Membrane Capacitance Properties - Ali El Ali

1. Question:

Following a change in the amplitude of a current injected to a plain bilayer membrane:

Is the slope of the voltage change directly proportional to the current amplitude? Should it be?

Answer:

Plain bilayer membranes work just like capacitors, following the basic equation(reference in Lecture 2, slide 64) $I = C\frac{\mathrm{dV}}{\mathrm{dt}}$. When we rearrange this to $\frac{\mathrm{dV}}{\mathrm{dt}} = \frac{I}{C}$, it becomes clear that the slope of voltage change is directly proportional to current amplitude as long as capacitance stays the same and that the capacitance remains constant. The equation for calculating the capacitor current follows the equation $I = C\frac{\mathrm{dV}}{\mathrm{dt}}$(which I later found out is called the capacitor I-V relationship). But to calculate the voltage change proportionality to the current amplitude, the equation needs to be rearranged to $\frac{\mathrm{dV}}{\mathrm{dt}} = \frac{I}{C}$.

Looking at the top graph, you can see that when I applied different currents (1-4 nA) to the membrane, the voltage changes were linear with time. The slopes increased proportionally with current - the 2 nA current produced a slope twice as steep as the 1 nA current, and so on.

By plotting the bottom graph, I could see the comparison made with the current amplitude against the voltage change. The line through the origin point confirms that the voltage change is directly proportional to the current amplitude only if the capacitance remains constant. An RC circuit has an analogous mechanism with how capacitors and voltages change scale based on the current.

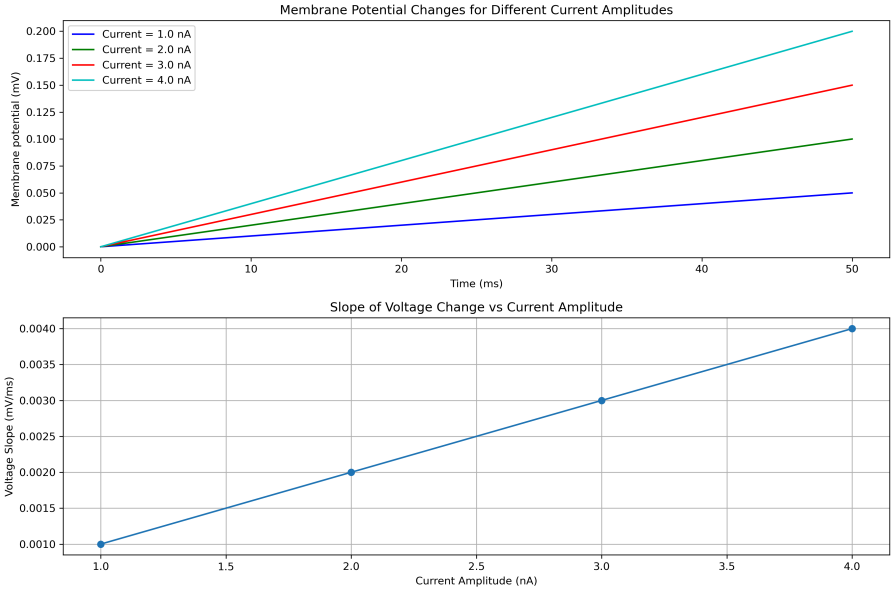


Figure 1: Demonstration of voltage changes for different current amplitudes and the resulting proportional relationship between current amplitude and voltage slope.

(par(body: strong(body: [1b. Question:])),)How is the slope of the voltage change related to the capacitance?

Answer:

From the capacitor I-V relationship(Lecture 2, slide 65) when $I = C\frac{\mathrm{dV}}{\mathrm{dt}}$ is rearranged to $\frac{\mathrm{dV}}{\mathrm{dt}} = \frac{I}{C}$ we are then able to observe that the voltage change is inversely proportional to capacitance. So when:

- capacitance increases, the slope of voltage change decreases
- capacitance decreases, the slope of voltage change increases

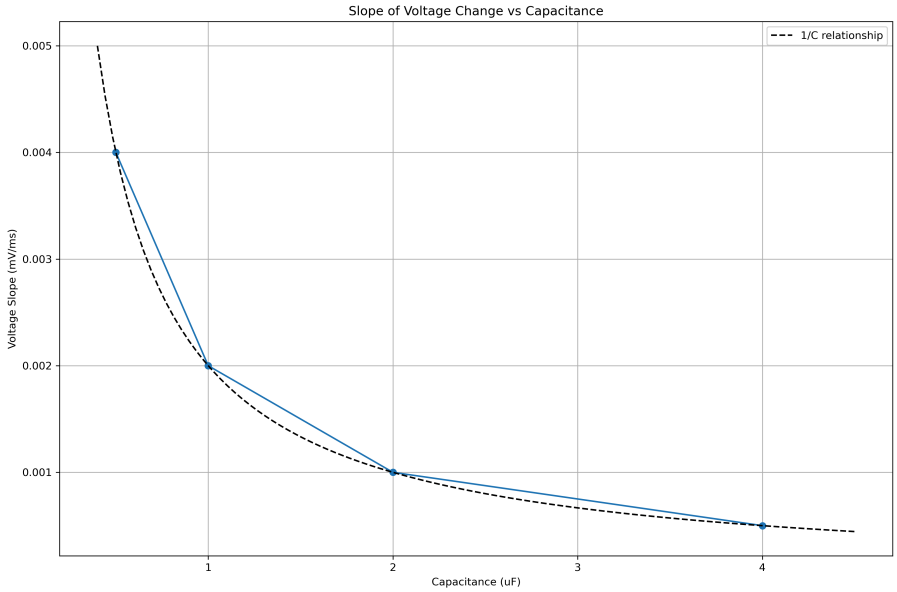


Figure 2: Voltage change slowing as the capacitance increases

2. Question:

Does the value of the resting potential affect the slope of the voltage ramp in response to a current pulse?

Answer:

No, the value of the resting potential doesn't affect the slope of the voltage ramp in response to a current pulse. The slope is determined by the current amplitude and membrane capacitance(Lecture 2, slide 67). The only determinant is by the capacitor I-V equation: $\frac{\mathrm{dV}}{\mathrm{dt}} = \frac{I}{C}$. Which shows that the rate of voltage change will remain the same regardless of the starting voltage. See figure 1.

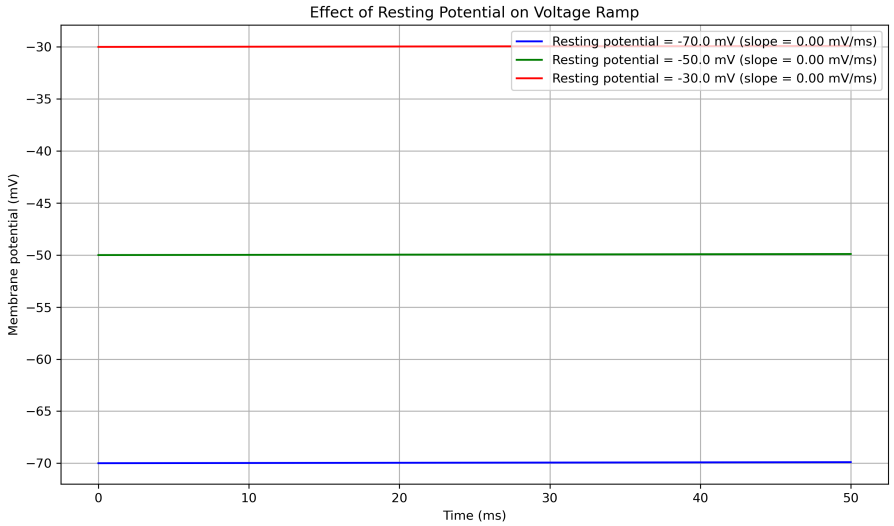


Figure 3: Voltage change depends only on current and capacitance. Not on the initial voltage level

3. Question:

If you double or halve the stimulus current amplitude, does the steady-state level follow in proportion to these changes? Should it?

Answer:

According to Ohm's law(Lecture 2, slide 48) $V = \text{IR}$ the voltage across a resistor is directly proportional to the current flowing through ti when resistance remains constant. So for a membrane with leak channels(Lecture 2, slide 29) , the steady state voltage follows that kind of relationship. For clarity -

$$V =$$

the steady state voltage $I =$ the stimulus current amplitude

$$R =$$

membrane resistance. This all lines up with the expectation that if you double the stimulus current amplitude, the steady-state voltage will also double with the assumption that the membrane resistance stays constant. Just to drive the intuition home - if you halve the stimulus current, the steady-state voltage will also be halved.

This is expected by how the leak channels have a linear current-voltage relationship. And those leak channels maintain a relatively constant conductance. This happens regardless of the membrane potential.

To answer the final part, yes, the steady-state level should follow in proportion to the changes in stimulus current amplitude when dealing with leak channels. This is what I learned to be `ohmic` behaviour.

4. Question:

If you reduce or increase the membrane capacitance, what happens to tau? What happens to the steady state level of the voltage?

Answer:

tau(the membrane time constant) is affected by membrance capacitance. The membrane time constant is defined as $\tau = \text{RC}$. With $R =$ membrane resistance and $C =$ membrane capacitance. This relationship shows that:

- when membrane capacitance increases, tau increases proportionally
- when membrane capacitance decreases, tau decreases proportionally

(Lecture 3a, slide 44) This points to how changes in capacitance directly affects how quickly the membrane potential reaches its steady state. But not the final voltage level it reaches. Within a membrane with leak channels, doubling or halving the current will proportionally change the steady-state voltage level. But changing the capacitance won't affect the steady-state value.

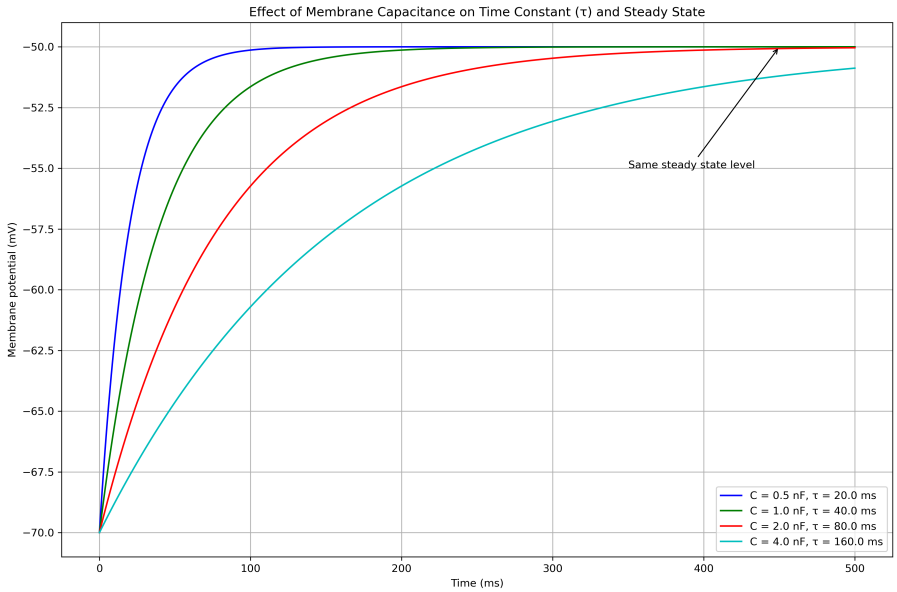


Figure 4: plot showing that curves all reach the same steady-state level at different rates. Higher capacitance is slower(larger tau), while lower capacitance would result in faster approaches(higher tau)

5. Question:

At what point in the action potential does the capacitive current cross zero? At what point in the action potential the capacitive current is at its peak?

Answer:

The capactive current crosses zero when the action potential hits its peak. This is the moment the rate of change of the voltage is zero. The capactive current reaches its peak during the fasted rising phase of the action potential. It hits its maximum when the action potential is changing at its most rapid. This is that upward tick of the action potential. The amplitude of the current is largest during the initial rapid depolarisation - that is a change within the cell where there is a shift in electric charge distribution.

6. Question:

What value of K_o^+ will cause EK to be exactly zero and why?

Answer:

The equilibrium potential(EK) will be zero when the extracellular potassium concentration $K + o$ equals the intracellular potassium concentration $K + i$. This comes from the Nernst equation:

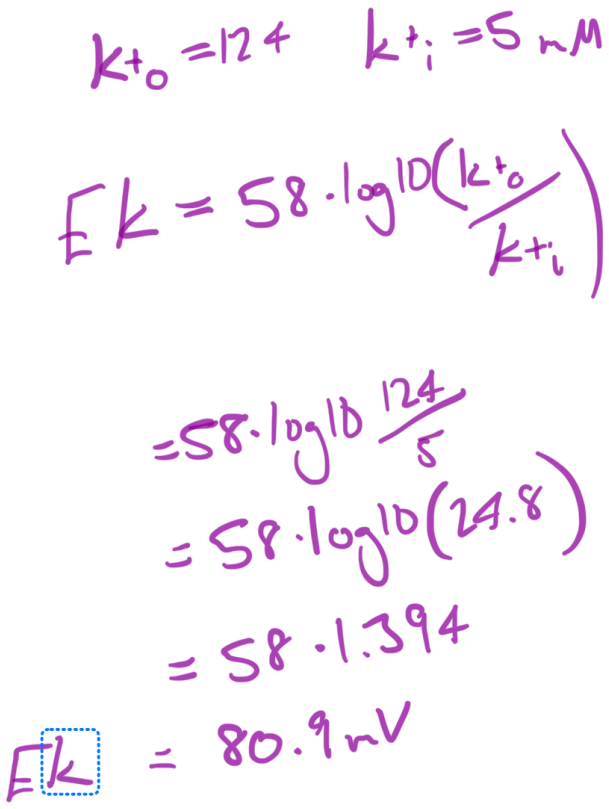
$$\mathrm{EK} = \left(\frac{\mathrm{RT}}{\mathrm{zF}}\right) \times \ln\left(\frac{K_o^+}{K_i^+}\right)$$

When the potassium concentrations are identical on both sides of the membrane, there is no concentration gradient driving the movement of K^+ ions and so no electrical potentials is needed to counteract the diffusion forces.

(par(body: strong(body: [6b. Question:])),)For the same values of K_o^+ and K_i^+, will EK be different in a mammal than in these simulations?

Answer:

The equilibrium potential would be approx. 80.9mV. See working out below:



(par(body: strong(body: [6c. Question:])),)For the same values of K_o^+ and K_i^+, will EK be different in a mammal than in these simulations?

Answer:

Yes, EK is different in a mammal compared to room temperature(Lecture 2, slide 50). Mammalian body temperates are at 37°C, with the coefficient changes from 58mV to roughly 61mV. Applying the same working out as above, see the below working:

$K^+_o = 124 \quad K^+_i = 5\ mM$

$$Ek = \cdot \log 10\left(\frac{K^+_o}{K^+_i}\right)$$

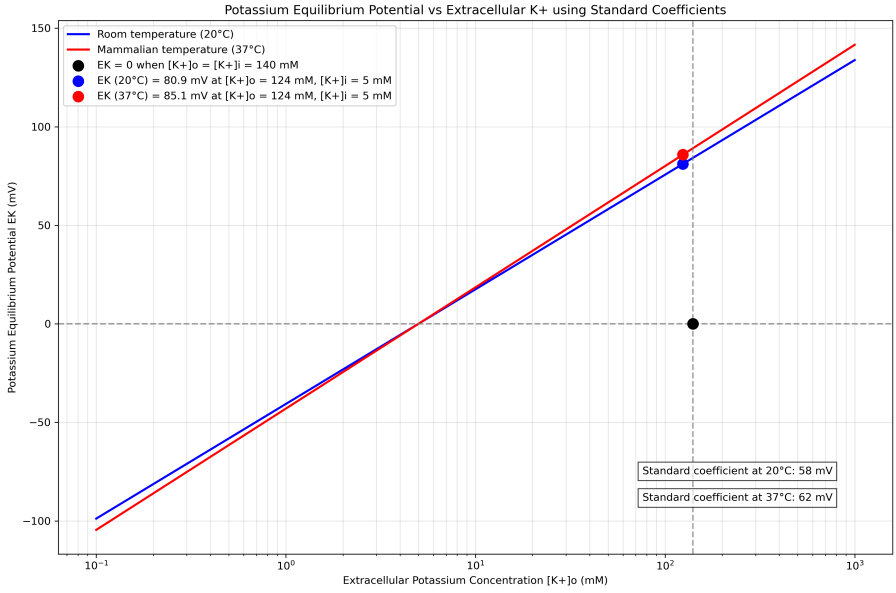
$$= 61 \cdot \log 10 \frac{124}{5}$$

$$= 61 \cdot \log 10(24.8)$$

$$= 61 \cdot 1.394$$

$$Ek = 85.0\ mV$$

Figure 6: A mammals' equilibrium potential is 85.0mV, which is higher than at room temperature(80.1mV)



7. Question:

What determines the “resting potential” and how does it depend on ion concentrations?

Answer:

Resting membrane potential is determined by the relative conductances of the membrane to different ions and their EK. When a membrane is permeable to multiple ions, the resting potential follows the Goldman-Hodgkin-Katz (GHK) equation: $\text{Vm} = \frac{\text{gK + gNa*ENa + gCI*ECI}}{\text{gK + gNa + gCI}}$

The ion concentrations affect the resting potential in two ways:

- directly determining the EK for each ion
- changes in ion concentrations can affect the conductances of ion channels

So if K_o^+ increases, EK becomes less negative and that shifts teh resting potential towards positivity.

8. Question:

Why is the resting potential so insensitive to the Na concentration when K+ is 50 times more permeant than Na+?

Answer:

The resting potential is relatively insensitive to sodium concentration changes due to a few reasons:

- When referencing the GHK equation’s contribution is weighted by its relative conductance/permeability.
- When K^+ is 50 times more permeable than Na^+, the weight of EK determining Vm is 50 times greater than the weight of ENa
- Which points to significant changes in Na^+ concentrations having minimal effect on Vm because ENa has such a small weight in the equation as a whole. The experimental results by Hodgkin and Huxley(Lecture 2 slide 39) demonstrated that changing extraceullar K^+ concentrations had a significant effect on membrane potential, yet Na^+ concentration has a negligible impact.