Action Potentials Practical

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a) Determine the relation between the sign (=direction: inward, outward) of the injection current parameter, the signs of (1) resistive and (2) capacitive currents and the sign (3) of the end value of membrane voltage.

The sum of all the currents needs to be 0, therefore we cannot have only positive or only negative currents. Also, the membrane voltage V_m is identical for both the resistor and the capacitor and that R_m and C_m must always be positive, therefore the signs of I_r and I_c are identical and determined solely by the sign of V_m.
Considering the aforementioned facts and the given formula 4a, i.e. $I_{inj} + \frac{V_m}{R_m} + C_m \frac{dV_m}{dt} = 0$, we can conclude that a positive injection current will lead to a negative I_r and I_c and, consequently, a negative membrane voltage. By using the same logic, we can demonstrate that a negative injection current will lead to a positive membrane voltage. (Figure 2)

b) Using the default parameters, measure the initial rate at which the membrane voltage rises (=the slope dVm(t)/dt). Use a short time window just after having started the current injection at t=10 ms We can make use of

$$I_{inj} + \frac{V_m}{R_m} + C_m \frac{dV_m}{dt} = 0$$

to extract $\frac{dV_m}{dt}$. First, we move I_{inj} and I_r to the right-hand side, yielding us:

$$C_m \frac{dV_m}{dt} = -(I_{inj} + \frac{V_m}{R_m})$$

. We then move C_m on the right-hand side, resulting in formula 4b:

$$\frac{dV_m}{dt} = -\frac{1}{C_m}(I_{inj} * \frac{V_m}{R_m})$$

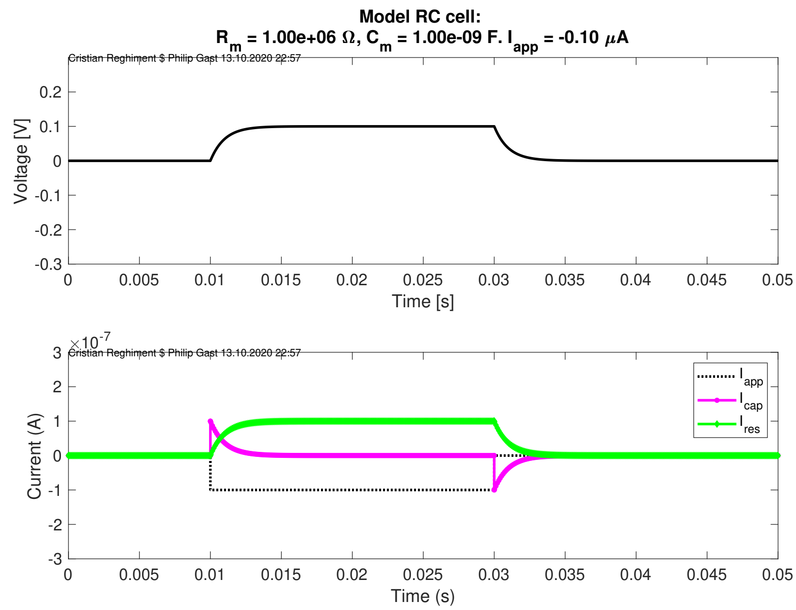

Figure 1: Voltage and currents of the membrane with the default values.

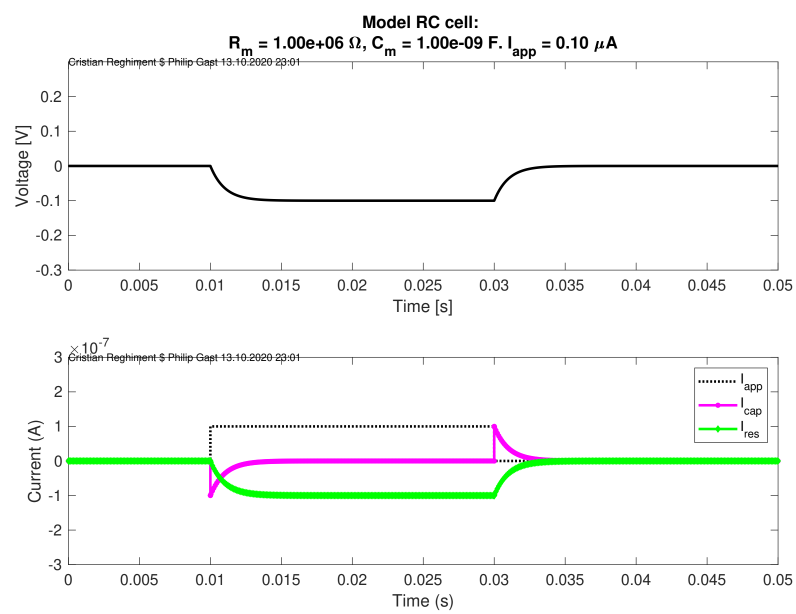

Figure 2: Voltage and currents of the membrane with the negated injection current.

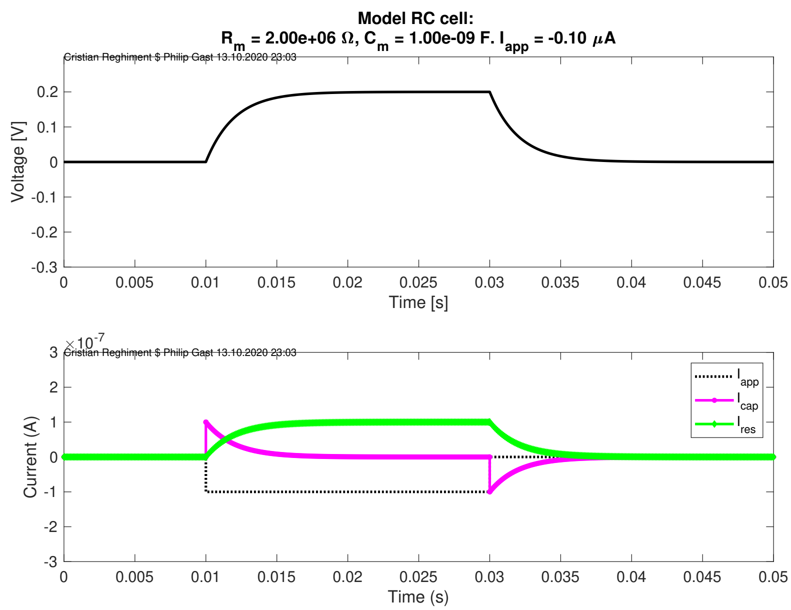

Figure 3: Voltage and currents of the membrane with doubled resistance.

Plugging the default parameters,i.e. $R_m = 10^6$, $C_m = 10^{-9}$ and $I_{inj} = -10^{-7}$, in formula 4b and considering $V_m = 0$, as there was no current before that point, we get:

$$\frac{dV_m}{dt} = -\frac{1}{10^{-9}}(-10^{-7} + 0) = \frac{10^{-7}}{10^{-9}} = 10^2 = 100V/s$$

c) Double the resistance and set the default injection current. Measure the initial voltage rate and the end voltage value. Since the pulse is time-limited, measure the end voltage value just before the end of the pulse.

After doubling the resistance, the end voltage value is $V_m = 0.2$V (see Figure 3). We determined the initial voltage rate by using the formula in the previous exercise.

$$\frac{dV_m}{dt} = -\frac{1}{10^{-9}}(-10^{-7} + \frac{0}{2 * 10^6}) = 100$$

The initial voltage rate is determined by the capacitance C_m and injected current I_{inj} only. Thus, the initial voltage slope is $-\frac{I_{inj}}{C_m}$.

d) Use the default resistance, change the capacitance to five-fold and set the default injection current. Measure the initial voltage rate and the end voltage value. After incrementing the capacitance, we

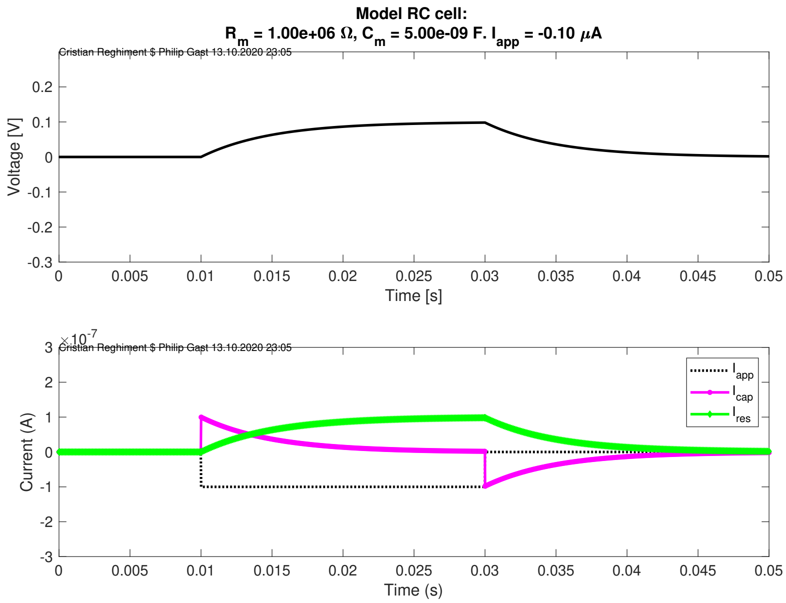

Figure 4: Voltage and currents of the membrane with five-fold capacitance.

see an immediate drop in the voltage slope (Figure), the initial voltage slope being $= -\frac{I_{inj}}{C_m} = \frac{-10^{-7}}{5*10^{-9}} = 20$. For the rest of the time course the slope will also be reduced, because of an increase in capacitance. We can conclude that the capacitance determines how quickly the potential can respond to injected current.

e) Which parameters are determining the initial voltage rate? Which parameters are determining the end voltage value? The initial slope is

determined by the capacitance C_m. The end voltage V_m is mostly influenced by the injected current I_{inj} and the resistance R_m.

2

a) Normal blood serum sodium concentration (i) is [Na+]ext 140 mM, while a red blood cell (RBC) has [Na+]int = 5 mM. Severe (ii) hypernatremia (due to severe dehydration) and (iii) hyponatremia (maybe due to downing too many beers) occur at serum concentrations 160 mM and 120 mM, respectively. Calculate the Nernst potentials for the cases (i),(ii),(iii). Supplying the Nernst potential equation

with the values of the constants, room temperature, and the sodium charge of

+1, we get:

$$E_{Na} = \frac{RT}{zF} \ln \frac{[Na]_{ext}}{[Na]_{int}} = 0.058 \log \frac{[Na]_{ext}}{[Na]_{int}}$$

where log is base 10. We can now calculate the Nernst potential. For normal blood serum sodium concentration (i) $[Na^{+}]_{ext} = 140mM$:

$$E_{Na} = 0.058 \log \frac{5 * 10^{-3}}{140 * 10^{-3}} \approx -0.0839V = -83.9mV$$

For hypernatremia (ii) $[Na^{+}]_{ext} = 160mM$:

$$E_{Na} = 0.058 \log \frac{5 * 10^{-3}}{160 * 10^{-3}} \approx -0.0873V = -87.3mV$$

For hyponatremia (iii) $[Na^{+}]_{ext} = 120mM$:

$$E_{Na} = 0.058 \log \frac{5 * 10^{-3}}{120 * 10^{-3}} \approx -0.08V = -80mV$$

Since we are taking into consideration the extracellular environment, the concentrations have therefore negative values.

b) Now take the previous values and (iv-vi) suppose the two concentrations were exchanged. (vii) Suppose that the sodium inside the RBC is the same as outside in the serum. Deduce these Nernst potentials from the previously calculated values without new calculations.

$[Na]_{ext} = [Na]_{int}$ and because of the logarithm, the resulting concentration is negative. Therefore:

$$\text{(iv) } E_{Na} = 83.9mV, \text{ (v) } E_{Na} = 87.3mV$$

and

$$\text{(vi) } E_{Na} = 80mV$$

Because $[Na]_{ext} = [Na]_{int}$,

$$\text{(vii) } E_{Na} = 0mV$$

c) Use the default parameters (Iinj-100 nA, GNa = 1S) for the simulation. What is the membrane potential in equilibrium (=when the traces are flat) when there is no current injection, and during current injection? Confirm the two values by comparing to the relevant equations. Result of the simulation with default parameters from `param2` in

Figure 5.

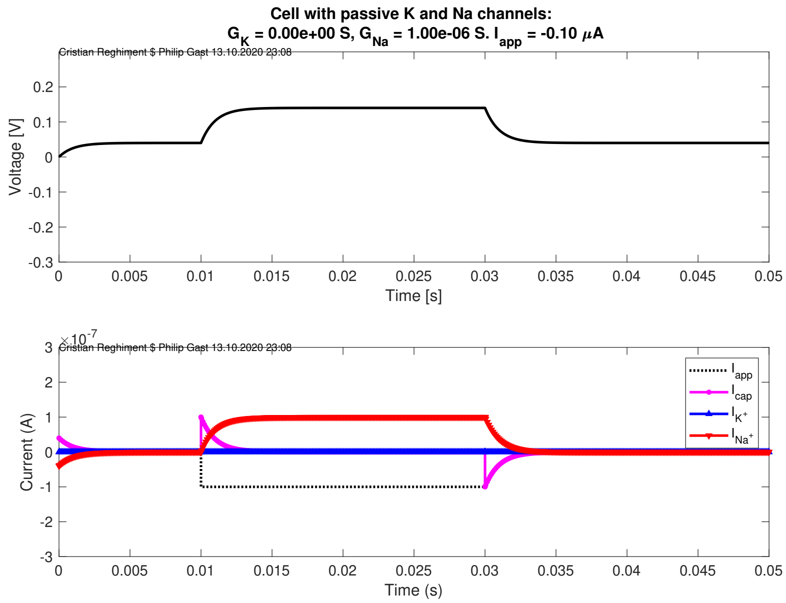

Figure 5: Plot of voltage and currents of the membrane simulation with default parameters from param2

The equilibrium is at $V_m = 40mV$. That is because the membranes resting potential is (assuming we neglect the Cl-current)

$$E_r = \frac{G_{Na}E_{Na} + G_K E_K}{G_{Na} + G_K} = \frac{10^{-6} * 0.04 + 0 * (-0.08)}{10^{-6} + 0} = 0.04V = 40mV$$

The potassium has no influence on the potential because its conductance is 0.

The membrane finds its equilibrium at $V_m = 140mV$ in response to the injected current.

d) Find (or calculate) the injection current that will bring the membrane potential to 0 mV. What is the sign of the sodium current and what is the flow direction of sodium ions in this case? Setting V_m to 0

and making use of the equation $I_{Na} = G_{Na}(V_m - E_{Na})$ and the given parameters , we can compute the value of I_{Na}:
$I_{Na} = 10^{-6} * (-4) * 10^{-2} = -4 * 10^{-8}A$.
Since this simulation leaves out all but the sodium channels, I_{inj} for this case would simply be $4 * 10^{-8}A$

e) Change the parameter for sodium conductance to GNa = 2 S and 0.5 S. Explain whether (+why or why not) does the changed con-

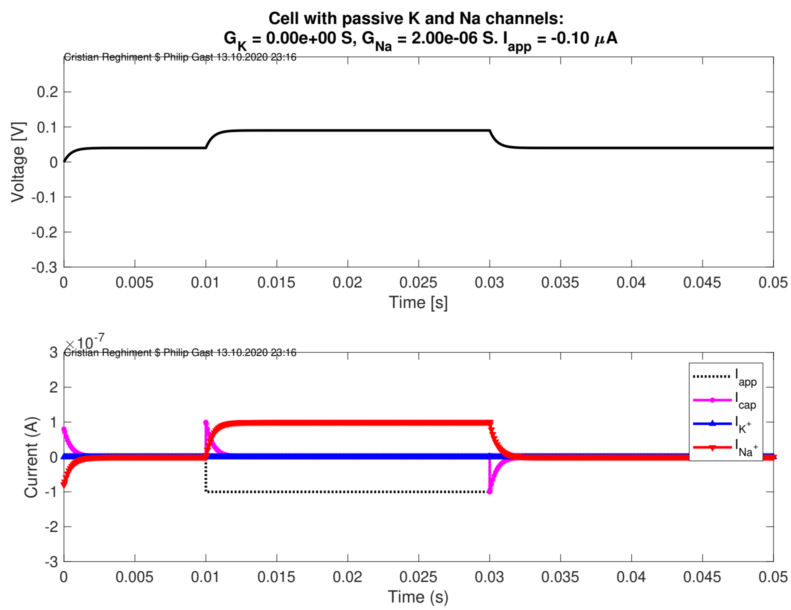

Figure 6: Voltage and currents of the membrane in the case of $G_{Na} = 2\mu S$

ductance influence the membrane voltage when there is no pulse?

The plot of the currents and the voltages of the membrane for $G_{Na} = 2\mu S$ and $G_{Na} = 0.5\mu S$ are shown in figures 6 and 7, respectively.
Since conductance serves as the inverse of electrical resistance, a higher conductance indicates that the ions(in our case, sodium ions) are transferred at a faster rate, allowing for a higher rate of change of I_{Na}. As it can also be seen from the aforementioned figures, a higher conductance(i.e. 2 μS) will help reach the equilibrium position faster, in about 0.03 seconds, as opposed to the case of lower conductance(i.e. 0.5 μS), which will reach equilibrium after almost 0.04 seconds.

f) Using GNa =2, 1, 0.5, 0 S, explain the relation between the conductance and the equilibrium membrane voltage during the pulse, and the relation between the conductance and the initial voltage slope. Explain the situation with zero conductance. The cases of $G_{Na} = 1\mu, 2\mu$

and $0.5\mu S$ were already plotted in previous exercises and can be seen in figures 5, 6 and 7, respectively. The case of $G_{Na} = 0\mu S$ can be seen in Figure 8.
As we can see in the plots, the idea that a higher conductance helps reach the equilibrium position faster still holds, in the case of 1,2 and 0.5. Also, it can be clearly seen from the graphs that a higher conductance will mean a more shallow initial voltage slope. For $G_{Na} = 2\mu S$, the membrane voltage barely

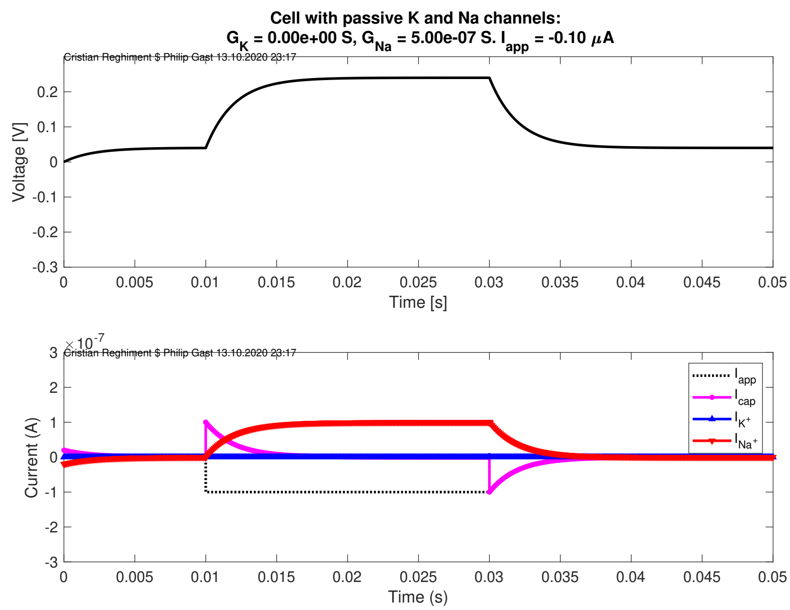

Figure 7: Voltage and currents of the membrane in the case of $G_{Na} = 0.5\mu S$

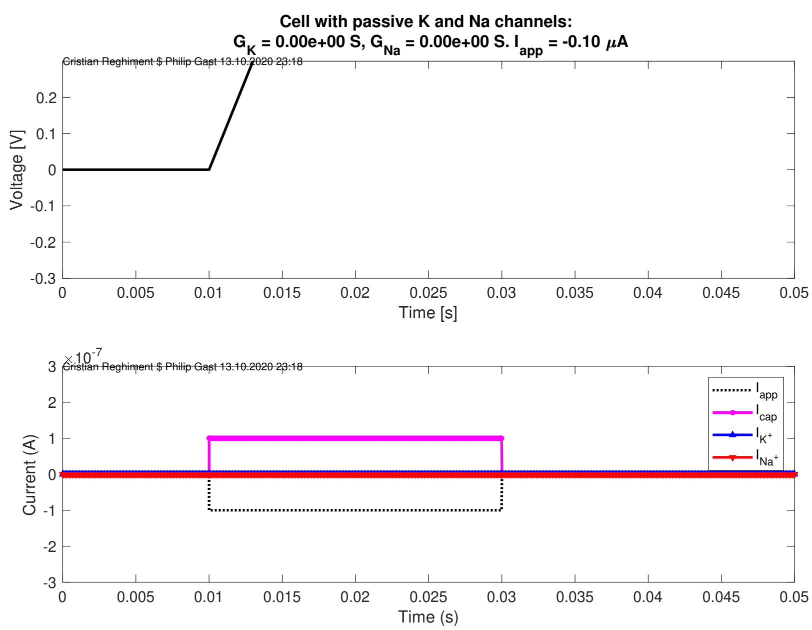

Figure 8: Voltage and currents of the membrane in the case of $G_{Na} = 0\mu S$

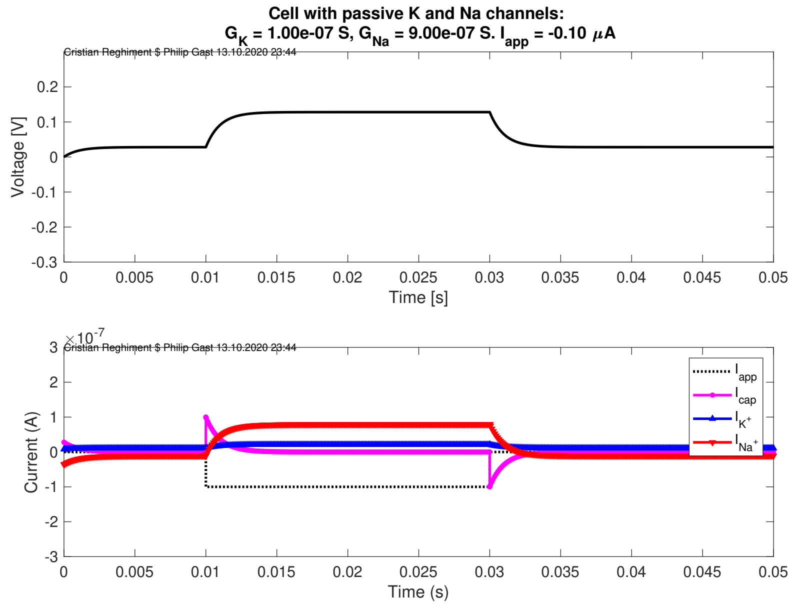

Figure 9: Voltage and currents of the membrane with $G_{Na} = 0.9\mu S$ and $G_K = 0.1\mu S$.

changes, for $G_{Na} = 1\mu S$, the difference becomes considerable, for $G_{Na} = 0.5\mu S$ the difference is far more significant, while for $G_{Na} = 0$, it is skyrocketing.
The case of $G_{Na} = 0$ is a special one in our situation, since it means that no sodium ions will pass through, meaning that the equilibrium position will never be reached, also since G_K is set to 0 through the entire simulation.

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g) Determine the membrane potential by setting the sodium versus potassium conductance ratios to e.g. 9:1, 4:1, 1:1, 1:4, 1:9 while keeping the sum conductance at 1 S. What happens if you take GNa= 0 S, or alternatively, GK=0 S? What is the range of possible values for the resting potential without any applied current, given the ENa and EK used in the simulations? Observe the equation (12).

The range of possible values for the resting potential can be calculated by plugging in all possible values of the conductances in equation (12), such that:

$$V_m = \frac{G_{Na}E_{Na}+G_KE_K}{G_{Na}+G_K} = \frac{0.9*10^{-6}*0.04+0.1*10^{-6}*(-0.08)}{0.9*10^{-6}+0.1*10^{-6}} = 28mV. \text{ (Figure 9)}$$

$$V_m = \frac{G_{Na}E_{Na}+G_KE_K}{G_{Na}+G_K} = \frac{0.8*10^{-6}*0.04+0.2*10^{-6}*(-0.08)}{0.8*10^{-6}+0.2*10^{-6}} = 16mV.$$

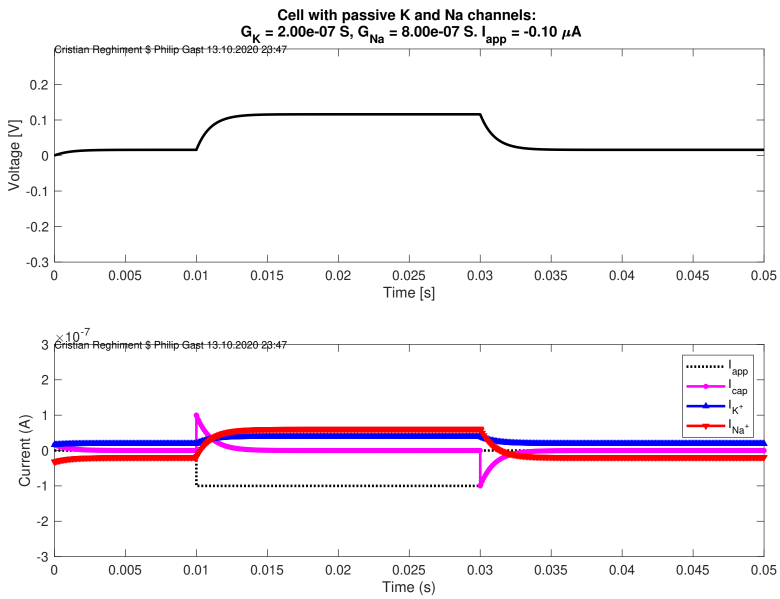

Figure 10: Voltage and currents of the membrane with $G_{Na} = 0.8\mu S$ and $G_K = 0.2\mu S$.

$V_m = \frac{G_{Na}E_{Na}+G_KE_K}{G_{Na}+G_K} = \frac{0.5*10^{-6}*0.04+0.5*10^{-6}*(-0.08)}{0.5*10^{-6}+0.5*10^{-6}} = -20mV.$
$V_m = \frac{G_{Na}E_{Na}+G_KE_K}{G_{Na}+G_K} = \frac{0.2*10^{-6}*0.04+0.8*10^{-6}*(-0.08)}{0.2*10^{-6}+0.8*10^{-6}} = -56mV.$
$V_m = \frac{G_{Na}E_{Na}+G_KE_K}{G_{Na}+G_K} = \frac{0.1*10^{-6}*0.04+0.9*10^{-6}*(-0.08)}{0.1*10^{-6}+0.9*10^{-6}} = -68mV.$ The range is, therefore, [-68mV,28mV]

h) How do the currents through the sodium and potassium channels relate to each other in terms of amplitude and direction?

The currents will be of the same magnitude and opposite sign. More current will go through the membranes as we increase the capacitance, which in turn increases the magnitudes of both Na and K currents. Both currents have the same amplitude but opposite directions because of this.

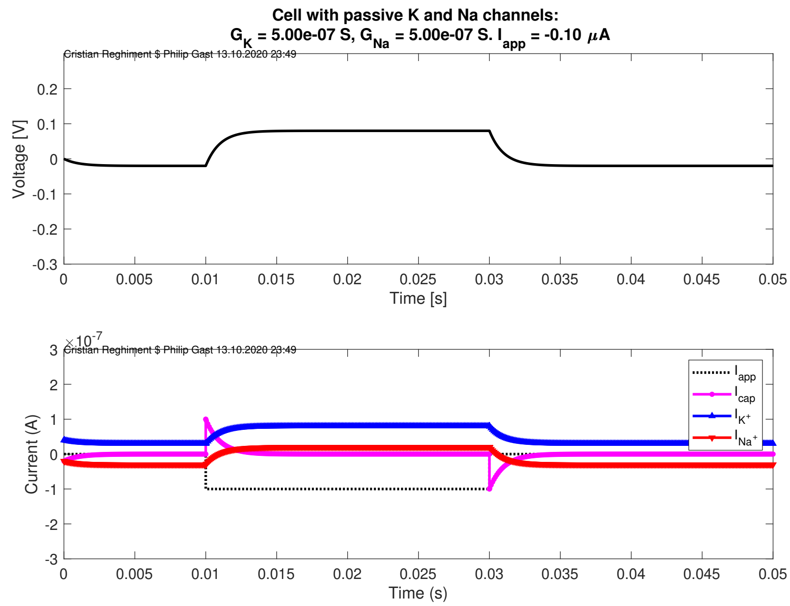

Figure 11: Voltage and currents of the membrane in the case of $G_{Na} = 0.5\mu S$

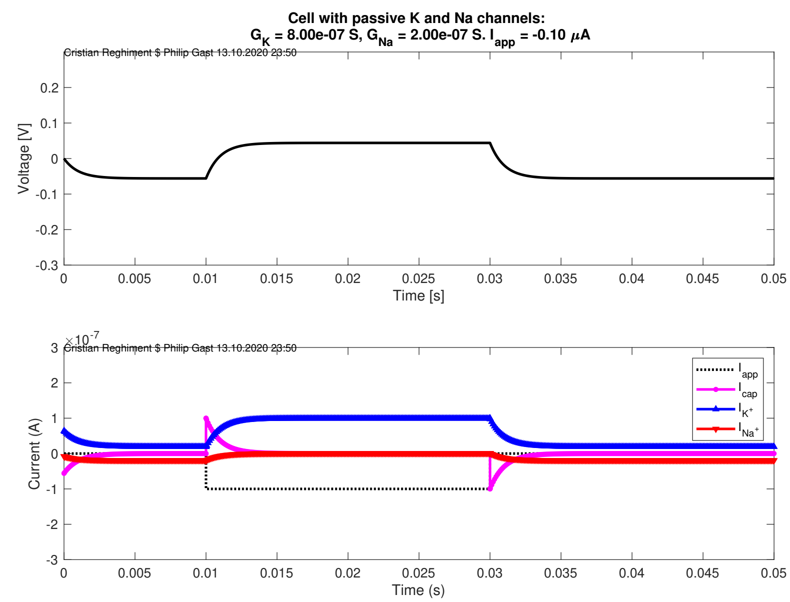

Figure 12: Voltage and currents of the membrane with $G_{Na} = 0.2\mu S$ and $G_K = 0.8\mu S$.

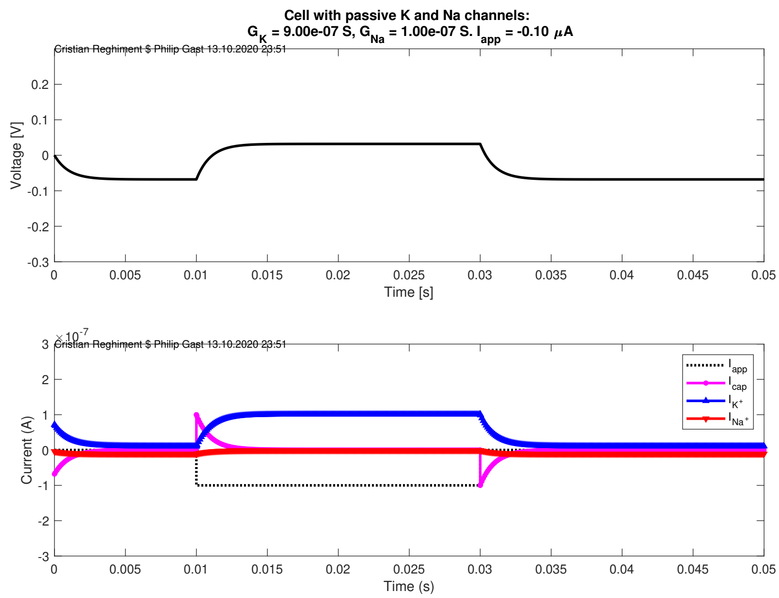

Figure 13: Voltage and currents of the membrane with $G_{Na} = 0.1\mu S$ and $G_K = 0.9\mu S$.