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Lecture 7
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Exercise 7.1: Equivalent Circuit for a Synapse

Fig. 1 depicts a simplified neuron, represented by an equivalent circuit including a fast chemical synapse. V_{rest} is the resting potential of the cell (in other exercises denoted as the reversal potential of the leakage current E_L), R_L is the input resistance and $V_m(t)$ the membrane potential which depends on time t. E_{syn} is the equilibrium potential of the synapse and g_{syn} is the synaptic conductance, which also depends on time. By Ohm's law you obtain the postsynaptic current I_{syn} due to a single synapse (left hand side of the diagram):

$$I_{\mathrm{syn}} = g_{\mathrm{syn}}(t)\,(V_m(t) - E_{\mathrm{syn}})$$

Note that the synaptic conductance is a function of time, which depends on the opening of the synaptic ionic channels. The complete equation for the above circuit (by Kirchhoff's law) yields:

$$0 = I_{\mathrm{syn}} + I_L = g_{\mathrm{syn}}(t)\,(V_m(t) - E_{\mathrm{syn}}) + (V_m(t) - V_{\mathrm{rest}})\,/R_L$$

Assume g_{syn} to be switched 'on' at $t = 0$, so that current may pass through (when a presynaptic action potential arrives at the synapse) and is switched 'off' at $t = 1\mathrm{ms}$ (when all neurotransmitter has been cleared from the synaptic cleft) such that:

$$g_{\mathrm{syn}}(t) = \begin{cases} 0 & \text{for } t < 0, \\ 1\mathrm{nS} & \text{for } 0 < t \leqslant 1\mathrm{ms}, \\ 0 & \text{for } t > 1\mathrm{ms} \end{cases}$$

Assume $V_{\mathrm{rest}} = -70\mathrm{mV}$ and $R_L = 2\mathrm{G}\Omega$.

1. Let $E_{\mathrm{syn}} = 10\mathrm{mV}$. Is this an excitatory or inhibitory synapse? Calculate I_{syn} and the amplitude of the postsynaptic potential (*i.e.* $V_m(t)$ for $0\mathrm{ms} < t < 1\mathrm{ms}$).
2. Let $E_{\mathrm{syn}} = -90\mathrm{mV}$. Is this an excitatory or inhibitory synapse? Calculate I_{syn} and the amplitude of the postsynaptic potential.
3. Let $E_{\mathrm{syn}} = -70\mathrm{mV}$. Calculate I_{syn} and the amplitude of the postsynaptic potential. Calculate g_{total} (total membrane conductance). What effect will this synapse have on the responsiveness of the membrane? Is this an excitatory or inhibitory synapse?
4. What circuit element can you add to make the circuit more realistic (hint: think of the time-course of the responses)?

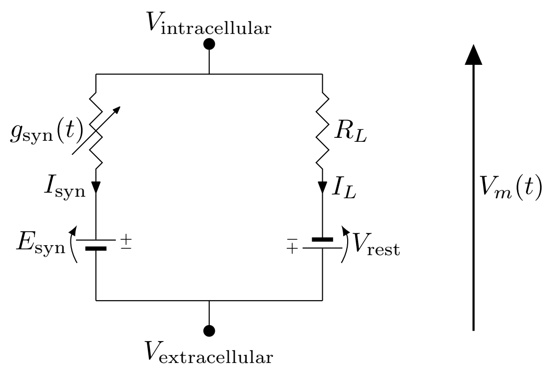

Figure 1: An equivalent circuit for a fast excitatory chemical synapse. The arrow through the resistor representing the synaptic conductance g_{syn} means that the resistance/conductance is *variable* (dependent on time). Instead, R_L has always the same value.

Exercise 7.2: Inhibitory Synapses

1. The most important sources for inhibition in the central nervous system are mediated by GABA and glycine receptors. These channels are selective for anions, such as Cl^- or HCO_3^-. For most neuronal cell bodies, the equilibrium potential for anions is more negative than the resting potential (because Cl^- is pumped out of the cell). However, in some cells, the equilibrium potential for anions is sometimes more positive than the resting membrane potential, and the opening of GABA or glycine channels produces a depolarization. In this case, how could the effect still be inhibitory?

2. Fig. 2 shows the effect of an unknown peptide on such a receptor-channel. The effect is described in terms of the difference in the synaptic current if the peptide is added vs. not added:

$$\Delta i_m = I_{\text{syn, with peptide}} - I_{\text{syn, without peptide}}.$$

Now, the figure shows how this Δi_m depends on the membrane potential V_m.

(a) What is the reversal potential of this channel?

(b) Does the peptide have a tendency to open the channel or close the channel?

(c) Remember that by definition a flux of positive charge going outward is a positive current. If the ions flowing through this channel (when it is open) are negative (anions), do they go outward or inward at the resting potential of –70 mV?

(d) If this peptide was designed to be an anti-epileptic drug, would it be a good candidate?

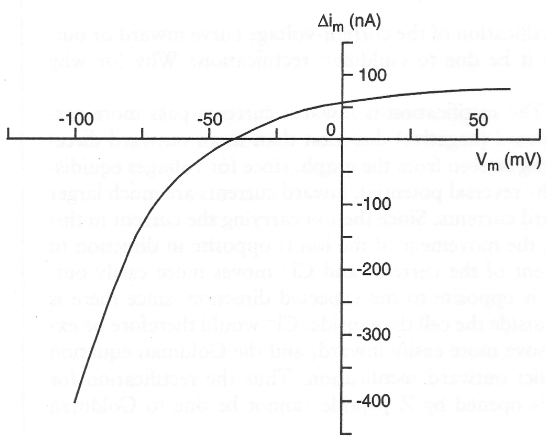

Figure 2: Effect of our mysterious peptide at different voltages (note that the y-axis shows the difference of current with the peptide)