Reprinted from

NEUROCOMPUTING

Neurocomputing 26–27 (1999) 735–742

Cortical and thalamic components of augmenting responses: A modeling study

Arthur R. Houweling[a,*], Maxim Bazhenov[b], Igor Timofeev[c], Mircea Steriade[c], Terrence J. Sejnowski[b,d]

[a]*Sloan Center for Theoretical Neurobiology, The Salk Institute, La Jolla, CA 92037, USA*
[b]*Howard Hughes Medical Institute, The Salk Institute, Computational Neurobiology Laboratory, La Jolla, CA 92037, USA*
[c]*Laboratory of Neurophysiology, School of Medicine, Laval University, Québec, Canada G1K 7P4*
[d]*Department of Biology, University of California San Diego, La Jolla, CA 92093, USA*

Accepted 18 December 1998

ELSEVIER

NEUROCOMPUTING

Neurocomputing Letters
for rapid publication of special short communications

The journal invites authors to submit letters, concise papers and short communications aimed at rapid publication. Such communication shall be made subject of a special fast procedure if the following conditions are met:
The submitted papers must fit within the general Aims and Scope of the journal and be:
- no longer than 5 pages in typeset form (or 8 A4 pages typed in double spacing); and
- about a new development which is served by rapid publication; or
- about remarkable preliminary results of current research.

Please send your submission directly to our Letters Editor. If, according to the Letters Editor, the submitted paper meets the stated conditions, it will be made subject of a special, rapid procedure:
- the author can expect a referee report on his paper within 10 weeks after submission;
- the paper shall be accepted or rejected without the possibility of revisions. Revised papers will only be considered for the regular part of the journal;
- upon acceptance of the paper, publication will take place in the first available issue of the journal, within approximately the next 3 to 4 months, if the author agrees to skip the phase of checking printer's proofs.

Author's instructions for regular papers and for submissions for the Letters section can be found on the back inside cover.

ELSEVIER

Neurocomputing 26–27 (1999) 735–742

NEUROCOMPUTING

www.elsevier.com/locate/neucom

Cortical and thalamic components of augmenting responses: A modeling study

Arthur R. Houweling[a,*], Maxim Bazhenov[b], Igor Timofeev[c], Mircea Steriade[c], Terrence J. Sejnowski[b,d]

[a]*Sloan Center for Theoretical Neurobiology, The Salk Institute, La Jolla, CA 92037, USA*
[b]*Howard Hughes Medical Institute, The Salk Institute, Computational Neurobiology Laboratory, La Jolla, CA 92037, USA*
[c]*Laboratory of Neurophysiology, School of Medicine, Laval University, Québec, Canada G1K 7P4*
[d]*Department of Biology, University of California San Diego, La Jolla, CA 92093, USA*

Accepted 18 December 1998

Abstract

Augmenting responses in neocortical pyramidal cells can be elicited by cortical or thalamic repetitive stimulation around 10 Hz. A realistic model of a cortical pyramidal (PY) cell and an interneuron (IN) was developed to explore possible intracortical mechanisms. The interaction between strong feedforward hyperpolarizing inhibition, deinactivation of a low-threshold Ca^{2+} current and depression of fast inhibitory currents in the PY cell resulted in only weakly augmented responses. The incremental nature and frequency dependence of intracortical augmenting responses was reproduced in the model pair of cortical cells that included short-term plasticity of inhibitory, lateral and thalamocortical synapses. Hyperpolarization-activated currents were not needed in the model to obtain these effects. Thalamic stimulation in a simplified thalamocortical model with short-term plasticity of cortical connections resulted in a small additional cortical augmentation of the already augmented thalamocortical inputs.

Keywords: Augmenting response; Short-term synaptic plasticity; Neocortex; Thalamus; Computational model

1. Introduction

When thalamically stimulated at frequencies between 5 and 15 Hz cortical responses grow in size and may carry an increased number of action potentials. These

* Corresponding author.

0925-2312/99/$ – see front matter
PII: S0925-2312(98)00142-8

'augmenting' responses [20] have been reported in motor cortex [5–7,23,27], somatosensory cortex [19] and association cortex [21], as well as in visual cortex [10] and auditory cortex [18]. Cortical augmenting responses can be evoked by stimulation of specific thalamic nuclei, white matter [7,19], ipsilateral [7,27] and contralateral cortical areas [21], but not from prethalamic stimulation sites [4]. Augmenting responses are modulated by behavioral state [5,25] and may develop into seizure-like self-sustained oscillatory activity in cortical neurons [27].

Recent evidence indicates there are two separate components contributing to augmenting responses: an intrathalamic and an intracortical component. The intrathalamic component was recently investigated in decorticated animals [26,32] and the underlying mechanisms have been explored in computer models of the thalamus [3]. The possible role of thalamically generated augmenting responses in the development of cortical incremental responses was investigated *in vivo* [27] and in a modeling study [4]. The occurrence of incremental responses in cortical slices [7] and in thalamus-lesioned animals [19] corroborates an additional purely intracortical component.

In this paper we test two possible mechanisms underlying intracortical augmenting responses. The first mechanism involves the interaction between strong feedforward hyperpolarizing inhibition and (dein)activation of hyperpolarization-activated currents in layer 5 cells [7]. The second mechanism depends on short-term synaptic plasticity of cortical connections. Growing evidence indicates short-term synaptic plasticity is a ubiquitous property of neocortical circuitry: connections between various excitatory cortical cell types display short-term depression [1,31,33], connections from excitatory cells onto inhibitory cells either facilitate [17,30] or depress [2,29], inhibitory currents in excitatory cells depress [7,8,24,29], and thalamocortical synapses depress [11,12,28]. If short-term plasticity is a common characteristic of cortical synapses, cortical networks are expected to display use-dependent phenomena when electrically or naturally stimulated.

2. Methods

Model description and parameters are given in detail elsewhere [14]. Briefly, neocortical pyramidal cells (PY) and interneurons (IN) were described using a two-compartment model [16] including voltage-dependent currents described by Hodgkin–Huxley type of kinetics. Our cortical model was a reduced network version consisting of a single PY-IN cell pair (Fig. 1A). The PY cell was connected to itself and the IN cell through an AMPA synapse, the IN cell was connected to the PY cell with a $GABA_A$ synapse. Both cells received a thalamocortical AMPA synapse. Maximal synaptic conductances in the model were $\bar{g}_{py-in} = 0.06\ \mu S$, $\bar{g}_{in-py} = 0.10\ \mu S$, $\bar{g}_{tc-py} = 0.05\ \mu S$, $\bar{g}_{tc-in} = 0.02\ \mu S$, $\bar{g}_{py-py} = 0.04\ \mu S$ with and $\bar{g}_{py-py} = 0.01\ \mu S$ without short-term plasticity of the PY-PY synapse. To model short-term synaptic plasticity we used a phenomenological description of the synaptic conductance [1,33]. Parameters of synaptic plasticity were estimated from experimental data (see [14]).

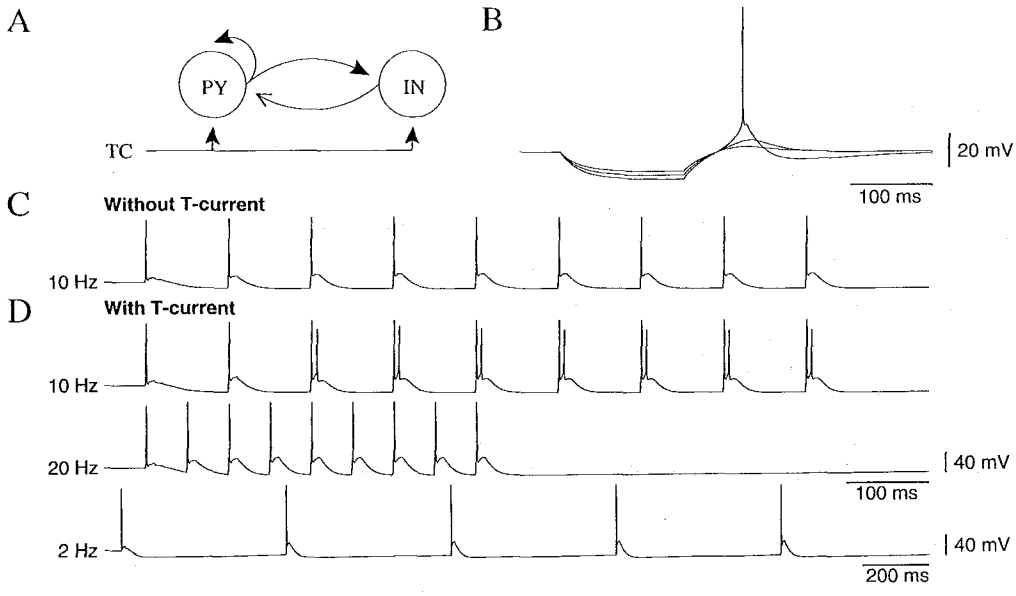


Fig. 1. (A) Schematic of the reduced cortical network model. (B) Rebound response of the PY cell at different strengths of hyperpolarization when a T-current was included ($pT = 20$ nm/s). (C) PY cell response to nine cortical shocks at 10 Hz in the model without T-current. (D) PY cell responses at different frequencies of stimulation in the model with T-current.

Electrical stimulation of the cortex was modeled as a brief activation of all synapses in the model. Activation of the thalamocortical synapses alone gave similar results. As a thalamic model we used an interconnected thalamocortical (TC) cell and nucleus reticularis (RE) cell described elsewhere [3]. All simulations were run using NEURON [13].

3. Results

To test the proposal that the initiation of augmenting responses depends on intrinsic properties of layer 5 cells [7] we added a low-threshold Ca^{2+} (T-) current [15] to the dendrite of the PY cell. The permeability of the T-channel was of intermediate strength such that a 150 ms hyperpolarization toward -85 mV resulted in a single sodium spike upon release from inhibition (Fig. 1B). We added a $GABA_B$ component [9] to the IN-PY synapse to obtain a slow IPSP that hyperpolarized the PY cell 15 mV from rest ($\bar{g} = 0.01$ μS). None of the synapses displayed short-term plasticity except the inhibitory $GABA_A$ synapse, which depressed. The model without T-current did not show augmentation upon 10 Hz stimulation (Fig. 1C). In contrast, when the T-current was added 10 Hz stimulation resulted in weakly incremented responses (Fig. 1D). At frequencies > 11 Hz and < 3 Hz responses were not

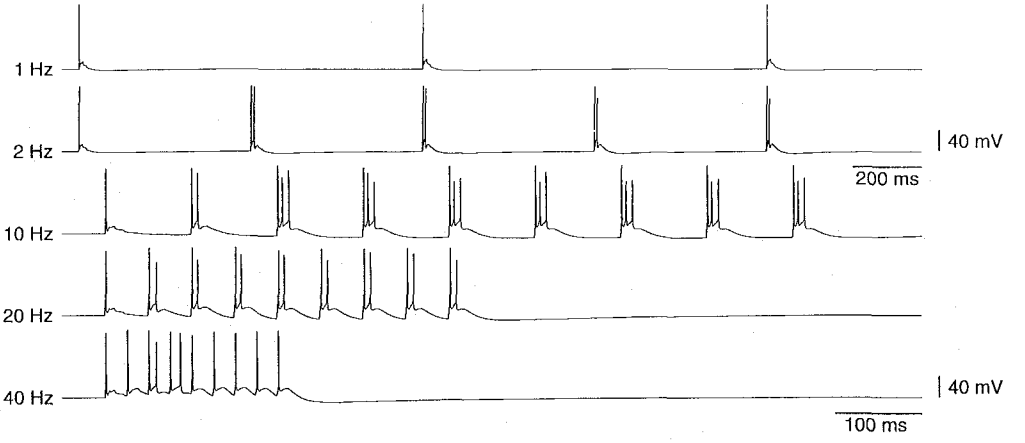


Fig. 2. PY cell responses to cortical shocks at different frequencies in the model including short-term synaptic plasticity.

augmented (Fig. 1D). When the inhibitory synapse did not depress, addition of the T-current did not result in incremental responses for any value of the inhibitory conductance (data not shown).

Next, we tested whether short-term plasticity of cortical synapses without T-current could generate incremental responses. In this model of cortical short-term plasticity the inhibitory synapse depressed with a paired-pulse depression of 30% at short intervals and a slow time constant of recovery ($U_{se} = 0.3$, $\tau = 1000$ ms) [7,24]. The PY-PY excitatory synapse depressed strongly at short intervals and recovered fast ($U_{se} = 0.75$, $\tau = 50$ ms) [31] and similar dynamics governed the thalamocortical synapses ($U_{se} = 0.4$, $\tau = 100$ ms) [11,28]. No T-current was present in the model. At 10 Hz stimulation PY cell responses augmented strongly carrying one, two and three spikes for the first three shocks respectively (Fig. 2). After the third shock responses stabilized to three spikes per shock. At high frequencies of stimulation incremental responses were reduced. For example, at 20 Hz a steady-state response of two spikes per shock was reached after the second shock, and at 40 Hz the steady-state was not augmented. At frequencies < 4 Hz augmentation was either reduced (at 2 Hz) or absent (at 1 Hz). IN cell responses were augmented similarly (data not shown). Frequency-dependent incremental responses were observed for a wide range of plasticity parameter values.

Finally, we tested whether thalamic stimulation could support cortical augmenting responses in the short-term plasticity model. A reciprocally coupled pair of RE-TC cells was stimulated at 10 Hz and the spike train of the TC cell was taken as an input to the cortical cells (Fig. 3, upper trace). The response of the TC cell was strongly augmented as a result of the deinactivation of the low-threshold Ca^{2+} current in this neuron and displayed characteristic poststimulus oscillations around 4 Hz [3]. In the cortical model without short-term plasticity the PY cell responded by closely reproducing the input pattern of spikes (Fig. 3, middle trace; see also [4]). In the cortical

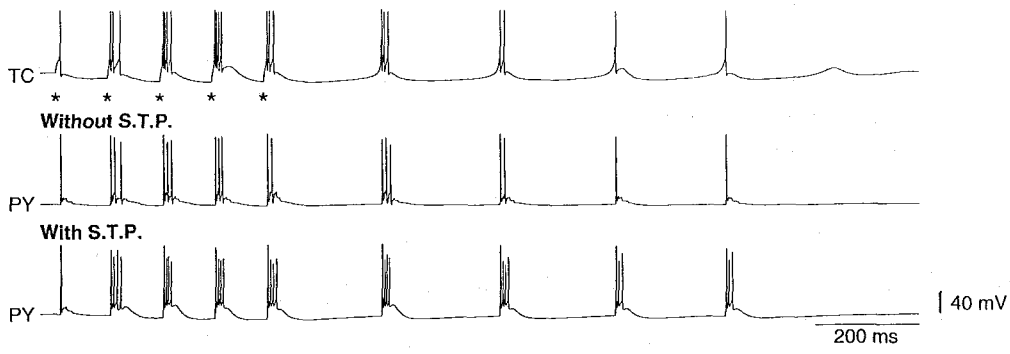


Fig. 3. PY cell responses to five thalamic shocks (indicated by *) at 10 Hz. TC cell response (upper), PY cell response in the model without short-term synaptic plasticty (S.T.P.) (middle), and PY cell response in the model with short-term synaptic plasticty (lower).

model with short-term plasticity, the PY cell responded to each shock with an equal or increased number of spikes compared to the thalamocortical input train (Fig. 3, lower trace), and the thalamic poststimulus oscillations were amplified.

4. Discussion

We tested two possible mechanisms underlying intracortical augmenting responses in a computational model of a pair of cortical cells. The first mechanism involved the deinactivation of a low-threshold Ca^{2+} current as a consequence of strong hyperpolarizing inhibition in pyramidal cells. This mechanism resulted in weakly augmented pyramidal cell responses for reasonably strong conductance values of the T-current. Small amplitude low-threshold spikes were obtained in only 15% of neocortical pyramidal cells [22]. Moreover, cells displaying augmenting responses often lack the strong hyperpolarization needed to deinactivate the T-current. These findings suggest this mechanism may contribute to cortical augmenting responses although it probably is not the most prominent one.

The incremental nature and frequency dependence of intracortical augmenting responses was reproduced in the model pair of cortical cells that included short-term plasticity of inhibitory, lateral and thalamocortical synapses. Hyperpolarization-activated currents were not needed in the model to obtain these effects. In a forthcoming paper we explore this mechanism in a large cortical network model [14]. Thalamic stimulation in a simplified thalamocortical model with short-term plasticity of cortical connections resulted in a small additional cortical augmentation of the already augmented thalamocortical inputs. Given the facilitory nature of corticothalamic feedback connections [34], thalamic and cortical circuits are likely to reciprocally reinforce thalamocortical oscillatory activity around 10 Hz.

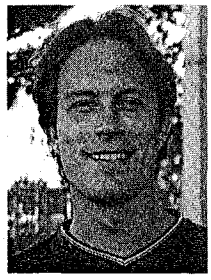
Acknowledgements

This research was supported by the Sloan Center for Theoretical Neurobiology, the Howard Hughes Medical Institute, Human Frontier Science Program, and the Medical Research Council of Canada.

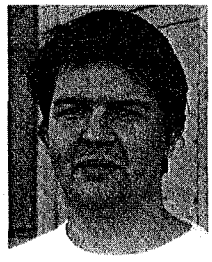
References

[1] L.F. Abbott, J.A. Varela, K. Sen, S.B. Nelson, Synaptic depression and cortical gain control, Science 275 (1997) 220–224.
[2] M.C. Angulo, J. Rossier, E. Audinat, Excitatory unitary synaptic inputs to GABAergic fast-spiking interneurons in the rat neocortex, Eur. J. Neurosci. 10 (10) (1998) 84.
[3] M. Bazhenov, I. Timofeev, M. Steriade, T.J. Sejnowski, Cellular and network models for intrathalamic augmenting responses during 10-Hz stimulation, J. Neurophysiol. 79 (5) (1998) 2730–2748.
[4] M. Bazhenov, I. Timofeev, M. Steriade, T.J. Sejnowski, Computational models of thalamocortical augmenting responses, J. Neurosci. 18 (16) (1998) 6444–6465.
[5] M.A. Castro-Alamancos, B.W. Connors, Short-term plasticity of a thalamocortical pathway dynamically modulated by behavioral state, Science 272 (1996) 274–277.
[6] M.A. Castro-Alamancos, B.W. Connors, Spatiotemporal properties of short-term plasticity in sensorimotor thalamocortical pathways of the rat, J. Neurosci. 16 (8) (1996) 2767–2779.
[7] M.A. Castro-Alamancos, B.W. Connors, Cellular mechanisms of the augmenting response: short-term plasticity in a thalamocortical pathway, J. Neurosci. 16 (23) (1996) 7742–7756.
[8] R.A. Deisz, D.A. Prince, Frequency-dependent depression of inhibition in guinea-pig neocortex in vitro by GABAB receptor feed-back on GABA release, J. Physiol. 412 (1989) 513–541.
[9] A. Destexhe, T. Bal, D.A. McCormick, T.J. Sejnowski, Ionic mechanisms underlying synchronized oscillations and propagating waves in a model of ferret thalamic slices, J. Neurophys. 76 (1996) 2049–2070.
[10] D. Ferster, S. Lindstrom, Augmenting responses evoked in area 17 of the cat by intracortical axon collaterals of cortico-geniculate cells, J. Physiol. 367 (1985) 217–232.
[11] Z. Gil, B.W. Connors, Y. Amitai, Differential regulation of neocortical synapses by neuromodulators and activity, Neuron 19 (3) (1997) 679–686.
[12] Z. Gil, B.W. Connors, Y. Amitai, Quantal properties and release characteristics of thalamocortical and intracortical synapse in layer 4 of neocortex, Eur. J. Neurosci. 10 (10) (1998) 137.
[13] M.L. Hines, N.T. Carnevale, The NEURON simulation environment, Neural Comput. 9 (6) (1997) 1179–1209.
[14] A.R. Houweling, M. Bazhenov, I. Timofeev, M. Steriade, T.J. Sejnowski, Intra cortical augmenting responses mediated by short-term depression of cortical synapses, submitted.
[15] J.R. Huguenard, D.A. McCormick, Simulation of the currents involved in rhythmic oscillations in thalamic relay neurons, J. Neurophysiol. 68 (4) (1992) 1373–1383.
[16] Z.F. Mainen, T.J. Sejnowski, Influence of dendritic structure on firing pattern in model neocortical neurons, Nature 382 (1996) 363–366.
[17] H. Markram, Y. Wang, M. Tsodyks, Differential signaling via the same axon of neocortical pyramidal neurons, Proc. Natl. Acad. Sci. USA 95 (9) (1998) 5323–5328.
[18] R. Metherate, J.H. Ashe, Facilitation of an NMDA receptor-mediated EPSP by paired-pulse stimulation in rat neocortex via depression of GABAergic IPSPs, J. Physiol. 481 (2) (1994) 331–348.
[19] D. Morin, M. Steriade, Development from primary to augmenting responses in the somatosensory system, Brain Res. 205 (1) (1981) 49–66.
[20] R.S. Morison, E.W. Dempsey, Mechanism of thalamocortical augmentation and repetition, Am. J. Physiol. 138 (1943) 297–308.
[21] A. Nunez, F. Amzica, M. Steriade, Electrophysiology of cat association cortical cells in vivo: intrinsic properties and synaptic responses, J. Neurophysiol. 70 (1) (1993) 418–430.

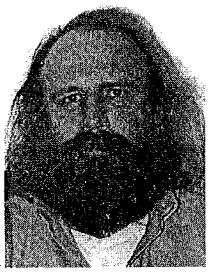
[22] D. Pare, E.J. Lang, Calcium electrogenesis in neocortical pyramidal neurons in vivo, Eur. J. Neurosci., 10 (10) (1998) 3164–3170.
[23] D.P. Purpura, R.J. Shofer, F.S. Musgrave, Cortical intracellular potentials during augmenting and recruiting responses. II. Patterns of synaptic activities in pyramidal and nonpyramidal tract neurons, J. Neurophysiol. 27 (1964) 133–151.
[24] S. Song, J.A. Varela, L.F. Abbott, S.B. Nelson, A quantitative description of synaptic depression at monosynaptic inhibitory inputs to visual cortical pyramidal neurons, Soc. Neurosci. Abstr. 23 (1997) 2362.
[25] M. Steriade, G. Iosif, V. Apostol, Responsiveness of thalamic and cortical motor relays during arousal and various stages of sleep, J. Neurophysiol. 32 (2) (1969) 251–265.
[26] M. Steriade, I. Timofeev, Short-term plasticity during intrathalamic augmenting responses in decorticated cats, J. Neurosci. 17 (10) (1997) 3778–3795.
[27] M. Steriade, I. Timofeev, F. Grenier, N. Durmuller, Role of thalamic and cortical neurons in augmenting responses and self-sustained activity: dual intracellular recordings in vivo, J. Neurosci. 18 (16) (1998) 6425–6443.
[28] K.J. Stratford, K. Tarczy-Hornoch, K.A. Martin, N.J. Bannister, J.J. Jack, Excitatory synaptic inputs to spiny stellate cells in cat visual cortex, Nature 382 (1996) 258–261.
[29] K. Tarczy-Hornoch, K.A. Martin, J.J. Jack, K.J. Stratford, Synaptic interactions between smooth and spiny neurones in layer 4 of cat visual cortex in vitro, J. Physiol. 508 (2) (1998) 351–363.
[30] A.M. Thomson, J. Deuchars, D.C. West, Single axon excitatory postsynaptic potentials in neocortical interneurons exhibit pronounced paired pulse facilitation, Neuroscience 54 (2) (1993) 347–360.
[31] A.M. Thomson, Activity-dependent properties of synaptic transmission at two classes of connections made by rat neocortical pyramidal axons in vitro, J. Physiol. 502 (1) (1997) 131–147.
[32] I. Timofeev, M. Steriade, Cellular mechanisms underlying intrathalamic augmenting responses of reticular and relay neurons, J. Neurophysiol. 79 (5) (1998) 2716–2729.
[33] M.V. Tsodyks, H. Markram, The neural code between neocortical pyramidal neurons depends on neurotransmitter release probability, Proc. Natl. Acad. Sci. USA 94 (2) (1997) 719–723.
[34] J.P. Turner, T.E. Salt, Characterization of sensory and corticothalamic excitatory inputs to rat thalamocortical neurones in vitro, J. Physiol. 510 (3) (1998) 829–843.



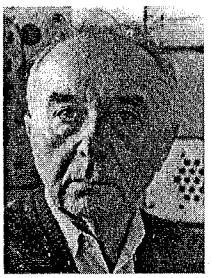
Arthur Houweling received his M.Sc. in biology from the University of Leiden, the Netherlands, in 1994. He is currently a doctoral student in the Computational Neurobiology Laboratory at the Salk Institute for Biological Studies and the Neurosciences Graduate Program at the University of California, San Diego. His research interests include the dynamic behavior and synaptic physiology of thalamocortical systems.



Maxim Bazhenov received his Ph.D. in physics and mathematics from Nizhny Novgorod State University in 1994, and joined the Institute of Applied Physics of Russian Academy of Sciences as a Research scientist. Since 1997 he has been a Research Associate in the Howard Hughes Medical Institute (The Salk Institute for Biological Studies, Computational Neurobiology Laboratory). His areas of research interests are: computational neuroscience, oscillations in thalamocortical and olfactory systems, pattern formation in neural networks.



Igor Timofeev received his Ph.D. from Bogomolets Institute of Physiology (Kiev, Ukraine) in 1993. He was employed as lecturer in the Department of Human and Animals Physiology at Odessa State University (Ukraine) and currently he is postdoctoral fellow at Laval University (Québec, Canada). His research interests are intrinsic vs. synaptic oscillations and plasticity in thalamocortical system.



Mircea Steriade was born in 1924, in Bucharest (Romania) where he obtained his M.D. and D.Sc. He made a postdoctoral stage with F. Bremer in Belgium. Since 1969 he is the head of the Laboratory of Neurophysiology at Laval University (Quebec, Canada) where he investigates the cellular bases of states of vigilance and seizures. He is a member of the Royal Society of Canada (Academy of Sciences).

Terrence Sejnowski is an Investigator with the Howard Hughes Medical Institute and a Professor at The Salk Institute for Biological Studies where he directs the Computational Neurobiology Laboratory. He is also Professor of Biology at the University of California, San Diego, where he is Director of the Institute for Neural Computation. Dr. Sejnowski received B.S. in physics from the Case-Western Reserve University, M.A. in physics from Princeton University, and a Ph.D. in physics from Princeton University in 1978. In 1988, Dr. Sejnowski founded Neural Computation, published by the MIT Press. The long-range goal of Dr. Sejnowski's research is to build linking principles from brain to behavior using computational models. This goal is being pursued with a combination of theoretical and experimental approaches at several levels of investigation ranging from the biophysical level to the systems level.

NEUROCOMPUTING

Instructions to authors

It is suggested that a prospective author who is not sure that his/her contribution fits into the Aims and Scope, before preparing a full-length manuscript, submits a proposal containing a description of the topic and how it meets the above criteria, an outline of the proposed paper, and a brief biography showing the author's qualification to write the paper (including reference to previously published material as well as the author's relation to the topic). If the proposal receives a favorable review, the author may prepare the paper, which after submittal will go through the standard review process. E-mail inquiries to the Editor-in-chief at dsanchez@san.rr.com

Letters: Short papers and communications (both containing no more than five printed pages) can be submitted for inclusion in the Letters section.

Papers, short papers, paper proposals, and *communications* (indicate which of these types of contribution should be taken into consideration) should always be submitted (2 copies) to the Editor-in-chief.

Upon acceptance of an article, the author(s) will be asked to transfer copyright of the article to the publisher. This transfer will ensure the widest possible dissemination of information.

The manuscript should be prepared for publication in accordance with the instructions given in the 'Instructions to Authors' (refer to the journal's homepage: www.elsevier.nl/locate/neucom), details of which are condensed below:

1. The manuscript must be typed on one side of the paper in double spacing with wide margins. A duplicate copy should be retained by the author.
2. The manuscript must include the complete affiliation, mailing address (including telephone/fax number and Email address), (short) biography of all authors, an abstract (max. 150 words) and a set of (max. 5) keywords. Upon final acceptance, a photo of each author and the original figures will be required and should be sent directly to: Olaf Meesters, Elsevier Science B.V., Issue Management, P.O. Box 103, 1000 AC Amsterdam, The Netherlands.
3. Footnotes, which should be kept to a minimum and should be brief, must be numbered consecutively and typed on a separate sheet in the same format as the main text.
4. Special care should be given to the preparation of the drawings for figures and diagrams. Except for a reduction in size, they will appear in the final printing in exactly the same form as they were submitted by the author; normally they will not be redrawn by the printer. In order to make a photographic reproduction possible, all drawings should be on separate sheets, with wide margins, drawn large size, in India ink and carefully lettered. Exceptions are diagrams only containing formulae and a small number of single straight lines (or arrows); these can be typeset by the printer.
5. References should be listed alphabetically, in the same way as the following examples:

   For a book:

   [1] Y.-H. Pao, *Adaptive Pattern Recognition and Neural Networks* (Addison Wesley, Reading, MA, 1989).

   For a paper in a journal:

   [2] S.-I. Amari, Backpropagation and stochastic gradient descent method, *Neurocomputing* 5 (4–5) (1993) 185–196.

   For a paper in a contributed volume:

   [3] D.S. Modha and R. Hecht-Nielsen, Multilayer functionals, in: J.G. Taylor, ed., *Mathematical Approaches to Neural Networks* (North-Holland, Amsterdam, 1993) 235–260.

   For an unpublished paper:

   [4] S.E. Fahlman and C. Lebiere, The cascade-correlation learning architecture, Report CMU-CS-90-100, School of Computer Science, Carnegie Mellon University, Pittsburgh, PA, 1990.

Books: Please send book announcements, names of books published, and book reviews directly to the Book reviews editor: Prof. K.J. Cios, University of Toledo, Dept. of Bioengineering, Toledo, OH 43606-3390, USA. Tel.: 1-419-537-2915, fax: 1-419-537-2450, E-mail: kcios@eng.utoledo.edu

Events: Please send announcements about meetings and call for papers as well as meeting reports directly to the section editor: G. Thimm, Design Research Center, School of Mechanical & Production Engineering, Nanyang Technological University, Singapore 639798. Tel: +65 790 5010, e-mail: mgeorg@ntu.edu.sg.

Letters: Please send letters directly to the section editor: Dr. F. Murtagh, Dept. of Computer Science, The Queen's University, Belfast BT7 1NN, Northern Ireland, UK. E-mail: fmurtagh@acm.org

---

Note to authors: Please mention your E-mail address on the first page of your manuscript. When submitting electronic files, please make sure that they are identical with the paper version.

Publication information

NEUROCOMPUTING (ISSN 0925-2312). For 1999 volumes 24–29 (18 issues) are scheduled for publication.

Subscription prices are available upon request from the publisher. Subscriptions are accepted on a prepaid basis only and are entered on a calendar year basis. Issues are sent by surface mail except to the following countries where air delivery via SAL is ensured: Argentina, Australia, Brazil, Canada, Hong Kong, India, Israel, Japan, Malaysia, Mexico, New Zealand, Pakistan, PR China, Singapore, South Africa, South Korea, Taiwan, Thailand, USA. For all other countries airmail rates are available upon request.

Claims for missing issues must be made within six months of our publication (mailing) date.

For orders, claims, product enquiries (no manuscript enquiries) please contact the customer Support Department at the Regional Sales Office nearest to you.

New York, Elsevier Science, P.O. Box 945, New York, NY 10159-0945, USA. Tel: (+1) 212-633-3730, [Toll Free number for North American Customers: 1-888-4ES-INFO (437-4636)], Fax: (+1) 212-633-3680, E-mail: usinfo-f@elsevier.com

Amsterdam, Elsevier Science, P.O. Box 211, 1000 AE Amsterdam, The Netherlands. Tel: (+31) 20-485-3757, Fax: (+31) 20-485-3432, E-mail: nlinfo-f@elsevier.nl

Tokyo, Elsevier Science K.K., 9-15, Higashi-Azabu 1-chome, Minato-ku, Tokyo 106-0044, Japan. Tel: (+81) 3-5561-5033, Fax: (+81) 3-5561-5047, E-mail: info@elsevier.co.jp

Singapore, Elsevier Science, No. 1 Temasek Avenue, #17-01 Millenia Tower, Singapore 039192. Tel: (+65) 434-3727, Fax: (+65) 337-2230, E-mail: asiainfo@elsevier.com.sg

USA mailing info. *Neurocomputing* (0925-2312) is published 16 times a year by Elsevier Science B.V. (Molenwerf 1, Postbus 211, 1000 AE Amsterdam). Annual subscription price in the USA US$ 1152.00 (valid in North, Central and South America), including air speed delivery. Application to mail at periodicals postage rate is pending at Jamaica, NY 11431.

USA POSTMASTER: Send address changes to *Neurocomputing,* Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003.

AIRFREIGHT AND MAILING in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003.

⊗ The paper used in this publication meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper).

Published 18 times a year 0925-2312/99 Printed in The Netherlands