Modeling Spike-Wave Discharges in the Brain with Small Neurooscillator Networks

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Introduction

Pathology of coupling architecture in the thalamo-cortical system is considered to be the main cause of absence epilepsy, which primary eletroencephalographic manifestation is spike-wave discharges (SWDs). In this study, we propose a simple mathematical model of 14 identical Fitzhugh–Nagumo neurons, organized in accordance with modern ideas about the thalamo-cortical brain network. In this model long transients in response to short-term pulse driving from a separate neuron, representing the nervus trigeminus, are shown to be a possible candidate for a SWD model.

Model

To simulate SWDs, it is important to take into account at least two thalamic nuclei: the reticular and ventroposteral medial, as well as the somatosensory cortex, which, in turn, consists of two types of cells: pyramids and interneurons. We used the scheme from [1] as a basis. In this case, the number of neurons was reduced in each of the populations to a minimum, so that we have the number of interneurons $N_{IN}=1$, the number of pyramids $N_{PY}=4$, the number of reticular cells $N_{RE}=4$ and the number of thalamocortical cells $N_{TC}=4$. In addition, an external input modeling the trigeminal nerve was introduced (one neuron, further designated as *NT*, $N_{NT}=1$).
Connections in the network are obtained using a pseudo-random number generator with imposition of restrictions that follow well-known laws of the anatomy of the thalamo-cortical system. In addition, some conditions were imposed, caused by rapidly used model neurons, since there are very few of them in comparison with the known network models [2, 3]: unconnected neurons, as well as neurons with only outgoing connections were prohibited. Also, all neurons were to influence each other directly or indirectly. The resulting network is depicted in Figure 1.

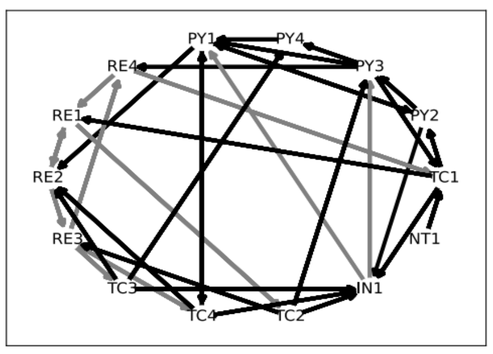

Figure: 1 Connection graph of 14 neurons of model (1). Positive links (for which $k_{i,j}>0$) are shown in black, negative ones ($k_{i,j}<0$) are shown in gray.

For an individual neuron, one of the simplest neuron models was used — the FitzHugh-Nagumo model in the simplified form (1), since such a form contains only one bifurcation parameter that simultaneously regulates the amplitude and frequency of oscillations, and is also convenient for further implementation in the form of an electrical circuit.

$$\varepsilon\frac{du_i}{dt}=u_i-\frac{u_i^3}{3}-v_i+\sum_{j=1,j\neq i}^{N}k_{i,j}u_i \qquad (1)$$
$$\frac{dv_i}{dt}=u_i+a_i$$

where the parameter a_i determines the characteristics of the conductivity of ion channels; $\varepsilon>0$ is the relative rate of change in slow ion currents; $k_{i,j}$ is the coefficient of connection between the *i*-th and *j*-th neurons..

Model equations (1) were solved using the *scipy.integrate.odeint* function from the *scipy* package, based on the *LSODA* standard library procedure, which in turn uses the Adams method and the "*back differentiation formula*" (*BDF*). The sampling step was equal to $\Delta t = 2^{-5}$. A transient of 15,000 values was discarded.

All connection coefficients $k_{i,j}$ that are not equal to zero took one of three values: k_{br} for positive connections within the network, $-k_{br}$ for negative connections within the network, and k_{NT} for the connection *NT*→*TC1*, that is, from the side of the external input to the network. All neurons were identical except for the *NT* neuron. The parameter $\varepsilon = 0.1$ was fixed, and the parameter $a_{i\neq NT} = a_{br}$ was changed to achieve the desired system behavior. The parameter $a_{NT} = 0.82$ was set in such a way that the trigeminal nerve neuron was always in an oscillatory mode: it was shown in [4] that the value $a = 1$ is bifurcational - there is an Andronov – Hopf bifurcation, and oscillations develop at $a < 1$.

Results

Oscillations in the autonomous model of thalamocortical network.

The Andronov - Hopf bifurcation, which exists in individual model neurons at $a = 1$, is preserved at small k_{br} in the autonomous system. However, starting from approximately $k_{br} \approx 0.02$, the generation of oscillations occurs rigidly through the bifurcation of the creation of a cycle from the condensation of phase trajectories. In this case, the Andronov - Hopf bifurcation does not disappear anywhere, it just happens later - with a smaller value of a_{br}. Subsequently, with an increase in k_{br}, more and more new bifurcations of the cycle of birth from condensation, for example, at $k_{br} \approx 0.11$, $k_{br} \approx 0.20$ and $k_{br} \approx 0.23$, as can be seen in Fig. 2, where there are discontinuities on cycle birth lines at the corresponding k_{br}.

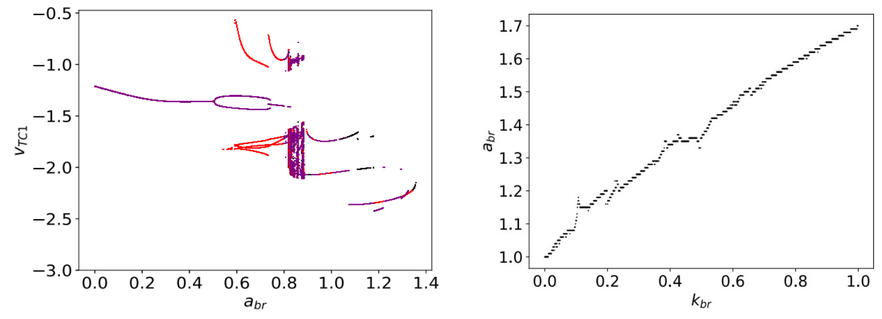

Figure: 2 Bifurcation diagram in the a_{br} parameter for the *TC1* neuron at k_{br} = 0.4, constructed by superimposing diagrams calculated under three different initial conditions (black, red, and lilac, respectively) - (a) and the bifurcation line of the birth of the limit cycle in model (1) at different levels of connections within the thalamo-cortical network on the plane (k_{br}, a_{br}) – (b).

Thus, in the system consistently with an increase in the strength of internal connections, more and more mechanisms for the implementation of oscillatory dynamics with hard excitement while maintaining the previous ones. These mechanisms allow to realize oscillations with ever larger a_{br}, that is, ever farther from the excitation threshold of an individual neuron. At the same time, far (below) from the line shown in Figure 2, b, multistability takes place, when several oscillatory modes are present at once, since the previous bifurcations do not disappear, but with an increase in k_{br} they shift towards large a_{br}, which is clearly seen from the bifurcation diagram (see Figure 2 , a), where different colors (black, red and lilac) denote points obtained under different initial conditions. Slightly below the line itself (except for very small $k_{br} \leq 0.02$) bistability occurs: the coexistence of a stable point and a cycle.

Induced oscillations

It was shown in [5] that stimulation of the trigeminal nerve can be one of the possible scenarios for the transition to epileptiform activity. Further, we assume that a relatively short sequence of pulses arrives in the thalamus from the trigeminal nerve, triggering oscillations in the network. These oscillations are at first forced, and then, after the end of the impact, they continue for some time. The possibility of continuing oscillations after the end of the driving is due to the setting of the a_{br}, parameter so that the system is in a non-oscillatory excitable state near the bifurcation of the cycle birth from the condensation of phase trajectories. In such a situation, after the termination of the external influence, the system enters the concentration of phase trajectories and continues to oscillate for some time, as shown in Figure 3. In fact, such oscillations represent a long transient process. They are largely regular, but at the same time not exactly periodic, which is also typical of experimentally observed peak-wave discharges.

The number of oscillations v after the end of the impact depends on several factors. First, the driving must be long enough (see Fig. 3, a), since otherwise it does not have time to exite the entire network. Second, the number v depends on the proximity to the bifurcation curve: a small change in parameters significantly changes the number of residual oscillations. Third, the number of residual oscillations depends not only on the duration of the driving, but, starting from a certain minimum duration, primarily on its phase (i. e. on the driving termination moment t_{fin}). The dependence $v(t_{fin})$ in Figure 4 has a pronounced periodic structure, although longer transient processes are more common with increasing driving length.

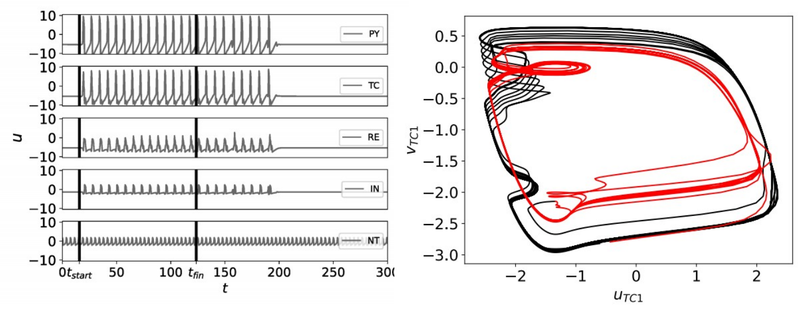

Figure: 3 Part (a) - time series summed up by the types of neurons, oscillations *u* of the thalamo-cortical network model before connecting, during and after disconnecting the action from the trigeminal nerve (neuron *NT*) at a_{br} = 1.337, a_{NT} = 0.82, k_{br} = 0.4, k_{NT} = 0.4. Black lines indicate the beginning and end of the impact. Part (b) is the projection of the phase trajectory onto the plane of the variables of the *TC1* neuron at the same time interval as shown in fragment (a), where non-autonomous dynamics are denoted in red, and autonomous dynamics are denoted in black, including 9 residual oscillations immediately after the end of the action.

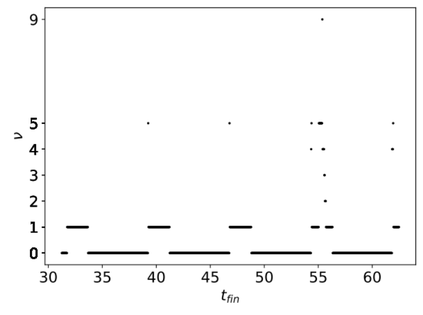

Figure: 4 Dependence of the number of residual oscillations v in system (1) on the duration (final moment t_{fin}) of external influence

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