

## SYNAPTIC DRIVE: QUESTIONS

### • Q1. CHANNEL NOISE

Though not directly related to synaptic drive, it is instructive to look at the level of noise in a group of  $N$  channels that spontaneously open at a rate  $\alpha$  and close at a rate  $\beta$ . Use  $x_k = 1$  to signify channel  $k$  is open and  $x_k = 0$  to signify it is closed.

[Q] By considering the total opening and closing rates of channels, calculate  $\langle x \rangle$  the probability that a channel is open in the steady state.

Let  $\gamma$  be the conductance of a single channel, and  $E_x$  be its reversal potential. Assume that the voltage  $V$  remains constant: the voltage of a cell can be fixed using the *voltage clamp* mode of intracellular voltage recording.

[Q] Write down a form for the instantaneous current flowing through all  $N$  channels as a function of the  $x_k$ s.

[Q] What is the average current?

Let  $X$  be equal to the total number of open channels

$$X = \sum_{k=1}^N x_k. \quad (1)$$

You have already calculated its average value  $\langle X \rangle = \sum_{k=1}^N \langle x_k \rangle = N \langle x \rangle$ . The aim now will be to calculate its variance, so we can examine the strength of the current fluctuations through the opening and closing channels.

[Q] First calculate the average value of  $X^2$ . Assume that different channels are uncorrelated. It is also useful to note that  $x_k^2 = x_k$  for the values that  $x_k$  can take.

The variance  $\sigma_I^2$  of the current is defined as  $\sigma_I^2 = \langle I_x^2 \rangle - \langle I_x \rangle^2$ .

[Q] Use the results of  $\langle X^2 \rangle$  and  $\langle X \rangle$  to calculate the current variance.

The standard deviation  $\sigma_I$  has units of current. A convenient dimensionless measure of the noise strength is  $\sigma_I / \langle I \rangle$ .

[Q] Calculate this quantity.

[Q] How does the relative strength of fluctuations scale with the channel number?

[Q] If the total conductance  $N\gamma$  remains constant, so the current is constant, how does the variance scale with the single channel conductance  $\gamma$ ? What are the implications?

### • Q2. SHUNTING INHIBITION

In this question we will examine the role of inhibition and see if it is subtractive or divisive. First we consider the voltage response to injected current. The voltage equation is

$$C \frac{dV}{dt} = g_L(E_L - V) + I \quad (2)$$

The current is initially zero but at time  $t = 0$  jumps to a constant value  $I_0$ .

[Q] After a long time has passed, what is the voltage increase  $\Delta V = V - E_L$ ?

[Q] What quantity in equation (2) determines the excitability of the cell (i.e. how easy it is to increase the voltage)?

The amplitude of a weak post-synaptic potential (PSP) is proportional to the difference between the resting potential  $E_L$  and the reversal potential of the synapse  $E_s$ , i.e. to  $(E_s - E_L)$ . The resting potential is typically around  $-65\text{mV}$  and for excitation  $E_e = 0\text{mV}$ , giving an amplitudinal factor of  $65\text{mV}$ . For inhibition  $E_i$  is around  $-70\text{mV}$  giving an amplitudinal factor over 10 times weaker. In fact in many cases  $E_i = E_L$  and so inhibitory synapses have zero amplitude.

Nevertheless, the presence of inhibition can significantly reduce the response of the neuron to excitatory synaptic drive. Consider the extreme case where  $E_i = E_L$ . The voltage equation is

$$C \frac{dV}{dt} = g_L(E_L - V) + g_i(E_i - V) + g_e(E_e - V) \quad (3)$$

[Q] Assume first that  $g_i = g_e = 0$ . What is the leak time constant  $\tau_L$  of the neuron?

Now assume that there is a steady barrage of inhibition so  $g_i = g_{i0} > 0$ .

[Q] What is the total conductance of the neuron now? What is the effective time constant? Is it larger or smaller than  $\tau_L$ ? How will this affect any EPSPs that arrive? How does this affect the neuron as a coincidence detector?

Imagine the excitatory input can be modelled as a constant conductance  $g_{e0}$ .

[Q] What is the value of  $\Delta V = V - E_L$  in the absence of inhibition?

[Q] What is its average value in the presence of constant inhibition  $g_{i0}$ ?

[Q] Excitatory drive is largely additive. Does inhibitory drive have a subtractive or divisive effect?

• Q3. MEAN-VARIANCE ANALYSIS

We will now review a simple method for extracting, from experiment, the number of vesicle release sites  $n$  and the voltage amplitude  $a$  (assuming this quantity has no variance) that each released vesicle causes. The total amplitude of the PSP due to the arrival of a presynaptic pulse at the release sites is

$$\mathcal{A} = a \sum_{k=1}^n y_k \quad (4)$$

where  $y_k = 1$  with probability  $p$  (or  $p_m$  if this particular event is part of a train of pulses) if a vesicle is released and  $y_k = 0$  with probability  $1 - p$  if no vesicle is released. Hence  $\langle y \rangle = p$ .

[Q] What is the mean amplitude  $\langle \mathcal{A} \rangle$ ?

[Q] Show that the variance of  $\mathcal{A}$  takes the form

$$\sigma_{\mathcal{A}}^2 = a^2 np(1 - p). \quad (5)$$

[Q] Re-express  $p$  as a function of the mean  $\mathcal{A}$  and use it to remove the explicit  $p$ -dependence of  $\sigma_{\mathcal{A}}^2$ . What is the functional relationship between the mean and variance?

[Q] How might this result be used to calculate  $n$  and  $a$ ?