A cortical network model for clinical EEG data analysis

Yuqiao Gu[1], Geir Halnes[1], Hans Liljenström[12] and Björn Wahlund[3]

[1]Dept. of Biometry and Informatics, SLU
S-750 07 Uppsala, Sweden

[2] Agora for Biosystems
P.O. Box 57
S-193 22 Sigtuna, Sweden

[3] Dept. of Clinical Neuroscience, Karolinska Instititute,
Section of Psychiatry, St. Görans Hospital, S-112 81 Stockholm, Sweden

Abstract

We use computational methods to investigate how cortical neurodynamics depend on network properties and intrinsic and external signals and fluctuations. In this paper, we investigate the role of network properties and external input on human EEG dynamics, in particular relating to electroconvulsive treatment (ECT) of patients with major depression. We use a neural network model based on neo-cortical circuitry, aiming at a deeper understanding of the mechanisms behind EEG signal generation and its relation to cortical structure and dynamics. We discuss how these methods can be used as a complementary tool to clinical and experimental methods in psychiatry and neuroscience.

Introduction

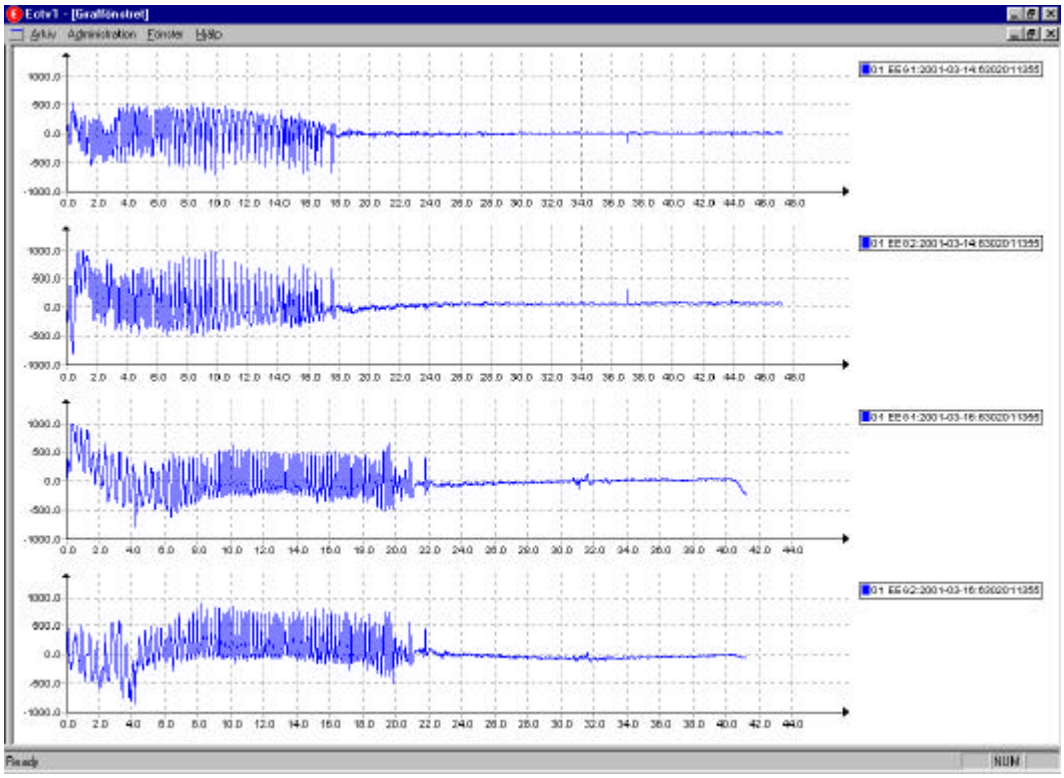
We use computational methods to investigate how cortical neurodynamics depend on network properties and on intrinsic and external signals and fluctuations. We have previously demonstrated plausible relations between structure, dynamics and function (primarily pattern recognition and associative memory) of a neural network model of the olfactory cortex and hippocampus (Liljenström 1991, Liljenström & Hasselmo 1995, Liljenström & Wu 1995, Liljenström & Århem 1997). Here, we investigate the role of network properties and external input on electroencephalography (EEG) dynamics, in particular relating to electroconvulsive treatment (ECT) of patients with major depression.

ECT is by far the most effective method to treat severe depression. Although the EEG after ECT-stimulation in general exhibits a specific pattern of seizure in the central nervous system (CNS), preliminary data show that there are differences between individuals depending on seizure threshold, stimulus doses and sub-diagnosis of major depressed (Wahlund et al., 2003). Moreover, in a series of several treatments, the first post-ECT EEG pattern contain most of the variation of information of how an individual respond the electrical stimulation (Abrams 2002; Wahlund et al., 2003). Thus, post-ECT EEG data overall shows similarities but with stochastical variation, as shown in Fig 1a) and b).

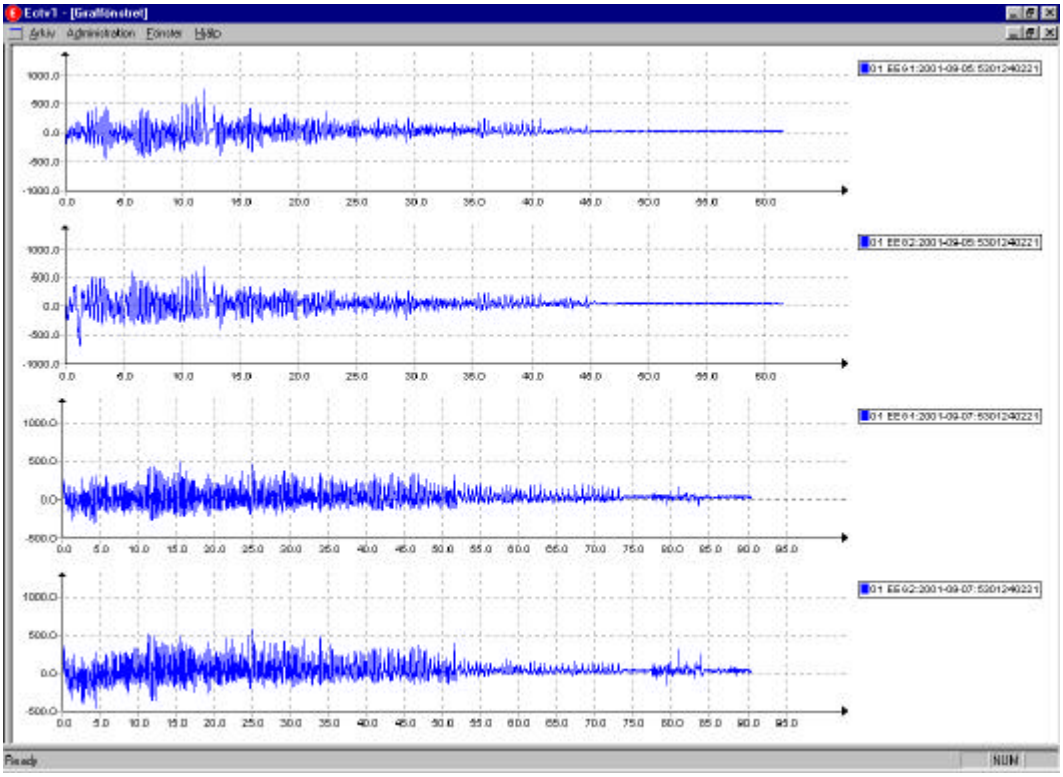
This paper approaches a quantitative description of the mechanisms underlying the EEG-signal. We also discuss to what extent computational methods of the kind described here can be used as a complementary tool to clinical and experimental methods in furthering our understanding of the complex brain dynamics and functions.

Methods

Using a computational model based on neo-cortical circuitry, and with realistic parameter values, we analyzed EEG-like time series by varying the connection patterns between neurons and by using different types of input. Our model is based on a previous model by Giannakopoulos *et al* (2001), but with modified connections, aimed at more realism (see below). Pairs of excitatory and inhibitory neurons form the basis of the previous model, and are organized in a square lattice with lattice distance being 0.2mm. The excitatory and inhibitory neurons of each pair are mutually connected. In addition, the inhibitory neurons were also connected through self-inhibition, while the excitatory neurons are connected only to other excitatory neurons in the network, in addition to inhibitory neurons.



a



b

Fig 1. Human EEG traces after ECT in two individuals with recurrent major depression using left prefrontal-to-ipsilateral electrodes (Fp1 and Fp2 according to the 10-20 system). 1a) The two first EEG recordings on top represents the CNS seizure immediately after the first ECT-stimulus ended (see label on right). The EEG on top represents the left EEG recording (Fp1) and the EEG just below this represents the right recording (Fp2). The two EEG recordings below represents the post-ECT stimulus EEG at the second treatment, as described above. 1b) Data from another patient, but with a different CNS seizure pattern (for explanations, please see above under 1a).

Connections are modeled with distance-dependent delays. The delays were due to a 1 ms synaptic delay, and also to the time a signal takes to travel through the axonal and dendritic trees between the output and target neurons with the propagation velocity 0.5 m/s. Neurons were modeled as continuous output units with realistic time constants.

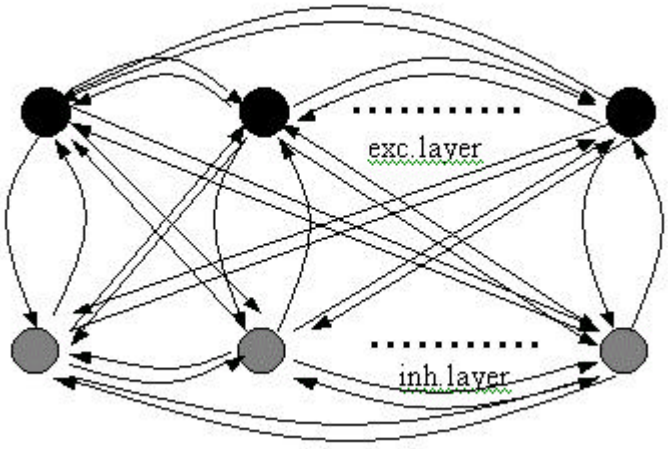


Fig 2. The basic circuitry of the neural network model used.

The cortical model uses continuous output units, of a Fitzhugh-Nagumo type, see below:

$$\dot{v}(t) = c(w(t) + v(t) - \tfrac{1}{3} v(t)^3) + I \qquad (1)$$

$$\dot{w}(t) = (a - v(t) - bw(t))/c \qquad (2)$$

where v is the membrane potential and w describes auxiliary variables, I is the current generated by synaptic inputs, $a, b, c > 0$ are appropriate constants which guarantee the existence of the oscillation interval.

Our model may be regarded as a generalization of the model described above. We included the possibility to have excitatory-inhibitory, inhibitory-excitatory and inhibitory-inhibitory connections between neurons belonging to different pairs. The inhibitory-inhibitory connections may replace the self-inhibition applied in the model (Giannakopoulos *et al* (2001)), and would thus represent a more realistic situation. In addition to this, we allowed for some of the inhibitory neurons to be eliminated, so that our model can reflect the anatomical findings that about 80% of the neo-cortical neurons are excitatory (see for instance G.M.Shepherd, 1998).

The values of the network parameters were mainly taken from the paper published by F. Giannakopoulos *et al* (2001). The ECT-stimulus doses parameters we used were predetermined according to age and sex, and had a frequency-range of 60-80 Hz and pulse width of 1 ms (Wahlund et al., 2003). For practical reasons, the ECT input used in our simulations was applied with a shorter duration than in the clinical case, everything else being similar.

Our simulations were run on a PC, mostly with the choice of 10x10 network units, with periodic boundary conditions for the connections. We developed a graphical user-friendly interface, which made it easy to control the parameters, (the connection strengths, the number of excitatory and inhibitory neurons) in the model and the input.

Results

Simulations were run with differences in connections, external input, parameters and number of inhibitory neurons. The dynamics of the network were quite different in the different cases. The graphs in the figures below show the membrane potential on the y-axis and time (1 unit = 0.1 ms) on the x-axis. The mean activity is taken as the EEG readout.

Figure 3 shows the user interface of our software. A network with 100 inhibitory and 100 excitatory neurons was applied to give the signal shown in the figure.

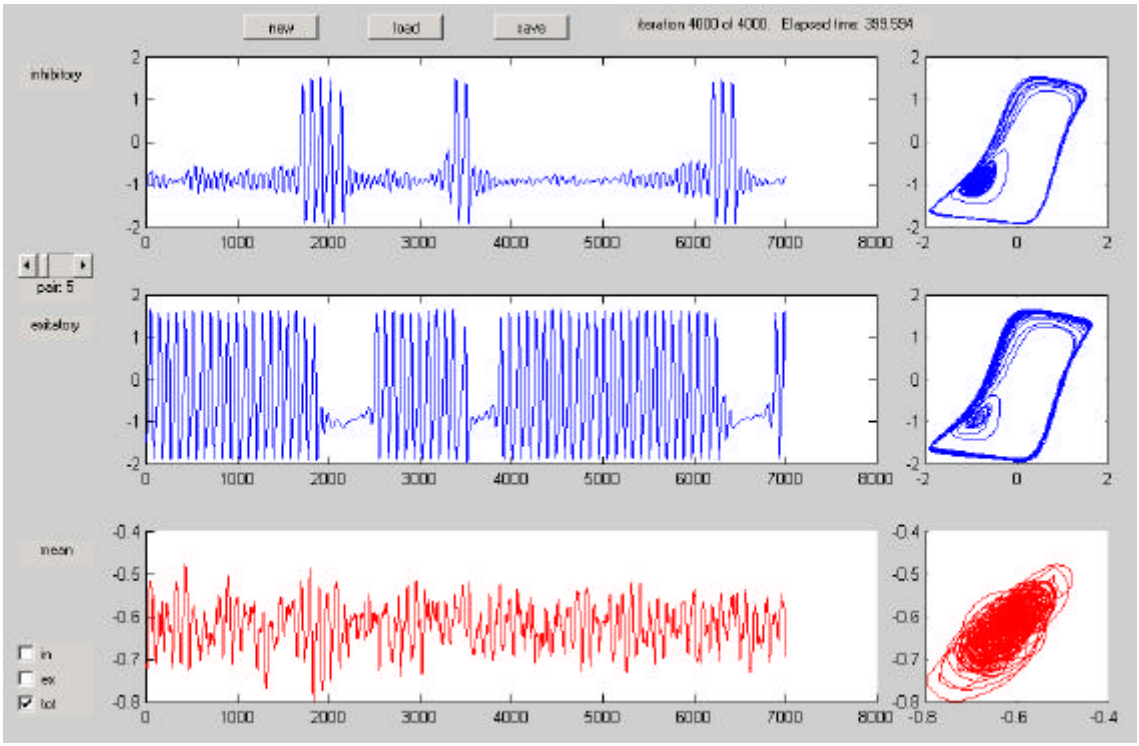


Fig. 3. The user interface of our software. The upper figures shows the membrane potential of a arbitrary inhibitory neuron in the network, and phase portrait of this activity. The middle figures show the same for an excitatory neuron. The figures at the bottom show the mean activity of the network units. The phase portrait implies that there is chaos in the mean activity. The network used, was a strongly connected one, concisting of 100 inhibitory and 100 excitatory neurons. The input signal was constant.

In Fig. 4 we show how the mean activity of the network in Fig.3 responds to an ECT-input. We see clearly the burst-like activity, showing that the ECT-input has synchronized the network. Note also that the amplitude is much larger for the post-ECT-activity.

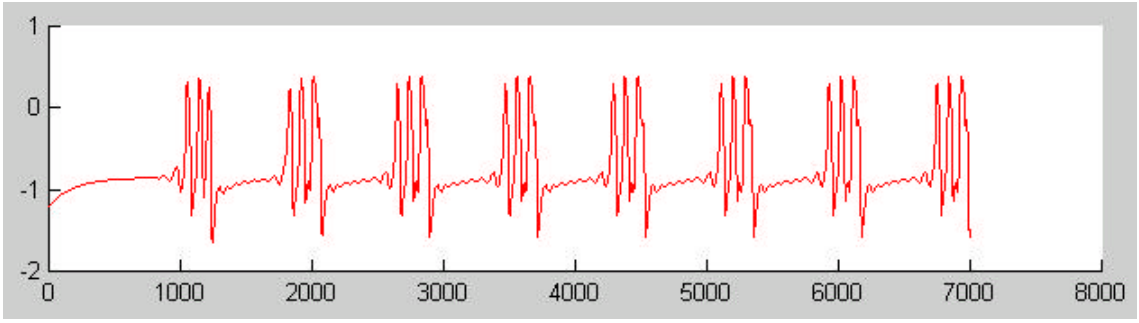


Fig. 4. Simulations with the same network as in Fig 3. An ECT input was applied.

We created a new network structure by removing 75 of the inhibitory neurons from the one described above, so that 80% of the total number of neurons were excitatory. This we did in order to mimic the situation in the real neo-cortex. The figures 5 and 6 show the mean activity of the network with a constant input and with ECT input, respectively. Note the difference between this network and the network above, in their reactions to ECT.

In the network with only 25 inhibitory neurons, the ECT-response (Fig. 6) is rather similar to the clinically measured response, as shown in Figure 1. Note that the ECT increased amplitude in Figure 6 gradually decreases towards the post-ECT amplitude in Figure 5.

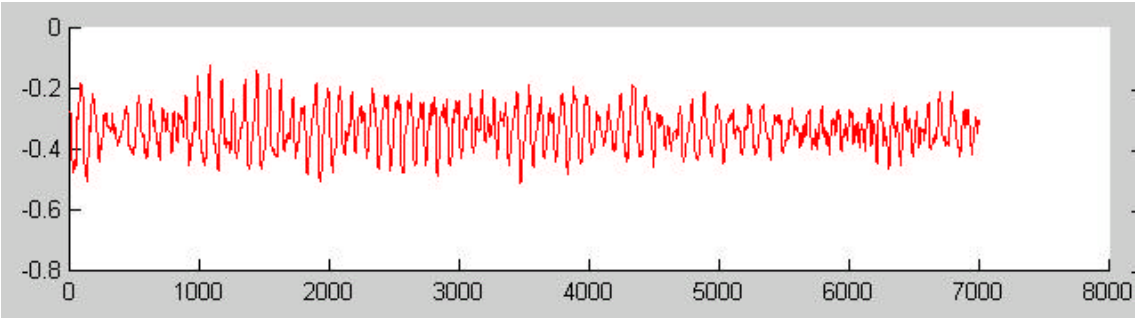


Fig. 5. The mean activity of a network with 100 excitatory and 25 inhibitory neurons. The input signal was constant.

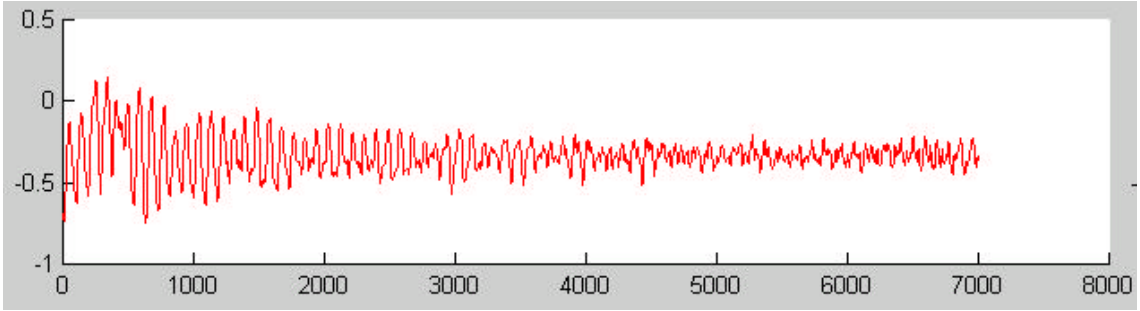


Fig. 6. Mean activity as the network in Fig. 5 responds to an ECT-like input. The increase in amplitude gradually dies out.

By increasing the strength of the inhibitory connections, we obtained a network that reacted on ECT in a way shown in Figure 7. Apparently, there are some similarities with the clinical signal shown in Figure 1b. As argued in the introduction, there are individual differences in the EEG response to ECT. The results we present suggest that these individual differences could be reflected by the strength of the inhibitory connections.

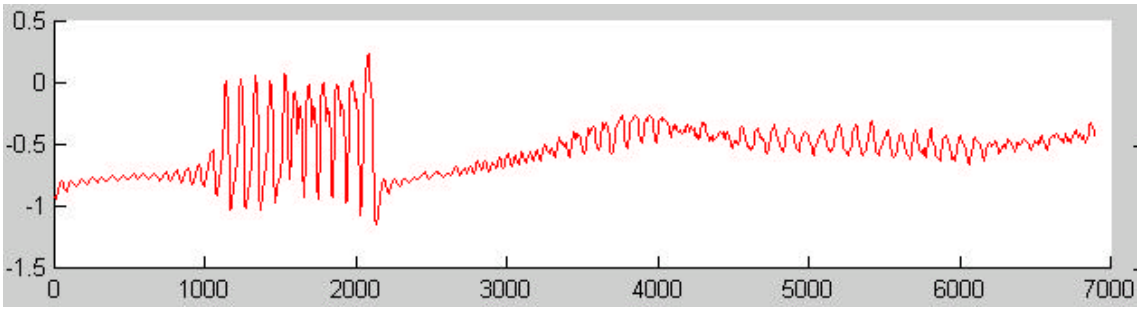


Fig. 7. Post ECT-activity of a network with strengthened inhibitory connections. The graph shows a silent (post-ictal-like) period, followed by a burst that in a sudden way dies out.

Discussion

Some of the similarities we have pointed out between the model-generated activity and the clinically measured EEG could seem rather “far-fetched”. Obviously, the quite oversimplified circuitry we used in our model is only a cartoon of the real neo-cortical circuitry, but can function as a first abstraction. The model shows, however, that even a simple network like the one we propose, can generate many different forms of complex activity.

An aim for our further studies is to advance the model presented above, in order to include more aspects from the realistic neurobiological neo-cortical circuitry. By eventually including major neuronal loops, such as the cortico-thalamic loops, as well as connections to hippocampus and amygdala, we hope to get even more realistic computer simulations. Moreover, by adding input from variation in the major neuromodulator systems, such as serotonin and noradrenaline, and with their nuclei in the brainstem, the simulation are expected to become even more "realistic".

Our results will be discussed in the more general framework of EEG and treatment of mental disorders and brain function. The simulation models mimicking the experimental signals in terms of post-ECT stimulus EEG opens a possibility to determine optimal ECT stimulus doses for clinical effect. Moreover, by use of our currently increasing database, including post-ECT EEG and other physiological parameters and clinical data, it is possible to include statistical variation in the computer models. By use of these new stochastically based computer models, it is conceivable to get a better understanding of brain dynamics, in terms of neuromodulation and balance between excitation and inhibition in the CNS.

Acknowledgement

This work was made possible through grants from the Swedish Research Council.

References

Abrams, R (2002) *Electroconvulsive Therapy*. New York: Oxford University Press Inc.

Giannakopoulos, F., Bihler, U., Hauptmann, C. and Luhmann, H.J. (2001) Epileptiform activity in a neocortical network: a mathematical model. *Biol. Cybern*. 85,257-268.

Liljenström, H. (1991) Modeling the Dynamics of Olfactory Cortex Using Simplified Network Units and Realistic Architecture. *Int. J. Neural Systems* 2, 1-15.

Liljenström, H. & Hasselmo, M.E. (1995) Cholinergic modulation of cortical oscillatory dynamics. J. Neurophysiol. 74:288–297.

Liljenström, H. & Wu, X. (1995) Noise-enhanced performance in a cortical associative memory model. Int. J. Neural Syst. 6:19-29.

Liljenström H. and Århem, P. (1997) Investigating Amplifying and Controlling mechanisms for Random Events in Neural Systems.In: *Computational Neuroscience*, (Ed. J.M. Bower), New York: Plenum Press.

Sheperd, Gordon M. (1998) The synaptic organisation of the brain. Oxford University press, Inc.

Wahlund B, Piazza P, von Rosen D, Castillio-Restrepo J (2003) Frequency distribution of ictal EEG patterns after ECT stimulation in subgroups of major depressed. A preliminary study. (Submitted for publication).