Principles of Computational Modelling in Neuroscience

The nervous system is made up of a large number of elements that interact in a complex fashion. To understand how such a complex system functions requires the construction and analysis of computational models at many different levels.

This book provides a step-by-step account of how to model the neuron and neural circuitry to understand the nervous system at many levels, from ion channels to networks. Starting with a simple model of the neuron as an electrical circuit, gradually more details are added to include the effects of neuronal morphology, synapses, ion channels and intracellular signalling. The principle of abstraction is explained through chapters on simplifying models, and how simplified models can be used in networks. This theme is continued in a final chapter on modelling the development of the nervous system.

Requiring an elementary background in neuroscience and some high school mathematics, this textbook provides an ideal basis for a course on computational neuroscience.

An associated website, providing sample codes and up-to-date links to external resources, can be found at www.compneuroprinciples.org.

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Abbreviations

ADP	adenosine diphosphate
AHP	afterhyperpolarisation
AMPA	α-amino-3-hydroxy-5-methyl-4-isoxalone propionic acid
AMPAR	AMPA receptor
ATP	adenosine triphosphate
BAPTA	bis(aminophenoxy)ethanetetraacetic acid
BCM	Bienenstock–Cooper–Munro
BPAP	back-propagating action potential
cAMP	cyclic adenosine monophosphate
cDNA	cloned DNA
cGMP	cyclic guanosine monophosphate
CICR	calcium-induced calcium release
CNG	cyclic-nucleotide-gated channel family
CNS	central nervous system
CST	corticospinal tract
CV	coefficient of variation
DAG	diacylglycerol
DBS	deep brain stimulation
DCM	Dual Constraint model
DNA	deoxyribonucleic acid
DTI	diffusion tensor imaging
EBA	excess buffer approximation
EEG	electroencephalogram
EGTA	ethylene glycol tetraacetic acid
EM	electron microscope
EPP	endplate potential
EPSC	excitatory postsynaptic current
EPSP	excitatory postsynaptic potential
ER	endoplasmic reticulum
ES	evolution strategies
GABA	γ-aminobutyric acid
GHK	Goldman–Hodgkin–Katz
GPi	globus pallidus internal segment
HCN	hyperpolarisation-activated cyclic-nucleotide-gated channel family
HH model	Hodgkin–Huxley model
HVA	high-voltage-activated
IP_3	inositol 1,4,5-triphosphate
IPSC	inhibitory postsynaptic current
ISI	interspike interval
IUPHAR	International Union of Pharmacology
KDE	kernel density estimation
LGN	lateral geniculate nucleus
LTD	long-term depression

LTP	long-term potentiation
LVA	low-voltage-activated
MAP	microtubule associated protein
MEPP	miniature endplate potential
mGluR	metabotropic glutamate receptor
MLE	maximum likelihood estimation
MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
MRI	magnetic resonance imaging
mRNA	messenger RNA
NMDA	N-methyl-D-aspartic acid
ODE	ordinary differential equation
PDE	partial differential equation
PDF	probability density function
PIP_2	phosphatidylinositol 4,5-bisphosphate
PLC	phospholipase C
PMCA	plasma membrane Ca^{2+}–ATPase
PSC	postsynaptic current
PSD	postsynaptic density
RBA	rapid buffer approximation
RC	resistor–capacitor
RGC	retinal ganglion cell
RNA	ribonucleic acid
RRVP	readily releasable vesicle pool
SERCA	sarcoplasmic reticulum Ca^{2+}–ATPase
SSA	Stochastic Simulation Algorithm
STDP	spike-timing-dependent plasticity
STN	subthalamic nucleus
TEA	tetraethylammonium
TPC	two-pore-channels family
TRP	transient receptor potential channel family
TTX	tetrodotoxin
VSD	voltage-sensitive domain

Preface

To understand the nervous system of even the simplest of animals requires an understanding of the nervous system at many different levels, over a wide range of both spatial and temporal scales. We need to know at least the properties of the nerve cell itself, of its specialist structures such as synapses, and how nerve cells become connected together and what the properties of networks of nerve cells are.

The complexity of nervous systems make it very difficult to theorise cogently about how such systems are put together and how they function. To aid our thought processes we can represent our theory as a computational model, in the form of a set of mathematical equations. The variables of the equations represent specific neurobiological quantities, such as the rate at which impulses are propagated along an axon or the frequency of opening of a specific type of ion channel. The equations themselves represent how these quantities interact according to the theory being expressed in the model. Solving these equations by analytical or simulation techniques enables us to show the behaviour of the model under the given circumstances and thus addresses the questions that the theory was designed to answer. Models of this type can be used as explanatory or predictive tools.

This field of research is known by a number of largely synonymous names, principally computational neuroscience, theoretical neuroscience or computational neurobiology. Most attempts to analyse computational models of the nervous system involve using the powerful computers now available to find numerical solutions to the complex sets of equations needed to construct an appropriate model.

To develop a computational model in neuroscience the researcher has to decide how to construct and apply a model that will link the neurobiological reality with a more abstract formulation that is analytical or computationally tractable. Guided by the neurobiology, decisions have to be taken about the level at which the model should be constructed, the nature and properties of the elements in the model and their number, and the ways in which these elements interact. Having done all this, the performance of the model has to be assessed in the context of the scientific question being addressed.

This book describes how to construct computational models of this type. It arose out of our experiences in teaching Masters-level courses to students with backgrounds from the physical, mathematical and computer sciences, as well as the biological sciences. In addition, we have given short computational modelling courses to biologists and to people trained in the quantitative sciences, at all levels from postgraduate to faculty members. Our students wanted to know the principles involved in designing computational models of the nervous system and its components, to enable them to develop their own models. They also wanted to know the mathematical basis in as far as it describes neurobiological processes. They wanted to have more than the basic recipes for running the simulation programs which now exist for modelling the nervous system at the various different levels.

This book is intended for anyone interested in how to design and use computational models of the nervous system. It is aimed at the postgraduate level and beyond. We have assumed a knowledge of basic concepts such as neurons, axons and synapses. The mathematics given in the book is necessary to understand the concepts introduced in mathematical terms. Therefore we have assumed some knowledge of mathematics, principally of functions such as logarithms and exponentials and of the techniques of differentiation and integration. The more technical mathematics have been put in text boxes and smaller points are given in the margins. For non-specialists, we have given verbal descriptions of the mathematical concepts we use.

Many of the models we discuss exist as open source simulation packages and we give links to these simulators. In many cases the original code is available.

Our intention is that several different types of people will be attracted to read this book and that these will include:

The experimental neuroscientist. We hope that the experimental neuroscientist will become interested in the computational approach to neuroscience.

A teacher of computational neuroscience. This book can be used as the basis of a hands-on course on computational neuroscience.

An interested student from the physical sciences. We hope that the book will motivate graduate students, post doctoral researchers or faculty members in other fields of the physical, mathematical or information sciences to enter the field of computational neuroscience.

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