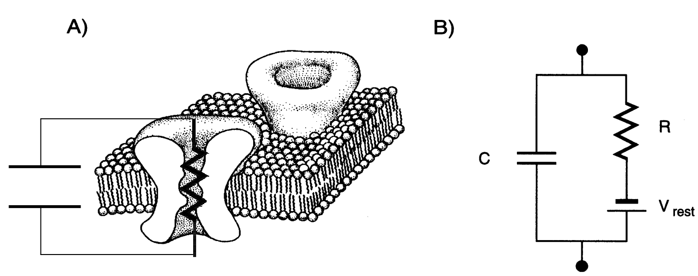
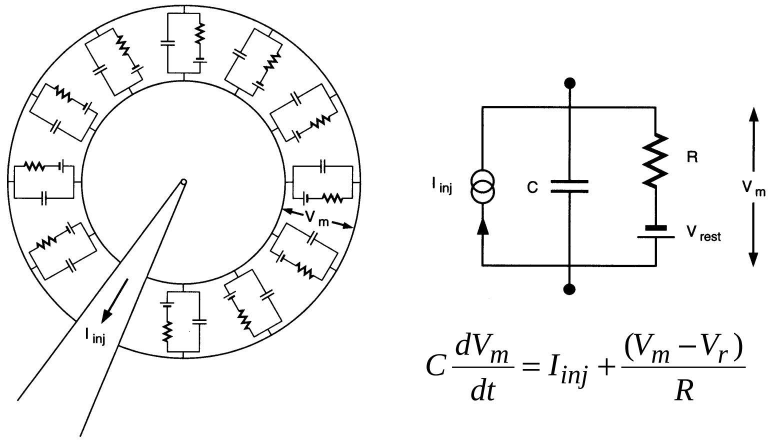
Membrane Models and the Hodgkin/Huxley Model of the Action Potential

1. Passive Membrane
2. Resting Potential
3. Dendrites/Axons as Cables
4. Properties of Action Potential
5. Hodgkin/Huxley Model

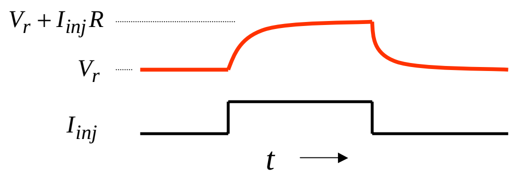
Passive Membrane Model

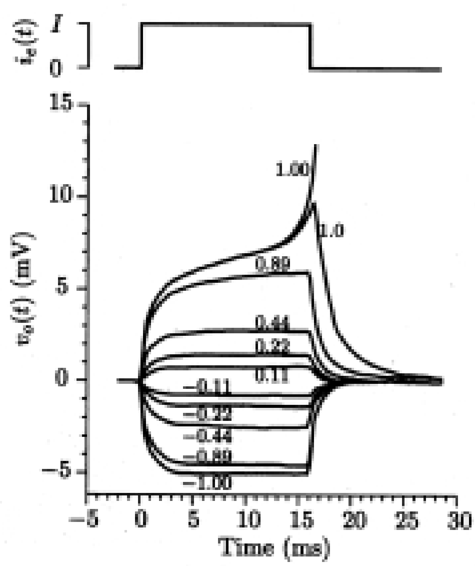


$C \approx 1 \mu F / cm^2$



$$C\frac{dV_m}{dt} = I_{inj} + \frac{(V_m - V_r)}{R}$$

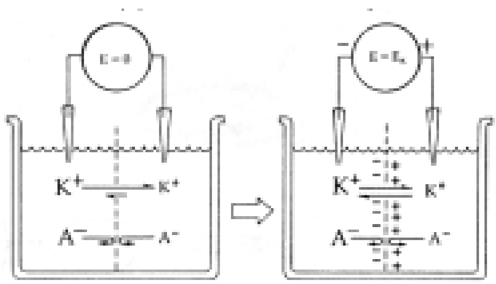




Nernst Potential

$$E_K = V_K = \frac{k_B T}{q} \ln \frac{[K]_{ext}}{[K]_{int}} = \frac{RT}{zF} \ln \frac{[K]_{ext}}{[K]_{int}}$$

$$E_K = V_K = \frac{58mV}{z} \log \frac{[K]_{ext}}{[K]_{int}}$$



An ionic gradient leads to a voltage gradient.

$[K]_{int} > [K]_{ext}$

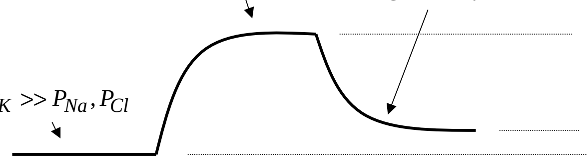
↓

resting potential is negative

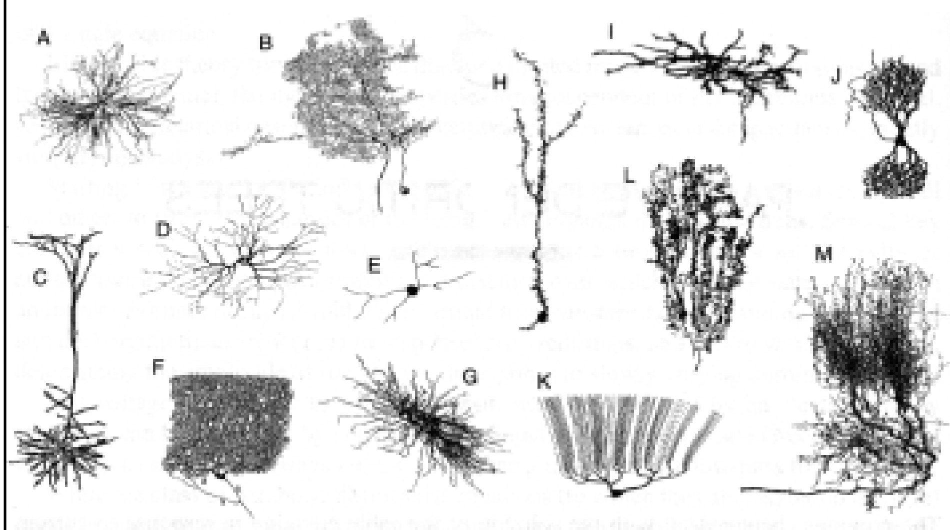
Goldman Hodgkin Katz Equation

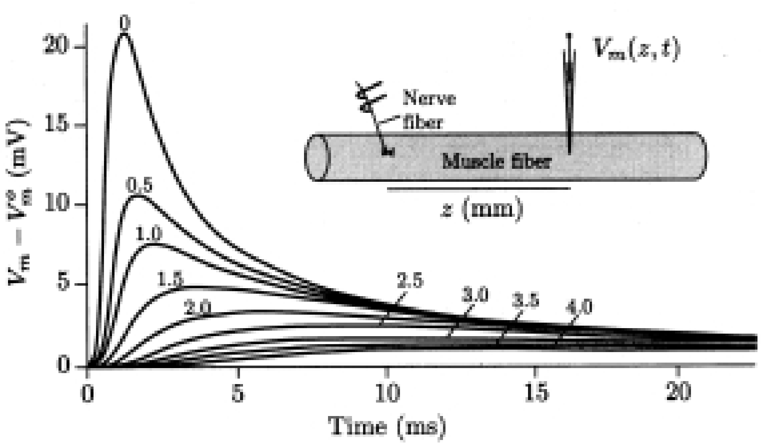
$$V = 58 \log \frac{P_K [K]_{ext} + P_{Na} [Na]_{ext} + P_{Cl} [Cl]_{int}}{P_K [K]_{int} + P_{Na} [Na]_{int} + P_{Cl} [Cl]_{ext}}$$

$P_K : P_{Na} : P_{Cl}$ relative permeabilities



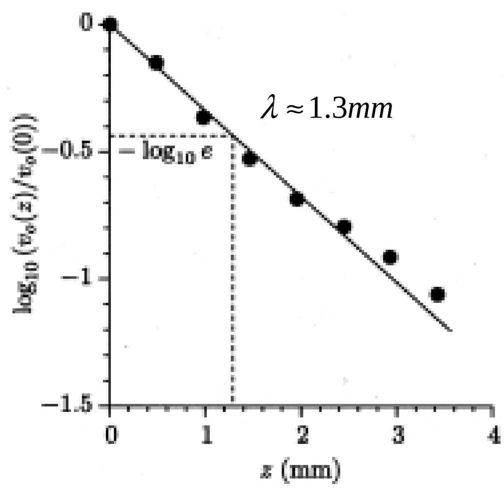
Spheres and Cables



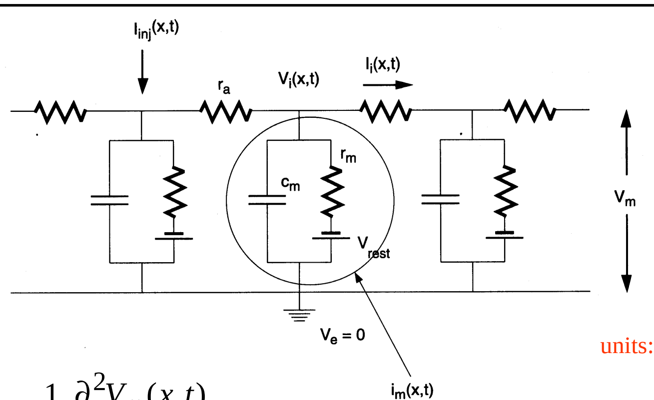


Frog muscle fiber (Fatt and Katz, 1951)

Membrane potential decay from point of constant current injection



lobster axon, Hodgkin and Rushton, 1946



$$\frac{1}{r_a}\frac{\partial^2 V_m(x,t)}{\partial x^2} = i_m(x,t)$$

$$i_m(x,t) = \frac{V_m(x,t)-V_{rest}}{r_m} + c_m\frac{\partial V_m}{\partial t} - I_{inj}(x,t)$$

$$\lambda^2 \frac{\partial^2 V_m(x,t)}{\partial x^2} = \tau_m \frac{\partial V_m(x,t)}{\partial t} + (V_m(x,t)-V_{rest}) - r_m I_{inj}(x,t)$$

units:

r_m: ohm-cm

r_a: ohm/cm

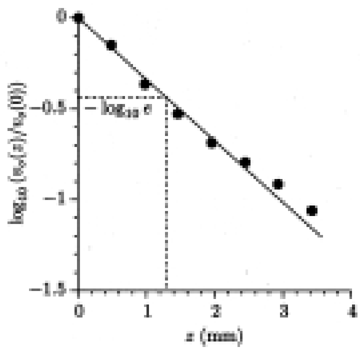
i_m: A/cm

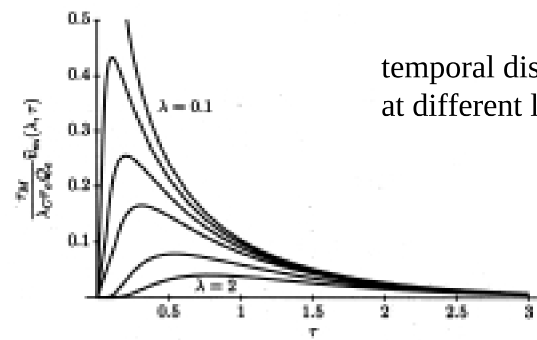
c_m: F/cm

$$\tau_m = r_m c_m$$

$$\lambda = \sqrt{\frac{r_m}{r_a}}$$

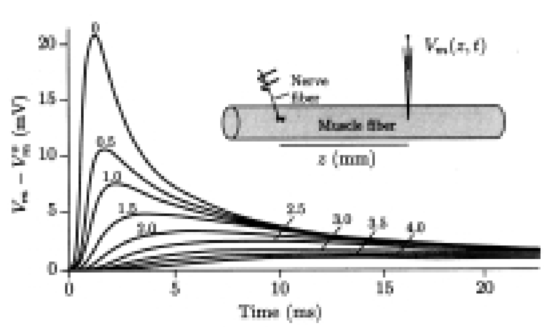
$$V(x) = V_0 \exp(-|x| / \lambda)$$



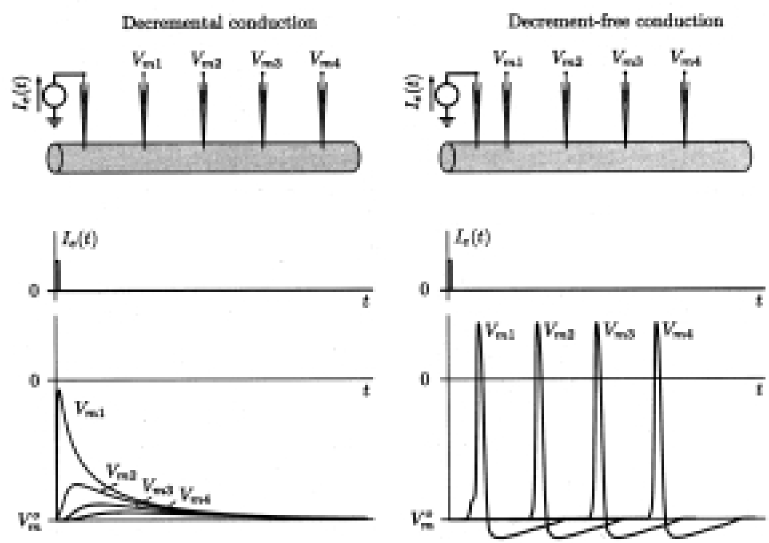


temporal distribution
at different locations

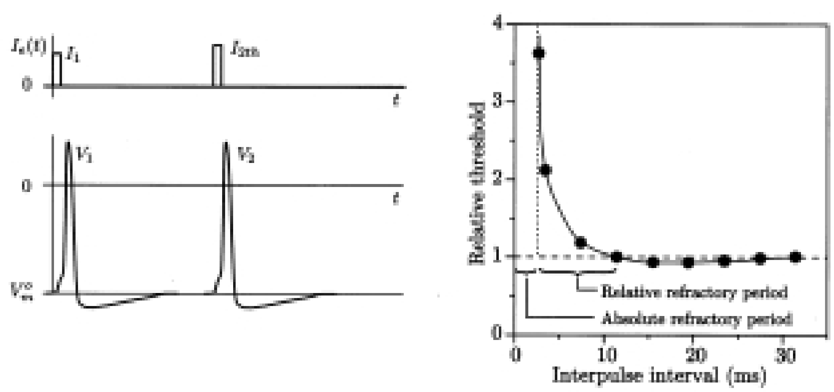
theory



experiment

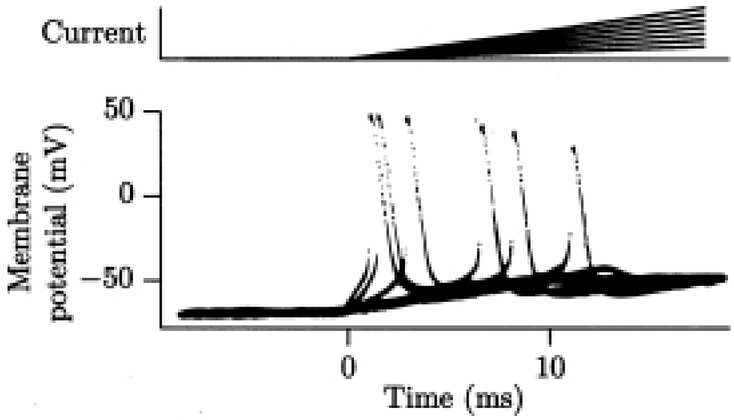


refractory period



Adrian and Lucas, 1912

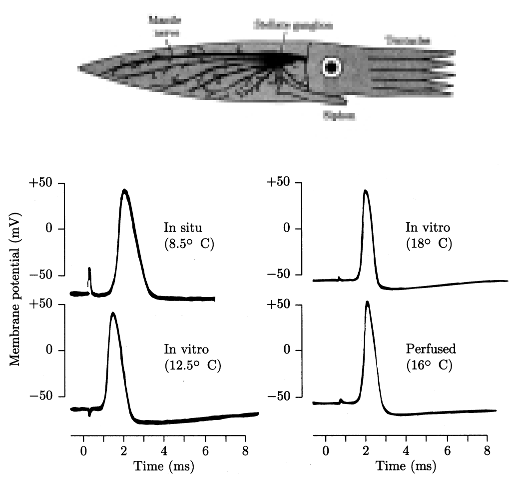
Accomodation

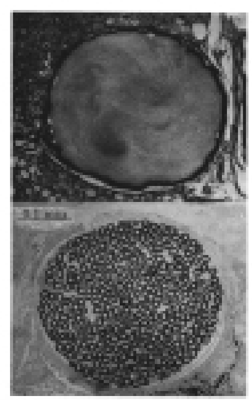


Xenopus laevis nerve fiber

Valibo, 1964

Squid Giant Axon





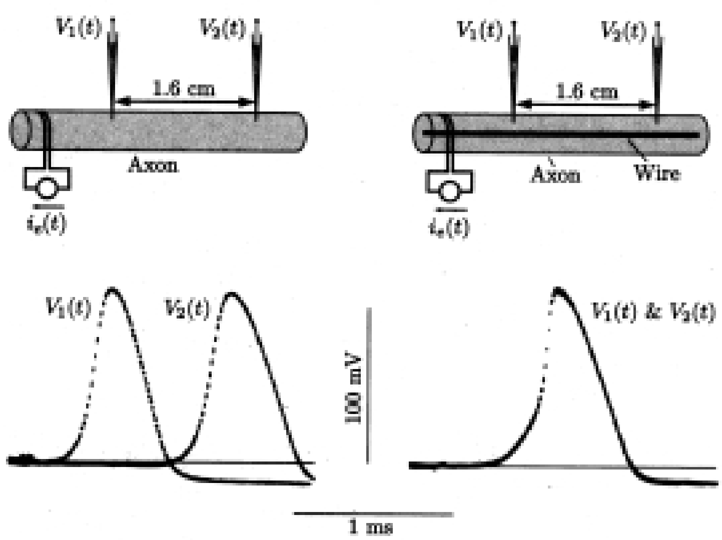
Substance	Axoplasm	Blood	Seawater
Water	865	870	966
Protein	20	0.15	—
Major ions			
K^+	323–400	20–22	8.3–10
Na^+	44–65	440–456	423–460
Cl^-	40–151	560–578	506–580
Ca^{++}	0.4–7	10–11	9.3–10
Mg^{++}	6.4–20	54–55	48–53
Isethionate$^-$	164–250	1.6	—
SO_4^{++}	7.5	8.1	28.2
PO_4^{---}	2.5–17.8	—	—
Major amino acids			
Aspartate	33–100	—	—
Glutamate	6.2–8.4	—	—
Arginine	0.36–2.2	—	—
Alanine	1.7–16	—	—
Glycine	4.5–18.4	—	—
Taurine	81–106.7	3.5	—
Homarine	20.4	3.4	—
Betaine	73.7	4.4	—
Major carbohydrates			
Glycerol	4.35	—	—
Glucose	0.24	—	—
Mannose	0.92	—	—
Fructose	0.24	—	—
Succinate and fumarate	17	—	—
High energy phosphates			
ATP	0.7–1.7	—	—
Arginine phosphate	1.8–5.7	—	—

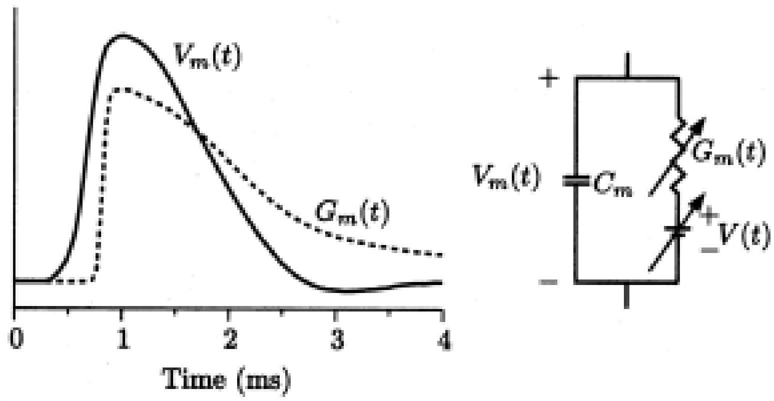
$$V_K = -77mV$$

$$V_{Na} = +50mV$$

$$V_L = -54.4mV$$

Space Clamp/Voltage Clamp

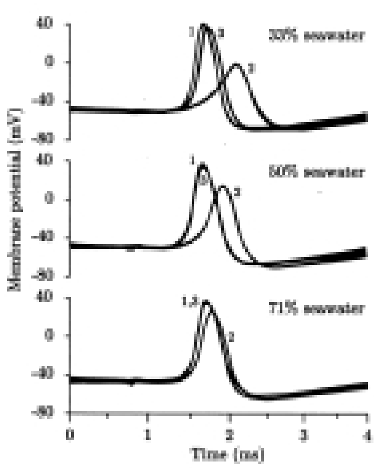


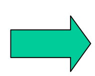


Cole, 1968

Bernstein Theory

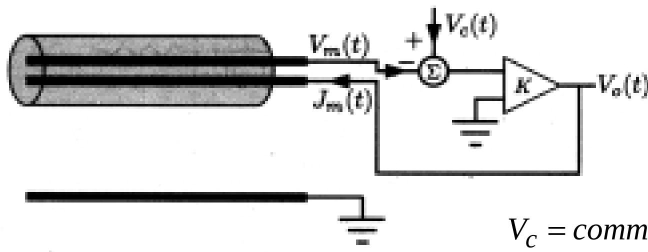
Permeability to K at rest
Membrane breaks down transiently





Na^+ permeability change associated with peak

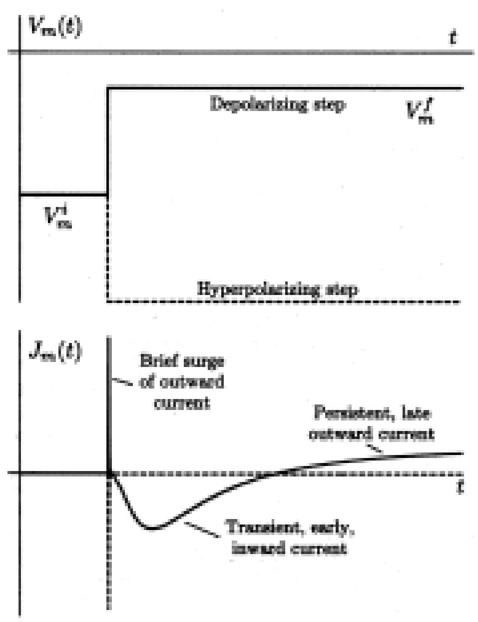
Voltage Clamp

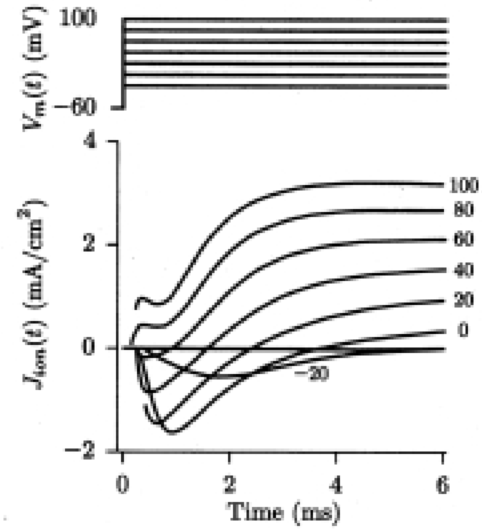


$V_c = command\ \ voltage$

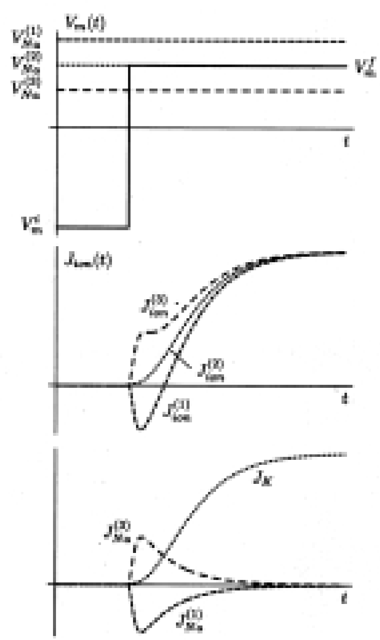
$$V_o = V_m = K(V_c - V_m)$$

$$V_m = \frac{K+1}{K} V_c$$

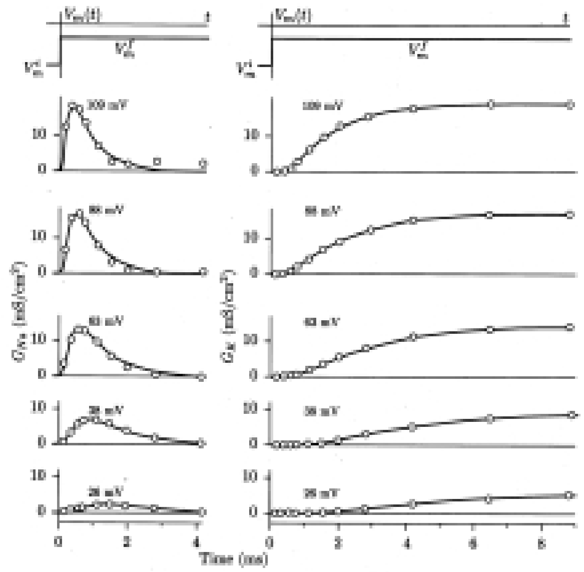




command
voltages



separating the currents
by altering Nernst
potential



gating driving force

$$I_K = g_K (V - V_K)$$

$$I_{Na} = g_{Na} (V - V_{Na})$$

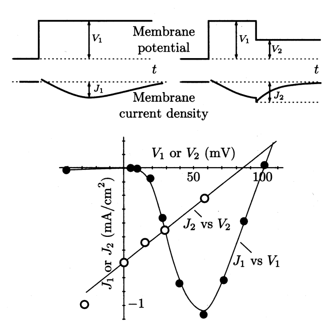
$$I_L = g_L (V - V_L)$$

units:

I : µA/cm^2

g : m mho/cm^2

V: mV



Ohmic for each state

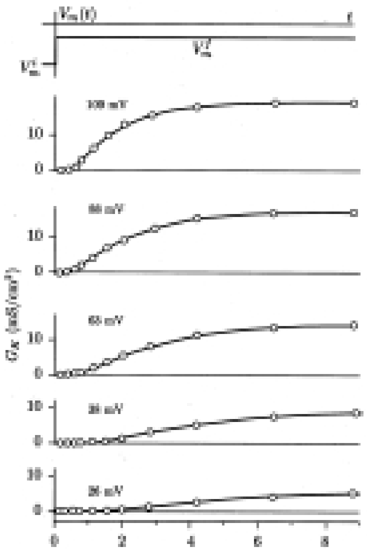
maximum conductance (constant)

$$g_K(V,t) = \bar{g}_K n^4(V,t)$$

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

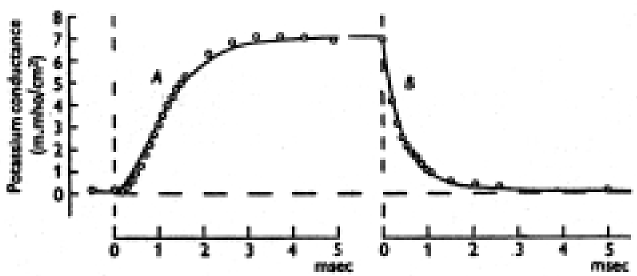
$$n(t) = n_\infty - (n_\infty - n_0)\exp(-t/\tau_n)$$

$$n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n} \qquad \tau_n = \frac{1}{\alpha_n + \beta_n}$$



units:

- n : [0,1]
- τ: msec
- g : m mho/cm^2
- α,β: msec^{-1}



$$g_K = \bar{g}_K n^4 (V - V_K)$$

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

$$n \approx 0 \Rightarrow \frac{dn}{dt} \approx \alpha_n \;\; \Rightarrow \; n(t) \approx \alpha_n t \; \Rightarrow g_K \approx (\alpha_n t)^4$$

$$n \approx 1 \Rightarrow \frac{dn}{dt} \approx -\beta_n n \; \Rightarrow n(t) \approx \exp(-\beta_n t) \Rightarrow g_K \approx \exp(-4\beta_n t)$$

$$g_{Na}(V,t) = \bar{g}_{Na} m^3(V,t) h(V,t)$$

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

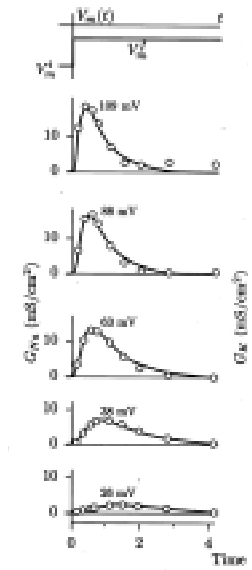
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)(h)$$

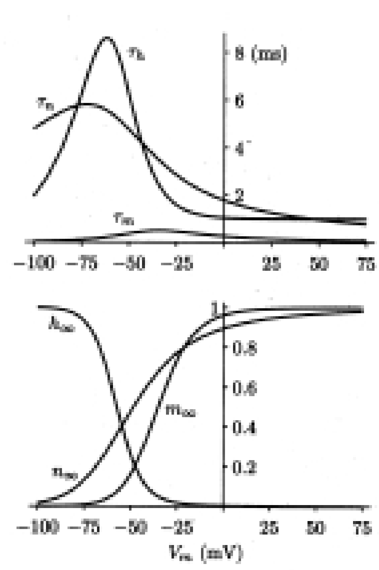
units:

m,h : [0,1]

g : m mho/cm^2

α,β: msec^{-1}





m fast

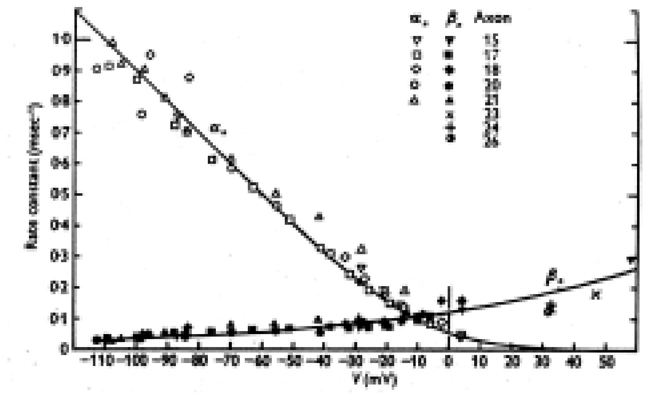
m,n activate with depolarization

h inactivates with depolarization

$$\alpha_n = \frac{n_\infty}{\tau_n} \qquad \beta_n = \frac{1 - n_\infty}{\tau_n}$$

units: V: mV

α,β: msec[-1]



$$\alpha_n = \frac{n_\infty}{\tau_n} \qquad \beta_n = \frac{1 - n_\infty}{\tau_n}$$

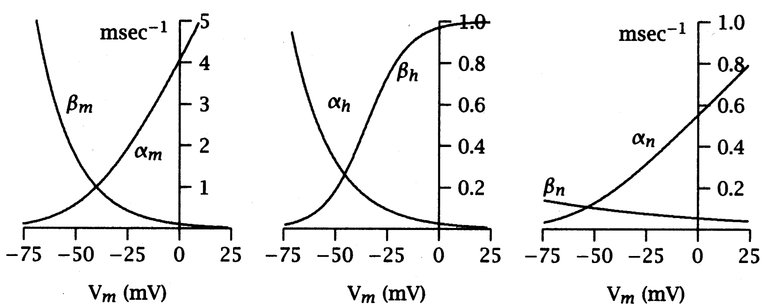
units: V: mV

α,β: msec[-1]

$$\alpha_n(V) = \frac{0.01(V+55)}{1-\exp[-(V+55)/10]} \qquad \beta_n(V) = 0.125\exp[-(V+65)/80]$$

$$\alpha_m(V) = \frac{0.1(V+40)}{1-\exp[-(V+40)/10]} \qquad \beta_m(V) = 4\exp[-(V+65)/18]$$

$$\alpha_h(V) = 0.07\exp[-(V+65)/20] \qquad \beta_h(V) = \frac{1}{1+\exp[-(V+35)/10]}$$



Space Clamped Hodgkin/Huxley Model

$$C\frac{dV}{dt} = I - \bar{g}_{Na} m^3 h (V - V_{Na}) - \bar{g}_K n^4 (V - V_K) - g_L (V - V_L)$$

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

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

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

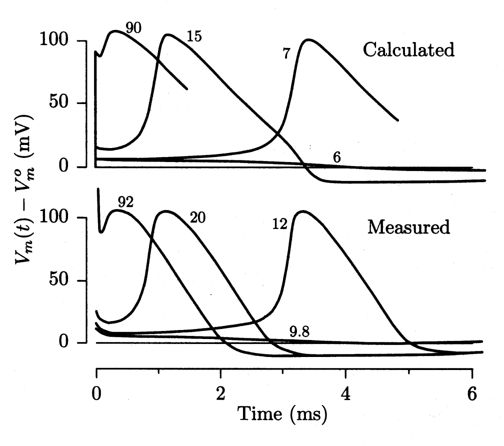
$\bar{g}_{Na} = 120 mmho/cm^2$
$\bar{g}_K = 36 mmho/cm^2$
$g_L = 0.3 mmho/cm^2$
$V_{Na} = 50 mV$
$V_K = -77 mV$
$V_L = -54.4 mV$
$C = 1 \mu F/cm^2$
$I : \mu A/cm^2$
$V : mV$

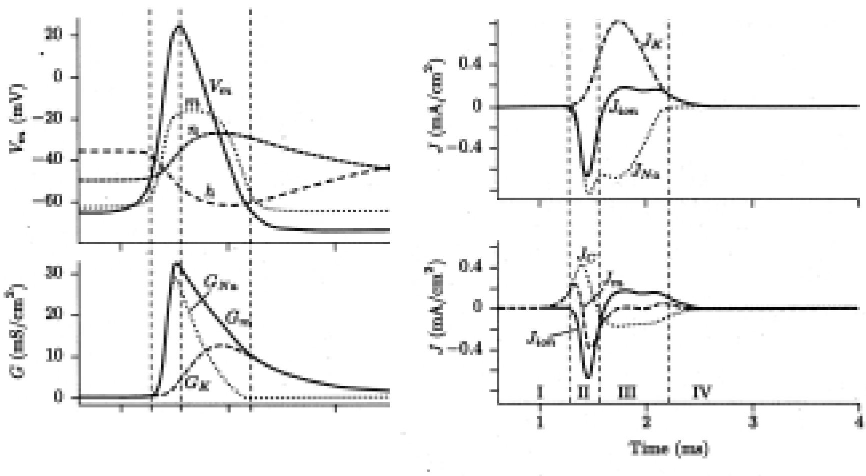
$$\alpha_m(V) = \frac{0.1(V+40)}{1-\exp[-(V+40)/10]} \qquad \beta_m(V) = 4\exp[-(V+65)/18]$$

$$\alpha_h(V) = 0.07\exp[-(V+65)/20] \qquad \beta_h(V) = \frac{1}{1+\exp[-(V+35)/10]}$$

$$\alpha_n(V) = \frac{0.01(V+55)}{1-\exp[-(V+55)/10]} \qquad \beta_n(V) = 0.125\exp[-(V+65)/80]$$

numerical integration of H/H equations





$$I = C\frac{\partial V}{\partial t} + \bar{g}_{Na} m^3 h (V - V_K) + \bar{g}_K n^4 (V - V_K) + g_L (V - V_L)$$

$$I = \frac{a}{2R}\frac{\partial^2 V}{\partial x^2}$$

a = radius (cm)

R = specific intracellular resistivity (kΩcm)

θ = propagating velocity (cm/msec)

assume $V(x,t) = V(x - \theta t)$

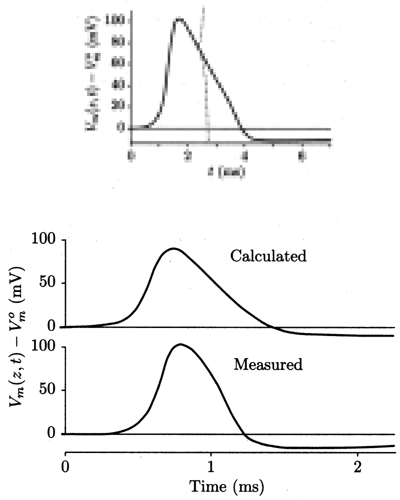
$$\frac{\partial^2 V}{\partial x^2} = \frac{1}{\theta^2}\frac{\partial^2 V}{\partial t^2}$$

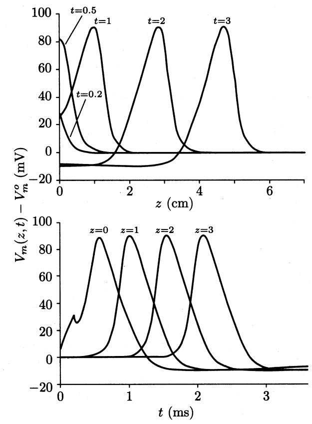
$$\frac{a}{2R\theta^2}\frac{d^2 V}{dt^2} = C\frac{dV}{dt} + \bar{g}_{Na} m^3 h (V - V_K) + \bar{g}_K n^4 (V - V_K) + g_L (V - V_L)$$

guess θ, numerically integrate

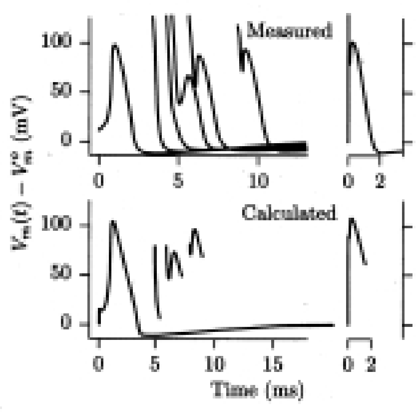
ODE

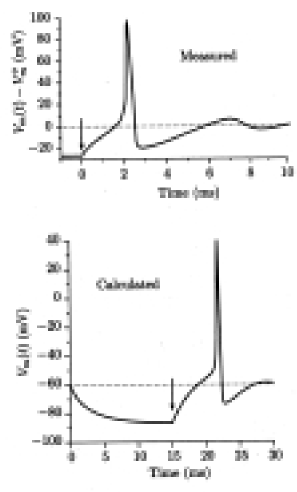
PDE

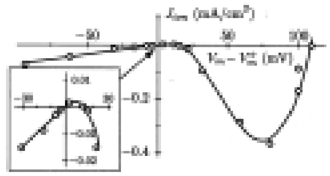


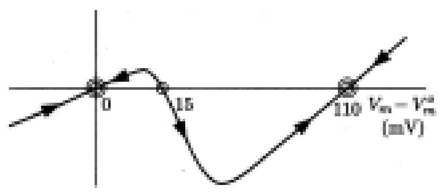


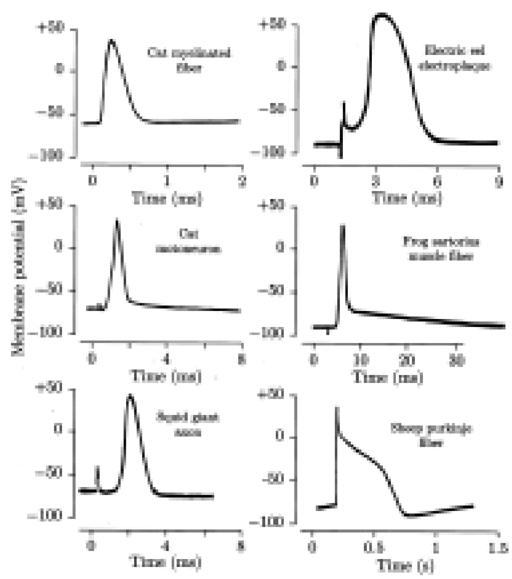
Cooley & Dodge

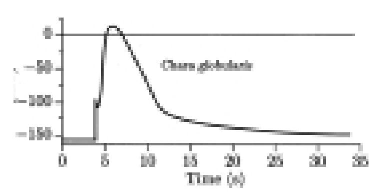





J_{ion} (mA/cm^2)
−50
50
100
$V_m - V_m^o$ (mV)
−0.2
−0.4


0
15
110
$V_m - V_m^o$
(mV)


Cat myelinated fiber
Electric eel electroplaque
Cat motoneuron
Frog sartorius muscle fiber
Squid giant axon
Sheep purkinje fiber
Membrane potential (mV)
Time (ms)
Time (s)


Chara globularis
Time (s)