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Dynamical effects of antiepileptic drugs on neurons affect network synchronizability

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Epilepsy is characterized by periods of excessive neuronal activity called seizures. While much is known about population behaviors of neurons during seizures, as measured by EEG electrodes, very little is known about the activity at the cellular level. The etiology of the disease can often be traced to specific mutations in particular ion channels [1]. These same ion channels are often the targets of antiepileptic drugs. Bridging the molecular scale causes and treatment of epilepsy to the network scale phenotype is a multi-scale problem that needs to be solved in order to develop more rational approaches to treating epilepsy.

Our research seeks to understand the basic mechanisms of epilepsy by understanding how network synchrony is affected by molecular level changes caused by epileptogenic mutations and antiepileptic drugs. Our approach is guided by experimental evidence, in a rat model of epilepsy, indicating that synchrony in the network changes over the different phases of the seizure [2]. Changes in synchrony may hold a key to understanding the causes and developing novel treatments for epilepsy. However, why synchrony changes during a seizure is still a mystery.

To better understand how neurons synchronize, we use pulse coupled oscillator theory [3]. The dynamics of the neuron are reduced to a simple input-output relationship, measuring how synaptic inputs applied at different phases of a periodically firing neuron advances or delays the spike, resulting in a Phase-Response Curve (PRC). From the measured PRC, it is possible to predict how a network of neurons will synchronize [4,5]. We then measure how epileptogenic mutations and antiepileptic drugs affect the neuron's PRC to infer how it changes the synchronizability of the network. By measuring the effects of these changes at the molecular level we know causes epilepsy, we can bridge the effect to a population.

Computational simulations and *in vitro* experiments measuring PRCs from neurons will be presented. We find that epileptogenic mutations in voltage gated sodium channels and potassium channels affect the neurons' PRCs to increase network synchrony while antiepileptic drugs decrease synchrony. We hypothesize that while many antiepileptic drugs have very different mechanisms of action, their common feature may be that they decrease network synchrony.

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References

1. Meldrum BS, Rogawski MA: **Molecular targets for antiepileptic drug development.** *Neurotherapeutics* 2007, **4(1)**:18-61.
2. Netoff TI, Schiff SJ: **Decreased neuronal synchronization during experimental seizures.** *J Neurosci* 2002, **22(16)**:7297-7307.
3. Winfree AT: **The geometry of biological time.** Springer 2001.
4. Ermentrout GB, Kopell N: **Fine structure of neural spiking and synchronization in the presence of conduction delays.** *Proc Natl Acad Sci U S A* 1998, **95(3)**:1259-164.
5. Netoff TI, Banks MI, Dorval AD, Acker CD, Haas JS, Kopell N, White JA: **Synchronization in hybrid neuronal networks of the hippocampal formation.** *J Neurophysiol* 2005, **93(3)**:1197-1208.

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