Biophysical Foundations

BENG/BGGN 260 Neurodynamics

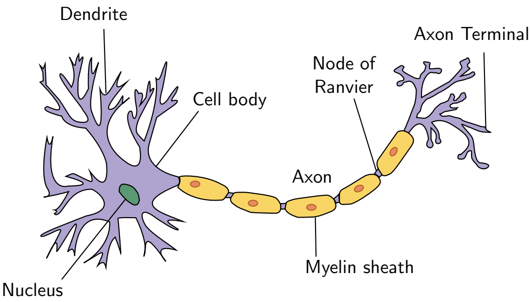
University of California, San Diego

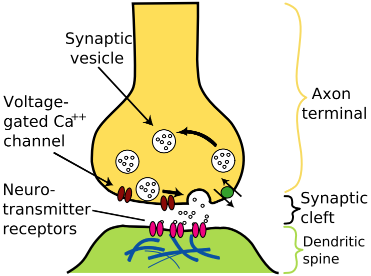
Week 1

Reading Material

- B. Hille, *Ion Channels of Excitable Membranes*, Sinauer, 2001, Ch. 1 and 10, pp. 1-21 and 309-326.
- C. Koch, *Biophysics of Computation*, Oxford Univ. Press, 1999, Ch. 1, pp. 5-13.
- P. Dayan and L. Abbott, *Theoretical Neuroscience*, MIT Press, 2001, Ch. 5, pp. 153-162.
- E.M. Izhikevich, *Dynamical Systems in Neuroscience*, MIT Press, 2007, Ch. 2, pp. 25-28.

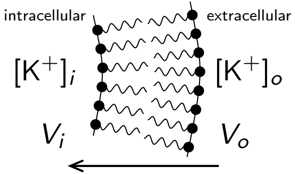
Neurodynamics: Overview





Membrane Dynamics	**Temporal Coding Signal Propagation**	**Adaptation and Learning**
Action Potential Generation	Axon Dynamics	STDP, reinforcement, ...
~ 1 ms	$\sim 10 - 100$ ms	~ 1 s – years

Nernst Potential



$$V_m = V_i - V_o$$

membrane potential

density ratio

energies per molecule

energies per mol

$$\frac{[K^+]_o}{[K^+]_i} = \frac{n_o}{n_i} = e^{-\frac{\mathcal{E}_o - \mathcal{E}_i}{kT}} \left(= e^{-\frac{U_o - U_i}{RT}} \right)$$

Boltzman constant

absolute temperature

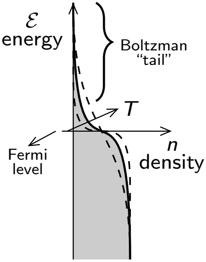
gas constant

$$= e^{-\frac{V_o - V_i}{kT/q}}$$

charge per molecule
$= 1.6\ 10^{-19}$C per valence index

$$\Rightarrow E_{rest} = V_m\big|_{equilibrium} = \overbrace{\frac{kT}{q}}^{\text{25mV @ room T}} \quad \ln \frac{[K^+]_o}{[K^+]_i}$$

$$= \underbrace{\frac{kT}{q} \ln 10}_{\text{62mV @ room T}} \quad \log_{10} \frac{[K^+]_o}{[K^+]_i}$$



Nernst Potential

TABLE 1.3 Free Ion Concentrations and Equilibrium Potentials for Mammalian Skeletal Muscle

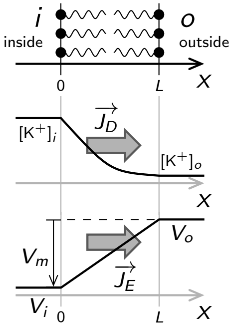
Ion	Extracellular concentration (mM)	Intracellular concentration (mM)	$\frac{\text{Ion}_o}{\text{Ion}_i}$	Equilibrium potential[a] (mV)
Na^+	145	12	12	+67
K^+	4	155	0.026	−98
Ca^{2+}	1.5	100 nM	15,000	+129
Cl^-	123	4.2[b]	29[b]	−90[b]

[a] Calculated from Equation 1.11 at 37°C $\left(E_{rest} = \frac{kT}{q} \ln \frac{[\text{Ion}]_o}{[\text{Ion}]_i}\right)$.

[b] Calculated assuming a −90-mV resting potential for the muscle membrane and that Cl^- ions are a equilibrium at rest.

Hille 2001, p. 17

Nernst-Planck



Equilibrium between **diffusion** and **drift**:

(chemical) (electrical)

Diffusion: $\overrightarrow{J_D} = qD \cdot \left(-\vec{\nabla}[K^+]\right)$

Drift: $\overrightarrow{J_E} = q[K^+]\mu \cdot \vec{E} = q\mu[K^+]\left(-\vec{\nabla}V\right)$

$$\Rightarrow \overrightarrow{J_{K^+}} = \overrightarrow{J_D} + \overrightarrow{J_E} = 0 \quad \text{equilibrium}$$

$$\Rightarrow -qD\frac{d[K^+]}{dx} - q\mu[K^+]\frac{dV}{dx} = 0 \Rightarrow \frac{D}{\mu}\boxed{\frac{d[K^+]}{[K^+]}} \underset{d\left(\ln[K^+]\right)}{=} -dV$$

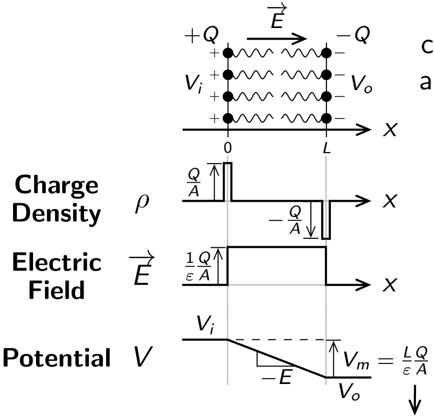
$$\Rightarrow \frac{D}{\mu}\ln\frac{[K^+]_o}{[K^+]_i} = -\left(V_o - V_i\right) = V_m \quad = E_{rest} \text{ with } \frac{D}{\mu} = \frac{kT}{q}$$

indeed, $D = \frac{kT}{q} \cdot \mu$

Dissipation-fluctuation

(Einstein)

Membrane Capacitance



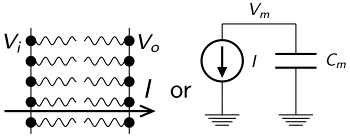
capacitance = differential charge accumulation with voltage across insulator (membrane)

$$\vec{\nabla}\vec{E} = \frac{\rho}{\varepsilon}\text{ , or }\frac{dE}{dx} = \frac{\rho}{\varepsilon}$$

$$\vec{\nabla}V = -\vec{E}\text{ , or }\frac{dV}{dx} = -E$$

$Q = C_m \cdot V_m$ with $C_m = \varepsilon \cdot \frac{A}{L}$ $\quad \frac{\varepsilon}{L} \approx 0.01\ \mathrm{F/m^2}$

Dynamics:



$$: \ C_m \frac{dV_m}{dt} = -I(V_m, \ldots)$$

Membrane Dynamics

- K^+: current density $\overrightarrow{J_K} = -q\mu[K]\left(\frac{kT}{q}\vec{\nabla}\ln[K] + \vec{\nabla}V\right)$

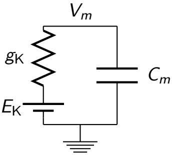
$\Downarrow$ approximate arguments ... more rigorous later

current $I_K \approx -q\mu\overline{[K]}\frac{A}{L}\left(\frac{kT}{q}\ln\frac{[K]_o}{[K]_i} + V_o - V_i\right) = g_K\left(V_m - E_K\right)$

average concentration

membrane thickness

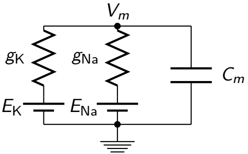
effective cross-section



$$\begin{cases} g_K = q\mu\overline{[K]}\frac{A}{L} \\ E_K = \frac{kT}{q}\ln\frac{[K]_o}{[K]_i} \end{cases}$$

Ohmic approximation

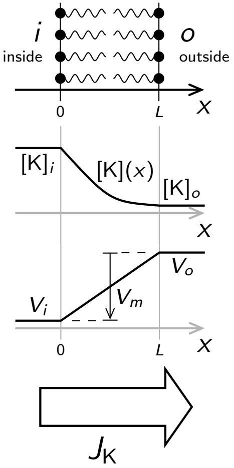
- K^+, Na^+:



Equilibrium: $E_{rest} = V_m = \dfrac{g_K E_K + g_{Na} E_{Na}}{g_K + g_{Na}}$

Not quite...

Goldman-Hodgkin-Katz



$$\vec{J}_\mathrm{K} = -q\mu\left(\frac{kT}{q}\vec{\nabla}[\mathrm{K}] + [\mathrm{K}]\vec{\nabla}V\right)$$

CURRENT DENSITY, $\mu A/cm^2$ DIFFUSION DRIFT

1-D, along x perpendicular to membrane:

$$J_\mathrm{K} = -q\mu\left(\frac{kT}{q}\frac{d[\mathrm{K}]}{dx} + [\mathrm{K}]\frac{dV}{dx}\right)$$

- $J_\mathrm{K} =$ constant (flow conservation)
- $\frac{dV}{dx} =$ constant (assumption!)
  $= -\frac{V_m}{L}$

$$\Rightarrow \frac{kT}{q}\frac{d[\mathrm{K}]}{dx} = -\frac{J_\mathrm{K}}{q\mu} + \frac{V_m}{L}\cdot[\mathrm{K}]$$

Goldman-Hodgkin-Katz Continued

$$\frac{kT}{q}\frac{d[\mathrm{K}]}{dx} = -\frac{J_\mathrm{K}}{q\mu} + \frac{V_m}{L}\cdot[\mathrm{K}] \;\Rightarrow\; \frac{d[\mathrm{K}]}{-\frac{J_\mathrm{K}}{q\mu} + \frac{V_m}{L}\cdot[\mathrm{K}]} = \frac{dx}{\frac{kT}{q}} \;\Rightarrow$$

$$\frac{L}{V_m}\, d\left[\ln\left(-\frac{J_\mathrm{K}}{q\mu} + \frac{V_m}{L}\cdot[\mathrm{K}]\right)\right] = \frac{dx}{\frac{kT}{q}} \;\Rightarrow\; \frac{V_m}{\frac{kT}{q}} = \ln\frac{-J_\mathrm{K} + \frac{q\mu V_m}{L}[\mathrm{K}]_o}{-J_\mathrm{K} + \frac{q\mu V_m}{L}[\mathrm{K}]_i} \;\Rightarrow$$

$$J_\mathrm{K}\left(1 - e^{-V_m/\frac{kT}{q}}\right) = \frac{q\mu V_m}{L}\left([\mathrm{K}]_i - e^{-V_m/\frac{kT}{q}}[\mathrm{K}]_o\right) \;\Rightarrow$$

$$J_\mathrm{K} = \frac{q\mu V_m}{L}\cdot\frac{[\mathrm{K}]_i - e^{-V_m/\frac{kT}{q}}[\mathrm{K}]_o}{1 - e^{-V_m/\frac{kT}{q}}}$$

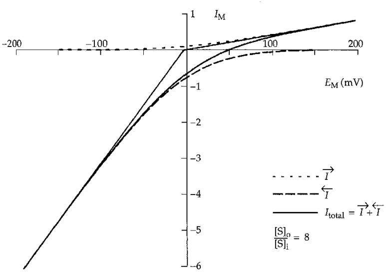
"GHK current equation"

Ohm's limit: $[\mathrm{K}]_i = [\mathrm{K}]_o = [\mathrm{K}]$

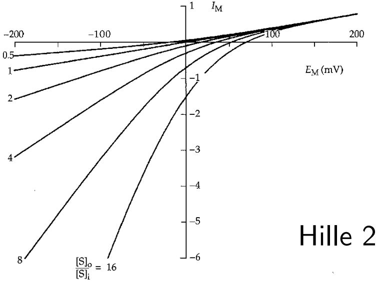
$$\Rightarrow J_\mathrm{K} = \frac{q\mu V_m}{L}\cdot[\mathrm{K}]$$

Goldman-Hodgkin-Katz Current Law

(A) UNIDIRECTIONAL FLUXES



(B) CONCENTRATION DEPENDENCE



Hille 2001, Fig. 14.2, p. 447

Goldman-Hodgkin-Katz Limits

$$J_{\mathrm{K}} = \frac{q\mu_{\mathrm{K}} V_m}{L} \cdot \frac{[\mathrm{K}]_i - e^{-V_m/V_t}[\mathrm{K}]_o}{1 - e^{-V_m/V_t}} \qquad V_t = \tfrac{kT}{q} \approx 25.9mV$$

① $J_{\mathrm{K}} = 0$ for $[\mathrm{K}]_i = e^{-V_m/V_t}[\mathrm{K}]_o$, or $V_m = V_t \ln \frac{[\mathrm{K}]_o}{[\mathrm{K}]_i} = E_K$ (OK!)

② $$\begin{tikzcd} & \frac{q\mu_{\mathrm{K}}}{L}[\mathrm{K}]_i\, V_m = P_{\mathrm{K}}[\mathrm{K}]_i\, V_m \\ J_{\mathrm{K}} \arrow[ur, "\mathrm{V_m} \gg \mathrm{V_t}"] \arrow[dr, "V_m \ll -V_t"'] & \\ & \frac{q\mu_{\mathrm{K}}}{L}[\mathrm{K}]_o V_m = P_{\mathrm{K}}[\mathrm{K}]_o V_m \end{tikzcd}$$

$$P_{\mathrm{K}} = \tfrac{q\mu_{\mathrm{K}}}{L}$$

"permeability"

$\Rightarrow$ Current asymptotes to a linear conductance limited by the **sourcing** concentration at active terminal.

③ $J_{\mathrm{K}} \approx g_{\mathrm{K}}(V_m - E_K)$ for $J_{\mathrm{K}} \approx 0 \quad (V_m \approx E_K)$ **?**

GHK Ohmic Approximation

$$V_m \approx E_K = \frac{kT}{q} \ln \frac{[\mathrm{K}]_o}{[\mathrm{K}]_i} \Rightarrow e^{-\frac{V_m}{\frac{kT}{q}}} = e^{-\frac{E_K}{\frac{kT}{q}}} e^{-\frac{V_m - E_K}{\frac{kT}{q}}} \approx \frac{[\mathrm{K}]_i}{[\mathrm{K}]_o} \left(1 - \frac{V_m - E_K}{\frac{kT}{q}} \right)$$

$$\Rightarrow J_{\mathrm{K}} \approx \frac{q \mu E_K}{L} \cdot \frac{\cancel{[\mathrm{K}]_i} - \frac{[\mathrm{K}]_i}{\cancel{[\mathrm{K}]_o}}(\cancel{1} - \frac{V_m - E_K}{\frac{kT}{q}}) \cdot \cancel{[\mathrm{K}]_o}}{1 - \frac{[\mathrm{K}]_i}{[\mathrm{K}]_o}(1 - \cancel{\frac{V_m - E_K}{\frac{kT}{q}}})}$$

or: $J_{\mathrm{K}} \approx g_{\mathrm{K}}(V_m - E_K)$

$$\text{with} \quad \underbrace{g_{\mathrm{K}}}_{\substack{\text{channel}\\ \text{conductance}}} = \underbrace{\frac{q\mu}{L}}_{\text{permeability}} \cdot \underbrace{\ln \frac{[\mathrm{K}]_o}{[\mathrm{K}]_i} \cdot \frac{[\mathrm{K}]_i [\mathrm{K}]_o}{[\mathrm{K}]_o - [\mathrm{K}]_i}}_{\text{average concentration}}$$

Goldman-Hodgkin-Katz Equilibrium

$$J_{\mathrm{K}} = \frac{q\mu_{\mathrm{K}} V_m}{L} \qquad \frac{[\mathrm{K}]_i - e^{-\frac{V_m}{kT/q}}[\mathrm{K}]_o}{1 - e^{-\frac{V_m}{kT/q}}}$$

$$J_{\mathrm{Na}} = \frac{q\mu_{\mathrm{Na}} V_m}{L} \qquad \frac{[\mathrm{Na}]_i - e^{-\frac{V_m}{kT/q}}[\mathrm{Na}]_o}{1 - e^{-\frac{V_m}{kT/q}}}$$

Equilibrium : $J_{\mathrm{K}} + J_{\mathrm{Na}} \equiv 0$, neglecting common terms :

$$\mu_K \left([\mathrm{K}]_i - e^{-\frac{V_m}{kT/q}}[\mathrm{K}]_o\right) + \mu_{\mathrm{Na}} \left([\mathrm{Na}]_i - e^{-\frac{V_m}{kT/q}}[\mathrm{Na}]_o\right) \equiv 0$$

$$E_{rest} = V_m = \frac{kT}{q} \ln \frac{\mu_K[\mathrm{K}]_o + \mu_{Na}[\mathrm{Na}]_o}{\mu_K[\mathrm{K}]_i + \mu_{Na}[\mathrm{Na}]_i}$$

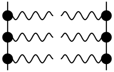
usually expressed in terms of permeabilities:

$$P_{\mathrm{K}} = \frac{q\mu_{\mathrm{K}}}{L} \text{ and } P_{\mathrm{Na}} = \frac{q\mu_{\mathrm{Na}}}{L}$$

GHK Neuromorphism

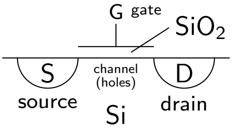
(for the silicon enthusiast)

LIPID BILAYER :
(K^+)

$[K]_i$  $[K]_o$

$$J_K \cong \begin{cases} P_K[K]_i & \text{for } V_m \gg V_t \\ P_K[K]_o & \text{for } V_m \ll -V_t \end{cases}$$

SILICON MOSFET :
(pMOS)*



$$J_p \cong \begin{cases} J_0 e^{\kappa \frac{V_g}{V_t}} \cdot e^{\frac{V_s}{V_t}} & \text{for } V_{ds} \gg V_t \\ J_0 e^{\kappa \frac{V_g}{V_t}} \cdot e^{\frac{V_d}{V_t}} & \text{for } V_{ds} \ll -V_t \end{cases}$$

neuromorphisms :
(imperfect)

$P_K \rightarrow J_0 e^{\kappa \frac{V_g}{V_t}}$ controlled by V_g, **gate** voltage

$[K]_i \rightarrow e^{-\frac{V_s}{V_t}}$ controlled by V_s, **source** voltage

$[K]_o \rightarrow e^{-\frac{V_d}{V_t}}$ controlled by V_d, **drain** voltage

$V_m \rightarrow V_{ds} = V_d - V_s$, i.e. :

$V_i \rightarrow -V_s$

$V_o \rightarrow -V_d$

* C.A. Mead, *Analog VLSI and Neural Systems*, Addison-Wesley, 1989