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Lecture 7
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Solution 7.1: Equivalent Circuit for a Synapse

An excitatory synapse has a reversal potential more positive than the threshold for the generation of an action potential: it tends to make V_m cross the threshold. Instead, an inhibitory synapse has a reversal potential more negative than the threshold. Intuitively, this rule can be understood by realizing that an EPSP will tend to depolarize the membrane potential so that it exceeds threshold, whereas an IPSP will always act to keep the membrane potential more negative than the threshold potential.
We first solve the given equation for $V_m(t)$:

$$0 = g_{\text{syn}}(t)\left(V_m(t) - E_{\text{syn}}\right) + \left(V_m(t) - V_{\text{rest}}\right)/R_L$$

$$V_m(t) = \frac{g_{\text{syn}}(t)E_{\text{syn}} + V_{\text{rest}}/R_L}{g_{\text{syn}}(t) + 1/R_L}$$

1. We substitute the given values into the equation for $V_m(t)$ with $0 < t \leqslant 1\text{ms}$:

$$\begin{aligned} V_m(t) &= \frac{1\text{nS} \cdot 10\text{mV} - 70\text{mV}/(2\text{G}\Omega)}{1\text{nS} + 1/(2\text{G}\Omega)} \\ &= -16.67\text{mV} \end{aligned}$$

   This synapse increases $V_m(t)$ from –70mV to –16.67mV, in other words it 'pulls' the V_m towards 10mV. Since 10mV is more depolarized than the typical threshold for the initiation of action potentials in neurons, the synapse has an excitatory effect.
   To calculate I_{syn} we insert our values into the given equation:

$$\begin{aligned} I_{\text{syn}} &= g_{\text{syn}}\left(V_m(t) - E_{\text{syn}}\right) \\ &= 1\text{nS}\left(-16.67\text{mV} - 10\text{mV}\right) \\ &= -26.67\text{pA} \end{aligned}$$

2. Similarly we find:

$$V_m(t) = -83.33\text{mV}$$

$$I_{\text{syn}} = 6.67\text{pA}$$

   Which makes this an inhibitory synapse.

3. Similarly we find:

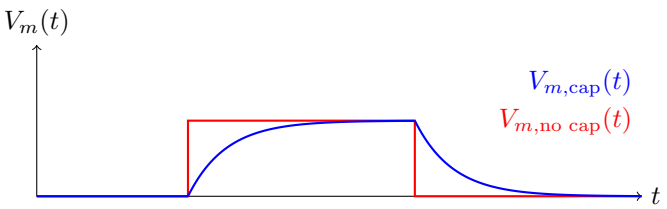
$$V_m(t) = -70\text{mV}$$

$$I_{\text{syn}} = 0\text{pA}$$

$$g_{\text{total}} = g_{\text{syn}} + 1/R_L$$

   This is an inhibitory synapse (**shunting inhibition**). Any inflowing current (is a depolarizing current) can now flow out not only over $g_{\text{mem}} = 1/R_L$, but also over g_{syn}. Thus $V_m(t)$ becomes less responsive.

4. By adding a capacitor we can make the time course of the voltage transition more realistic (not just a step function).



Solution 7.2: Inhibitory Synapses

1. As you have seen in exercise 6.1.3 about shunting inhibition, the opening of a synaptic channel whose reversal potential is below the threshold increases the minimal conductance of an excitatory synapse necessary to bring V_m over the threshold. In this way it can be inhibitory even if it increases the membrane potential. Another way to think about it is that in a time point when $V_m(t)$ is between the reversal potential of such a channel and threshold, the opening of this channel will reduce $V_m(t)$ and thus have a clear inhibitory effect. However, if you additionally take temporal dynamics into account the distinction between excitation and inhibition is not completely obvious.

2. (a) At the reversal potential, there is no net current flowing through the channel: $I_{\text{syn, with peptide}} = I_{\text{syn, without peptide}} = 0$. On the graph, at –37 mV we see no difference when we apply the peptide: $\Delta i_m = 0$. This is obviously the case at the reversal potential, since it makes no difference if the channel is open or not when nothing flows through it. Therefore, $E_{\text{syn}} = -37$ mV.

   (b) Remember that $I_{\text{syn}} = g_{\text{syn}}(V_m - E_{\text{syn}})$. So

$$\underbrace{\frac{\Delta i_m}{V_m - E_{\text{syn}}}}_{(*)} = g_{\text{syn, with peptide}} - g_{\text{syn, without peptide}}$$

   Now, for $V_m \neq E_{\text{syn}}$ the fraction $(*)$ is always > 0 because from the graph you can see that:

   - at $V_m > E_{\text{syn}}$: $\Delta i_m > 0$.
   - at $V_m < E_{\text{syn}}$: $\Delta i_m < 0$.

   Taken together, we conclude that $g_{\text{syn, with peptide}} > g_{\text{syn, without peptide}}$, so addition of the peptide leads to an opening of the channel.

   (c) At –70 mV we see a negative current I_{syn}, *i.e.* positive charges flowing into the cell or negative charges flowing out. Since Cl^- is negative, the ions are leaving the cell.

   (d) Most anti-epileptic drugs (AEDs) decrease membrane excitability by interacting with neurotransmitter receptors or ion channels. They prevent the neurons from being overexcitated. To answer the question whether the peptide is a good candidate or not we must know the threshold for the generation of action potentials. Only if the threshold is clearly above E_{syn}, the proposed drug is a good candidate.