Electric Brain Signals

Foundations and Applications of Biophysical Modeling

Brain activity is commonly studied by measuring the extracellular electric potentials inside or outside the brain. Interpreting such measurements requires knowledge of the physical processes underlying the recorded signals. This book introduces the electromagnetic and biophysical theory required for simulating neural activity and its extracellular potentials. Written by leading experts in the field, it presents results from long-term research into forward modeling of extracellular brain signals and illustrates the link between theory and real recorded signals under various conditions. Practical code examples for modeling real neural systems are included throughout and supported by an online code repository, making this volume a valuable resource for students and scientists who wish to analyze electric brain signals through biophysics-based modeling.

GEIR HALNES is a research scientist with a background in physics and theoretical biology. For the last one-and-a-half decades, he has worked in the Computational Neuroscience Lab at the Norwegian University of Life Sciences. His research focuses on the fundamental physical processes in neurons, glial cells, and brain tissue.

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GAUTE T. EINEVOLL is Professor of Physics at the Norwegian University of Life Sciences and the University of Oslo, working on the modeling of nerve cells, networks of nerve cells, brain tissue, and brain signals as well as the development of neuroinformatics software tools, including LFPy.

"*Electric Brain Signals*, by the Norwegian group founded by Gaute Einevoll, is the definitive how-to guide for detailed, biophysical modeling of brains, building up from the minuscule ionic currents traversing the cellular membrane, to the observed macro-variables across spatial scales, from the extracellular action potential and local field potential to EEG and MEG signals recorded inside or outside the skull. The book beautifully encapsulates, with easy-to-read prose and associated code, the sophistication of quantitative, mechanistic neuroscience of the twenty-first century necessary to understand the brain and the mind at the time scale of sensory input, motor action, and thought, in both health and disease."

Christof Koch, Allen Institute for Brain Science, USA; and author of *Biophysics of Computation*

"If you love physics, are fascinated with the brain, and wish that neural circuits could be understood from first principles, this book is for you! Gaute Einevoll and his team put together a masterpiece educational resource. Depending on the background and stage of training, the reader can consume it front to back, or use it as a reference book. The first part covers, in detail, the biophysical theory governing generation of the transmembrane and extracellular electrical potential. The second part is a comprehensive guide to simulations of these signals with the focus on data-driven modeling, from the microscopic level of single neurons and neural networks to macroscopic signals observable with noninvasive electro- and magneto-encephalography. This didactic organization, depth of coverage, and impeccable expertise of the authors make this book a top candidate as a textbook for computational neuroscience courses. Supplementary simulation software, freely available on GitHub, is a fantastic addition for research and teaching."

Anna Devor, Professor of Biomedical Engineering, Boston University, USA

"The brain is an electrochemical organ. The laws of electricity are simple. Yet how currents spread in a heterogeneous, non-isotropic milieu, such as the brain, is super complex. This long needed outstanding book provides all the necessary ingredients to comprehend this complexity. Done with the utmost care, this volume is a must-read for both novices and experts in electrophysiology and I bet it will become the foundation of elective graduate courses for many years to come. The text is the systems neuroscience equivalent of the single-neuron Hodgkin–Huxley model."

György Buzsáki, NYU Neuroscience Institute, USA; and author of *Rhythms of the Brain* and *The Brain from Inside Out*

"This book is a fantastic resource for the computational neuroscience community and beyond. The introductory 'guide' is outstanding in its clarity and description for readers with a range of backgrounds. The presentation is rigorous and detailed with many mathematical equations, and yet readable and understandable, with many figures. The authors are to be commended for their clearly defined terminologies and presentation of complex concepts. A gem of a read for anyone wanting to develop an in-depth understanding of electrical brain recordings and models of them."

Frances K. Skinner, Krembil Brain Institute, University Health Network and University of Toronto, Toronto, Ontario, Canada

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it was not a closed system

meteorites fell to earth
cracks appeared

through cracks we were born
with our own cracks

we used them
to eat structure and crap chaos

in this way
order could feed in us
and we developed the most wonderful brains

the brains were cracks

trees fell in
and became trees to us
mountains fell in
and became mountains to us

meteors sent electric sprinkles
across the visual cortex
and chills down our spines

Geir Halnes, *Mor Rom* (*Mother Space*). Transcreated to English by Geir Halnes and Ida Kock.

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Preface

Neurons in the brain communicate via electric signals that can be recorded with electrodes placed either inside the neurons, in the space between neurons, or outside the brain and head. The foundation for interpreting the signals recorded intracellularly was laid through the pioneering works of Hodgkin, Huxley, Rall, and others in the 1950s. The biophysics-based approach to modeling neurons proposed by these scientists gave predictions that could be compared directly with experimental recordings and represented a “quantitative revolution” in neuroscience.

The relationship between neural activity and what is measured extracellularly is less trivial, partly because an extracellular electrode picks up overlapping signals from many neurons simultaneously and partly because a neuron’s contribution to the recorded signal depends on various (typically unknown) factors such as, for example, the neuron’s morphology and its position relative to the electrode. As a further complication, extracellular signals may contain “noisy” contributions that are difficult to control for in an experimental setting – for example, from ongoing muscle activity or recording equipment.

The extracellular signal that is the easiest to interpret is the “spike,” which is the extracellular signature of a neuronal action potential. For this reason, the analysis of extracellular potentials has largely been limited to inferring spike times of a relatively small number of neurons located in the vicinity of recording contacts. Although this is well and good, the extracellularly recorded potentials contain information beyond spike times that is not taken advantage of in these kinds of analyses.

Given the proper theoretical tools, extracellular recordings could putatively be used to answer questions regarding, for example, the positioning of contributing neurons, the number of contributing neurons, the types of neurons that contribute the most, the distributions of synaptic input onto neurons, etc. Such questions have, however, lacked quantitative answers grounded in biophysics. In the absence of precise biophysics-based tools for interpreting extracellular potentials, “rules of thumb” for interpretation have been spread in our neuroscience community. These are not always well-founded and have often been based on intuition and “folk physics” rather than actual biophysics.

Over the last 20 years, our research group at the Norwegian University of Life Sciences and the University of Oslo has worked on forward-modeling of brain signals from biophysically detailed (multicompartment) models of neurons and networks of neurons. In the process, we have developed the open-source simulation tool LFPy (https://LFPy.readthedocs.io) and related tools to facilitate the biophysics-based

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modeling of extracellular signals. Most of our work has focused on electric signals recorded with electrodes placed inside brain tissue to detect spikes, which are revealed in the high-frequency part of the signal, or the local field potential (LFP), which is the term for the low-frequency part of the signal. However, we have in recent years extended our research interests to include also electric signals recorded on the cortical surface (ECoG) or on the scalp (EEG), as well as magnetic signals (MEG). As all these types of signals essentially have the same neural origin, they can be modeled using conceptually and methodologically similar computational schemes. By establishing a link between neural activity and extracellularly measured signals, these biophysically founded schemes can make the analysis of extracellular signals more quantitative and informative. These modeling schemes and the insights drawn from them are the main topics of this book.

The amount of data being routinely gathered in modern-day neuroscience experiments is enormous. For example, the number of micro-electrode contacts used to record spikes and LFPs within a single in vivo experiment is often in the hundreds, and is steadily increasing with the ongoing technological development. We anticipate that the biophysics-based modeling that we advocate will become an increasingly important tool for interpreting these ever-expanding data sets. However, getting to grips with this ever-growing amount of incoming data requires a team effort. This book has been written with the hope that students and scientists wish to join in the ambitious endeavor of trying to understand the brain through biophysics-based modeling of neurons, neural networks, and the extracellular signatures of their activity. For this reason, the computer code used in many of the simulations and corresponding figures presented in this book has been made publicly available in the online code repository (https://github.com/LFPy/ElectricBrainSignals), also accessible via www.cambridge.org/electricbrainsignals, so that interested readers can download and modify the simulation codes. Unless otherwise noted, figures in this book are provided by the authors (CC-BY 4.0 International license).

Our work on extracellular brain signals over the last 20 years has been based on collaborations with numerous scientists, including Evrim Acar, Jose-Manuel Alonso, Sebastian Amundsen, Costas Anastassiou, Ole A. Andreassen, Anton Arkhipov, Pooja N. Babu, Aslak Wigdahl Bergersen, Kosio Beshkov, Yassan Billeh, Erin Bjørkeli, Daniel M. Bjørnstad, Patrick Blomquist, Christine Brinchmann, Alessio Buccino, Miguel Cavero, Chaitanya Chintaluri, Hermann Cuntz, David Dahmen, Anders M. Dale, Alain Destexhe, Anna Devor, Markus Diesmann, Andrew G. Edwards, Ada Ellingsrud, Torbjørn Elvsåshagen, Rune Enger, Janne C. Fossum, Felix Franke, Marianne Fyhn, Justen Geddes, John Gigg, Torbjørn L. Gjerberg, Helena Głąbska, Sergey Gratiy, Sonja Grün, Torkel Hafting, Don Hagler, Eric Halgren, Ken Harris, Eivind Hennestad, Jørgen Hoel, Ulf Indahl, Karoline Jæger, Daniel Keller, Amir Khosrowshahi, Jan Fredrik Kismul, Christof Koch, Anders Lansner, Szymon Łeski, Henrik Lindén, Glenn T. Lines, Charl Linssen, Steinn H. Magnusson, Tuomo Mäki-Marttunen, Anders Malthe-Sørensen, Pablo Martínez-Cañada, Alberto Mazzoni, Nicolo Meneghetti, Stéphanie Miceli, Abigail Morrison, Jonas Nilsen, Eivind S. Norheim, Stig Omholt, Stefano Panzeri, Łukasz Paszkowski, Bijan Pesaran, Hans Ekkehard Plesser, Jan Potworowski,

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Reserved Physical Symbols and Quantities

Symbol	Unit	Description
t	s	time
f	Hz	frequency
q	C	electric charge
T	K	absolute temperature
$\mathbf{r}$	m	position vector
$u \in \{x, y, z\}$	m	location on u-axis
$E, \mathbf{E}$	V/m	electric field (scalar, directed)
$B, \mathbf{B}$	T	magnetic field (scalar, directed)
$F_k, \mathbf{F}_k$	N	force (scalar, directed) on particle k
$V, V_\mathrm{i}, V_\mathrm{e}, V_\mathrm{m}$	V	electric potential (general, intracellular, extracellular, membrane)
$[k]$	mol/m^3	ion concentration of species k
D_k	m^2/s	diffusion constant of ion species k
f_k	mol/(m^{3}s)	source density of ion species k
$J_k, \mathbf{J}_\mathrm{k}$	mol/s	flux of ion species k (scalar, directed)
$j_\mathrm{k}, \mathbf{j}_\mathrm{k}$	mol/(m^{2}s)	flux density of k (scalar, directed)
$I, \mathbf{I}$	A	electric current (scalar, directed)
$\mathcal{I}$	A/m	electric current per unit length (scalar)
$i, \mathbf{i}$	A/m^2	electric current density (scalar, directed)
$P, \mathbf{P}$	Am	current-dipole moment (scalar, directed)
C	A/m^3	current-source density
$\sigma, \sigma_\mathrm{t}$	S/m	conductivity (general, for tissue) for volume currents
r_m	Ωm^2	specific membrane resistivity
r_a	Ω/m	specific axial resistivity
c_m	F/m^2	specific membrane capacitance
g_k	S/m^2	specific membrane conductance for ion species k
E_k	V	reversal potential for ion species k
l	m	length of dendritic stick
τ, τ_m	s	time constant (general, membrane)
$h(\tau)$	arbitrary	temporal filter/impulse response (1D)
$H(\mathbf{r}, \tau)$	arbitrary	spatiotemporal filter/impulse response

F	96 485.332 12 C/mol	Faraday constant
R	8.314 462 618 153 24 J/(Kmol)	gas constant
N_A	$6.022\,140\,76 \times 10^{23}$ 1/mol	Avogadro constant
c	299 792 458 m/s	speed of light
e	$1.602\,176\,62 \times 10^{-19}$ C	elementary charge
ϵ_0	$8.854\,187\,812\,8 \times 10^{-12}$ F/m	vacuum permittivity
μ_0	$1.256\,637\,062\,12 \times 10^{-6}$ N/A^2	vacuum permeability

Abbreviations

AP	action potential
CSD	current-source density
CSF	cerebrospinal fluid
ECoG	electrocorticography
EEG	electroencephalography
FEM	finite element method
LFP	local field potential
MC	multicompartment (model of neuron)
MC+VC	multicompartment (neurons) + volume-conductor (theory)
MEA	micro-electrode array
MEG	magnetoencephalograpy
MoI	method of images
MUA	multi-unit activity
PSD	power-spectral density
VC	volume conductor