Modeling limbic seizure initiation with an ensemble of delay coupled neorooscillators

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Abstract. A mathematical model of initiation mechanism for focal limbic seizures is proposed. The epileptic focus is assumed to be a relatively small network of neurons distributed over the hippocampus, generating an epileptic activity. This activity frequency is a function of the main loop length and coupling delays. This frequency can change by activating or deactivating some network elements. FitzHugh–Nagumo equations are used for network nodes.

Introduction

The limbic (temporal lobe) epilepsy is a widespread neurological disease, characterized by spontaneous seizures. Large amplitude oscillations in different areas are highly synchronized and well studied both in humans [1] and in animal models [2]. But the initial pathological activity source (epileptic focus) is somewhere in the hippocampus, with its localization being still not completely understood [3]. Here we hypothesize that the focus is not a spatially local phenomenon, but a partly isolated circuit consisting of relatively small number of neurons, which is distributed over large part of hippocampus (hippocampal pyramid neurons are know to have many long range projections, including projections to hippocampus itself). This circuit can "sleep" for a long time, and cannot be detected since there are no clinical symptoms, and moreover, even for animal models where the epilepsy is prospected, local field potential electrodes cannot measure its activity due to relatively small number of cells in the circuit, and consequently, small impact of this circuit into the local field. The single unit intra- or extracellular electrodes are unlikely to be located in the right place for the same reason, and the circuit stays unrevealed. But at some point, elements of the focal circuit become involved in the larger hippocampal networks, and start to translate their dynamics to the other regions, forcing the synchronized oscillations. This is seizure generalization. The models of the proposed type — network mesoscale epilepsy models — are not very popular since it is hard to find the balance between incorporation of individual cell properties like different GABA, glutamate and CB1 receptors from one hand, and correct representation of cell numbers and networks in different brain regions. Still, some recent models were successfully constructed [4, 5].

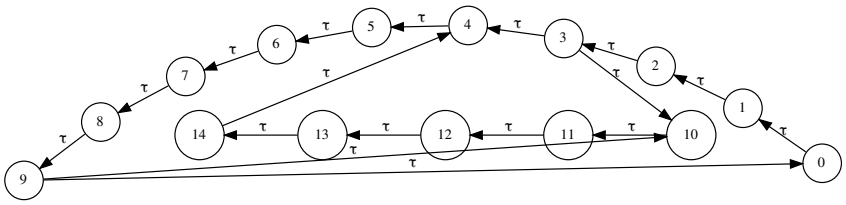

Figure 1: A scheme of the proposed network organization with two circuits major and minor, for changing the generation frequency.

Results and discussion

Networks of 15–50 FitzHugh–Nagumo oscillators coupled in the way, presented were constructed, with the parameters for individual nodes taken from [5]. It was shown that the oscillation shape and frequency can be managed with changing the delay time τ and a small number of couplings (switches) in the system. The delay time and the number of oscillators were set in the way to match the physiologically proven values. Such a circuit can be used as a model of epileptic focus, in which the main loop length determines the oscillation frequency. With additional switches turned on and off, the main frequency can both slowly decrease and rapidly change during the seizure as it usually seen in real electroencephalograms.

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