Available online at www.sciencedirect.com
ScienceDirect
Neurocomputing 70 (2006) 3–8
NEUROCOMPUTING
www.elsevier.com/locate/neucom

A computational model of the primary auditory cortex exhibiting plasticity in the frequency representation

Marilene de Pinho[a,*], Marcelo Mazza[b], Antônio C. Roque[b]

[a]Departamento de Neurologia, Psiquiatria e Psicologia Médica, FMRP, USP, 14049-900 Ribeirão Preto, SP, Brazil
[b]Departamento de Física e Matemática, FFCLRP, USP, 14040-901 Ribeirão Preto, SP, Brazil

Available online 18 August 2006

Abstract

Many studies have demonstrated that classical conditioning retunes single neurons in the primary auditory cortex (AI). Recent works suggest that this functional plasticity is related to alterations in the area of representation of the conditioned stimulus frequency in AI. In this work, we present a computational model of AI and pre-cortical structures involved with auditory processing (cochlea and medial geniculate body) which reproduces some properties of tonotopic maps in AI. The model is used to simulate a classical conditioning experiment, which causes retuning of certain neurons to the conditioned frequency. This retuning is accompanied by an expansion of the cortical representation area of the conditioned frequency.

Keywords: Computational neuroscience; Classical conditioning; Cortical plasticity; Auditory system

1. Introduction

Extensive studies on auditory systems of several species have revealed that the linear arrangement of characteristic frequencies (CF) present in the cochlea is topographically represented across the primary auditory cortex (AI) [11]. Until relatively recently it was thought that such tonotopic maps were fixed and immutable in adults but several studies in the past 20 years have shown that they can be altered as a consequence of both central and peripheral lesions, and classical conditioning [3,8,12–14]. In particular, experiments of classical conditioning [8,14] resulted in alterations of the tuning curves of neurons and groups of neurons so that their responses to the conditioned frequency was increased. In some cases the conditioned frequency became the new CF of the retuned neurons.

The plasticity of single neuron tuning curves suggests that the tonotopic representation of the cochlea across AI is altered during a classical conditioning experiment. However, the tonotopic map itself has not been directly studied during such an experiment [7]. Besides, the underlying mechanisms responsible for the classical conditioning-induced retuning of a neuron's response are still poorly understood. Weinberger [15] proposed that Hebbian mechanisms might be involved in such reorganization process. The main candidate for being responsible for a Hebbian-like process in the brain is the NMDA synaptic receptor [2].

In this work we use a computational model of the auditory system, which simulates neural circuits believed to be involved with classical conditioning phenomena [14], to study the behavior of the cortical area of representation of the conditioned stimulus frequency during a simulation of classical conditioning experiment. The model also is used to study the possible involvement of NMDA receptors in the plasticity phenomenon.

2. The model

The computational model is an extended version of an early model developed by us [4–6]. The model contains four structures: cochlea, ventral division of the medial geniculate body (MGBv), medial division of the medial geniculate body (MGBm) and primary AI. There is also a source of

*Corresponding author.
E-mail addresses: mpinho2001@yahoo.com.br (M. de Pinho), mazzamb@yahoo.com.br (M. Mazza), antonior@neuron.ffclrp.usp.br (A.C. Roque).

0925-2312/$ - see front matter © 2006 Published by Elsevier B.V.
doi:10.1016/j.neucom.2006.07.004

excitatory stimuli which represents the unconditioned stimulus (US). The model's generic scheme is given in Fig. 1. The model cochlea is a 47-receptor linear layer with 16 2-receptor regions specifically sensitive to orderly frequencies (from 1 to 16, in arbitrary units) alternated with 15 1-receptor overlapping sensitivity areas which have one-third of the sensitivity of the specifically sensitive regions [4].

Fig. 2 shows a scheme of the model cochlea.

Each thalamic nucleus (MGBv or MGBm) contains 564 excitatory relay cells arranged in an array of 94×6 nodes and 186 inhibitory interneurons arranged in an array of 31×6 nodes. These areas were constructed so that each relay cell receives connections both from cochlear cells and thalamic interneurons, and sends excitatory outputs either to other relay cells or to cortical cells. Relay cells at the MGBm also receive the unconditioned input.

The cortical area (AI) consists of 3384 excitatory pyramidal cells arranged in an array of 188×12 nodes and 1128 inhibitory basket cells arranged in an array of 94×12 nodes. Each pyramidal cell receives excitatory inputs from thalamic relay cells (both from MGBm and MGBv) and other cortical pyramidal cells. Pyramidal cells also receive inhibitory inputs from cortical basket cells. Cortical basket cells receive excitatory inputs from cortical pyramidal cells. Fig. 3 shows a scheme of the connectivity of the model.

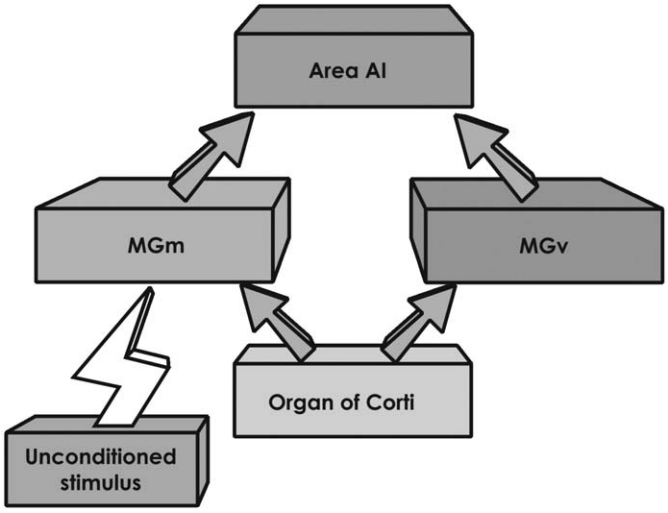

Fig. 1. Scheme of the model.

The passive and active properties of the model cells are adaptations to the auditory system of properties of model cells used by us in a simulation of the somatosensory system [10].

The thalamic relay cell model has four compartments: a soma and three dendrites. The following ionic channels were placed at the soma: transient sodium (Na), low threshold inactivating calcium (Ca), fast calcium and voltage-dependent potassium (K_c), slow calcium-dependent potassium (K_{ahp}), and delayed rectifier potassium (K_d). AMPA, NMDA and GABA synaptic receptors were distributed in the dendrites of the relay cells in the following way: the MGBv relay cells have only AMPA and GABA receptors placed in their dendrites. The MGBm cells have GABA receptors at their soma and AMPA and NMDA receptors at their dendrites. A thalamic interneuron model has only two compartments: a soma and a dendrite. Its soma has the following ionic channels: transient Na, slow potassium (K_s), and K_d. Thalamic interneurons only have AMPA receptors at their single dendrites.

A cortical pyramidal cell model has six compartments: a soma, two basal dendrites, and an apical dendrite divided into three compartments (distal, medial and proximal). The following ionic channels were placed at the soma: transient Na, K_s, and K_d. AMPA receptors were placed at the two basal dendrites and at the distal and proximal segments of the apical dendrite. NMDA receptors were placed at one of the basal dendrites. GABA receptors were placed at the soma. A cortical basket cell model has only two compartments: a soma and a dendrite. Its soma has the following ionic channels: transient Na, K_s, and K_d. AMPA receptors were placed at its single dendrite.

The architecture of the model is the following: each cochlear cell sends excitatory inputs to a neighborhood of 27 (3×9) MGBv relay cells and to a neighborhood of 45 (5×9) MGBm relay cells. In the MGBm, each relay cell is connected to itself and to other relay cells in its first ring of neighbors with a probability of 80% (for a description of how these probabilities are set refer to [10]). It also is connected to all interneurons in its third and fourth neighborhood rings and to interneurons in its first and second neighborhood rings with probability of 60%. Each thalamic interneuron is connected to its first relay cell neighbor and to all relay cells in its first ring of neighbors; it also is connected to relay cells in its second ring of neighbors with a probability of 60%. In the MGBv, each

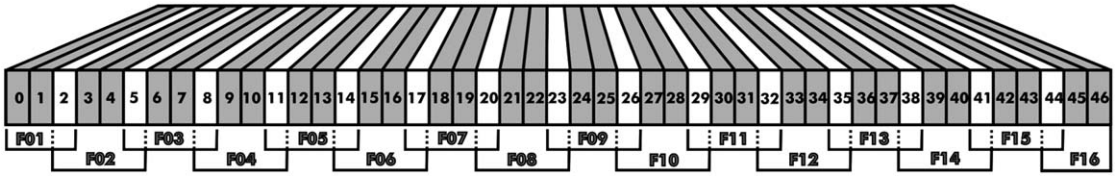

Fig. 2. Scheme of the frequency representation along the 47-receptor model cochlea. Receptor pairs painted gray are maximally sensitive to their corresponding frequencies while receptors in white have only one-third of the sensitivity to the frequencies of their neighbors.

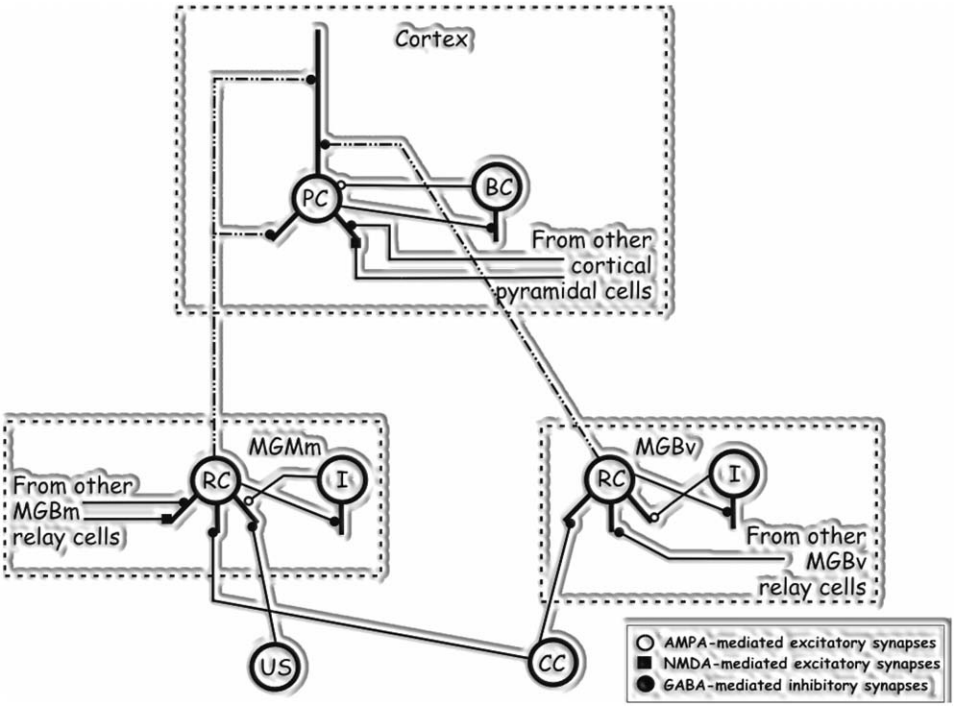

Fig. 3. Scheme of the connectivity of the model. US = unconditioned stimulus; CC = cochlear cell; RC = thalamic relay cell (excitatory); I = thalamic interneuron (inhibitory); PC = cortical pyramidal cell (excitatory); BC = cortical basket cell (inhibitory).

relay cell is connected to itself and to a neighborhood of 5×3 relay cells with a probability of 80%. It also is connected to all interneurons in its third and fourth rings of neighbors and to interneurons in its first and second rings of neighbors with probability of 60%. Each interneuron is connected to the closest relay cell and to all relay cells in its first ring of neighbors, and has a probability of 60% of being connected to relay cells in its second ring of neighbors.

Each thalamic relay cell (both from MGBv and MGBm) sends inputs to an area of 27 (9×3) pyramidal cells in the cortical area. In the cortex, each pyramidal cell is connected to itself and all pyramidal cells in its first ring of neighbors, and has a probability of 50% of being connected to pyramidal cells in its second ring of neighbors. A pyramidal cell also is connected to its closest basket cell and to all basket cells in its third and fourth neighborhood rings, and to basket cells in its first and second rings of neighbors with a probability of 60%. Each basket cell is connected to itself and to all pyramidal cells in its first ring of neighbors, and is connected to pyramidal cells in its second ring of neighbors with 50% of probability.

3. Experiments done with the model

Once the model was "assembled" in the computer it was submitted to two *in silico* experimental protocols. Fig. 4 shows a scheme of the two protocols with their respective phases.

The objective of Protocol 1 was to allow the study of the behavior of area AI before, during and after the simulated classical conditioning experiment. This protocol was divided into three phases. The first phase took 2400 simulation steps (a simulation step in the model corresponds to 0.05 ms so this corresponds to 0.12 s). In this phase, each one of the 16 frequencies was randomly chosen to be presented to the system for a period of 15 time steps (0.75 ms) so that the cochlea as a whole was stimulated for 10 times. The second phase also took 2400 simulation steps and consisted in the classical conditioning. In this phase the cochlea was stimulated as in the first phase but every time the frequency chosen to be the conditioned stimulus (frequency 11) was presented, the MGBm received the US as well. In the third phase the source of the US was inactivated and the system was submitted again to the same kind of stimulation of the first phase for 1200 time steps (0.06 s).

Protocol 2 was similar to Protocol 1 with the difference that, at the beginning of phase 2 (simulation step 2401), all synaptic receptors of the NMDA type in area AI were blocked. The objective of this protocol was to investigate the role of the NMDA synaptic receptors in the process of classical conditioning in the primary AI.

4. Results

The measure chosen to evaluate the activity level of area AI was the sum of the membrane potentials at the soma of all excitatory neurons in this area.

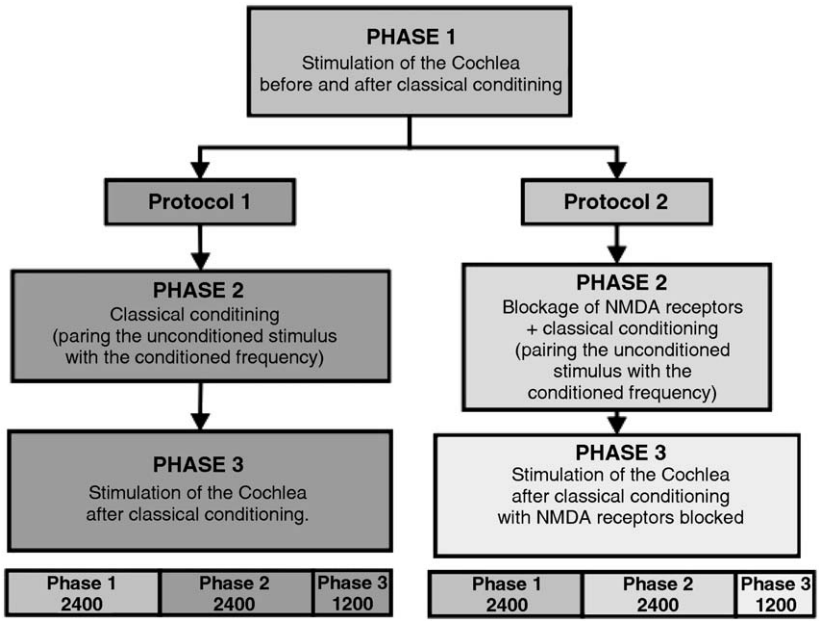

Fig. 4. Schematic representation of the three phases of each one of the two experimental protocols.

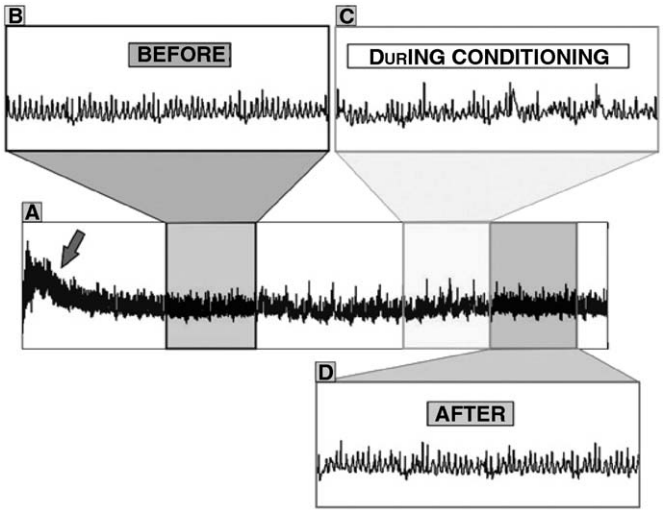

Fig. 5. (A): Activity level of area AI during Protocol 1. (B–D): Details of the activity level for the three phases of Protocol 1.

Fig. 5 shows how the measure of activity level of area AI varies during the three phases of Protocol 1. Fig. 6 shows the behavior of this measure of activity level of area AI during Protocol 2 in comparison with its behavior during Protocol 1.

Observing the behavior of the activity level of area AI during Protocol 1 (Fig. 5), one sees that after a transient phase the activity level reaches a stable state. After the attainment of this stable state we can make measurements of the spiking activities of excitatory cell in AI to determine the tonotopic map [9]. During the presentation of a given frequency, its cortical map was determined by registering only those excitatory cells in AI that spiked in that period. The same procedure was used to determine frequency maps in the MGBm and MGBv. These tonotopic maps are shown in Fig. 7.

Fig. 7 shows that there are areas whose neurons respond exclusively to a single frequency and there are superposition areas whose neurons respond to two neighboring frequencies.

The behavior of the representation area of the frequency corresponding to the conditioned stimulus (frequency 11) was studied as well. We observed that after the classical conditioning experiment with the NMDA receptors working normally (phase 3 of Protocol 1) there was an important expansion of the area of representation of frequency 11. On the other hand, when the NMDA synaptic receptors were blocked there was a small shrinkage of the area of representation of frequency 11. This can be seen in Fig. 8.

5. Discussion

Aversive classical conditioning to sound stimuli is an important experimental paradigm in the investigation of how the brain represents internal representations of the external world [1]. The model described by Weinberger [14] is a synthesis of the neural circuits involved in this process. Based on his model, Weinberger suggested that the cortical alterations which occur as a consequence of classical conditioning should result in an expansion of the area of representation of the conditioned frequency [7,14]. Weinberger also proposes that Hebbian mechanisms might be responsible for the retuning of AI neurons which favors the conditioned frequency [14,15]. The main candidate for implementing a Hebbian mechanism in the brain is the glutaminergic synaptic receptor of the NMDA type [2].

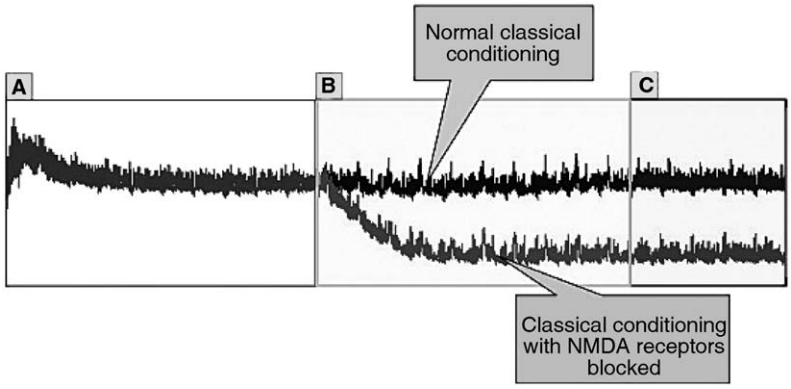

Fig. 6. Activity level of area AI during the two experimental protocols. The letters A, B and C indicate the three phases of each protocol.

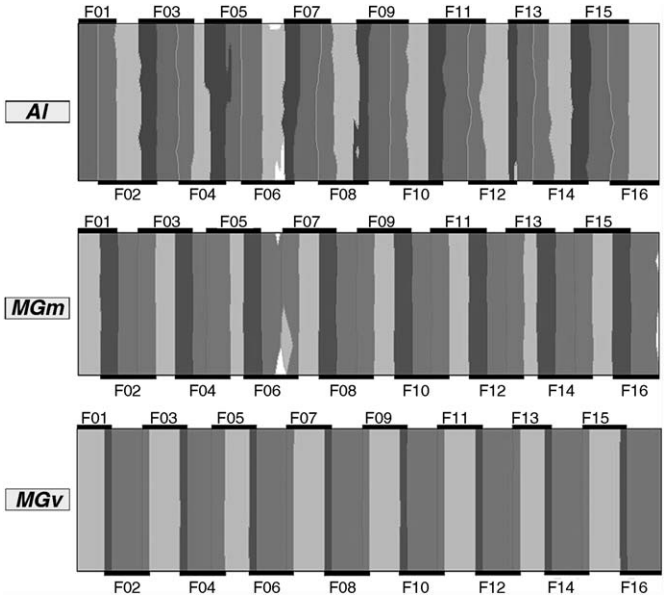

Fig. 7. Tonotopic maps in area AI and in the thalamic nuclei MGBm and MGBv. The black bars above and bellow the maps indicate the areas of representation of the frequencies written above them.

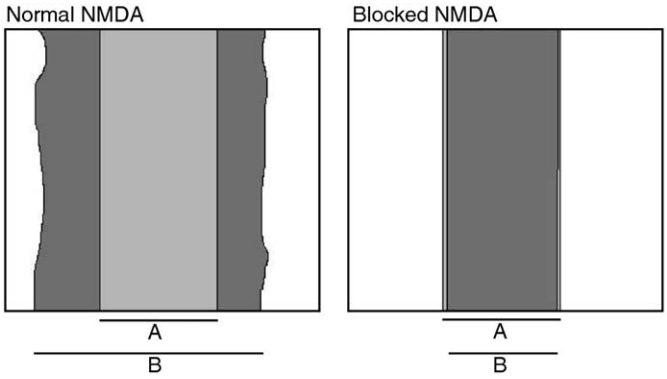

Fig. 8. Areas of representation of the conditioned frequency (frequency 11), in the normal situation and in the situation with NMDA receptors blocked. (A) Area before conditioning; (B) area after conditioning.

In this work we wanted to study (1) the behavior of the area of cortical representation of the conditioned frequency before, during and after a classical conditioning experiment, and (2) the possible involvement of NMDA receptors in the alteration of this area.

The results of our simulations indicate that there is an expansion of the area of representation of the conditioned frequency after a classical conditioning experiment. This expansion is not present, moreover there is even a shrinkage, when the NMDA synaptic receptors are blocked.

Even taking in consideration that these results were obtained with a computational model with several simplifications and limitations in relation to real systems, they can be used to support the view that classical conditioning modifies specifically the information processing capability of the brain relative to the conditioned frequency, and that the mechanism responsible for this modification is somewhat related with the NMDA receptor.

Acknowledgment

The authors would like to thank the São Paulo State Research Foundation (FAPESP), which supported this work.

References

[1] J.S. Bakin, N.M. Weinberger, Classical conditioning induces CS-specific receptive field plasticity in the auditory cortex of the guinea pig, Brain Res. 536 (1990) 271–286.
[2] D.V. Buonomano, M.M. Merzenich, Cortical plasticity: from synapses to maps, Ann. Rev. Neurosci. 21 (1998) 149–186.
[3] A. Das, Plasticity in adult sensory cortex: a review, Network 8 (1997) R33–R76.
[4] M. de Pinho, A.C. Roque-da-Silva, A realistic computational model of formation and variability of tonotopic maps in the auditory cortex, Neurocomputing 26–27 (1999) 355–359.
[5] M. de Pinho, M.B. Mazza, A.C. Roque, A biologically plausible computational model of classical conditioning induced reorganization of tonotopic maps in the auditory cortex, Neurocomputing 32–33 (2000) 685–691.
[6] M. de Pinho, M.B. Mazza, J.R.C. Piqueira, A.C. Roque, Shannon's entropy applied to the analysis of tonotopic reorganization in a computational model of classical conditioning, Neurocomputing 44–46 (2002) 359–364.
[7] V.V. Galván, N.M. Weinberger, Long-term consolidation and retention of learning-induced tuning plasticity in the auditory cortex of the guinea pig, Neurobiol. Learn. Memory 77 (2002) 78–108.

[8] D.R.F. Irvine, Injury- and use-related plasticity in the adult auditory system, J. Commun. Disord. 33 (2000) 293–312.
[9] M.B. Mazza, M. de Pinho, A.C. Roque, Biologically plausible models of topographic map formation in the somatosensory and auditory cortices, Int. J. Neural Syst. 9 (1999) 265–271.
[10] M. Mazza, M. de Pinho, J.R.C. Piqueira, A.C. Roque, A dynamical model of fast cortical reorganization, J. Comput. Neurosci. 16 (2004) 177–201.
[11] H.L. Read, J.A. Winer, C.E. Schreiner, Functional architecture of auditory cortex, Curr. Opin. Neurobiol. 12 (2002) 433–440.
[12] G.H. Recanzone, C.E. Schreiner, M.M. Merzenich, Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys, J. Neurosci. 13 (1993) 87–103.
[13] D. Robertson, D.R.F. Irvine, Plasticity of frequency organization in auditory cortex of guinea pig with partial unilateral deafness, J. Comp. Neurol. 282 (1989) 456–471.
[14] N.M. Weinberger, Retuning the brain by fear conditioning, in: M.S. Gazzaniga (Ed.), The Cognitive Neurosciences, MIT Press, Cambridge, MA, 1995, pp. 1071–1089.
[15] N.M. Weinberger, Physiological memory in primary auditory cortex: characteristics and mechanisms, Neurobiol. Learn. Memory 70 (1998) 226–251.

Marilene de Pinho is a clinical psychiatrist born in Teresina, Piauí, Brazil, where she graduated in medicine in 1993 and concluded her medical residence in 1996. She received her Ph.D. in psychobiology from the University of São Paulo in Ribeirão Preto, Brazil, and worked in the Department of Psychiatry of this same university studying the organization of a psychiatric ward with methods of Information Theory. She is now working in the publication of the results of this research.

Marcelo Mazza graduated in Physics at the University of Teresina, Brazil, and received his Ph.D. in medical physics from the University of São Paulo in Ribeirão Preto, Brazil. He worked with neural networks and data mining in brain images of schizophrenic patients in the Department of Psychiatry of the University of São Paulo in Ribeirão Preto from 2002 to 2004. Now he is working in the Institute of Research and Teaching of the Albert Einstein Hospital in São Paulo, Brazil, with non-linear analysis of EEG in epilepsy and computational modeling of brain functions.

Antônio C. Roque was born in São Paulo, SP, Brazil in 1963. He received his BS degree in physics from the State University of Campinas, Brazil, in 1983, and his Ph.D. degree in cognitive science and artificial intelligence from the University of Sussex, Brighton, UK, in 1992. He joined the faculty of the Department of Physics and Mathematics of the University of São Paulo at Ribeirão Preto, Brazil, in June 1993. In 1996 he founded the Laboratory of Neural Systems (SisNe), which is being active since then in the field of computational neuroscience. He also is the organizer of the Latin American School on Computational Neuroscience (LASCON), which has the objective of promoting computational neuroscience among Latin American students and researchers.