Theoretical Neuroscience I

Exercise 5: Operating point of a spiking neuron

Due: Wednesday, 4 December 2019

1 Introduction

Neurons typically integrate hundreds or thousands of excitatory and inhibitory synaptic inputs. Although excitation and inhibition are balanced on average, they cause the membrane potential to fluctuate considerably. It is the amplitude and frequency of fluctuations that determines output spikes

In this exercise, you will vary the number of synaptic inputs and, separately, alter the balance between excitatory and inhibitory inputs. The goal is to understand the **operating point** of a spiking neuron.

2 Opening and closing of synaptic conductances

To simulate the time-course $P_{ex}(t)$ and $P_{in}(t)$ of the opening and closing of excitatory and inhibitory synaptic conductances, you are provided with the matlab function **synaptic_activation.m**. It takes as arguments the number of synapses, $N_{ex} = 1$ or $N_{in} = 1$, the frequency of presynaptic spikes, $\nu_{ex} = 20\,Hz$ or $\nu_{in} = 20\,Hz$, the synaptic time-constant, $\tau_{ex} = 1\,ms$ or $\tau_{in} = 2\,ms$, and the vector of time-points at which an output is desired. From these arguments, it generates a Poisson sequence of presynaptic spikes and, superimposes the resulting synaptic conductances, generates a time-course, as shown in Fig. 1. The figure was generated with the Matlab function **plot_synaptic_activation.m**.

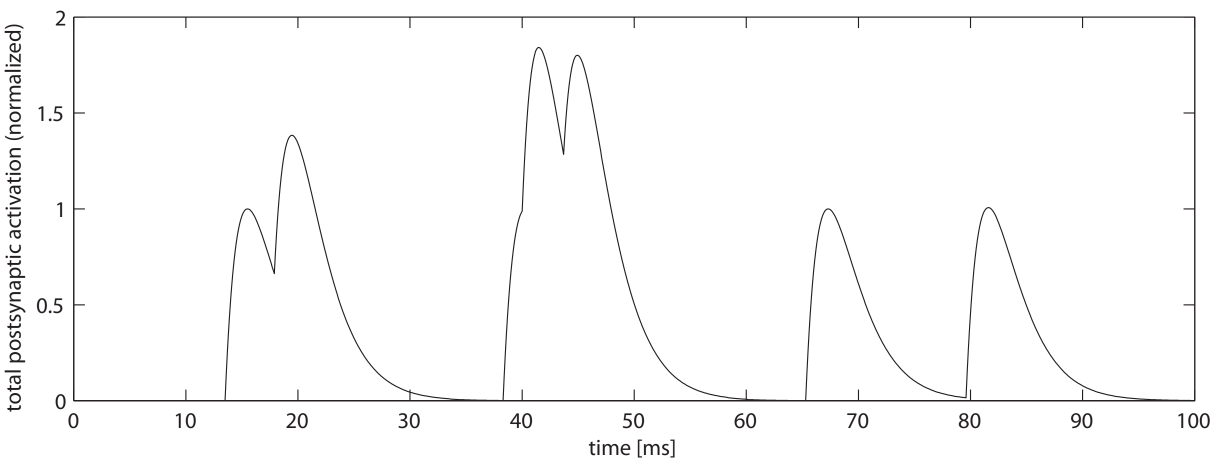

Figure 1: Multiple synaptic activation.

3 Programming assignments

Iteratively integrate the dynamic equation of the membrane potential of a LIF neuron. As always, use $V_m(t)$ to compute $V_m(t+\Delta t)$. Assume that all other state variables – $P_{ex}(t)$, $P_{in}(t)$, $\tau_{\text{eff}}(t)$, and $V_\infty^{\text{eff}}(t)$ remain constant during the interval $(t, t+\Delta t)$. Our iteration rule is then

$$V_m(t+\Delta t) = V_\infty^{\text{eff}}(t) + \left[V_m(t) - V_\infty^{\text{eff}}(t)\right] \exp\left(-\frac{\Delta t}{\tau_{\text{eff}}(t)}\right) \quad if \quad V_m(t+\Delta t) < V_{th}$$

$$V_m(t+\Delta t) = V_{reset} \qquad if \quad V_m(t+\Delta t) \geq V_{th}$$

Please see Appendix for details and for parameter values.

To write your program, follow these steps:

1. Define variables for all parameters and assign their values.
2. Define a suitable vector of time points, going from $0\,ms$ to $1000\,ms$ in steps of $\Delta t = 0.1\,ms$.
3. Obtain the synaptic input. You need to call 'synaptic_activation' *twice* twice, to get both excitatory and inhibitory activations. Start with $N_{ex} = 1$ excitatory and $N_{in} = 1$ inhibitory synapses.
4. Use V_{reset} as the initial value of $V_m(t)$.
5. Iteratively compute the time-dependent variables $V_\infty^{\text{eff}}(t)$, $\tau_{\text{eff}}(t)$, and $V_m(t)$.
6. Plot the time-evolution of the membrane voltage in a first graph.

Next, modify your program to *additionally* compute a membrane potential $V_{ns}(t)$, with *no output spikes*:

1. Add a time-dependent membrane potential $V_{ns}(t)$ (no spikes).
2. Plot the time-evolution of the $V_{ns}(t)$ in a second graph.

Finally, compute and save a vector of output spike times t_i (the times at which the membrane voltage exceeds threshold and is reset), a vector of inter-spike intervals t_{isi} (use the Matlab-function 'diff()'), and the average inter-spike interval (use 'mean()')

$$\langle t_{isi} \rangle = \text{mean}(t_{isi})$$

the standard deviation of inter-spike-intervals (use 'std()')

$$\sqrt{\langle t_{isi}^2 \rangle - \langle t_{isi} \rangle^2} = \text{std}(t_{isi})$$

the coefficient of variation of inter-spike-intervals

$$c_v = \frac{\sqrt{\langle t_{isi}^2 \rangle - \langle t_{isi} \rangle^2}}{\langle t_{isi} \rangle} = \frac{\text{std}(t_{isi})}{\text{mean}(t_{isi})}$$

and the average spike rate

$$\nu_{spk} = \frac{n_{spk}}{t_{end}}$$

where $n_{spk} = \text{length}(t_i)$ is the number of output spikes and t_{end} is the duration of your simulation.

4 Analysis assignment

4.1 Excitation only, $N_{in} = 0$

For a fixed (presynaptic) input rate of $\nu_{ex} = 20\,Hz$, determine how the (postsynaptic) output rate ν_{spk} increases with the number of excitatory inputs N_{ex}! Try to attain output rates between $\nu_{spk} \approx 10\,Hz$ and $\nu_{spk} \approx 70\,Hz$. To be efficient, begin with short simulations of $t_{end} = 2000\,ms$.

After finding the desired range of excitatory inputs, increase t_{end} to $20,000\,ms$ (or more) to obtain more reliable estimates of ν_{spk}. For each simulation, compute the coefficient of variation c_v of intersipike intervals t_{isi}, starting with the vector of output spikes, as described above. Finally, for each simulation, compute the average non-spiking membrane potential, $\langle V_{ns} \rangle$.

Plot your values of ν_{spk} as a function of N_{ex}! Plot your values of c_v as a function of $\langle V_{ns} \rangle$! What kind of relationships between these quantities do you observe? Do higher membrane potential produce more variable firing, or is it the other way round?

4.2 Excitation and inhibition, $N_{ex} = 100$

Using a fixed number of $N_{ex} = 100$ excitatory inputs, determine how the (postsynaptic) output rate ν_{spk} changes with the number of inhibitory inputs N_{in} (each firing with $\nu_{in} = 20\,Hz$)! Try to attain output rates between $\nu_{spk} \approx 10\,Hz$ and $\nu_{spk} \approx 70\,Hz$. Begin with short simulations of $t_{end} = 2000\,ms$ before proceeding to long simulations with $t_{end} = 20000\,ms$ (or more). For each simulation, determine also the coefficient of variation, c_v, and the average non-spiking membrane potential, $\langle V_{ns} \rangle$

Plot your values of ν_{spk} as a function of N_{ex}! Plot your values of c_v as a function of $\langle V_{ns} \rangle$! What kind of relationships between these quantities do you observe?

4.3 Operating point of the neuron, $N_{ex} = 100$ (optional)

Using $N_{ex} = 100$ excitatory inputs, determine the number of inhibitory inputs that maximizes c_v. Plot c_v as a function of the average non-spiking membrane potential $\langle V_{ns} \rangle$. At which distance to the threshold V_{th} do you obtain the maximal variability of output firing?

This is the neuron's operating point, where output firing is most sensitive to variations in synaptic input.

5 Appendix: Dynamic equation

The dynamic equation of a LIF neuron with synaptic conductances is:

$$c_m \frac{dV_m(t)}{dt} = -g_L\,[V_m(t) - E_L] - \underbrace{g_s\,P_s(t)\,[V_m(t) - E_s]}_{postsynaptic\ current}$$

where g_s is maximal synaptic conductance, $P_s(t)$ synaptic time-course, and E_s synaptic reversal potential. The other parameters are membrane conductance g_L, membrane capacitance τ_m, and resting potential EL. We approximate the time-course as follows (alpha function)

$$P_s(t - t_i) = \left[\frac{t - t_i}{\tau_s} \exp\left(1 - \frac{t - t_i}{\tau_s}\right) \right]_+$$

where τ_s is synaptic time-constant, t_i presynaptic spike time, and $[]_+$ denotes positive arguments (negative arguments are set to zero).

In the general case, we consider N_{ex} excitatory neurons, each of which sends K_{ex} spikes at times t_{ij}, and N_{in} inhibitory neurons, each of which sends K_{in} spikes at times t_{kl}. The total postsynaptic time-courses are then

$$P_{ex}(t) = \sum_{i=1}^{N_{ex}} \sum_{j=1}^{K_{ex}} P_s(t - t_{ij}) \qquad\qquad P_{in}(t) = \sum_{k=1}^{N_{in}} \sum_{l=1}^{K_{in}} P_s(t - t_{kl})$$

and the dynamic equation is

$$c_m \frac{dV_m(t)}{dt} = -g_L\,[V_m(t) - E_L] - g_{ex}\,P_{ex}(t)\,[V_m(t) - E_{ex}] - g_{in}\,P_{in}(t)\,[V_m(t) - E_{in}]$$

After rearranging terms, we obtain the dynamic equation in its standard form:

$$\frac{dV(t)}{dt} = \frac{1}{\tau_{\text{eff}}(t)} \left[V_{\infty}^{\text{eff}}(t) - V(t)\right]$$

$$\tau_{\text{eff}}(t) = \frac{c_m}{g_L + g_{ex} P_{ex}(t) + g_{in} P_{in}(t)} \qquad V_{\infty}^{\text{eff}}(t) = \frac{g_L E_L + g_{ex} P_{ex}(t) E_{ex} + g_{in} P_{in}(t) E_{in}}{g_L + g_{ex} P_{ex}(t) + g_{in} P_{in}(t)}$$

The parameter values are

$$\begin{array}{ccc} V_{th} = -54\,mV & V_{reset} = -70\,mV & c_m = 10\,nF/mm^2 \\ g_L = 1.2\,\mu S/mm^2 & g_{ex} = 0.1\,\mu S/mm^2 & g_{in} = 0.5\,\mu S/mm^2 \\ E_L = -65\,mV & E_{ex} = 0\,mV & E_{in} = -80\,mV \end{array}$$