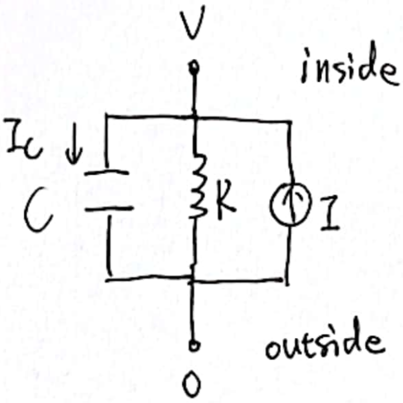
Models of the Neuron



$CV = Q$

$\Rightarrow C\frac{dV}{dt} = \frac{dQ}{dt} = I_c = -\frac{V}{R} + I$

$\Rightarrow \frac{dV}{dt} = -\frac{V}{RC} + \frac{I}{C}$ ...... ①

assume a general form: $\frac{dy}{dx} = \alpha y + \beta$ Let $y = ae^{bx} + d$

$\frac{dy}{dx} = abe^{bx}$, $abe^{bx} = \alpha \cdot [ae^{bx} + d] + \beta \Rightarrow abe^{bx} = \alpha ae^{bx} + \alpha d + \beta$

We have $\begin{cases} ab = a\alpha \\ \alpha d + \beta = 0 \end{cases} \Rightarrow \begin{cases} b = \alpha \\ d = -\frac{\beta}{\alpha} \end{cases}$ a is determined by boundary conditions

in ①, $\alpha = -\frac{1}{RC}$, $\beta = \frac{I}{C}$ $\therefore b = -\frac{1}{RC}$, $d = \frac{-\frac{I}{C}}{-\frac{1}{RC}} = IR$

$\therefore \boxed{V = a \cdot e^{-\frac{t}{RC}} + IR}$

Let $\tau = RC$, ① becomes $\boxed{\tau\frac{dV}{dt} = -V + RI}$ ... ②

give unit impulse at $t=0$ $\Rightarrow \begin{cases} V(0^+) = \frac{1C}{C} \\ I(0^+) = 0 \end{cases} \Rightarrow V(0^+) = \frac{1}{C}$ dimensionless

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i.e., dirac delta function : $\delta(t)$

$\Downarrow$

$a = \frac{1}{C}$

$\Rightarrow$ for $t > 0$, $V(t) = \frac{1}{C}e^{-\frac{t}{\tau}} \triangleq h(t)$ unit impulse response

$h(t) = \frac{1}{C}e^{-\frac{t}{\tau}}$

$I(t) = \sum_i q_i \delta(t - t_i)$ $q_i = I(t_i) \cdot dt$ very small, so do integral.

$$\boxed{\begin{aligned} V(t) &= V(0)e^{-\frac{t}{\tau}} + \frac{1}{C}\int_0^t e^{-\frac{(t-t')}{\tau}} \cdot I(t') \cdot dt' \\ &= V(0)e^{-\frac{t}{\tau}} + \frac{1}{C}\int_0^t h(t-t') \cdot I(t') dt' \end{aligned}}$$ Convolution.

	Actual values in discrete circuit	Definition per unit length	Conventional definition	
Capacitance	$\hat{c}$	$c=\hat{c}/h$	$C=\hat{c}/S$	C per unit area
Membrane resistance	$\hat{r}_m$	$r_m=\hat{r}_m h$	$R_m=\hat{r}_m\cdot S$	R_m per unit area
Internal resistance	$\hat{r}_i$	$r_i=\hat{r}_i/h$	$R_i=\hat{r}_i\cdot\frac{A}{h}$	R_i resistivity

$\hat{c}=c\cdot h$ $\quad$ $\hat{c}=C\cdot S$

$\hat{r}_m=r_m/h$ $\quad$ $\hat{r}_m=R_m/S$

$\hat{r}_i=r_i\cdot h$ $\quad$ $\hat{r}_i=R_i\cdot\frac{h}{A}$

$$\boxed{\begin{aligned} S&=hl\\ l&=\pi d\\ A&=\pi\left(\frac{d}{2}\right)^2 \end{aligned}}$$

cable equation

$$\tau\frac{\partial V(x,t)}{\partial t}=-V(x,t)+\lambda^2\frac{\partial^2 V(x,t)}{\partial x^2}+R_m I(x,t)$$

$$\begin{cases}\text{Time constant} & \tau=\hat{r}_m\cdot\hat{c}=r_m\cdot c=R_m\cdot C\\ \text{space constant} & \lambda=\sqrt{\dfrac{\hat{r}_m h^2}{\hat{r}_i}}=\sqrt{\dfrac{r_m}{r_i}}=\sqrt{\dfrac{R_m d}{4R_i}}\end{cases}$$

$I(x,t)$ is from outside to inside.

$I(x,t)$ is the extra current.

Cable equation with external resistance

$$\tau\frac{\partial V(x,t)}{\partial t}=-V(x,t)+\lambda^2\frac{\partial^2 V(x,t)}{\partial x^2}+R_m I(x,t)$$

$$\begin{cases}\text{Time constant} & \tau=r_m\cdot c\\ \text{space constant} & \lambda=\sqrt{\dfrac{r_m}{r_o+r_i}}\end{cases}$$ (the only difference).

Flat state of the cable equation

Assume $V(x,t)=V(t)$ (same voltage along the cable).

we have $\tau\frac{dV(t)}{dt}=-V(t)+R_m I(t)$ → identical to that of the standard RC circuit.

General Solution for discrete model

$$c_i \dot{V}_i = -V_i/r_i + \sum_{j, j\neq i} (V_j - V_i)/r_{ij} + I_i \quad , \quad i=1,2,\cdots,n.$$

$\Downarrow$

$$\boxed{c_i \dot{V}_i = \sum_{j=1}^{n} g_{ij} V_j + I_i \quad , i=1,\cdots,n.}$$

$$g_{ij} = \begin{cases} -1/r_i - \sum_{k,k\neq i} 1/r_{ik} \ , & \text{if } i=j, \\ 1/r_{ij} \ , & \text{if } i\neq j. \end{cases}$$

$G = \{g_{ij}\}$. $g_{ij} = g_{ji}$, G is symmetric.

$\underbrace{v = [c_1^{1/2} V_1, \cdots, c_n^{1/2} V_n]^T}_{\text{scaled voltage vector}}$, $\underbrace{z = [c_1^{-1/2} I_1, \cdots, c_n^{-1/2} I_n]^T}_{\text{scaled input vector}}$. $C = \text{diag}\{c_1, \cdots, c_n\}$

input: current.

$\Downarrow$

$C^\alpha = \text{diag}\{c_1^\alpha, \cdots, c_n^\alpha\}$

vector-matrix form: $\dot{v} = W \cdot v + z$, $W = C^{-1/2} G C^{1/2}$

W is symmetric ($W^T = W$) $\quad W = U \Lambda U^T = \sum_{k=1}^{n} \lambda_k u_k u_k^T$ with $UU^T = I$

$\Lambda = \text{diag}\{\lambda_1, \cdots, \lambda_n\}$ diagonal matrix

λ_k ↳ eigenvalue

$U = [u_1, u_2, \cdots u_n]$ ↳ orthogonal matrix

u_k ↳ eigenvector

see Handout 1.pdf 2.6.3 general solution for discrete model for details.

Kernel for impulse response

Kernel $K_{ij}(t)$ is the voltage response at node i to a Dirac delta impulse current $\delta(t)$ dilivered to node j. $\quad K_{ij}(t) = \frac{1}{\sqrt{c_i c_j}} \sum_{k=1}^{n} e^{\lambda_k t} u_{k,i} u_{k,j}$.

~~repo~~ reciprocity

$\Uparrow$

$K_{ij}(t) = K_{ji}(t)$ due to the symmetry $W^T = W$. Finally, we have $V_{a,b}(t) = V_{b,a}(t)$.

3

Entropy formulas and Boltzmann distribution. The logic ~~relash~~ relationship of these formulas is organized on page 6.

- Clausius $dS = \frac{dQ}{T}$ heat over temperature
- Boltzmann $S = k \ln W$ W is the number of microscopic states
- Gibbs $S = -kN \sum_{i=1}^{n} p_i \ln p_i$ for N molecules with n energy states
- Shannon $S = -\sum_i p_i \log_2 p_i$ for random variable.

Maximizing entropy leads to Boltzmann distribution

$p_i \propto e^{-\beta E_i}$, p_i is the probability of state with energy E_i.

$\beta = \frac{N_A}{RT} = \frac{1}{kT}$

Why maximizing the entropy?
It can be thought of as being derived from the second law thermodynamics.

Nernst equation of equilibrium potential (reversal potential)

$$\underbrace{V = \frac{kT}{q} \ln \frac{C_o}{C_i}}$$

V is the Nernst potential or the equilibrium potential.

$q = ez$; e: elementary charge ; z: valence

derived based on Boltzmann distribution (max entropy)

Fick's law of diffusion $\boxed{J = -D\frac{\partial C}{\partial x}}$

J: diffusion flux mol/(m²·s)
D: diffusion coefficient (diffusivity) m²/s

no time terms

We have $\boxed{\frac{\partial C}{\partial t} = -\frac{\partial J}{\partial x}}$ according to the conservation of mass.
the continuity equation ☆

$$\frac{\partial C}{\partial t} = -\frac{\partial}{\partial x}\left(-D\frac{\partial C}{\partial x}\right) = D\frac{\partial^2 C}{\partial x^2}$$

with time terms

Fick's ~~law~~ second law of diffusion $\boxed{\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2}}$

If we consider diffusion with drift, then Fick's law $J = -D\frac{\partial c}{\partial x}$ is replaced by $J = -D\frac{\partial c}{\partial x} + vc$.

v → drift velocity. same

Then the Fick's second law is replaced by Fokker-Planck equation. (diffusion equation with drift)

Fick's second law $\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}$

⇓

Fokker-Planck equation $\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} - \frac{\partial (vc)}{\partial x}$ ~~Focker~~

drift velocity ↑ $v = \mu E$

It's from

Ohm's law for flux of ions $J = -\mu c\frac{\partial u}{\partial x}$ (only considering drift)

μ: electrical mobility ($m^2/(V\cdot s)$)

$J = vc = -\mu c\frac{\partial u}{\partial x}$

~~Ernst~~ Nernst-Planck equation adds together Fick's law and Ohm's law.

$$\boxed{J = -D\frac{\partial c}{\partial x} - \mu c\frac{\partial u}{\partial x}}$$

use the continuity equation $\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x}$

introduce time

Then the Fokker-Planck equation becomes. $\boxed{\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} - \mu\frac{\partial}{\partial x}\left(c\frac{\partial u}{\partial x}\right)}$

At equilibrium, Nernst-Plank equation also implies Nernst equation.

Let $J = -D\frac{\partial c}{\partial x} - \mu c\frac{\partial u}{\partial x} = 0 \Rightarrow V = \frac{D}{\mu}\ln\frac{C_o}{C_i} = \frac{kT}{q}\ln\frac{C_o}{C_i}$

$\Rightarrow$ Einstein relation $D = \mu kT/q$

The logic relationship between entropy, Boltzmann distribution, Nernst equation, Fick's law, Fick's second law, the continuity equation, Fokker-Planck equation, Nernst-Planck equation, Ohm's law, and Einstein relation.

Entropy with different form (but should be equivalent).

⇓ maximize entropy (the second law of thermodynamics)

$\beta = \frac{N_A}{RT} = \frac{1}{kT}$ (demonstrated from physics)

Boltzmann distribution $P_i \propto e^{-\beta E_i}$

1st part

⇓ directly implies

Nernst equation of equilibrium potential $V = \frac{kT}{q} \ln \frac{C_o}{C_i}$

Considers drift, i.e., **Ohm's law** $J = vC = -\mu C \frac{\partial u}{\partial x}$ (Another form of $U = IR$)

Fick's law $J = -D\frac{\partial C}{\partial x}$

Nernst-Planck equation $J = -D\frac{\partial C}{\partial x} - \mu C \frac{\partial u}{\partial x}$

⇓ use **the continuity equation** $\frac{\partial C}{\partial t} = -\frac{\partial J}{\partial x}$

⇓ use **the continuity equation**

Fick's second law $\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2}$

Fokker-Planck equation $\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} - \mu \frac{\partial}{\partial x}\left(C\frac{\partial u}{\partial x}\right)$

demonstrated by mass conservation.

2nd part

Nernst equation and **Nernst-Planck equation** are from two separate parts above. But at equilibrium, they ~~are~~ are related and implies **Einstein relation**

$J = -D\frac{\partial C}{\partial x} - \mu C \frac{\partial u}{\partial x} = 0 \Rightarrow V = \frac{D}{\mu} \ln \frac{C_o}{C_i} \quad V = \frac{kT}{q} \ln \frac{C_o}{C_i}$

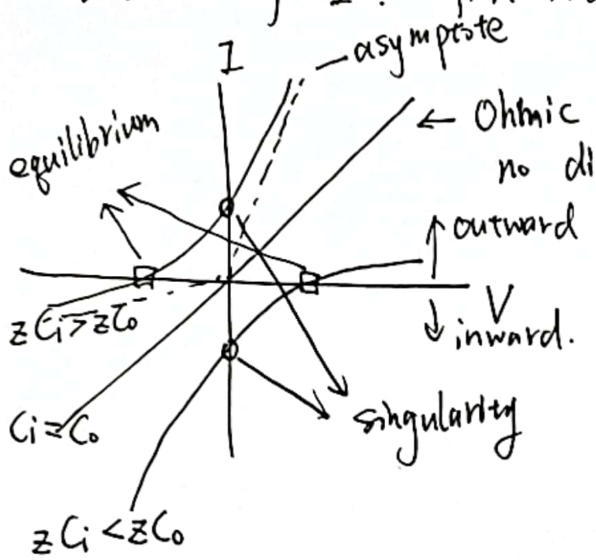
$D = \frac{\mu k T}{q}$

$\boxed{\text{Goldman-Hodgkin-Katz current equation.}}$

comes from Nernst-Planck equation with assuming J, $c(x)$, U don't change with time

$$I = PFz^2 \frac{eV}{kT} \frac{C_i - C_o e^{-zeV/kT}}{1 - e^{-zeV/kT}}, \quad P = D/L \text{ is the membrane permeability.}$$

direction of I: from inside to outside. i.e., $\begin{cases} I > 0 & \text{outward current} \\ I < 0 & \text{inward current} \end{cases}$



singularity point: diffusion only, no ohmic current.

equilibrium point: can be used to derive the reversal potential E (equilibrium potential)

$$I = 0 \Rightarrow C_i = C_o e^{-zeV/kT} \Rightarrow V = \frac{kT}{ze} \ln \frac{C_o}{C_i}$$

E should be ~~as large~~ same as $\frac{kT}{ze} \ln \frac{C_o}{C_i}$ to keep the ~~ba~~ equilibrium.

$$\boxed{E = \frac{kT}{ze} \ln \frac{C_o}{C_i}}$$

positive slope at equilibrium points implies stable equilibrium. Because as I increases, charges go out, ~~resulting~~ resulting in a lower voltage, then according to the positive slope, I decreases.

$\boxed{\text{Goldmann-Hodgkin-Katz voltage equation}}$

After applying GHK current equation to each single ionic species, and letting the total current $I = I_K + I_{Na} + I_{Cl} = 0$, we will get the GHK voltage equation:

$$V = E = \frac{kT}{e} \ln \frac{P_{Na}[Na^+]_o + P_K[K^+]_o + P_{Cl}[Cl^-]_i}{P_{Na}[Na^+]_i + P_K[K^+]_i + P_{Cl}[Cl^-]_o}$$

special case for a single ion: $E = \frac{kT}{ze} \ln \frac{C_o}{C_i}$ (Nernst equation)

(the term P (permeability) is canceled out)

Equilibrium potential for monovalent ions.

If including divalent ions, the equation will be more complex.

Hodgkin-Huxley model (1952)

Gating variable first-order kinetics

$$1-p \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} p$$

$\alpha = \alpha(V)$ is the rate for gate opening
$\beta = \beta(V)$ is the rate for gate closing
both are voltage-dependent.

$$\frac{dp}{dt} = \alpha(1-p) - \beta p$$

p is between 0 and 1.

Example: gating variable n for potassium channel.

$$\frac{dn}{dt} = \alpha(1-n) - \beta n \Rightarrow \frac{dn}{dt} = -(\alpha+\beta)n + \alpha \Rightarrow \frac{1}{\alpha+\beta}\frac{dn}{dt} = -n + \frac{\alpha}{\alpha+\beta}$$

$$\Rightarrow \boxed{\tau \frac{dn}{dt} = -n + n_\infty}$$

we define

$\boxed{\tau = \frac{1}{\alpha+\beta}}$ time constant

$\boxed{n_\infty = \frac{\alpha}{\alpha+\beta}}$ steady-state value

$$\Leftrightarrow \begin{cases} \alpha = \frac{n_\infty}{\tau} \\ \beta = \frac{1-n_\infty}{\tau} \end{cases}$$

$$\frac{dn}{dt} = \alpha(1-n) - \beta n \Rightarrow \text{solution } n(t) = Ae^{-(\alpha+\beta)t} + \frac{\alpha}{\alpha+\beta} = \boxed{A \cdot e^{-\frac{t}{\tau_n}} + n_\infty}$$

$$A = n_0 - n_\infty$$

$$\boxed{n(t) = (n_0 - n_\infty)e^{-\frac{t}{\tau_n}} + n_\infty}$$

for small t: $e^{-t/\tau_n} \approx 1 - t/\tau_n$

$$n(t) \simeq n_0 + (n_\infty - n_0)\,t/\tau_n$$

$$g_{Na} = \bar{g}_{Na} m^3 h \qquad\qquad g_K = \bar{g}_K n^4$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)\, m$$

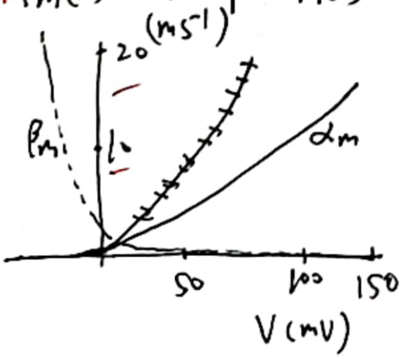
$$\begin{cases} \alpha_m(V) = \dfrac{0.1(25-V)}{\exp((25-V)/10) - 1} \\ \beta_m(V) = 4\exp(-V/18) \end{cases}$$

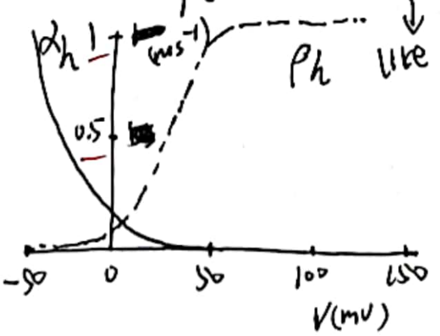
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)\, h$$

$$\begin{cases} \alpha_h(V) = 0.07\exp(-V/20) \\ \beta_h(V) = \dfrac{1}{\exp((30-V)/10) + 1} \end{cases}$$

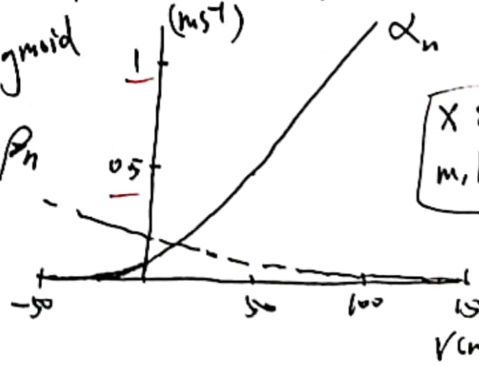
$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)\, n$$

$$\begin{cases} \alpha_n(V) = \dfrac{0.01(10-V)}{\exp((10-V)/10) - 1} \\ \beta_n(V) = 0.125\exp(-V/80) \end{cases}$$





β_h like sigmoid



X stands for m, h, n

$$\tau_x(V) = \frac{1}{\alpha_x(V) + \beta_x(V)}, \quad x_\infty(V) = \frac{\alpha_x(V)}{\alpha_x(V) + \beta_x(V)}, \quad \alpha_x(V) = \frac{x_\infty(V)}{\tau_x(V)}, \quad \beta_x(V) = \frac{1 - x_\infty(V)}{\tau_x(V)}$$

Hodgkin-Huxley Model (1952)

$$C\frac{dV}{dt} = g_{Na}(E_{Na} - V) + g_K(E_K - V) + g_L(E_L - V) + I$$

$$\left(I_{total} = -(I_{Na} + I_K + I_L) + I\right)$$

$$\begin{cases} I_{Na} = g_{Na}(V - E_{Na}) & g_{Na} = \bar{g}_{Na} m^3 h \\ I_K = g_K(V - E_K) & g_K = \bar{g}_K n^4 \\ I = g_L(V - E_L) & g_L \text{ is a constant} \end{cases}$$

set the resting state's $V = 0$

then $E_K = -12\,mV$

$E_{Na} = 115\,mV$

$I: \begin{cases} \text{inward} & \text{positive} \\ \text{outword} & \text{negative} \end{cases}$

$I_{Na}, I_K, I_L \begin{cases} \text{inward} & \text{negative} \\ \text{outward} & \text{positive} \end{cases}$

Fitzhugh-Nagumo model.

$$\begin{cases} \dot{V} = V - V^3/3 - W + I \\ \tau \dot{W} = -W + AV + B \end{cases}$$

$(A = 1.2,\ B = 0.8,\ \tau = 15)$

V-nullcline $\dot{V} = 0$ $W = V - V^3/3 + I$

W-nullcline $\dot{W} = 0$ $W = AV + B$

$$\begin{cases} W_0 = V_0 - V_0^3/3 + I \\ W_0 = AV_0 + B \end{cases} \Rightarrow (A-1)V_0 + V_0^3/3 = I - B$$

equilibrium point (V_0, W_0)