

Simulation and Analyzing of Epilepsy and Seizure by Neuron

A seizure focus depends on the interplay between excitation (red) and inhibition (gray) in the neural circuits.

In this hypothetical neocortical seizure focus the neuron labeled a is in the focus and would show characteristic electrical properties such as paroxysmal depolarizing discharges. Activity in cell a can activate another pyramidal cell (b), and when many such cells fire synchronously, a spike can be recorded on the EEG. However, cell a also activates GABA-ergic inhibitory interneurons (gray), which through feedback inhibition can reduce the activity of cells a and b (temporal containment) as well as block the firing of cells outside the focus (cell c). This block is called the paroxysmal depolarizing shift (PDS) consisting of a large depolarization that triggers a burst of action potentials.

The depolarization is largely dependent on a large calcium conductance (gCa). After the depolarization, the cell is hyperpolarized by activation of GABA receptors and voltage-dependent K+ channels (gK). (Adapted from Lothman and Carnevale, 1994. New York: McGraw-Hill, 2000.)

The synaptic connections for cells a, b, c, and d are shown at the left. The activity at cell a in the focus consists of a paroxysmal depolarizing shift. However, cell c in the surround inhibition region is hyperpolarized because of GABA-ergic inhibition.

The conductances that underlie the paroxysmal depolarizing shift of a neuron in a seizure focus in a simple cortical circuit.

A. The paroxysmal depolarizing shift (PDS) consists of a large depolarization that triggers a burst of action potentials. The depolarization is largely dependent on a-amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) and L-glutamate (GluB). The former activates excitatory NMDA channels (P) and provides spatial containment of the seizure focus. This block is called the paroxysmal depolarizing shift (PDS) consisting of a large depolarization that triggers a burst of action potentials.

B. A simplified version of the circuitry impinging on a cortical pyramidal neuron. The pink terminals are excitatory, whereas the gray terminals are inhibitory. Recurrent axon branches activate inhibitory neurons and cause feedback inhibition of the pyramidal neuron. Extrinsic excitatory inputs can also activate feed-forward inhibition.

The Concept of Seizure Focus Spreading

Computational Procedures

\[ C_m \frac{dV}{dt} = -I_T - I_h - I_{Na} - I_K - I_{Na(P)} - I_L + I_{inject} \]

\[ I_T = g_T \cdot s_3(V) \cdot h \cdot (V - V_{Ca}) \]

\[ dX/dt = \phi_X (X - (V - X)) / \tau_X (V) \]

\[ I_h = g_h \cdot H^2 \cdot (V - V_h) \]

\[ I_K = g_K \cdot n^4 \cdot (V - V_K) \]

\[ I_{Na} = g_{Na} \cdot m^3h \cdot (\sigma_{Na} \cdot V) \cdot (0.85 - n) \cdot (V - V_{Na}) \]

\[ I_{Na(P)} = g_{Na(P)} \cdot m^3h \cdot (\sigma_{Na} \cdot V) \cdot (V - V_{Na}) \]

\[ I_L = g_L \cdot (V - V_L) \]

The Result: Simulation by Neuron

At first, we create five neuron units and link each of them as the second picture (the bottom side of this picture). Then, we give them the parameters that match its condition to simulate it by Wang’s algorithm. By the way, we let it be injected current at 3000ms for stabilizing and initialization of the model. Finally, we get the picture similar to the one that we expected.

The first one is the voltage about a, the second one is the voltage about b, the third one is the voltage about c, the fourth one is the voltage about inhibitory neuron affected by unit a, the fifth one is the voltage about inhibitory neuron affected by unit b, the sixth one is the current about a, b, c contributed by inhibitory condition, and the seventh one is the current about a, b, c contributed by excitatory condition.

Reference


