

MONOGRAPHS OF THE PHYSIOLOGICAL SOCIETY 49

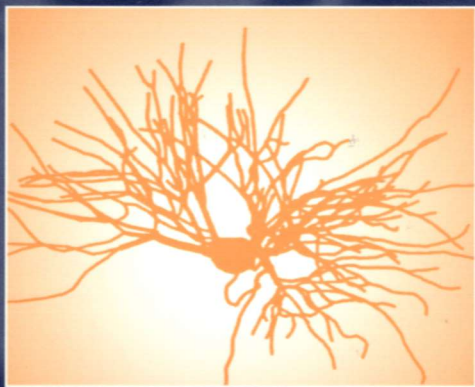
---

# Thalamocortical Assemblies

How ion channels, single neurons  
and large-scale networks organize  
sleep oscillations

---

Alain Destexhe & Terrence J. Sejnowski



OXFORD

## Thalamocortical Assemblies

# Monographs of the Physiological Society

## Members of the Editorial Board

- R. N. Lemon (Chairman), C. C. Michel, P. J. Harrison, N. B. Standen, R. E. J. Dyball
43. Dwain L. Eckberg and Peter Sleight, *Human Baroreflexes in Health and Disease*, 1992
  44. Christopher L-H. Huang, *Intramembrane Charge Movements in Striated Muscle*, 1993
  45. Robert Porter and Roger Lemon, *Corticospinal Function and Voluntary Movement*, 1993
  46. M. de Burgh Daly, *Peripheral Arterial Chemoreceptors and Respiratory-Cardiovascular Integration*, 1997
  47. Platon Kostyuk, *Plasticity in Nerve Cell function*, 1998
  48. David Price and David Willshaw, *Mechanisms of Cortical Development*, 2000

# Thalamocortical Assemblies

How Ion Channels, Single Neurons and Large-Scale Networks  
Organize Sleep Oscillations

---

Alain Destexhe

*Unité de Neurosciences Intégratives et Computationnelles, CNRS,  
UPR-2191, Avenue de la Terrasse, 91198 Gif-sur-Yvette, France*

*Département de Physiologie, Laval University,  
Québec G1K 7P4, Canada*

and

Terrence J. Sejnowski

*Computational Neurobiology Laboratory,  
The Howard Hughes Medical Institute,  
The Salk Institute for Biological Studies,  
10010 North Torrey Pines Road, La Jolla, California 92037, USA*

*Department of Biology, University of California San Diego,  
La Jolla, California 92093, USA*

**OXFORD**  
UNIVERSITY PRESS

# OXFORD

UNIVERSITY PRESS

Great Clarendon Street, Oxford OX2 6DP

Oxford University Press is a department of the University of Oxford.  
It furthers the University's aim of excellence in research, scholarship,  
and education by publishing worldwide in

Oxford New York

Athens Auckland Bangkok Bogotá Buenos Aires Cape Town  
Chennai Dar es Salaam Delhi Florence Hong Kong Istanbul Karachi  
Kolkata Kuala Lumpur Madrid Melbourne Mexico City Mumbai Nairobi  
Paris São Paulo Shanghai Singapore Taipei Tokyo Toronto Warsaw

with associated companies in Berlin Ibadan

Oxford is a registered trade mark of Oxford University Press  
in the UK and in certain other countries

Published in the United States  
by Oxford University Press Inc., New York

© Alain Destexhe and Terrence J. Sejnowski 2001

The moral rights of the authors have been asserted

Database right Oxford University Press (maker)

First published 2001

All rights reserved. No part of this publication may be reproduced,  
stored in a retrieval system, or transmitted, in any form or by any means,  
without the prior permission in writing of Oxford University Press,  
or as expressly permitted by law, or under terms agreed with the appropriate  
reprographics rights organizations. Enquiries concerning reproduction  
outside the scope of the above should be sent to the Rights Department,  
Oxford University Press, at the address above

You must not circulate this book in any other binding or cover  
and you must impose this same condition on any acquirer

British Library Cataloging in Publication Data  
Data available

Library of Congress Cataloging in Publication Data  
Destexhe, Alain.

Thalamocortical assemblies : how ion channels, single neurons, and large-scale  
networks organize sleep oscillations / Alain Destexhe and Terrence J. Sejnowski.  
p. cm.—(Monographs of the Physiological Society)

Includes bibliographical references.

1. Cerebral cortex. 2. Thalamus. 3. Sleep. 4. Electroencephalography. I. Sejnowski,  
Terrence J. (Terrence Joseph). II. Title. III. Series.

QP383 .D47 2001 612.8'21—dc21 2001031407

ISBN 0-19-8524250

10 9 8 7 6 5 4 3 2 1

Typeset by  
Newgen Imaging Systems (P) Ltd., Chennai, India  
Printed in Great Britain  
on acid-free paper by  
Biddles Ltd., Guildford & King's Lynn

*To Beatrice and Laurence, who helped us in many ways and  
for their forbearance with our sleep deprivation*

# Contents

---

<b>1</b>	<b>Introduction</b>	<b>1</b>
1.1	Brain rhythmicities	1
1.2	Early views on brain rhythmicity	2
1.3	Origin of brain rhythmicity	3
1.4	Identification of the key neuronal structures	5
1.5	Thalamocortical assemblies	6
<b>2</b>	<b>Biophysical models of the membrane potential and ionic currents</b>	<b>8</b>
2.1	Ionic bases of neuronal excitability	8
2.1.1	Membrane potential	8
2.1.2	Voltage-gated ion channels	9
2.1.3	The Hodgkin–Huxley model for action potentials	11
2.1.4	Biophysical bases for voltage dependence	18
2.2	Calcium-dependent ion channels	22
2.2.1	Intracellular calcium	22
2.2.2	Constant field equations	23
2.2.3	Calcium-activated channels	24
2.2.4	Oscillations with $I_{Ca}$	25
2.3	Markov models of voltage-dependent ion channels	26
2.3.1	Single-channel recordings	27
2.3.2	Markov kinetic models	29
2.4	Discussion	36
2.4.1	Hodgkin–Huxley models of ion channels	36
2.4.2	Markov models of ion channels	36
2.4.3	Applications to model single-cell and network behavior	37
2.5	Summary	38
<b>3</b>	<b>Electrophysiological properties of thalamic relay neurons</b>	<b>39</b>
3.1	The bursting properties of thalamic relay neurons	39
3.1.1	Experimental characterization of the rebound burst	39
3.1.2	Computational models of burst responses in TC cells	44
3.2	Oscillatory properties of thalamic relay cells	45
3.2.1	Experimental characterization of intrinsic oscillations	45
3.2.2	Models of oscillations in TC cells	45
3.3	Intrinsic waxing-and-waning oscillations in thalamic relay cells	51

3.3.1	Experimental characterization of waxing-and-waning oscillations	51
3.3.2	Models of waxing-and-waning oscillations from $\text{Ca}^{2+}$ regulation of $I_h$	52
3.3.3	Oscillatory behavior from $\text{Ca}^{2+}$ -regulated $I_h$	57
3.3.4	$\text{K}^+$ -dependent waxing-and-waning oscillations	57
3.3.5	Indirect modulation of $I_h$	60
3.4	Dendritic T-current in thalamic relay cells	64
3.4.1	Morphology	65
3.4.2	Passive properties and electrotonic structure	67
3.4.3	Model of dendritic $I_T$	69
3.4.4	Low density of T-current in the soma	71
3.4.5	Increased density of T-current in the dendrites	71
3.4.6	Dendritic T-currents affect current-voltage relations	73
3.4.7	Burst generation in TC cells with dendritic T-current	76
3.4.8	T-channels can be controlled more efficiently if they are dendritic	78
3.4.9	Simplified three-compartment models of TC cells	80
3.4.10	Simplified one-compartment model of TC cells	82
3.5	Discussion	84
3.5.1	The interplay of ionic currents in thalamic relay cells	84
3.5.2	Dendritic T-current in thalamic relay cells	86
3.6	Summary	88
<b>4</b>	<b>Electrophysiological properties of thalamic reticular neurons</b>	<b>89</b>
4.1	The rebound burst of thalamic reticular cells	89
4.1.1	Experimental characterization of rebound responses in RE cells	89
4.1.2	Model of the T-current and rebound burst in RE cells	91
4.2	Intrinsic oscillations in RE cells	92
4.2.1	Experimental characterization of repetitive bursting	92
4.2.2	Models of oscillatory properties of RE cells	93
4.3	Dendritic T-current in thalamic reticular cells	98
4.3.1	Experimental evidence for dendritic calcium currents	98
4.3.2	Model of dendritic calcium currents in thalamic reticular cells	99
4.3.3	Passive properties	104
4.3.4	Localization of the T-current	105
4.3.5	Properties of dendritically generated bursts	107
4.3.6	Properties of RE bursts <i>in vivo</i>	114
4.3.7	Reduced models	117
4.4	Discussion	119
4.4.1	The interplay of ionic currents in thalamic reticular cells	119



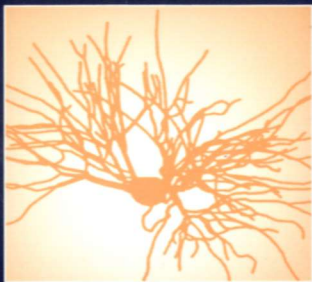
4.4.2	The role of the dendrites in the electrophysiology of thalamic reticular neurons	121
4.5	Summary	123
<b>5</b>	<b>Biophysical models of synaptic interactions</b>	<b>125</b>
5.1	Transmitter release	125
5.1.1	Experimental characterization of neurotransmitter release	125
5.1.2	Kinetic models of neurotransmitter release	127
5.1.3	Simplified models of the release process	128
5.2	Models for different types of postsynaptic receptors	131
5.2.1	Markov models of neurotransmitter-gated channels	132
5.2.2	Simplified models of neurotransmitter-gated channels	133
5.2.3	AMPA/kainate receptors	133
5.2.4	NMDA receptors	137
5.2.5	GABA <sub>A</sub> receptors	140
5.2.6	GABA <sub>B</sub> receptors	142
5.2.7	Simplified models of second-messenger gated channels	146
5.2.8	Noradrenergic and serotonergic receptors	146
5.2.9	Synaptic summation	147
5.3	Detailed models of GABAergic synaptic transmission in thalamus, hippocampus and neocortex	148
5.3.1	Model of neurotransmitter spillover	148
5.3.2	Time course of GABA in the synaptic cleft	150
5.3.3	Time course of GABAergic currents	152
5.3.4	Stimulus intensity dependence of GABAergic currents	153
5.3.5	Slow IPSPs in neocortex	155
5.4	Discussion	157
5.4.1	Modeling synaptic interactions	157
5.4.2	Detailed models of GABAergic synaptic transmission and spillover of GABA	159
5.5	Summary	162
<b>6</b>	<b>Spindle oscillations in thalamic circuits</b>	<b>164</b>
6.1	Experimental characterization of sleep spindle oscillations	164
6.2	Models of rhythmicity in the isolated reticular nucleus	170
6.2.1	Model networks of RE cells	173
6.2.2	Oscillatory behavior in simple circuits with GABA <sub>A</sub> synapses	174
6.2.3	Oscillatory behavior in two-dimensional networks with GABA <sub>A</sub> synapses	177
6.2.4	Spatiotemporal dynamics of two-dimensional networks with GABA <sub>A</sub> synapses	180
6.2.5	Oscillatory behavior in the presence of GABA <sub>B</sub> synapses	183

6.2.6	Oscillations with depolarizing GABA <sub>A</sub> synapses	187
6.3	Models of rhythmicity arising from thalamic relay-reticular interactions	190
6.3.1	Model of the TC-RE oscillator	190
6.3.2	Spindle oscillations in the simple TC-RE circuit	191
6.4	Why does the RE nucleus oscillate <i>in vivo</i> but not <i>in vitro</i> ?	192
6.4.1	Model of noradrenergic/serotonergic actions on RE cells	193
6.4.2	Neuromodulatory control of network oscillations in the RE nucleus	194
6.5	Network model of spindle oscillations in ferret thalamic slices	196
6.5.1	Networks of TC and RE cells	196
6.5.2	Small circuits of thalamic reticular neurons	196
6.5.3	Subharmonic bursting of TC cells	197
6.5.4	Minimal circuit for spindle oscillations	200
6.5.5	Oscillations in networks of TC and RE cells	202
6.5.6	Spatiotemporal patterns of discharges	205
6.5.7	Refractoriness of the network	207
6.6	Intrathalamic augmentation responses	211
6.6.1	Model for the intrathalamic augmenting response	213
6.7	Discussion	216
6.7.1	Spindle oscillations in the intact thalamus	216
6.7.2	Oscillations in the isolated reticular nucleus	223
6.8	Summary	226
<b>7</b>	<b>Spindle oscillations in the thalamocortical system</b>	<b>228</b>
7.1	Experimental characterization of spindle oscillations in the thalamocortical system	228
7.1.1	Early studies	228
7.1.2	The influence of corticothalamic projections	230
7.1.3	Propagating patterns of oscillations <i>in vivo</i>	235
7.2	A thalamocortical network model of spindle oscillations	241
7.2.1	The thalamocortical network	241
7.2.2	Inhibitory dominance in thalamocortical cells	248
7.2.3	Inhibitory dominance is optimal for triggering thalamic oscillations	250
7.2.4	Inhibitory dominance determines thalamic coherence	254
7.2.5	Refractoriness of the corticothalamic network	256
7.2.6	Refractoriness influences propagation	259
7.2.7	Spontaneous cortical discharges control spatiotemporal coherence	261
7.3	The large-scale synchrony of spindle oscillation during natural sleep	262
7.3.1	Spatiotemporal analysis of spindle oscillations in the cortex	265
7.3.2	Computational models of cortical excitability	270

7.3.3	Effect of enhancing the excitability of cortical pyramidal cells	271
7.3.4	Spatiotemporal coherence of simulated oscillations	275
7.3.5	Effects of enhancing the excitability of different cell types	277
7.4	Thalamocortical augmenting Responses	277
7.4.1	Thalamocortical augmenting	277
7.4.2	Augmenting responses in simple thalamocortical circuits	280
7.4.3	Augmenting responses in thalamocortical networks	280
7.4.4	Augmenting responses to cortical stimulation	282
7.4.5	Mechanisms underlying augmenting responses following cortical stimuli	284
7.5	Discussion	286
7.5.1	The coherence of spindle oscillations in the thalamocortical system	286
7.6	Summary	292
<b>8</b>	<b>Thalamocortical mechanisms for spike-and-wave epileptic seizures</b>	<b>294</b>
8.1	Experimental characterization of paroxysmal oscillations	294
8.1.1	Experimental models of absence seizures	294
8.1.2	Involvement of GABA <sub>B</sub> receptors	298
8.2	Modeling the genesis of paroxysmal discharges in the thalamus	301
8.2.1	Early models	301
8.2.2	Models of the activation properties of GABA <sub>B</sub> responses	305
8.2.3	Genesis of ~3 Hz oscillations in thalamic circuits	307
8.2.4	~3 Hz paroxysmal oscillations in thalamic networks	309
8.2.5	Spatiotemporal properties of thalamic paroxysmal oscillations	313
8.3	Model of spike-and-wave oscillations in the thalamocortical system	313
8.3.1	The thalamocortical model	316
8.3.2	Possible role of GABA <sub>B</sub> receptors in generating spike-and-wave field potentials	318
8.3.3	Intact thalamic circuits can be forced into ~3 Hz oscillations due to GABA <sub>B</sub> receptors	320
8.3.4	Suppression of intrathalamic GABA <sub>A</sub> inhibition does not generate spike-and-wave	322
8.3.5	Suppression of intracortical GABA <sub>A</sub> inhibition leads to ~3 Hz spike-and-wave	325
8.3.6	A thalamocortical loop mechanism for ~3 Hz spike-and-wave oscillations	328
8.3.7	Determinants of 3 Hz spike-and-wave oscillations	329

8.3.8	'Fast' 5–10 Hz spike-and-wave oscillations	332
8.4	Discussion	336
8.4.1	The importance of the nonlinear activation of GABA <sub>B</sub> responses	336
8.4.2	Paroxysmal discharges in the thalamus	337
8.4.3	3 Hz spike-and-wave in thalamocortical networks	339
8.4.4	Faster (5–10 Hz) spike-and-wave in thalamocortical networks	342
8.4.5	Predictions	343
8.4.6	Future directions	344
8.5	Summary	345
<b>9</b>	<b>A physiological role for sleep oscillations</b>	<b>347</b>
9.1	Impact of thalamic inputs on neocortical neurons	347
9.1.1	Experimental characterization of the thalamic input in neocortical pyramidal neurons	348
9.1.2	Computational models of thalamic inputs in neocortical pyramidal neurons	353
9.1.3	Modeling the consequences of spindles on neocortical pyramidal neurons	356
9.2	Oscillations during natural sleep and wakefulness	360
9.2.1	Spatiotemporal coherence of local field potentials during natural wake and sleep states	361
9.2.2	Correlations with unit discharges	363
9.2.3	Fast oscillations during slow-wave sleep	366
9.2.4	Origin of cortical slow waves	369
9.3	A possible function for sleep oscillations	377
9.3.1	Sleep oscillations as a trigger for plasticity	377
9.3.2	Slow oscillations	378
9.3.3	Network reorganization	380
9.4	A computational theory of sleep	381
9.4.1	Temporally asymmetric Hebbian plasticity	382
9.4.2	Thalamocortical assemblies	384
9.4.3	Sleep and memory consolidation	385
9.4.4	Reciprocal interactions between the hippocampus and the neocortex	387
9.4.5	Computational models of sleep	389
9.5	Summary	391
<b>Appendix A:</b>	<b>Ionic bases of the membrane potential</b>	<b>392</b>
A.1	Water and phospholipid membranes	392
A.2	Establishing a membrane potential	394
A.3	Passive properties of neuronal membranes	396
A.3.1	Leak channels	396
A.3.2	Time constant	398
A.3.3	Input resistance	398

<b>Appendix B: Optimized algorithms for simulating synaptic currents</b>	<b>401</b>
B.1 Single synapse	401
B.2 Multiple synapses	402
<b>Appendix C: Data available on the Internet</b>	<b>404</b>
C.1 NEURON simulation programs	404
C.2 Computer-generated animations	405
<b>References</b>	<b>406</b>
<b>Index</b>	<b>443</b>



## MONOGRAPHS OF THE PHYSIOLOGICAL SOCIETY

During sleep, the mammalian brain generates an orderly progression of low-frequency oscillations. The nature of these oscillations changes as the brain moves from sleep onset into deep sleep. Although readily measured and recorded, the underlying neural mechanisms involved and the purpose of these oscillations have remained unclear. However, as we learn more about the properties of neurons in the thalamus and cerebral cortex and their interactions, it has become possible to suggest a role for these occurrences.

This book reviews the molecular components and ionic mechanisms underlying sleep oscillations, including the properties of ion channels, synaptic receptors and the patterns of interconnectivity among thalamic and cortical neurons. These properties have been used to build detailed computational models of thalamocortical assemblies and their collective behavior.

The precise experimental data collected has provided a foundation for the study of dynamic activity in the central brain systems and it is now possible to suggest a role for thalamocortical oscillations in memory consolidation.

*Thalamocortical Assemblies* is for neuroscientists, neurobiologists, physiologists and other researchers interested in sleep and memory processes.



OXFORD  
UNIVERSITY PRESS

[www.oup.com](http://www.oup.com)