Methods in Computational Neuroscience

Single neuron modeling: action potential generation

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In this homework, we will explore how single neurons generate action potentials. In particular, we will investigate two simple models of how real neurons create action potentials: the Integrate-and-Fire and Hodgkin-Huxley models.
MAX PAGES for the report (ex 1 + ex 2) is 8

1. Integrate-and-Fire neuron.

1.1 Simulate the dynamics of the membrane potential. We will start by simulating the voltage across a neuron's membrane when a current $I = 1nA$ is injected. For a passive membrane, the voltage is given by the differential equation:

$$C\frac{dV(t)}{dt} = g_L\left(E_L - V(t)\right) + I \tag{1.1}$$

where $C = 1\mu F$ is the membrane capacitance, $gL = 0.1\mu S$ is the conductance of the membrane, and $E_L = -70mV$ its reversal potential. This equation (and any other differential equation) can be solved numerically using the Euler method, that is, using the approximation:

$$V(t + \Delta t) = V(t) + \frac{dV(t)}{dt}\Delta t. \tag{1.2}$$

Implement the Euler Method and plot the dynamics of the membrane potential $V(t)$. Use an initial condition $V(0) = E_L$, and choose a time step $\Delta_t = 1ms$. Iterate the model for $100ms$ (i.e. for 100 time steps).

1.2 Change I. Change the injected current and explain how the dynamics vary.

1.3 [Extra point] Solve the ODE. Compare the numerical solution with the exact solution to the differential equation (1.1).

1.4 Spiking mechanism. We will now equip the passive membrane with a very simple action-potential-generating mechanism. For that purpose, we will assume that every time the voltage V surpasses a threshold V_{th}, the neuron fires an action potential, and the membrane voltage is reset to $V = E_L$. Introduce this spiking mechanism in (1.1) and simulate again the dynamics of the membrane potential. Use $V_{th} = -63mV$ and $V_{max} = +30mV$, which denotes the maximum voltage reached during the spike.

1.5 How many spikes? How many spikes do you get within 100ms?
Change the input current and see:
• at what current does the neuron starts firing;
• how the current affects the number of spikes within 100ms. Plot the tuning curve of this neuron, i.e. the number of spikes within 100ms as a function of the input current I.

1.6 Noise and spike trains To make the dynamics more realistic, we introduce a white noise term into the simulation (1.1):

$$C\frac{dV(t)}{dt} = g_L\left(E_L - V(t)\right) + I + \sigma\eta(t). \tag{1.3}$$

Here, σ determines the amount of noise, and $\eta(t)$ is a random variable from a normal distribution with mean 0 and variance 1. Recall to include $\sqrt{dt}$ in the simulation, so that it is independent of the time step (see slides). Simulate again the dynamics of the membrane potential: try with different noise magnitudes and discuss the obtained results.

1.7 Time-varying input Create a time-varying stimulus $I(t)$: this means that the injected current is no longer constant, but it changes at each time step of the dynamics. The simplest time-varying input takes the form: $I = np.zeros(T),\ \ I[T_{on} : T_{off}] = 1$, meaning that the input is on for a limited period. Invent a time-varying input and see how this impacts the generation of spikes. Use a low level of noise. Plot the membrane potential dynamics, as well as the time-varying input.

2. Hodgkin-Huxley model

So far, we have treated the action potential as a simple threshold crossing of the voltage, without further specification of how exactly it comes about. In the Hodgkin-Huxley model, the generation of the action potential itself is explained through the action of active, voltage-dependent ion channels. The membrane voltage is given by

$$C\frac{dV}{dt} = g_L\left(E_L - V\right) + \bar{g}_\kappa n^4\left(E_{\mathrm{K}} - V\right) + \bar{g}_{\mathrm{Na}} m^3 h\left(E_{\mathrm{Na}} - V\right) + I \tag{2.4}$$

where the second term on the right-hand-side describes the current due to the *delayed-rectifier* K-channel and the third term the current due to the *fast* Na-channel. The parameters of this model are $C = 1\mu F/cm^2$, $g_L = 0.3mS/cm^2$, $E_L =$-$54.4mV$, $g_K = 36mS/cm^2$, $E_K =$-$77mV$, $g_{Na} = 120mS/cm^2$, and $E_{Na} = 50mV$.
The channel variables h,m, n all follow the 1rst-order kinetics, i.e. rate equations of the form

$$\frac{dx}{dt} = \alpha(V)(1-x) - \beta(V)x \tag{2.5}$$

and the opening and closing rates, $\alpha(V)$, and $\beta(V)$ are channel-specific and voltage-dependent:

$$\alpha_n = \frac{.01(V+55)}{1-\exp(-.1(V+55))} \quad \beta_n = 0.125\exp(-0.0125(V+65)) \tag{2.6}$$

$$\alpha_m = \frac{.1(V+40)}{1-\exp[-.1(V+40)]} \quad \beta_m = 4\exp[-.0556(V+65)] \tag{2.7}$$

$$\alpha_h = .07\exp[-.05(V+65)] \quad \beta_h = 1/(1+\exp[-.1(V+35)]) \tag{2.8}$$

2.1 HH dynamics Simulate the Hodgkin-Huxley model. Plot the dynamics of V,h,m and n on the same plot. [Here you have to simulate 4 differential equation **simultaneously**, with the Euler method.]

2.2 Vary I. Increase the injected current I from $I = 0nA$ to $I = 10nA$. At which value does the neuron start to spike repetitively? What is its lowest firing rate? What happens at the spiking threshold?