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Modelling of Biologically Plausible Excitatory Networks: Emergence and Modulation of Neural Synchrony

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Abstract. To emphasize the electrical nature of information processing in the brain we use a compartmental model of single neurons. The realistic simulation of wave-like activity in the recurrent excitatory network is similar to the intracellular activation in rat embryonal cerebral cortex cultures [1]. The natural structure of the network is reproduced by including interactions between different functional neurons. We start by reproducing spontaneous electrical activity of single neurons. After massive simulations selective influences are comparable to in vitro measured activity. We show adaptation of the network behavior by introducing external stimulation.

1 Introduction

Neurons of the embryonic cerebral cortex of vertebrates develop synchronous oscillatory network activity during the second week in culture. It is assumed that this early network activity is necessary to form a functional synaptic microcircuitry with self-organizing properties [1, 2], but the mechanisms involved are still unclear. Here we reproduce the biologically realistic parameters of the early cortical culture in a computer simulation. We hope to be able to make previsions about hidden parameters contributing to the network dynamics and to uncover hints for better design and initialization of artificial neural networks.

There are different approaches for modelling neural network activity, e.g. phenomenological descriptions on a systemic level [4], coupled oscillators like Wilson-Cowan-oscillators [8] or computationally efficient models such as the Integrate-and-Fire-model [6]. To adapt the simulation to experiments, we use a more realistic model of individual cells of different types with unique behaviors and connecting patterns. We focus on two types of neurons, namely glutamatergic-like projection neurons and GABAergic-like interneurons. Glutamatergic neurons are normally excitatory and more frequent than GABAergic interneurons, that are normally inhibitory in the adult networks. In the early cortical network GABAergic interneurons are however depolarizing [2] and are required for the development of

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oscillatory synchronous activity, probably working as integrator elements for synchronization [1].

2 Model Description

2.1 Neuron Model

We use a compartment model (Fig.1a) to simulate the neuronal behavior numerically [5]. A modeled neuron consists of two coupled cylindrical compartments that correspond to different subcellular compartments (Fig.1c). An input compartment simulates the signal integration of dendrites and contains several input synapses with specific time constants. In the excitable compartment (soma and axonal hillock) the impulse generation is produced by voltage-dependent active Hodgkin-Huxley Na^+ and K^+ channels. The axon is modeled by spike transmission with adjustable delay.

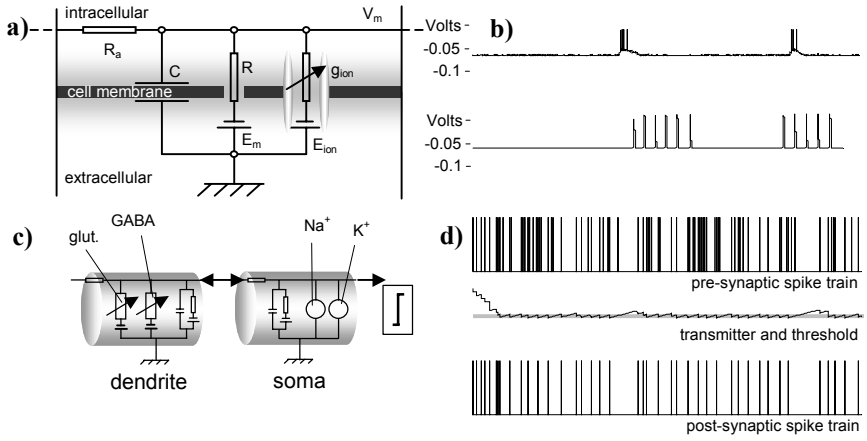

Fig.1 Neuron model. a) compartment model with voltage-dependent ion channel b) spontaneous activity clamped in real cultures and calculated in simulated networks in single neurons (somatic membrane potential), c) dendrite and soma as coupled compartments, d) synaptic depression: pre-synaptic spikes, availability of transmitter and post-synaptic spikes

Empirical pharmacological intervention in cell cultures showed a period of synaptic depression after each burst activity, that is probably caused by exhaustion of neurotransmitters at the synapse. This depression is the only attenuation of network activity in this network. An economical way to implement the depression in our model is to utilize an additional compartment reflecting the amount of transmitter available. If this amount is below a critical threshold spikes are not transmitted (Fig.1d).

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2.2 Network Model

To achieve a recurrent probabilistic network, we design populations of neurons and their connections stochastically. A section of the network is generated by adding a certain number of neurons with arbitrary positions. Unlike regular matrix-patterns where the number of units is limited to certain numbers, any density of neurons may be chosen in the arbitrary distribution used here. Considered as a spatial distribution, these set of positions can be de-clustered, scattered uniformly over the section's area with adaptive rules in terms of self-organizing-maps according to [7], which can be used to configure the spatial entropy of the distribution. This is done separately for each type of neurons, to homogenize the structure and prevent overlying of neuronal positions.
To generate the synaptic couplings in the network, we connect the neurons according to a probability model. For each pair (n_i, n_j) of neurons we calculate the probability of a possible connection between them. Each neuron has a terminal region defined by a random set direction and distance (axon length, $d_{min} < d < d_{max}$). Inside this terminal region the probability of a connection decreases with distance from the center by Gauß-Laplace distribution (standard deviation Φ).

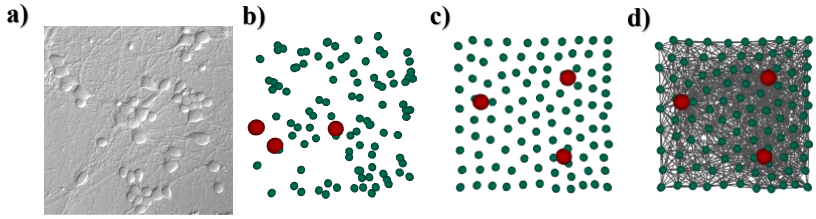

Fig.2 Network model. a) image of a real culture b) insertion of neurons, c) de-clustering d) generation of connections

The number of established connections in biological networks increase in time by a sigmoidal distribution (center t_m, scale factor c). To simulate this effect, each connection gets a time stamp, in which the activation time is stored. During simulation the connections are established by a script.

2.3 Parametrizing the Model

The free parameters for each of two different neurons (glutamatergic and GABAergic) can be set individually. Glutamatergic cells are numerous (100 in test region) and small (soma size *10.0 x 10.0 µm*; dendrite size *2.0 x 50.0 µm*) and make synapses with small time constants (*tau = 3.0 ms*). Additionally this cells discharge spontaneously (Poisson-distributed intrinsic spontaneous activity [3]). GABAergic cells are bigger (soma size *30.0 x 30.0 µm*; dendrite size *2.0 x 200 µm*), but less numerous (*0-5* in test region) and have synapses with larger time constants (*tau = 20.0 ms*).
The parameter of connections can be configured separately for each source target cell type combination. GABAergic neurons have larger terminal region and also receive

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more inputs (*glutamatergic to glutamatergic μ=0.1mm, σ=0.1mm; glutamatergic to GABAergic μ=0.2mm, σ=0.2mm; GABAergic to glutamatergic μ=0.2mm, σ=0.2mm; GABAergic to GABAergic μ=0.4mm, σ=0.1mm*). This values will be gradually optimized according to physiological experiments and literature.

3 Simulation and Results

3.1 Emergence of Wave-Like Activity by Coupling Neurons

First we simulate the network with a varied number of integrated GABAergic neurons. In Fig.3 three different network configurations and their outputs with 100 glutamatergic and zero, two and four GABAergic neurons are shown.

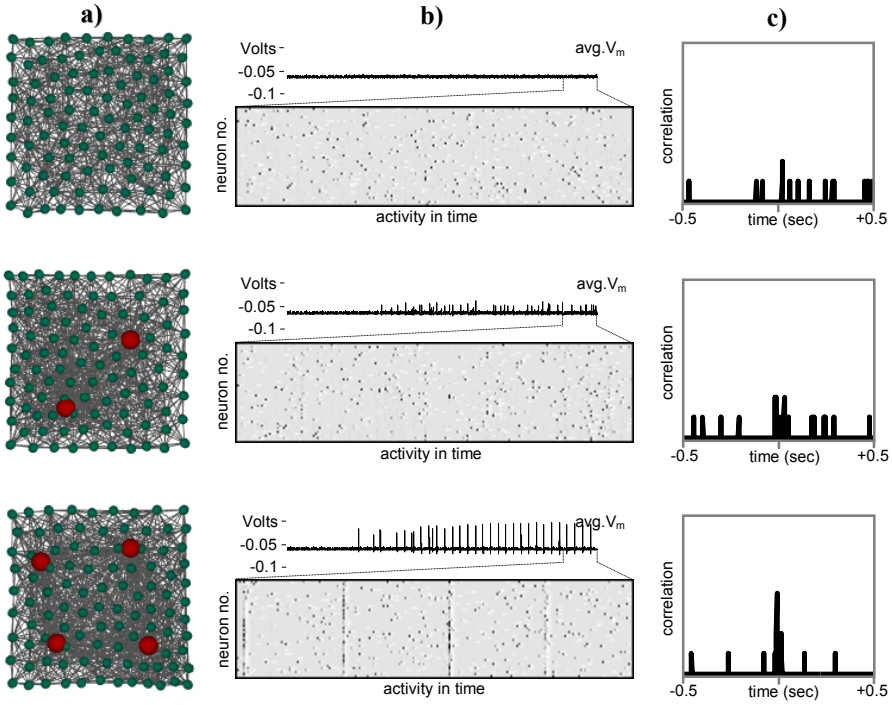

Fig.3 Influence of GABAergic neurons to the dynamic of network, a variation of 100 glutamatergic neurons and 0, 2, and 4 GABAergic neurons. a) network structure, b) network activity (average somatic membrane potential in Volts) and a section of the history, c) cross-correlograms between spiketrains of between two randomly selected glutamatergic cells.

The network unfolds an intrinsic behavior when gradually coupled. In a network without GABAergic neurons no synchronous behavior can be seen. A distinct synchrony in behavior can be observed with rising number of GABAergic neurons. They are assumed to act as activity-integrators by above described properties [1].

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A rhythmic wave-like dynamic emerges with a stable frequency, which depends on the depression time of the glutamate synapses, and amounts in biological early neurons to approximately one time per minute.
Firing neurons tend to synchronize their locally stored historical information, that in this case reflects the time point of reactivation state after synaptic depression. Neurons which are firing asynchronously (out of phase) with the wave-like dynamic state will be attracted to synchrony. This specific wave-like activity of synchronous firing is a emergent network characteristic.

3.2 External Stimulation

We can influence the rhythm by adding an external rhythmic input. For this purpose we define a receptive area which influences a subset of the neurons (Fig. 4a). The stimulation is achieved by adding extra synapses to the neurons inside the predefined receptive area.

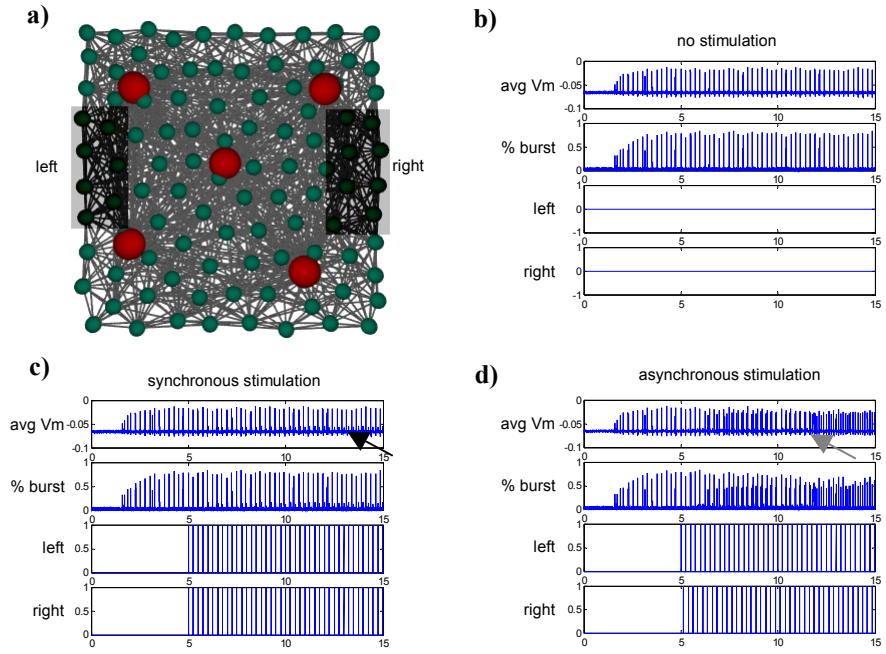

Fig.4 External stimulation of the network. a) local excitation areas, b) without stimulation (average membrane potential, network activity, left and right stimulus spike trains), c) synchronous (in-phase) stimulation, d) asynchronous (anti-phase) stimulation

In this simulation we use two of this receptive areas, localized at opposite border regions of the network. Each one is covering about five percent of the network and is feeding all neurons in these areas with stimulus patterns (Fig 4 b-d)

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This local stimulation modifies the activities of neurons in the whole network. In Fig.4 it can be seen how the stimulation progress influences the network behavior.
With just one excitatory pulse or several synchronous pulses the neurons are firing accumulated activity in the phases between the network bursts (Fig.4c black arrow). Applying several excitatory pulses (asynchronous, in phase opposition excitatory) leads to a forced de-synchronization and split up of the network (Fig.4d gray arrow).

4 Conclusion and Discussion

These are the first steps of modeling this network. We hope that biological experiments give further suggestions for improving this model. The appeared oscillation emerges as a network quality with GABAergic neurons without global clocks like pacemaker neurons.
In the next step we will add dynamic subcellular mechanisms like the development of glutamatergic receptors (from “silent” synapses to functional ones) and dynamic Hebb-like adaptation behavior. The stimulation patterns of the network can be extended toward images, to investigate the synaptic initialization and explore its potentialities for applications of associative memory modules.

Acknowledgments

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References

1. T. Voigt, T. Opitz, and A. de Lima: Synchronous Oscillatory Activity in Immature Cortical Network is Driven by GABAergic Preplate Neurons. The Journal of Neuroscience 15: 8895-8905, 2001.
2. T. Opitz, A. de Lima, and T. Voigt: Spontaneous Development of Synchronous Oscillatory Activity During Maturation of Cortical Networks In Vitro. The Journal of Neurophysiology 88: 000-000, 2002.
3. A. Harsch, H.P.C. Robinson: Postsynaptic Variability of Firing in Rat Cortical Neurons: The Roles of Input Synchronization and Synaptic NMDA Receptor Conductance. The Journal of Neuroscience 20(16): 6181-6192, 2000.
4. J. Tabak, W. Senn, M. O’Donovan, J. Rinzel: Modeling of Spontaneous Activity in Developing Spinal Cord Using Activity-Dependent Depression in an Excitatory Network. The Journal of Neuroscience 20(8): 3041-3058, 2000.
5. J.M. Bower, D. Beeman: The Book of GENESIS, 2nd edition. Springer-Verlag New York, 1999.
6. W. Maass and C.M. Bishop (Eds.): Pulsed Neural Networks. Cambridge, Ma.: The MIT Press / A Bradford Book, 1999.
7. B. Fritzke: Vektorbasierte Neuronale Netze. Shaker Verlag, Aachen, 1998.
8. T. Ueta, G. Chen: On Synchronization and Control of Couplet Wilson-Cowan Neural Oscillators. International Journal of Bifurcation and Chaos, Vol. 13, No. 1 (2003).