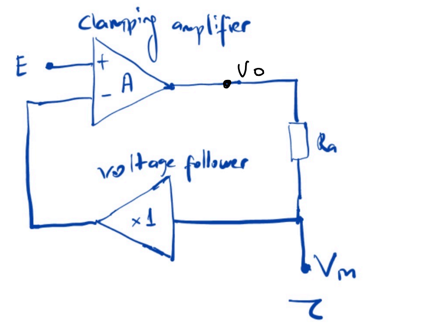
Q1) The question about the amplifier circuit for voltage clamp is shown in the HW2-Q1 file.
Explain how it can stabilize the voltage at a specific voltage level.
What is the condition that the control voltage (E) controls to have Vm approaching to E.
Discuss the electronic processes if the intracellular potential is less and more than the desired intracellular voltage. ?
How can we understand the ion flux in such a configuration.



Write the condition for A that will lead to Vm approaches to E.

+ Op-amp has three connections an "inverting and non inverting input" and "output".
" takes voltage difference btw inverting and non-inverting input, and multiplies some large number, and provides output.

+ If we connect the output of op amp to the inverting input, and your signal to the non-inverting input, something happens; The output equal to non-inverting input. Op amps draw no currents.
→ If we apply voltage to the non-inverting input(E) Vcmd, and put resistor Ra, voltage follower to the output and inverting input, Vo will drop some voltage over RF equal to current the op-amp has to pass to keep Vcmd equal to Vcmd - Ra×I
So the voltage Vo will be Vcmd − RaI . .
→ Inverting input connected to the cell and non-inverting input receives command voltage. Op-amp passes current to keep whole op-amp voltages equal, thus creates voltage at its output equal to Vcmd − Ra × I. All that is required is for the rest of circuitry to subtract of Vcmd, and divide voltage by Ra, and we get voltage proportional to passed current

The aim of ΔVcommand is to change the voltage with respect to resting potential

$t \to \infty$

condition?

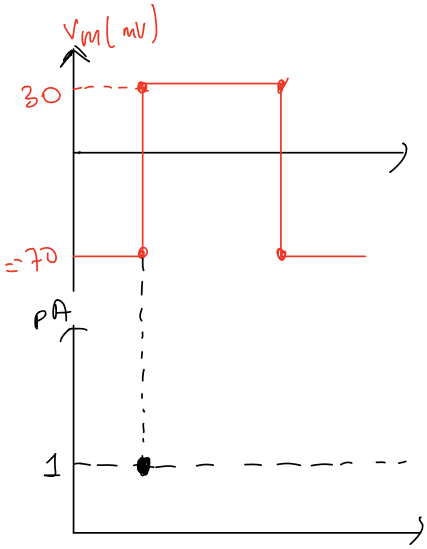
Vintra(t-τ) Vcommand + Vintra(0)

example:

+30 + (-65) = -35

t→∞ : -35mV +30 + (-65) = -35mV
t = 0 ; -65mV +30 + (-65) = -35 mV

→ To understand the ion flux in such configurational created example :



$$\Delta Q = C_m \cdot \Delta V_m \longrightarrow \Delta Q = 1\times10^{-6} \frac{F}{cm^2} \times 100\times10^{-3} V$$

$$= 10^{-7} \frac{C}{cm^2} = 10^{-15} \frac{C}{\mu m^2}$$

$$F = 96.487 \frac{C}{mol}$$

$$\frac{\Delta Q}{F} = \frac{10^{-15} \frac{C}{\mu m^2}}{96487 \frac{C}{mol}} \cong 10^{-20} \frac{mol}{\mu m^2}$$

$\approx 10^{-5}$

$$1\,mol = 6.02 \times 10^{23}$$

* One channel carrying 1pA in 1ms

$$1pA = 10^{-12} A = 10^{-12} \frac{C}{s}$$

$$\frac{10^{-12} \frac{C}{s}}{96487 \frac{C}{mol}} \cong 10^{-17} \frac{moles}{sec}$$

$$10^{-17} \frac{moles}{sec} \times \text{avagadro number} = 6\times10^{6} \frac{ions}{sec}$$

$$6 \times 10^{6} \frac{ions}{sec} \times \underbrace{1\,ms}_{10^{-3} sec} = 6\times10^{+3}\ ions$$

1ms & 1 pA → 6×10^{3} ions can move and generate 100mV voltage difference.

Q2) The following questions from the text book: 2, 5, 6, 7, 8, 9, 21, 22, 23, 24, 25, 26, 27 (pages 417-422 in 3rd Edition of the text book)

2. During the upstroke of an action potential in squid giant axon, the probability of a sodium channel being open changes. At rest the probability of an open channel is 0.01, while at the peak of an action potential it is 0.2. Consider 0.6 mm^2 of cell membrane. On the average, how many channels change from closed to open as the membrane moves from rest to peak, i.e., during the upstroke of the action potential?

Table 4.1. Conductance of Sodium and Potassium Channels

Preparation –	γ (pS)	Channels (number/μm^2)
Sodium		
$\boxed{\text{Squid giant axon}}$	4	330
Frog node	6–8	400–2000
Rat node	14.5	700
Bovine chromaffin	17	1.5–10
Potassium		
Squid giant axon	12	30
Frog node	2.7–4.6	570–960
Frog skeletal	15	30
Mammalian BK	130–240	—

$0.6\ mm^2 = 6 \times 10^5\ \mu m^2$

total amount of channels + N_K = (330 channel/μm^2) $\times$ ($6\times10^5\ \mu m^2$) = 198×10^6 channels

(0.2 x # of channels on membrane) − (0.01 x # of channels on membrane)

$= 0.19 \times 198 \times 10^6$ channels $= 37{,}620{,}000$ channels open.

5. Suppose a frog skeletal muscle cell is satisfactorily represented in the shape of a brick with edges (length, width, and depth) of 2,000, 25, and 10 μm. At rest the rate of potassium channel opening is 0.005, and the rate of channel closing is 0.48 msec^{-1}. The resting membrane voltage is –96 mV, and the temperature is 28 degrees C. What is the (macroscopic) potassium current in at rest?

①

$$\text{channel open} \underset{\beta}{\overset{\alpha}{\rightleftarrows}} \text{channel closed}$$

α: # of time per second gate open = 0.005 msec^{-1}

β: # " " " " closed = 0.48 msec^{-1}

$$p = \frac{\alpha}{(\alpha+\beta)} = \frac{0.005}{0.485} = 0.01030928$$

② dimensional cell = 2000x25x10

macroscopic current — total # of channels

$$I_K = n \cdot p \cdot \underbrace{\gamma_K \cdot (V_m - E_K)}_{I}$$

$=$

$n = 30 \times 2000 \times 25 \times 10 = 15 \times 10^6$

I = conductance α voltage (potential $= 15\times10^{-12} S \times (96\times10^{-3}\ V - (\underbrace{-98\times10^{-3}}_{\text{found on book}})) = 36.34\times10^{-15}$ Amp

$= 15\times10^6 \times \frac{5}{485} \times 36.34 \times 10^{-15}$

$= 5.62 \times 10^{-9}$ Amp

Exercises 6–13 involve the probabilities of channels being open and closed. In all questions, the number of channels is N, the probability of an open channel is p, the probability of a closed channel is q, and the channel density is D.

6. What is the formula for the expected number of open channels?

E[# open channels] $= N \cdot p$ from Engr200 course

7. What is the formula for the expected number of closed channels?

E[# closed channels] $= N \cdot q$

8. What is the sum $p + q$?

$p + q = 1$ ← union bound

9. What is the formula for the standard deviation of the number of open channels?

$\sigma^2 = Npq \rightarrow \sigma^2 = \sqrt{N \cdot p \cdot q}$

Model cell

surface area: 600 μm^2

channel density: D: 40 channels/μm^2

$\gamma = 10$ pS

$V_r = -60$ mV

$E_K = -80$ mV

$E_{Na} = +60$ mV

$$p = \frac{\alpha}{\alpha + \beta}$$

Exercises 21–26: Again examine the potassium channels and currents in the model cell, this time with V_m^1 of –55 mV and V_m^2 of 55 mV.

21. At steady state in phase 1, what is:

a. The probability p_1 that a K^+ channel is open?

$p_1 = 0.025$

b. The expected number of open K^+ channels?

$N \cdot p \longrightarrow 592$ open channels

c. The fluctuation in number of open channels, if the fluctuation is considered to be four times the standard deviation?

$\sigma = \sqrt{N \cdot p \cdot (1-p)} = 4 \times 24$ channels $\swarrow$ $\sqrt{Npq} = \sqrt{24000 \times 0.2469 \times 0.7531}$

d. During steady state for phase 1, what is the cell's K^+ current?

$= 600 \cdot 40 \cdot 10\,pS \cdot (-60+80) 10^{-3} = 1.48 \times 10^{-10}$ Amperes

22. During steady state in phase 2 what is:

a. The probability p_2 that a K^+ channel is open?

$p_2 = 0.894$

b. The expected number of open K^+ channels?

$N \cdot p \longrightarrow 21{,}467$ open channels

c. The cell's K^+ current?

$= 600 \cdot 40 \cdot 10\,pS\,(55-(-80))\,10^{-3} = 2.898 \times 10^{-8}$ Amperes

23. As judged by the results of exercises 21 and 22, if V_m^2 is greater than V_m^1, are more K^+ channels open?

Yes, at steady state since there is more channels.

24. Quantitatively compare the number of open channels during the steady state of phase 1 to the number open in the steady state of phase 2. What is the ratio of the expected numbers of open K^+ channels $N^2_{\text{open}}/N^1_{\text{open}}$?

$\frac{21{,}467}{592} =$ The ratio is 36.3, more channels in steady state in phase 2

25. Compare the K^+ current at steady state in phase 1 (I_K^1) to that at steady state in phase 2 (I_K^2). What is I_K^2/I_K^1? $195.81 \approx 196$. Much higher current flows at the steady state of phase 2. Ratio is higher than ratio of # of open channels

26. Compare the I_K current at time $t = t_a$, I_K^a, evaluated immediately after the transition of V_m, to I_K^1, the current just before. What is the ratio I_K^a/I_K^1?

2.86, much lower than that of preceding question

27. In a few sentences, explain why there is a difference between the answers to Exercises 25 and 26.

21)

a) $V_m' = (V_m - V_r) = (-55-(-60))\,mV = 5\,mV$

$$\alpha_n = \frac{0.01 \times (10 - V_m)}{\exp\left(\frac{10-V_m}{10}\right) - 1} = 0.0771\ msec^{-1}$$

$$\beta_n = 0.125 \exp\left(\frac{-V_m}{80}\right) = 0.1174\ msec^{-1}$$

$$n = \frac{\alpha_n}{\alpha_n + \beta_n} = \frac{0.0771}{0.1945} = 0.3964$$

$$p_1 = n^4 = 0.02469$$

b) $N_{K^+} = 600\,\mu m^2 \times 40\ ch/\mu m^2 = 24000$ channels

# of open channels $= N_{K^+} \cdot p_1 = 592$ channels

22)

a) $V_m^2 = (V_m - V_r) = (55-(-60))\,mV = 115\,mV$

$$\alpha_n = \frac{0.01 \times (10 - V_m^2)}{\exp\left(\frac{10-V_m^2}{10}\right) - 1} = 1.05\ msec^{-1}$$

$$\beta_n = 0.125 \exp\left(\frac{-V_m^2}{80}\right) = 0.0297\ msec^{-1}$$

$$n = \frac{\alpha_n}{\alpha_n + \beta_n} = \frac{0.0771}{0.1945} = 0.9725$$

$$p_1 = n^4 = 0.8944$$

b) $N_{K^+} = 2400$

# of open channels $= N_{K^+} \times p_2 = 21467$ channels

27) + Because it needs time to reach steady state, it will reach half of the expected current in τ, and grows exponentially but slowly after a while.

It is different because when entered phase 2, # of open channels change with time. After transmission, voltage changes to phase 2's voltage level.
# of open channels equivalent because of small change of time.