Karla Burelo

Resting potential

BIOLOGY

ELECTRICAL ENGINEERING

PLOTS

EQUATIONS

Things to keep in mind

1. Nernst Equation

$$E_{ion} = \frac{kT}{q} \ln \frac{[ion]_{out}}{[ion]_{in}}$$

The reversal potential of an ion, i.e. K^+, Na^+, Cl^-... depends on concentrations and temperature. None of these will change so take E_{ion} as a CONSTANT!

But if ions are flowing in and out the cell... why they do not change concentration?

To change conc. by 1 mol you need $6,022 \times 10^{23}$ molecules of that ion → huge number ain't gonna happen!

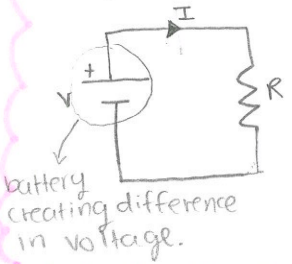
2. Resistor is an element that limits current flow

This is the symbol we use →

3. Ohm's law gives us the relationship between voltage, current and resistance:

$$V = RI \quad , R = \frac{V}{I} \quad , I = \frac{V}{R}$$

How to see this in a circuit?



4. What is resistivity?

In electrical engineering a resistor looks like this:

A resistor can be of any material each material has a resistivity. Think of a metal, metals are god conductors their ability of limiting current to flow is nothing.

$$\text{Resistance} = \text{resistivity} \frac{\text{length of resistor}}{\text{area of resistor}}$$

$$R = \rho \frac{L}{A}$$

In biology we talk about conductivity, we are basically talking about the inverse of resistivity.

Here we use g as symbol of conductivity.

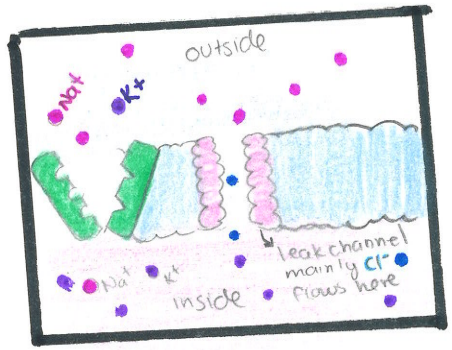
$$\rho = \frac{1}{g}$$

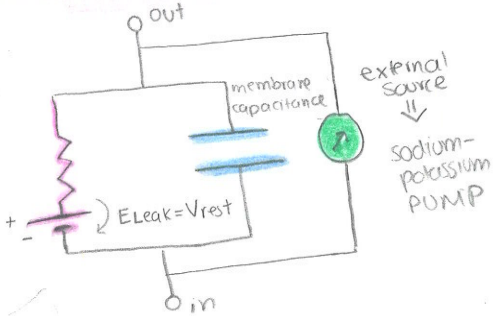
5. Conductivity? ability to conduct, to let current flow... easy!

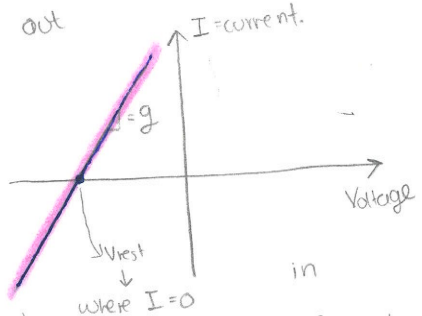
6. when we calculate currents here, the sign gives us the direction of the current. Because we define $V_{mem} \rightarrow \Delta V = V_{in} - V_{out}$

positive I → I flows in → out the cell

negative I → I flows out → in the cell







equation of a line? $y = b\,x$

b is the slope... what is b here?

See Ohms law! $I = \left(\frac{1}{R}\right) V$ → slope!

we said we'will talk in terms of resistivity in biology ∴ slope = $\frac{1}{\rho}$

$\frac{1}{\rho} = g$ → conductance!

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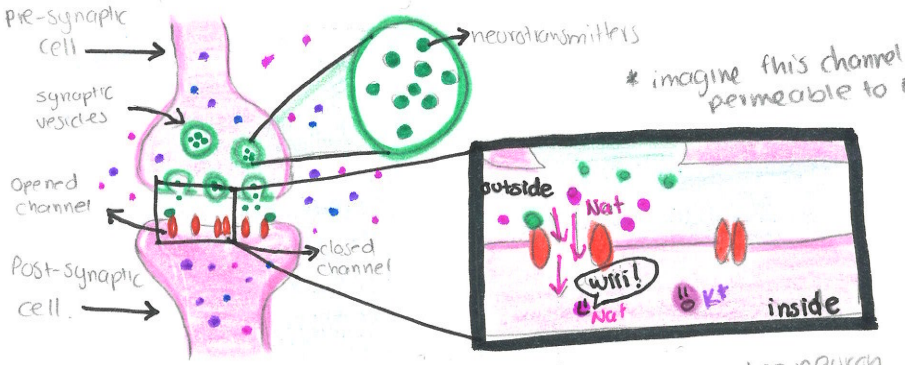
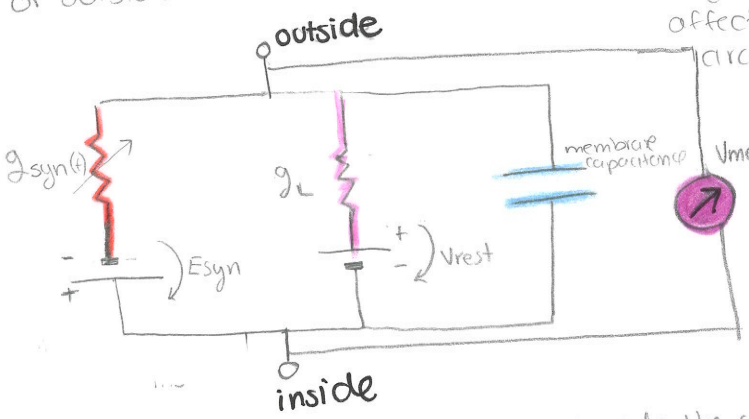
How to analyse what is happening during a synapse...

K^+ Na^+ Cl^-



* imagine this channel is permeable to Nat

During synaptic transmission, the presynaptic neuron releases **neurotransmitters**, for now let's keep it simple: neurotransmitter binds to a channel, this works like a 'key' and opens the channel. What happen? This channels are usually permeable to a specific ion, which goes crazy and flows inside if ion is positive (Na^+, Ca^{2+}) or outside if ion is negative. (Cl^-) → In any case we have a flux of current affecting our circuit.



Think about this: if we inject current inside the cell is because we allow ions to flow, by changing the conductivity of a **synapse** ($g_{syn} = 0$ for close channels, g_{syn} = value, for open channels) what happen to the **voltage across the membrane**? Ohm's law → it changes as well!

How do we know the value of V_{mem} now?

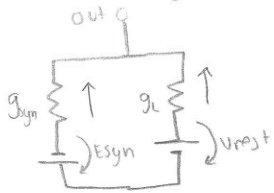
1. Ohm's law tells us that the current due to the synapse:

$$I_{syn} = g_{syn}(t)\left(V_m(t) - E_{syn}\right)$$

and due to leakage:

$$I_L = g_L\left(V_m(t) - V_{rest}\right)$$

we also have a current due to the capacitor but we will forget about it for now



2. Kirchoff's law says that the sum of all currents in a circuit is equal to zero.

$$\therefore I_{syn} + I_L = 0$$

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

$$g_{syn}(t) * V_m(t) - g_{syn}(t) * E_{syn} + g_L * V_m(t) - g_L * V_{rest} = 0$$

$$V_m(t) * \left(g_{syn} + g_L\right) - g_{syn}(t) * E_{syn} - g_L * V_{rest} = 0 \quad \text{(summing)}$$

$$V_m(t) * \left(g_{syn} + g_L\right) = g_{syn}(t) * E_{syn} + g_L * V_{rest} \quad \text{(dividing)}$$

$$V_m(t) = \frac{g_{syn} * E_{syn} + g_L * V_{rest}}{g_{syn} + g_L}$$

Clearly the effect of the synapse will depend on E_{syn}, g_{syn}, which in biology **E_{syn} depends on the concentration of the ion that is permeable to the channels that open during the synapse** and **g_{syn} will be the conductance → how many of those channels opened.** g_{syn} depends on time, meaning the channels will close again.

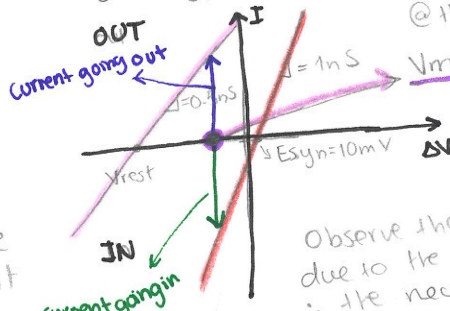
Lets see what happens when the neuron gets a new veq → meaning current flowing in is the same as going out & when the channels of synapse are still open:

Three cases:

* Excitatory synapse

The channel is permeable to an ion which $E_{syn} = 10mV$, g_{syn} (@ synapse + new veq) = 1nS

$g_L = \frac{1}{2GΩ} = 0.5nS$ (constant), $V_{rest} = -70mV$



@ the time of synapse $V_m = -16.67mV$

current flowing in

current flowing out

Observe that @ V_m, the current due to the synapse goes inside! ∴ the neuron will **depolarize**

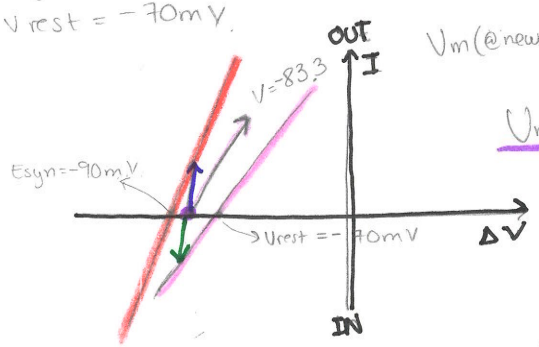
$V_m > V_{rest}$ ... is it excitatory?

If a synapse brings the V_{mem} to a value greater than the neuron threshold then YES

$V_{threshold} \approx -55mV$ for typical neurons.

* Inhibitory synapse

The channel is permeable to an ion which
$E_{syn} = -90mV$, $g_{syn} = 1nS$, $g_L = 0.5nS$
$V_{rest} = -70mV$



$$V_{m(@\,new\,eq)} = \frac{g_{syn} * E_{syn} + g_L * V_{rest}}{g_{syn} + g_L}$$

$V_m = -83.33mV$

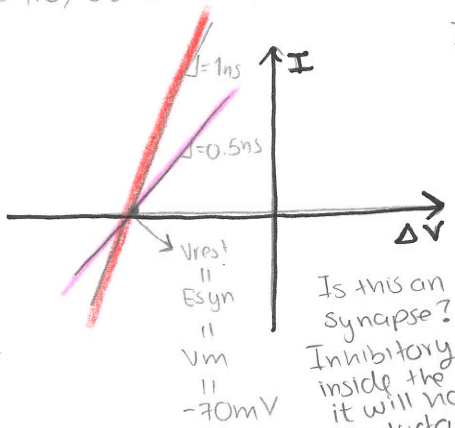
$I_{syn} = 1nS(-83 + 90)$

$I_{syn} \approx 7pA$ current flowing out or negative charges going in

Observe how now the current due to leak I_L is negative ∴ it is going inside the cell. The synaptic one is going outside ∴ causing an **hyperpolarization** on the neuron since this synapse does not help the neuron to get to Vthreshold, the synapse is inhibitory.

* Shunting inhibition

The channel is permeable to an ion which $E_{syn} = -70mV$
$g_{syn} = 1nS$, $g_L = 0.5mS$, $V_{rest} = -70mV$ @ equilibrium.



Is there current flowing?

Nope!

Is there hyperpolarization or depolarization?

No, none of them

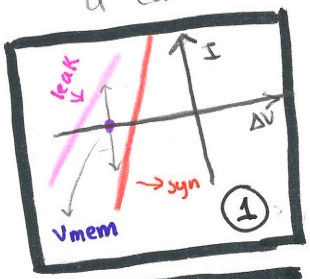
Is this an excitatory or inhibitory synapse?

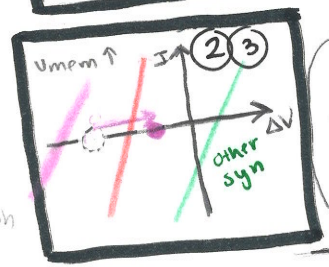
Inhibitory! Because any current going inside the neuron trying to depolarize it will have a hard time. Now the conductance that allows current to flow outside the neuron is higher
$g_{TOTAL} = g_L + g_{syn} = 1.5nS$
This synapse is trying to keep cell at -70mV!

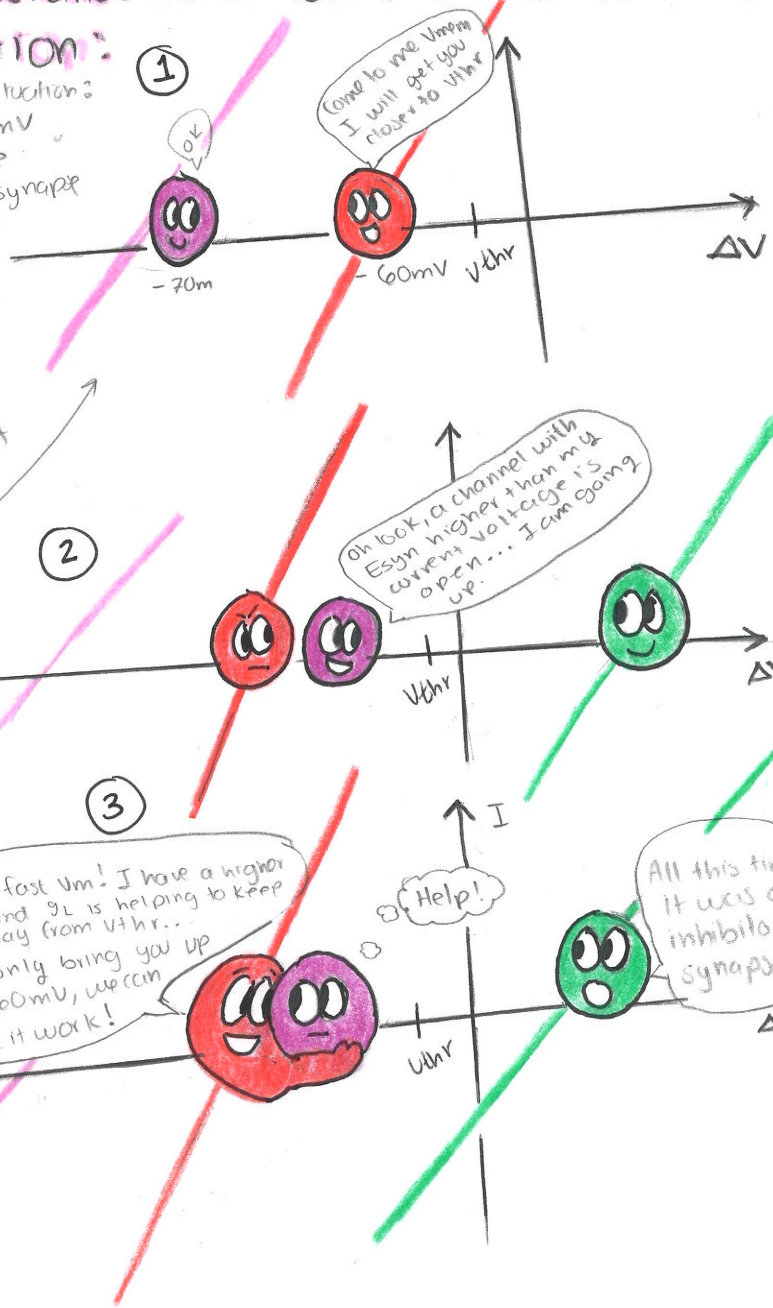
a way to understand inhibition even when there is depolarization:

Imagine the following situation:
V_{rest} due to leak = -70mV
$g_L = 0.5nS$. A synapse occurs. We know this synapse has $g_{syn} = 1nS$ and
$E_{syn} = -60mV$
say $V_{thr} = -30mV$
Is the synapse excitatory?

Voltage is a concept but for illustration purpose I will give it life as a cartoon.







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Lecture 6
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Solution 6.1: 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:

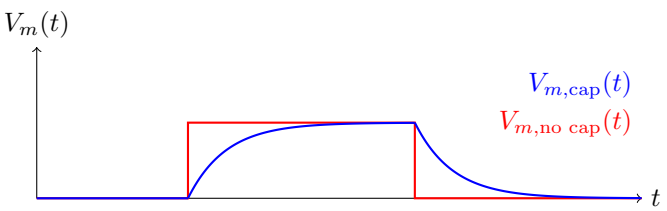
$$V_m(t) = -70\text{mV}$$

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

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

   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 6.2: Inhibitory Synapses

1. As you have seen in exercise 22.3 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.