), and learn how to construct more structured (integrative) models with greater biological insight than heretofore attempted. The book spans the range from gene expression, dendritic growth, and synaptic mechanics to detailed continuous-membrane modeling of single neurons and on to cell–cell interactions and signaling pathways, including nonsynaptic (ephaptic) interactions. In the final chapters, we deal with complex networks, presenting graph- and information-theoretic methods of analyzing complexity and describing in detail the use of robotic devices with synthetic model brains to test theories of brain function.

The book is neither a handbook nor an introductory volume. Some knowledge of neurobiology, including anatomy, physiology, and biochemistry is assumed, as well as familiarity with analytical methods including methods of solving differential equations. A background knowledge of elementary concepts in statistics and applied probability is also required. The book is suitable as an advanced textbook for a graduate-level course in neuronal modeling and neuroengineering. It is also suited to neurophysiologists and neuropsychologists interested in the quantitative aspects of neuroscience who want to be informed about recent developments in mathematical and computer modeling techniques. Finally, it will be valuable to researchers in neural modeling interested in learning new methods and techniques for testing their ideas by constructing rigorously realistic models based on experimental data.

The first edition of *Modeling in the Neurosciences* has contributed impressively to the analytical revolution that has so completely changed our perception of quantitative methods in neuroscience modeling. Nevertheless many different views persist regarding the most satisfactory approaches to doing theoretical neuroscience. The source of this plethora of interpretations is, perhaps, the fact that "computational" interpretations of brain function are not satisfactory, as discussed in the introductory chapter by G. Reeke. Thus, it seems appropriate in this book to attempt to obtain a more balanced picture of all the elements that must be taken into account to get a better understanding of how nervous systems in fact function in the real world where adaptive behavior is a matter of life or death. We hope the integrative viewpoint we advocate may serve as a Rosetta stone to guide the development of modern analytical foundations in the neurosciences.

To accomplish this, we have commissioned authors to provide in-depth treatments of a number of unresolved technical and conceptual issues which we consider significant in theoretical and integrative neuroscience, and its analytical foundations. We hope that this second edition will help and inspire neuroscientists to follow threads revealed herein for many years to come.

We acknowledge the support of the many colleagues who have made this book possible, in particular, the authors who have given so freely of their time to create the chapters now before you. We are also indebted to Dr. John Gillman, Publisher at Harwood Academic Publishers, Reading, UK, who authorized the commissioning of the second edition in the winter of 2001; Dr. Grant Soannes, Publisher at Taylor & Francis, London, UK, who contracted for the book in the fall of 2003; and Barbara Norwitz, Publisher at Taylor & Francis, Boca Raton, Florida, who finalized the arrangements in January of 2004. Last but not least, we thank Pat Roberson and her team for their continuing efforts in the production of a truly immaculate volume.

Sadly, one of the contributors, Aron M. Gutman, passed away soon after the launch of the first edition in the spring of 1999. Aron Gutman was born in Zhitomir, Ukraine in 1936. He received his Ph.D. (externally) from the Department of Physics of Leningrad University in 1962. From 1959 to 1999 he worked in the Neurophysiological Laboratory of Kaunas Medical Institute (now University). He was a prolific writer with more than 150 scientific publications, including two monographs (in Russian) and about 50 papers in international journals. As a distinguished biophysicist, particularly known for his work on the theory of N-dendrites, he has made a profound impact on the scientific community. In Gutman's own words: "small cells use dendritic bistability with slow rich logic."

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Foreword

Numerical modeling is common, but analytical theory is rare. Fast computers and software to generate formal models have become more accessible to experimentalists at their own peril. The art of specifying and validating models has not kept pace. The complexities and nonlinearities of neuronal systems require, on the part of the modeling practitioner, an unusual degree of neurophysiological and neuroanatomical insight, as well as skill in a repertoire of numerical methods. However, a computer simulation without an underlying theory is only of heuristic value; such a model cannot be properly tested because conceptual errors cannot be distinguished from inappropriate parameter choices.

At the cellular level, numerical models that discretize the neuronal membrane suffer from an excess of degrees of freedom; it is difficult or impossible to collect enough data to constrain all the parameters of such models to unique values. In such constructs, the continuity of the neuronal membrane is sliced into pieces to form compartments (or "spiking neuron" models in the computational neuroscience literature). Much better treatments of chemical diffusion and the spatial variation of ion concentrations inside and outside the cell are badly needed. The use of continuous-membrane (partial differential equation) models to resolve some of the issues mentioned here is a strong feature of the present volume.

There are also foundational problems at the systems biology level. The next step toward the construction of a solid theoretical foundation for brain science will require a precise clarification of the subtle problems afflicting current computational neuroscience (both conceptual and epistemological), together with the development of fully integrative models across all levels of multihierarchical neural organization. It will also require a new understanding of how perceptual categorization and learning occur in the real world in the absence of preassigned category labels and task algorithms. I congratulate the editors who have produced this second edition of *Modeling in the Neurosciences*, which epitomizes a trend to move forward toward the development of more conceptual models based on an integrative approach.

Professor G.A. Chauvet, M.D., Ph.D.
Chief Editor
Journal of Integrative Neuroscience
Imperial College Press, London, U.K.

About the Editors

George Reeke was born in Green Bay, Wisconsin in 1943. He trained as a protein crystallographer with Dick Marsh at Caltech and Bill Lipscomb at Harvard, where his Ph.D. thesis contained one of the first atomic coordinate sets for any protein, that of the enzyme carboxypeptidase A. He was brought to Rockefeller University in 1970 by Gerald Edelman, with whom he collaborated in a series of studies on the three-dimensional structures of proteins of interest for understanding the function of the immune system. He developed one of the first microprocessor-controlled lab instruments, an x-ray camera, and his Fourier synthesis software was used to solve many protein structures worldwide.

In recent years, his interest has turned to problems of pattern recognition, perceptual categorization, and motor control, which he has studied primarily through computer simulations of selective neural networks and recognition automata, including brain-based robot-like devices. With Allan Coop, he has developed a computationally efficient composite method for modeling the discharge activity of single neurons, as well as a new "analytic distribution" method for assessing the interval entropy of neuronal spike trains. At present, Dr. Reeke is an Associate Professor and head of the Laboratory of Biological Modeling at The Rockefeller University and a Senior Fellow of The Neurosciences Institute. He serves as a member of the editorial board of the Journal of Integrative Neuroscience and of the Biomedical Advisory Committee of the Pittsburgh Supercomputer Center.

Roman R. Poznański was born in Warsaw, the city of Frédéric Chopin. He is an influential neuroscientist noted for his modeling work in first pinpointing the locus of retinal directional selectivity as vindicated by recent experiments.

He continues to set the stage in revolutionizing the pioneering work undertaken in the 1950s and 1960s by the NIH duo: *Richard FitzHugh* and *Wilfrid Rall* through a complete analytical treatment of the most difficult partial differential equations in classical neurophysiology, namely the Frankenhaeuser–Huxley equations. He has been instrumental in the establishment of a new generation of neural networks and their application to large-scale theories of the brain. Dr. Poznański remains a heavyweight in both neural modeling and neuropsychology with the publication of an integrative theory of cognition in the *Journal of Integrative Neuroscience* (founded with *Gilbert A. Cháuvet*). His idea is to develop integrative models to represent semantic processing based on more biologically plausible neural networks. This would naturally lead to more sophisticated artificial systems: he has coined the term "neuromimetic robotics" (with *Olaf Sporns*) to designate real-world devices beyond neuroscience-inspired technology used in today's connectionist design protocols.

Currently, Dr. Poznański holds a research faculty appointment in the Claremont Research Institute of Applied Mathematical Sciences within the School of Mathematical Sciences at Claremont Graduate University.

"*His main supervisor W R Levick, FRS was one of the most imminent neuro-psychologists of our time. And here is where Roman made his first real contribution. In fact, I was surprised but warmed to see how influential his work has been.*"

Allan W. Snyder FRS
150th Anniversary Chair, University of Sydney
Peter Karmel Chair, Australian National University

Olaf Sporns was born in Kiel, Germany, in 1963. After studying biochemistry at the University of Tübingen in Germany, he entered the Graduate Program at New York's Rockefeller University. In 1990, he received a Ph.D. in neuroscience and became a Fellow in Theoretical Neurobiology at The Neurosciences Institute in New York. Since 2000, he has held a faculty position at the Department of Psychology at Indiana University in Bloomington. Dr. Sporns' main research interest is theoretical neuroscience. A main research focus is the development of integrative and synthetic models that can be interfaced with autonomous robots and can be used to study neurobiological and cognitive functions such as perceptual categorization, sensorimotor development, and the development of neuronal receptive field properties. Another focus is the development of anatomically and physiologically detailed models of neuronal networks to investigate the large-scale dynamics of neuronal populations. This work includes the development of statistical measures for characterizing global dynamics of neuronal networks as well as methods for analyzing the structure of neuronal connectivity patterns. Dr. Sporns is a member of the AAAS, the Society for Neuroscience, the Society for Adaptive Behavior, the Cognitive Neuroscience Society and Sigma Xi. He is a member of the editorial boards of the journals *BioSystems*, *Adaptive Behavior*, the *International Journal of Humanoid Robotics*, and *Neuroinformatics*.

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Contents

1 Introduction to Modeling in the Neurosciences

George N. Reeke

In this book, 40 distinguished authors explore possibilities for the creation of computational models of neuronal systems that capture biologically important properties of those systems in a realistic way that increases our understanding of how such systems actually work. The authors survey the theoretical basis for believing that such studies might be worthwhile, the kinds of methods that may be employed profitably in practice, and current progress.

This field stands today at a crossroads. While computational models of cognitive function have been constructed at least since the earliest days of electronic computers, progress has been slow. This has been due partly to the inadequate performance until recently of the available computational equipment, and perhaps even more due to the overwhelming acceptance of the key postulate of what has become known as cognitive science: the idea that the brain itself is a kind of computer. Whether the field stays on this path or takes another, while continuing to draw what inspiration it can from the computer metaphor, will largely determine the kinds of results we can expect to see in the coming decades and how fast we get there.

The postulate of the computational brain has been enormously successful in taking us away from the "black box" approach of the behaviorists. It has encouraged us to look inside the brain and analyze what goes on there in terms of the logical conditions that must be satisfied in order to get from the known input to the known output. This has helped us to see, for example, that the sensory affordances spoken of by the Gibsons (1966, 1979) are the beginning, not the end, of the story. Computational science tells us that it can be productive to ask just how it might be that an affordance is transformed into an action. Thinking in computational terms has brought about a great deal of refinement in the kinds of questions that are being asked about the control of behavior and the kinds of evidence that can be brought to bear on these questions.

Nonetheless, for some time, some of us have been saying that this emphasis is holding back our understanding of the brain (Reeke and Edelman, 1988; Bickhard and Terveen, 1996; Poznanski, 2002b). Now this claim, which until recently could be argued only on rather abstract theoretical grounds, has begun to take hold as the inadequacies of the formalistic computational approach have become more evident. Here I will go briefly over this ground, to remind readers of the issues involved, then discuss briefly the kinds of facts we know about the brain that need to be taken into account to arrive at models that truly explain, rather than just emulate, cognitive processes. I will then try to show how the chapters in this book reflect work that does take these facts into account, and indicate where such work might lead to in its maturity.

Just why is it that the computational analogy is inadequate? Surely it is correct that on–off signals (neural spikes) enter the brain via multiple sensory pathways and leave via motor pathways, just as binary signals enter and leave a computer via its input/output devices. Inside, various complex transformations are applied to the input signals in order to arrive at appropriate behavioral outputs. As Marr (1982) famously proposed, these transformations (call them computations if you wish) may be analyzed at the level of their informational requirements (without certain inputs, certain outputs can never be unambiguously obtained), at the level of algorithm (by what steps the appropriate transformations can be efficiently carried out), and at the level of implementation (what kind of devices are needed to carry out the algorithms). These levels of analysis apply also to, indeed, were derived from, processes carried out in computers. Thus, what Marr has proposed is to take what has already been learned about computation, beginning with the work of Turing (1950) and von Neumann, and apply this information to understanding the brain. The problem arises when this analogy is pushed too far, to the point where one falls into the temptation of calling everything the brain does a computation. One thus arrives at the curious circularity of logic espoused by Churchland and Sejnowski (1992, p. 61), who put it this way: "Notice in particular that once we understand more about what sort of computers *nervous systems* [authors' emphasis] are, and how they do whatever it is they do, we shall have an enlarged and deeper understanding of what it is to compute and represent." In this view, the study of the brain, which is already a big enough problem, takes on the additional burden of providing a new underpinning for computer science as well. This is necessary because conventional computer science cannot adequately explain what it is that the brain does. Either computer science must be expanded, as Churchland and Sejnowski suggest, or else we must study the brain on its own terms and stop calling it a computer, as we suggest in this book.

What then, are some of the problems with the computationalist view? First and foremost, the brain is not a programmed, or even a programmable, device. There is no evidence that neuronal circuits are genetically specified and constructed during development to carry out specific algorithmic manipulations of signals, except perhaps in the simplest invertebrate brains, nor can we see how they might be, given our current understanding of the epigenetic influences that preclude perfect realization of genetically specified templates during development. (Although Chomsky [1988] and Pinker [1994] have suggested that humans have genetically specified circuits that provide innate language capabilities, they have not explained what these circuits might be or how DNA could encode the details of their construction.) Similarly, there is no mechanism in view that could explain how the brain could make use of signals derived from behavioral errors to reshape its circuitry in a way specifically directed to correct those errors. Rather, the brain is a product of evolution, constructed of neurons, glia, blood vessels, and many other components in just such a way as to have the right sort of structures to be able to generate adaptive behavior in response to environmental inputs. It has no programs written down by a programmer and entered as instructions on some sort of tape. The mystery that we must try to solve with our modeling efforts, then, is how the brain organizes itself, without the good offices of a programmer, to function in an adaptive manner. In other words, on top of the mystery of what processes the brain might be carrying out, which the computational approach investigates, there is the further mystery of how those processes construct themselves. That mystery is generally ignored by the computational approach or else solved only by biologically unrealistic mechanisms such as back-propagation of error signals (Werbos, 1974; McClelland et al., 1986; Rumelhart et al., 1986) or so-called genetic algorithms (Holland, 1975), which make a caricature of the processes of mutation and recombination that occur during evolution, applying them incorrectly to specifications of procedures rather than of structures.

A second, closely related problem, concerns the question of how neural firings in the brain come to have meaning, that is, how they come to represent objects and actions in the world, and eventually, even abstract concepts such as black holes or Gödel's proof that have no obvious referents in the sensory world around us. In ordinary Turing machine computation, of course, the signals in the machine are assigned interpretations as numbers by the machine's designer, and these numbers are in turn assigned meanings in terms of a particular problem by a programmer. A great deal of work in artificial intelligence has gone into finding ways to free machine programs from their dependence on preassigned symbol definitions and prearranged algorithms to operate upon those symbols. This work has led to systems that can prove mathematical theorems (Wos and McCune, 1991), systems that can optimize their own learning algorithms ("learn how to learn") (Laird et al., 1986), even systems that can to a limited extent answer questions posed in natural human language (Zukerman and Litman, 2001). These systems have demonstrated to everyone's satisfaction that it is possible for a formal logic system, such as a computer, to construct rich webs of symbolic representation and to reason from them to reach conclusions that were not included in their initial programming.