Simulation of Neocortical Epileptiform Activity using Parallel Computing

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Summary

Clinical recordings of bioelectricity generated in the brain from epilepsy patients, reveal abnormal activity over large cortical areas containing hundreds of thousands of neurons. Therefore, this type of measurement doesn't reveal much detail of underlying activity at the cellular level or in the cortical microcircuitry. Studies in animal models of epilepsy, or in slices from resected tissue from epilepsy patients, described paroxysmal cellular behavior and network activity [e.g. 1,4,9,15,17,18]. Models of neural elements provide an alternative for the study of underlying processes of brain pathologic behavior. The cell's intrinsic properties or network parameters of the model can be examined as potential mechanisms for evoking and sustaining physiologic bursting patterns or pathologic seizure-like activity. Studies that focus on intrinsic membrane properties, small neural networks, or larger networks with reduced complexity at the cellular level were described previously [e.g. 3, 5, 7, 8, 11, 13, 20, 22].

Our objective was to create a network (scalable to 10^5 elements) with sufficient detail to examine both intrinsic properties and network function during epileptiform activity. We focused on neocortical structure because of our interest in pediatric epilepsy; epileptic foci in children are frequently found in different parts of neocortex, and (unlike in adults) often outside the temporal lobe. We included an EEG generator for comparison between simulated activity and clinical data. Individual cells are modeled as multi-compartment units with Hodgkin and Huxley type Na^+ and K^+ channels [10].

The neocortex is organized in six horizontal layers and shows vertical organization in modules, or (micro-)columns [14, 16, 19]. The canonical circuit for neocortex, first proposed by Douglas and Martin [6], was the basis for our model's cell types and connectivity (Fig. 1).

The major neural component of neocortex consists of two types of pyramidal cells.

1. the superficial neurons in layers 2,3 (S_, Fig. 1) and
2. deep cells in layers 5,6 (D_, Fig. 1).

The distinction between the superficial and deep cells also relates to the target of their axons: intracortical for the superficial cells and intracortical plus subcortical for the deeper ones.

Inhibitory units in neocortex are commonly subdivided into different subtypes [6, 16].

3. Basket cells (B, Fig. 1) inhibit the pyramidal cell's soma and receive inputs from the pyramidal cells. A part of the basket cell's connections is with other interneurons [16, 23]. Krimer and Goldman-Racik [12] identified 3 types of basket cells which were classified on the basis of the range of the axon arbor.
4. Chandelier cells (C, Fig. 1) inhibit the initial segment of the pyramidal cell and receive inputs from the pyramidal cells [6, 12].
5. Other types of inhibitory neurons were not included in the current model.

A scalable network was built on the pGENESIS neural simulator [2]. The simulation software runs on the Chiba City and Jazz clusters of Linux-based PCs at Argonne National Laboratory. We examined effects of strength of excitation and inhibition on spontaneous activity and bursting in a neural network; results obtained with an earlier version of our model were described previously [21]. We demonstrated synchronization of inhibitory neural activity by gap-junctions and the relative contributions of the inhibitory and excitatory neuronal populations on the EEG (Fig. 2).

Acknowledgement

Supported by the Falk Grant and by the Mathematical, Information and Computer Sciences Division subprogram of the Office of Advanced Scientific Computing Research, U.S. Department of Energy, contract W-31-109-ENG-38.

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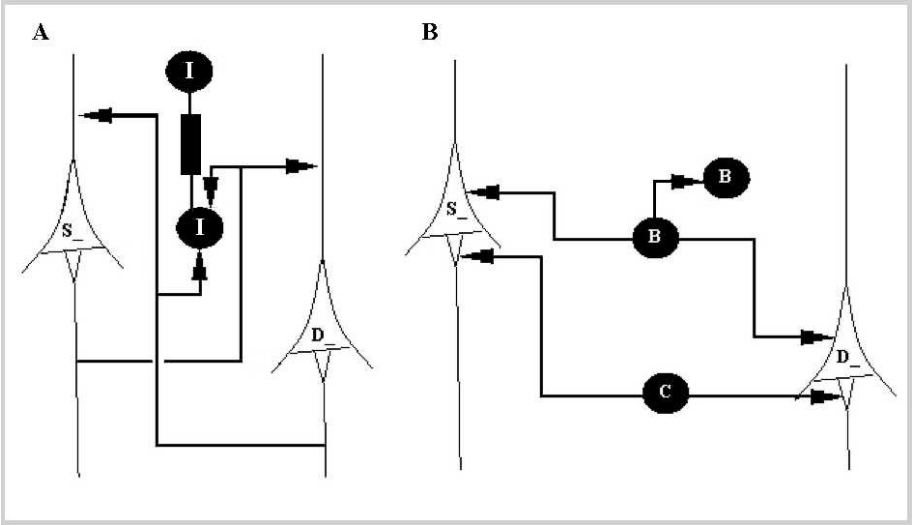
Fig. 1:
Overview of cell types and connectivity.

A. Excitatory contacts including gap-junctions depicted as a resistor between inhibitory cells (I); S_ and D_ symbolize the superficial and deep pyramidal cells.
B. Inhibitory synapses; Inhibitory neurons are symbolized by B and C (basket and chandelier cells respectively).

Fig. 2:
A 300 ms epoch of activity in a small 160-cell network. Both activities of pyramidal cell types are superimposed in the two upper traces. The next four traces are superimposed activities of inhibitory cell types; note the relatively strong synchrony. The two lower traces are the contributions of the excitatory and inhibitory populations to the EEG signal.


A
I
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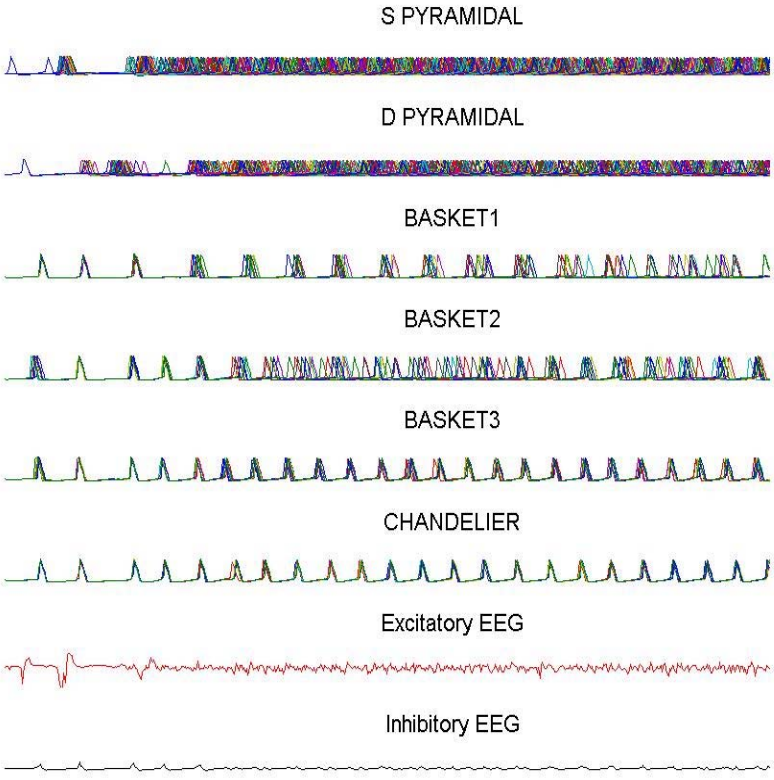
S PYRAMIDAL
D PYRAMIDAL
BASKET1
BASKET2
BASKET3
CHANDELIER
Excitatory EEG
Inhibitory EEG