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Tutorial 3.2

**1a. )**

Graphical user interface

Description automatically generated with medium confidence

In the absence of any input current, the Hodgkin-Huxley model stabilizes at about -70.2mV membrane potential. This value is notably more negative than the reversal potential. The first spike is simply an artifact of the model, as many computational models have to take this sort of “boot up” time to figure themselves out before behaving as expected.

**1b. )**

Chart

Description automatically generated

In the scenario where there is a small step change in current, the H-H model reacts as follows. There is a brief period of oscillation beginning when the current is introduced, first depolarization, then hyperpolarization, then depolarization again. Each cycle becomes less and less intense until eventually the membrane potential rests at a new steady state value. After current is discontinued, the model hyperpolarizes before quickly resuming the old steady state.

The H-H model is an oscillator, and therefore a type II neuron. If we were to increase the step change in current to a level that could produce spikes, the previously mentioned “new steady state” would be one above threshold for a spike, creating a discontinuous jump for firing rate from 0Hz to some value.

**1c. )**

Chart, histogram

Description automatically generated

Graphical user interface, chart, histogram

Description automatically generated

Many different values of a time delay between step pulses were unable to produce spikes (not pictured above.) However, beginning at about 10ms delay between pulses, spikes began to appear. This is because of the properties of an oscillator. All oscillator’s have a natural frequency, and much like with wave interference in physics (sound and light come to mind especially), additional oscillating systems can have varying impacts depending on how close they match the original oscillator’s frequency. In this case, we are providing the neuron with oscillating input. The input that matches closely with the frequency of the subthreshold oscillations will produce spikes (the resonant frequency).

Worth noting is the single spike produced by the 14ms delay. Very likely, this frequency is still close enough the subthreshold oscillations to produce the occasional spike, but far away enough that it takes a significant amount more time to get there. We can test this theory by running the simulation along a larger time scale with more total step pulses, but all other parameters remaining constant. (see below)

Chart, histogram

Description automatically generated

(Iapp vs time didn’t show up very well on this figure, but applied current and duration is identical to previous trial)

**1d. )**

Chart, histogram

Description automatically generated

In the above figure, instead of positive pulses being introduced after a time delay, larger inhibitory pulses are introduced. Hyperpolarization of sufficient strength will still produce spikes in the H-H model due an anode break. Much like with a slingshot or swing, the “pulling back” of membrane potential creates an action potential when released. This occurs because sodium channels are de-inactivated and potassium channels deactivated in hyperpolarization. These factors combine to create a neuron that is essentially hypersensitive to a sudden change in membrane potential, such as when the negative current is released. The gating variables will not have time to adjust to a more appropriate steady state before a spike is produced thanks to the “hyperpolarization primed” state of the gating variables.

**1e. )**

Graphical user interface, chart, histogram

Description automatically generated

Chart, histogram

Description automatically generated In the above trial, the neuron’s steady state prior to a change in input was enough to produce spikes. Should input have remained as just baseline current, the neuron would continue to spike. However, when input was increased during hyperpolarization, the neuron oscillated to a new steady state that was below the spiking threshold. Additionally when identical input is introduced later, the spiking “switches back on”. (see below) This would imply input is in the neuron’s bistable range.

While it may be difficult to see in the above figures, input is not increased until the cell is fully hyperpolarized. The rate of increase of the membrane potential away from hyperpolarization is slightly faster for the duration of the increased input, but there is a definite change in the slope after input is returned to normal. Introducing positive current and it disappearing when it does must therefore be influencing the sodium current in such a way that prevents it from helping to produce a subsequent spike. This makes sense, as input was introduced before sodium had a chance to deinactivate and potassium to deactivate. The introduction and subsequent disappearance of the input current is likely preventing the sodium deinactivation variable from behaving like it did prior, stopping the spikes. Using the swing analogy, the swing was essentially pushed in the opposite direction it was moving during the midpoint, slowing down movement tremendously. Later, when the same force is applied to a “still swing”, oscillations in activity resume.

**1f. )**

Graphical user interface, chart, histogram

Description automatically generated

During 1e, I used a subsequent figure in my explanation that actually is about the same phenomenon that this question is addressing. In this scenario, the gating variables are initialized in such a way to make the neuron quiescent prior to input. However, the applied current is still in the neuron’s bistable range. This means that all that would be required to produce spikes at this point in time is for a single spike to be introduced. Once spiking begins, the baseline current is more than adequate to continue to produce spikes. Following a spike, potassium channels are deactivated and sodium channels are deinactivated more than they would be in a steady state without spikes, making it easier to produce the next spike.