

# Rutgers 642:613 - Fall 2003

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Sections 2.6-on, Membrane Potentials, Cell Volume

<http://www.math.rutgers.edu/~sontag/613.html>

## Nernst Equation

inside cell, concentration of ions is different from that in surrounding liquid, and this difference in concentration generates an electrical potential

*electrical potential energy* (in joules) at point  $x$  in space due to voltage  $V$  (volts) on charge  $q$  (coulombs) is  $E(x) = qV(x)$

( $V$  in fact *defined* as potential energy per unit of + charge: work to move charge  $q$  from point  $x$  to  $y$  is  $q(V(y) - V(x))$ )

thermodynamics: probability that a molecule is in state of energy  $E$  proportional to the Boltzmann factor  $\exp(-E/kT)$ , where  $k$  is the Boltzmann constant and  $T$  the temperature

$\therefore$  for a positive ion with charge  $q$ ,

Prob(particle at (near) position  $x$ )  $\propto \exp(-qV(x)/kT)$

compare: Brownian motion, i.e. pure diffusion: if  $V \equiv 0$ , equal probabilities, i.e. pure random walk; but (if  $q > 0$ ) then lower prob where higher  $V$ : free positive charges move towards regions of lower voltage

concentration  $\propto$  Prob,  $\Rightarrow c(x) \propto \exp(-qV(x)/kT)$

$\therefore \frac{c_e}{c_i} = \exp(-q(V_e - V_i)/kT)$  or

$$V_S = \frac{kT}{q} \ln \left( \frac{[S]_e}{[S]_i} \right)$$

where  $V_S = V_i - V_e$  *Nernst potential*,

$[S]_e$  = external concentration of ion

$[S]_i$  = internal concentration of ion

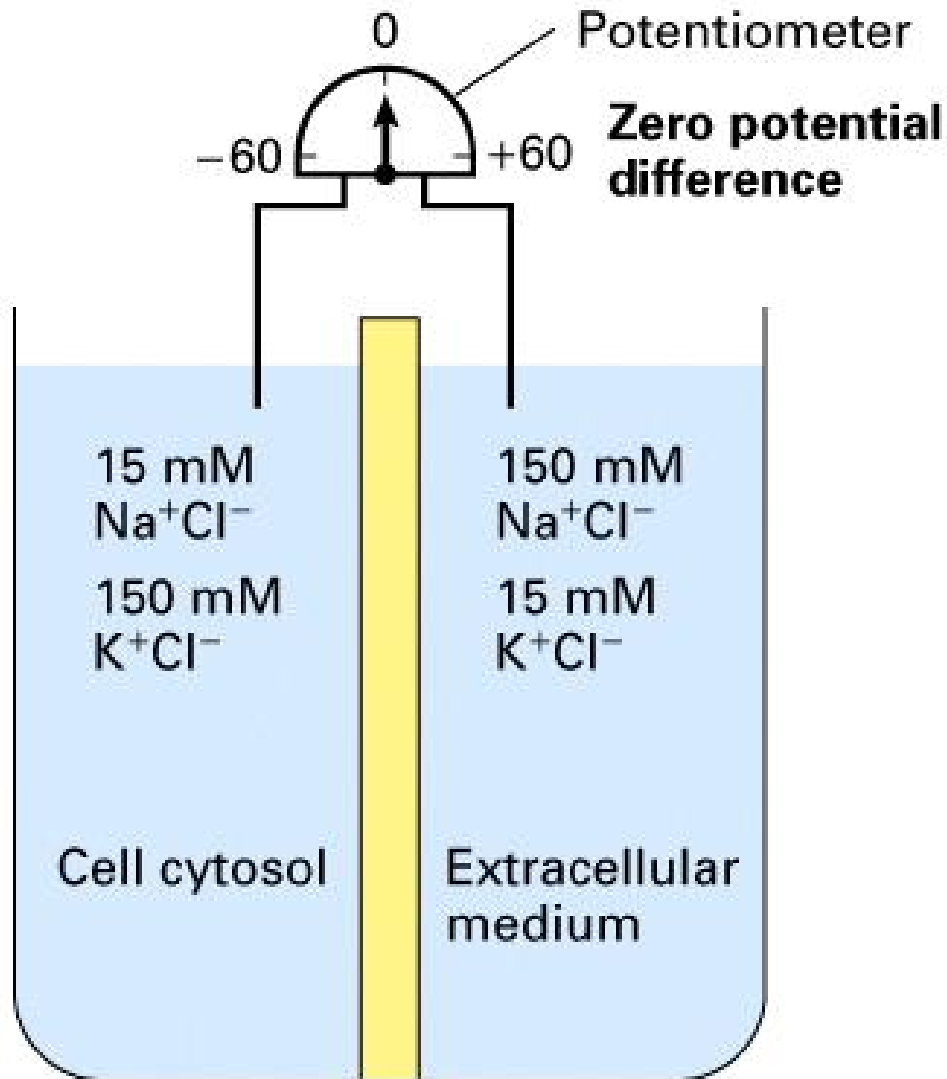
(book has “ $qz$ ”, where  $z$ =valence of ion,  $q$ =proton charge)

*at this potential difference, there is no net flow,  
& everything is in equilibrium*

e.g. (see Figs 2 and 3 that follow): if  $[S^+]_i > [S^+]_e$ ,  
diffusion (through ion-specific channels) would be  
interior  $\rightsquigarrow$  exterior; but if  $V_e > V_i$  then  $\exists$  electrical flow  
exterior  $\rightsquigarrow$  interior, and both *balance out*

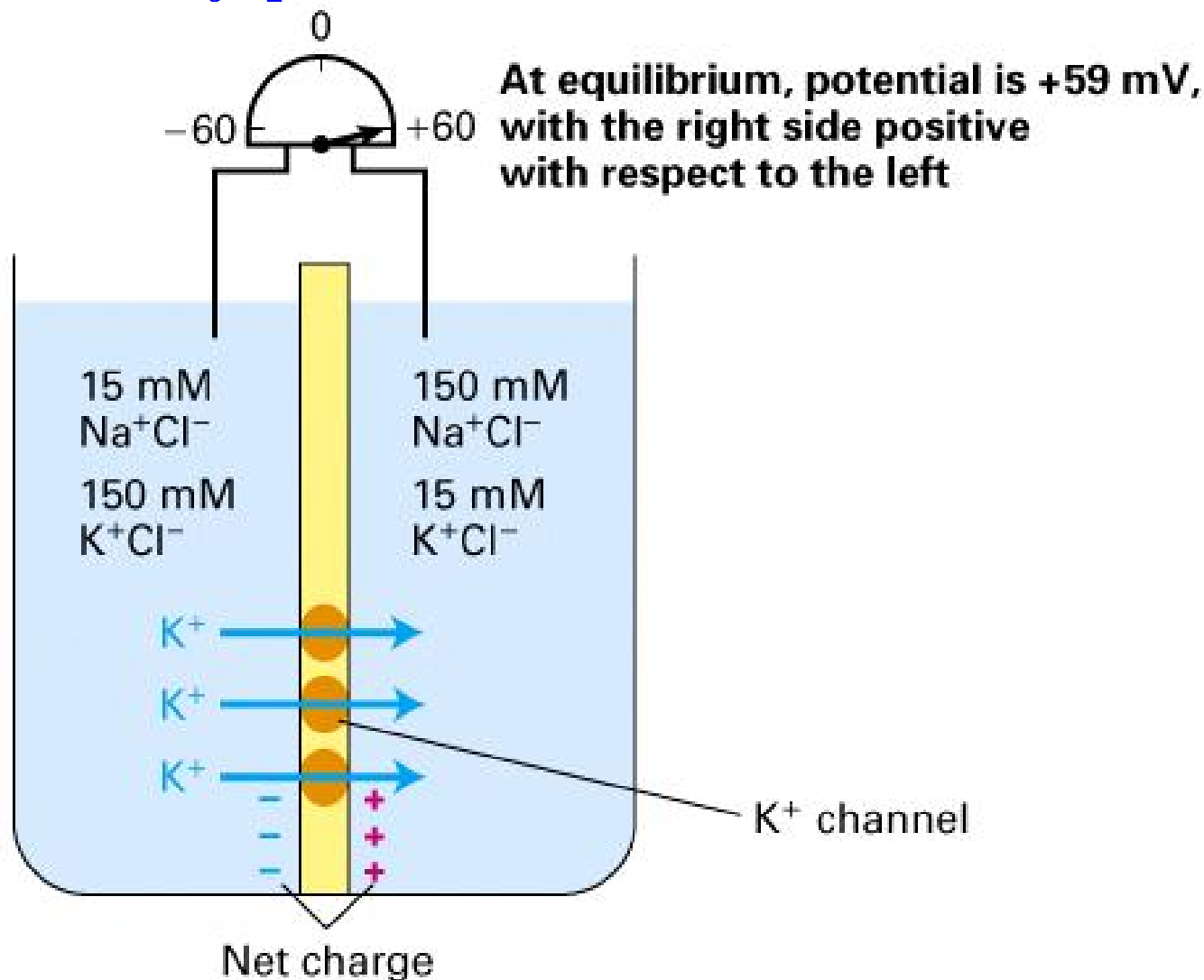
$\therefore$  current due to voltage  $V$  depends on *difference*  $V - V_S$

## impermeable membrane



<http://www.zoology.ubc.ca/~auld/bio350/lectures/Nernst.html>

## $K^+$ -only permeable membrane

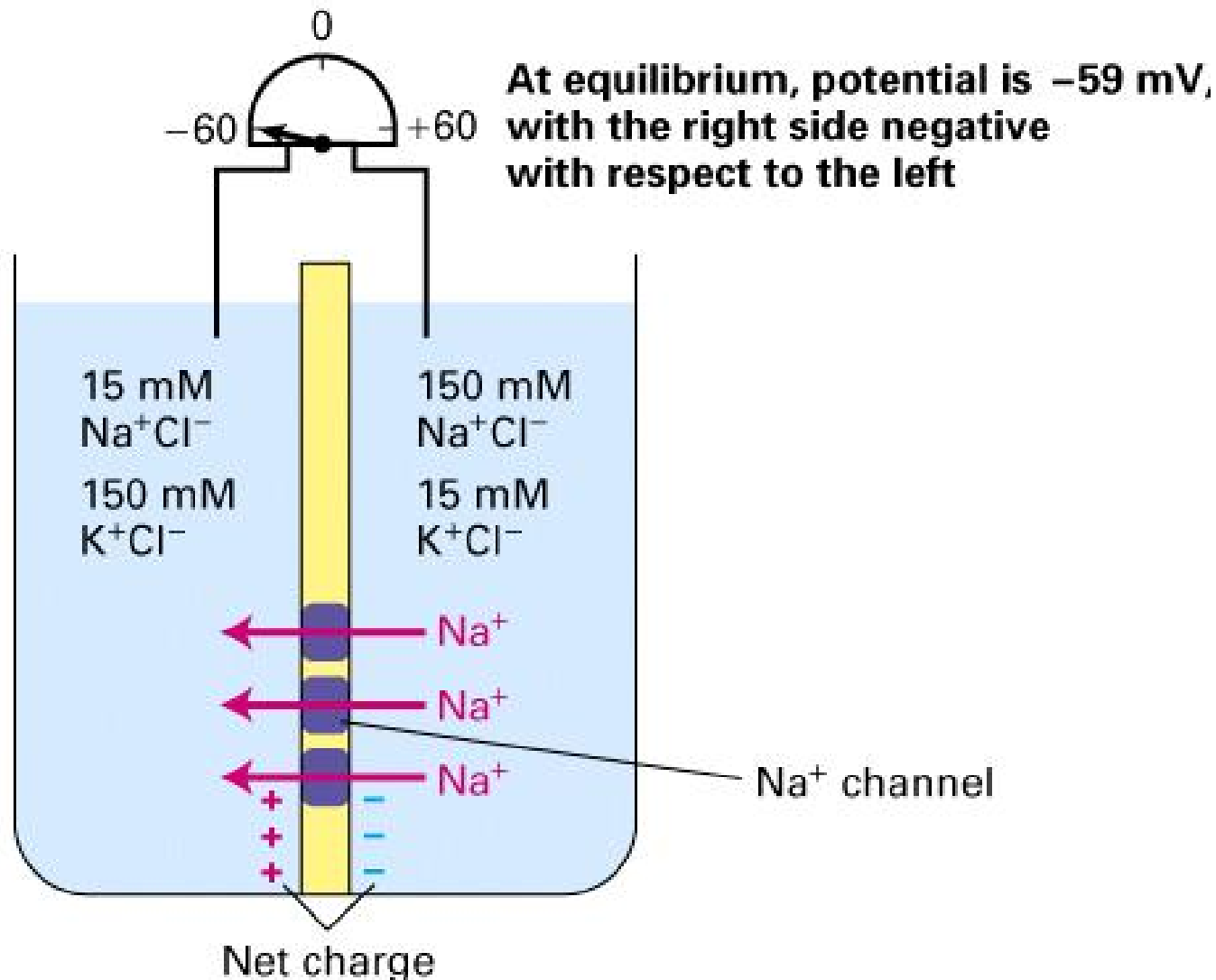


<http://www.zoology.ubc.ca/~auld/bio350/lectures/Nernst.html>

$$[K]_i > [K]_e, V_i < V_e$$

(sign of  $V$  opposite to book, where “internal - external”)

# Na<sup>+</sup>-only permeable membrane



<http://www.zoology.ubc.ca/~auld/bio350/lectures/Nernst.html>

$$[Na]_i < [Na]_e, V_i > V_e$$

(sign of  $V$  opposite to book, where “internal - external”)

applets for Nernst:

select:

“Ion Movements Generate a Membrane Potential”  
and  
“Case of a Membrane Permeable to Potassium”

<http://lessons.harveyproject.org/development/worksprogress.html>

# typical potentials and concentrations

concentrations in nM, potentials in mV

	Squid Giant Axon	Frog Sartorius Muscle	Human Red Blood Cell
Intracellular concentrations			
Na <sup>+</sup>	50	13	19
K <sup>+</sup>	397	138	136
Cl <sup>-</sup>	40	3	78
Mg <sup>2+</sup>	80	14	5.5
Extracellular concentrations			
Na <sup>+</sup>	437	110	155
K <sup>+</sup>	20	2.5	5
Cl <sup>-</sup>	556	90	112
Mg <sup>2+</sup>	53	1	2.2
Nernst potentials			
V <sub>Na</sub>	+56	+55	+55
V <sub>K</sub>	-77	-101	-86
V <sub>Cl</sub>	-68	-86	-9
Resting potentials			
	-65	-99	-6 to -10

## Current-Voltage Relations for Ion Channels

to find formula for current  $I_S$  through a channel for ion  $S$ , need to look at analog of “Ohm’s law” calculation for case when there is also an electrical potential (which acts on ion)

now consider not just flux due to diffusion (Fick’s law) but also flux due to electric field (Planck’s equation) then look for steady state solution of sum of both; leads to ODE, whose solution  $c(x)$  is *nonlinear* function, so flux  $J$  is not constant in this case; from flux, get current (flux  $\times$  charge of each ion):

section 2.5.2: *Goldman-Hodgkin-Katz equation*

$$I_S = P_S \frac{z^2 F^2}{RT} V \frac{[S]_i - [S]_e \exp\left(\frac{-zFV}{RT}\right)}{1 - \exp\left(\frac{-zFV}{RT}\right)}$$

where  $F$  = Faraday’s constant,  $R$  = universal gas constant,  $P_S$  = permeability of membrane to  $S$  (time-dependent  $I_S$ , since  $[S]_i, [S]_e, V$  depend on  $t$ )

note (set numerator to zero) that  $I_S(V) = 0$  exactly when

$$V = V_S = \frac{kT}{q} \ln \left( \frac{[S]_e}{[S]_i} \right) \frac{RT}{zF} \ln \left( \frac{[S]_e}{[S]_i} \right)$$

(consistent with previous equilibrium calculation)

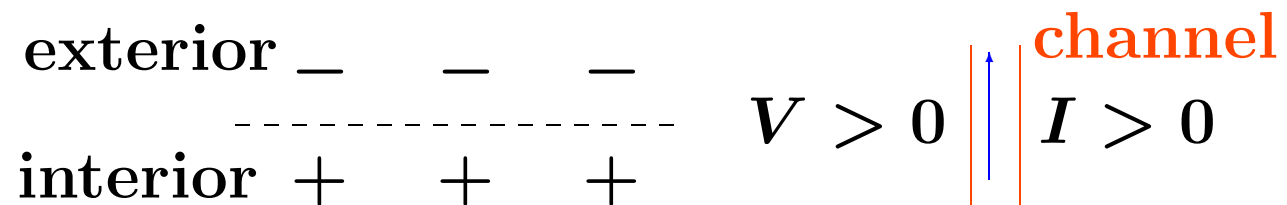
expanding  $\rightsquigarrow I_S(V) = g_S(V - V_S) + o(V - V_S)$

“linear  $I-V$  relation” when dropping nonlinear part good approximation for giant axon of squid, but not always

$g$  is called the *conductance* of the channel

total current = sum of  $I_S$ 's for different channels,  
 + applied external current (when looking at neurons, chap.4)  
 + currents due to active pumps

signs:  $V > 0$ : more positive inside;  $I > 0$ : flow outward)



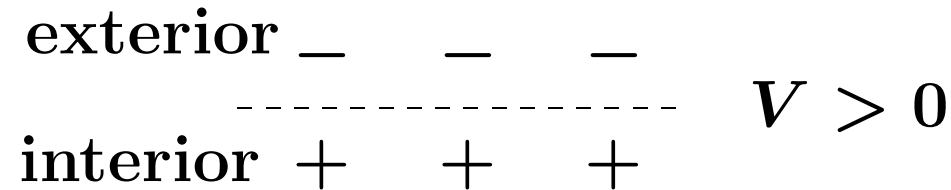
## membrane as capacitor

membrane is not perfect electrical insulator

charges collect on both sides  $\rightsquigarrow$  capacitor effect:

charges “stick” to two sides of membrane

(attracted to the opposite-sign charges on opposite side)



Faraday:  $CV = Q$ ,  $Q =$  net charge,  $C =$  “capacitance”

$C \propto$  area (larger  $\Rightarrow$  more room to stick)

$C \propto 1/\text{thickness}$  (larger  $\Rightarrow$  effect felt less)

$$Q(b) = Q(a) - \int_a^b I_{\text{total}}(t) dt$$

i.e. current charge = starting amount – total outflow,  $\rightsquigarrow$

$$C \frac{dV}{dt} = -I_{\text{total}}$$

## ion flows and charges

consider concentration of ion inside:  $[S]_i(t)$ ;

then, with  $q$  = charge of each ion (positive or negative)

and  $w$  = volume inside cell, total charge is  $wq[S]_i(t)$ , so:

$$wq[S]_i(b) = wq[S]_i(a) - \int_a^b I_S(t) dt$$

i.e., starting amount of charge minus total outflow of charge,

$$\therefore -wq \frac{d[S]_i}{dt} = I_S(t)$$

and when using linear  $I-V$  relation:

$$-wq \frac{d[S]_i}{dt} = \left[ V - \frac{RT}{zF} \ln \left( \frac{[S]_e}{[S]_i} \right) \right]$$

(book inconsistent, sometimes writing “ $zq$ ” instead of “ $q$ ”, where  $z$  = valence and  $q$  = charge of a proton)

note that signs get reversed when  $z = -1$ , i.e. negative ion, which is consistent with direction of current)

## other possible effects on $I_S$ : active pumps

e.g.  $Na - K$  pumps give rise to a “ $+3pq$ ” effect on  $I_{Na}$  and a “ $-2pq$ ” effect on  $I_K$ ,

where  $p$  = rate at which pumps operate,  
since 3  $Na$ 's go out for each 2  $K$ 's that go in  
( $p = p \cdot 1 = pz$  = charge in each ion)

summary, for three ions  $Na^+$ ,  $K^+$ , and  $Cl^-$ ,  
remembering  $z = -1$  (so “ $q$ ” is  $-1$ ) in the case of  $Cl$ ,  
and using linear  $I-V$  relation  $I_S = g_S(V - V_S)$ :

$$\begin{aligned} -q \frac{d[Na]_i}{dt} &= g_{Na} \left[ V - \frac{RT}{F} \ln \left( \frac{[Na]_e}{[Na]_i} \right) \right] + 3pq \\ -q \frac{d[K]_i}{dt} &= g_K \left[ V - \frac{RT}{F} \ln \left( \frac{[K]_e}{[K]_i} \right) \right] - 2pq \\ q \frac{d[Cl]_i}{dt} &= g_{Cl} \left[ V + \frac{RT}{F} \ln \left( \frac{[Cl]_e}{[Cl]_i} \right) \right] \end{aligned}$$

## total charges

total charge outside:

$$Q_i = qw ([Na]_i + [K]_i - [Cl]_i) + z_x q X$$

total charge inside:

$$Q_e = qw_e ([Na]_e + [K]_e - [Cl]_e)$$

where  $X$  represents other molecules (that cannot exit cell), all negatively charged and with valence  $z_x \leq -1$  and  $w$ ,  $w_e$  are amounts of internal, external water

book says  $CV =$  difference of these, but formula cannot be right: charge only matters near membrane; also, positive charges in just one side cannot affect capacitance, etc.  
Should assume  $Q$  is due to net effect of past currents, as with usual capacitors, to make physical sense?

## cell volume

change in volume assumed proportional to water flow  
(ions too small to affect cell volume)

osmosis general principle:  $r \frac{dw}{dt} = kT(c_i - c_e)$  where  
 $c$  = concentration of solutes (particles dissolved in water)  
 $r$  is “flow resistance” of membrane

e.g. more particles inside  $\Rightarrow$  more water flows in  
so here:

$$r \frac{dw}{dt} = kT \left( [Na]_i + [K]_i + [Cl]_i - [Na]_e - [K]_e - [Cl]_e + X/w \right)$$

(book has  $R$  instead of  $k$ : “small” error  $\approx 10^{23}$  :)

next: find (*steady state*) volume, assuming  $Q_i = Q_e = 0$ :  
*electroneutrality*: charges, on each side, separately balanced  
(“not true near membrane, but reasonable assumption”)  
and actually **each** external concentration  $[S]_e \equiv \text{constant}$

nondimensionalize (see book for details):

$$\nu = \frac{FV}{RT}, \quad P = \frac{pFq}{RTg_{Na}}, \quad \mu = \frac{w}{X}[Cl]_e, \quad y = e^{-\nu}$$

electroneutrality becomes:

$$\alpha y - \frac{1}{y} + \frac{z_x}{\mu} = 0$$

and osmotic balance

$$\alpha y + \frac{1}{y} + \frac{1}{\mu} - 2 = 0$$

with  $\alpha = \frac{[Na]_e e^{-3P} + [K]_e e^{2P\gamma}}{[Na]_e + [K]_e}$ ,  $\gamma = g_{Na}/g_K$ , and ion eqs:

$$\frac{[Na]_i}{[Na]_e} = e^{-3P} y$$

$$\frac{[K]_i}{[K]_e} = e^{-2P\gamma} y$$

$$\frac{[Cl]_i}{[Cl]_e} = 1/y$$

e.g.: derivation of  $\frac{[Na]_i}{[Na]_e} = e^{-3P}y$  from

$$0 = \dot{I}_{Na} = g_{Na} \left[ V - \frac{RT}{F} \ln \left( \frac{[Na]_e}{[Na]_i} \right) \right] + 3pq$$

is (using  $\nu = \frac{FV}{RT}$ ):

$$\frac{RT}{F} \ln \left( \frac{[Na]_i}{[Na]_e} \right) = -\frac{3pq}{g_{Na}} - \frac{RT\nu}{F}$$

so multiply by  $\frac{F}{RT}$  and take exponential

now solve  $\alpha y - \frac{1}{y} + \frac{z_x}{\mu} = 0$  for positive root and substitute into  $\alpha y + \frac{1}{y} + \frac{1}{\mu} - 2 = 0$ ; get

$$4(1 - \alpha)\mu^2 - 4\mu + 1 - z_x^2 = 0$$

so (since  $z_x^2 \geq 1$ )  $\exists$  positive root for  $\mu \sim$  volume iff  $\alpha < 1$

can get  $\alpha = \alpha(P) < 1$  for some  $P$  ( $\sim$  pump rate)?

claim:  $\alpha = \alpha(P) < 1$  for some  $P > 0 \Leftrightarrow \alpha'(0) < 0$

proof:

“ $\Leftarrow$ ” clear:  $\alpha(0) = 1$ , so  $\alpha'(0) < 0 \Rightarrow \alpha'(0^+) < 1$

“ $\Rightarrow$ ”: suppose  $\exists P_1$  such that  $\alpha(P_1) < 1$ , but  $\alpha'(0) \geq 0$

then: first assume  $\alpha'(0) > 0$ , which  $\Rightarrow \alpha(P) > 1$  for  $P \approx 0$ , so  $\alpha'$  must change sign, to be able to decrease to  $\alpha(P_1) < 1$ , but also also:  $\alpha(P) \rightarrow \infty$  as  $P \rightarrow \infty$ , so must increase again

thus  $\exists P, Q$  such that  $\alpha'(P) = \alpha(Q) = 0$

(if  $\alpha'(0) = 0$ , decreases to  $P_1$ , then increases, so again  $\exists$  another root of  $\alpha'$ )

however,  $\alpha'(P) = 0$  at most at one point  $P$ , since  $\alpha(P)$  has form  $ae^{-mx} + be^{nx}$ , so  $\alpha' = -mae^{mx} + nbe^{nx} = 0 \Rightarrow mae^{mx} = nbe^{nx} \Rightarrow e^{(m-n)x} = nb/ma$  and exp is 1-1  $\otimes$

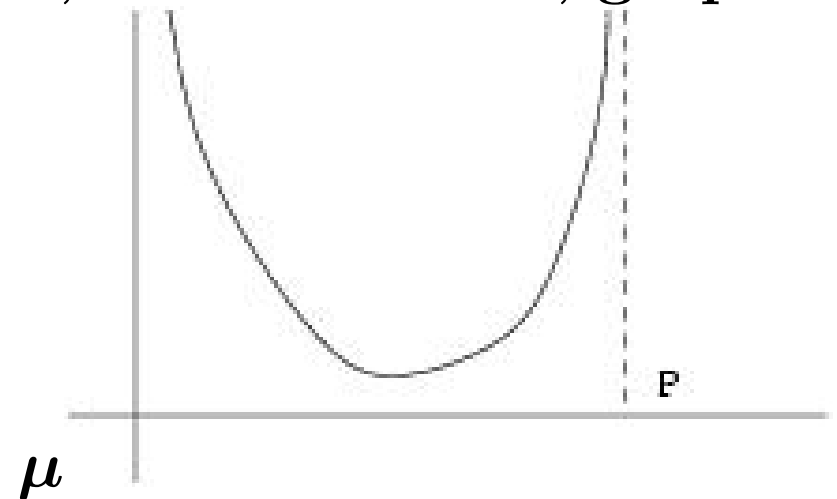
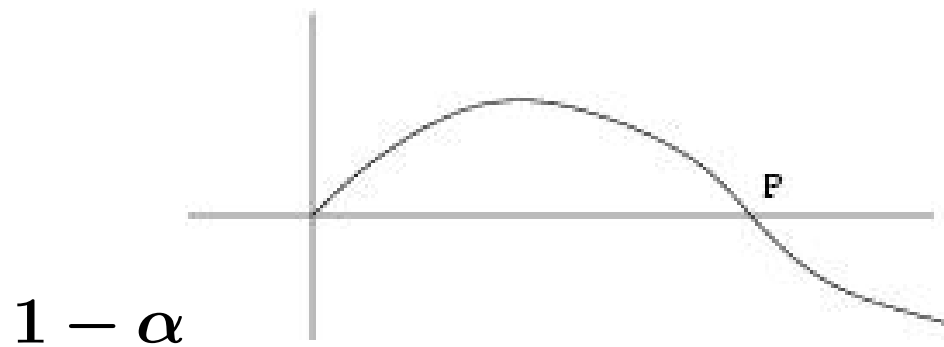
compute  $\alpha'(0) \rightsquigarrow$  condition in terms of  $[Na]_e$ , etc, OK!

graph of  $\mu$  (vol) vs  $P$  (pump rate)

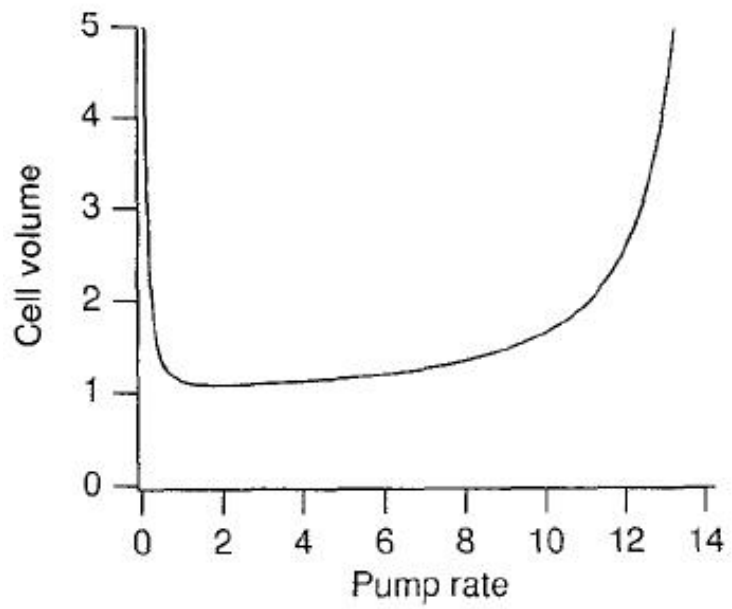
for simplicity,  $z_x = 1$ ; so quadric is  $4(1 - \alpha)\mu^2 - 4\mu = 0$  and positive root is

$$\mu = \frac{1}{1 - \alpha(P)}$$

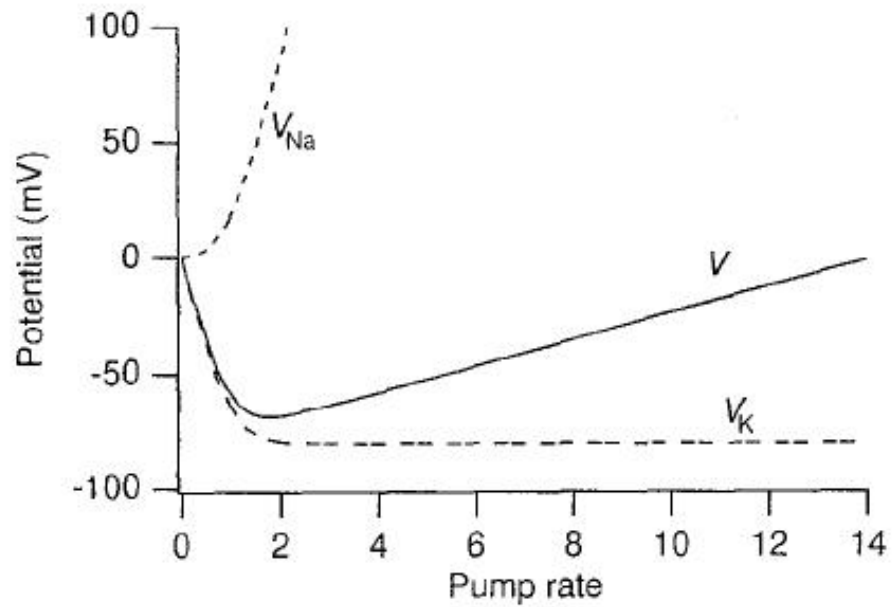
and since we know that  $\alpha$  decreases, then increases, graphs:



for actual parameters in book:



**Figure 2.13** Cell volume as a function of the pump rate.



**Figure 2.14** Membrane potential, sodium equilibrium potential, and potassium equilibrium potential as functions of the pump rate.

singularity at  $P = 0$ : add

$$\alpha y - \frac{1}{y} + \frac{1}{\mu} = 0, \quad \alpha y + \frac{1}{y} + \frac{1}{\mu} - 2 = 0$$

so  $y = 1$ , so  $\nu = 0$  (since  $y = e^{-\nu}$ , so from  $\frac{Na_i}{Na_e} = e^{-3P}y$ , have  $Na_i = Na_e$ , so in  $\dot{w}$  equation just the term  $X/w$  is left, and cell swells (e.g. when dead, no pumping))

interesting: min of  $\mu(P)$  is  $\approx$  observed values, so seems pumping rate is the one that minimizes volume

skip rest of chapter, next: excitable behavior in cells