

Biophysics I (BPHS 4080)

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Website: <http://www.yorku.ca/cberge/4080W2018.html>

Space-Clamp

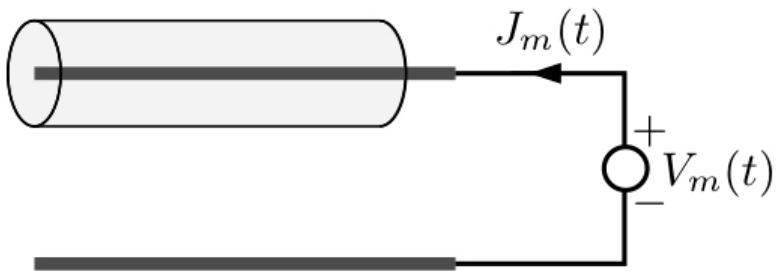


Figure 4.10

Kenneth Cole & George Marmont (1940s)

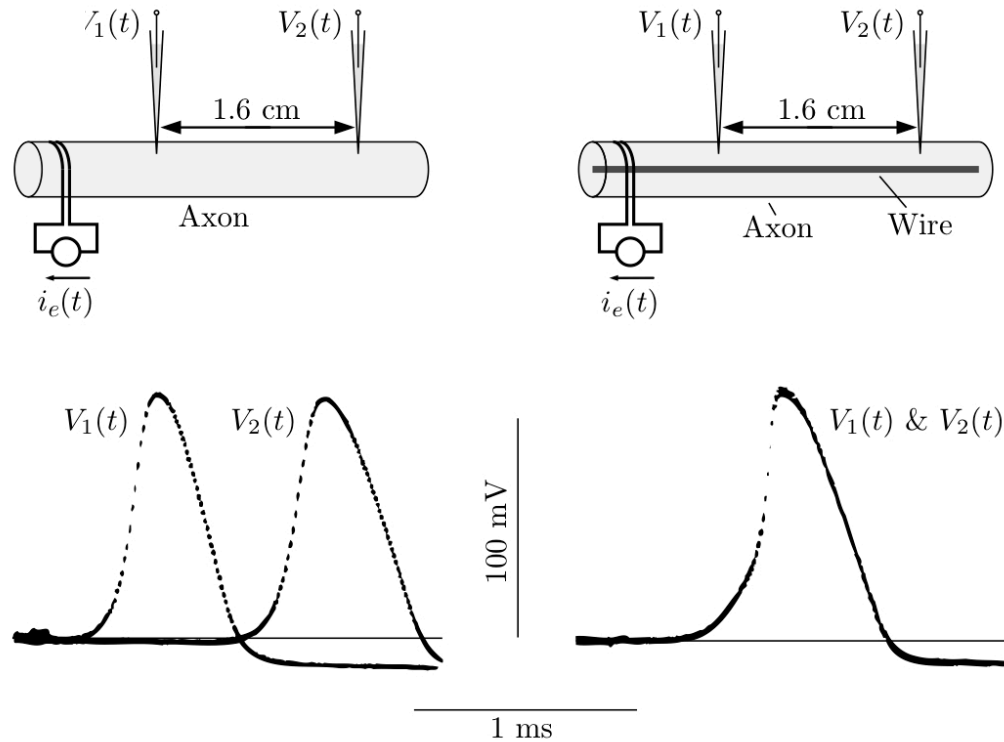


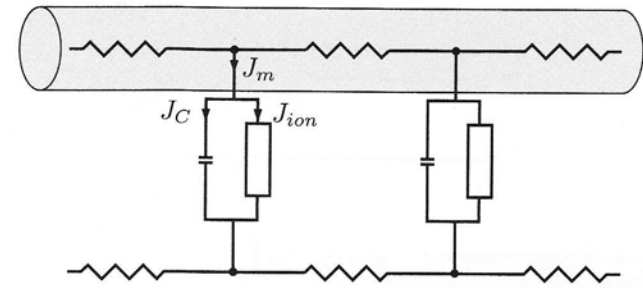
Figure 2.15

→ *Eliminates spatial dependence*
 (i.e., make an electrically large cell a small one)

Voltage-Clamp

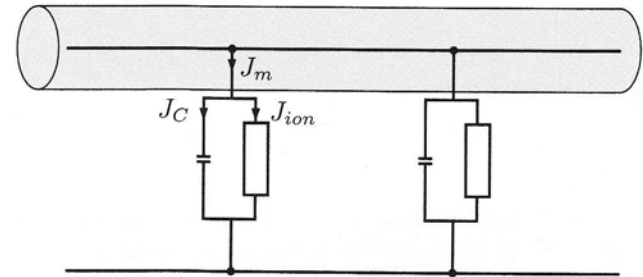
Note: No action potentials 'fire' under voltage clamp

→ Provides a means to study ionic currents



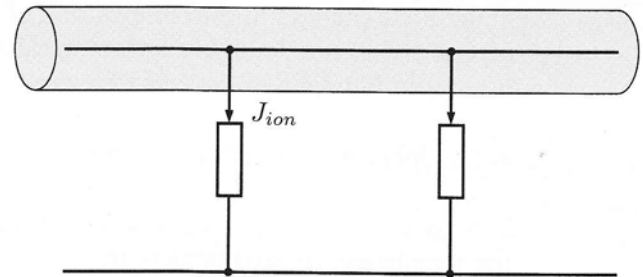
Space clamp

$$\frac{\partial V_m}{\partial z} = 0$$

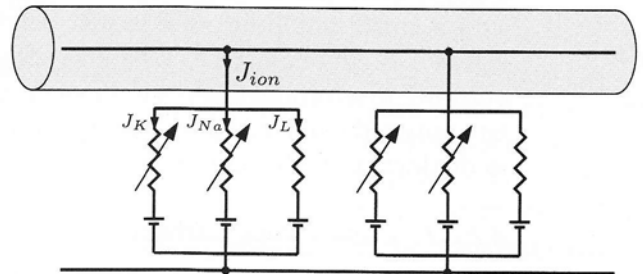


Step voltage clamp

$$\frac{\partial V_m}{\partial z} = \frac{\partial V_m}{\partial t} = 0$$



Separation of ionic currents



Separating Ionic Currents

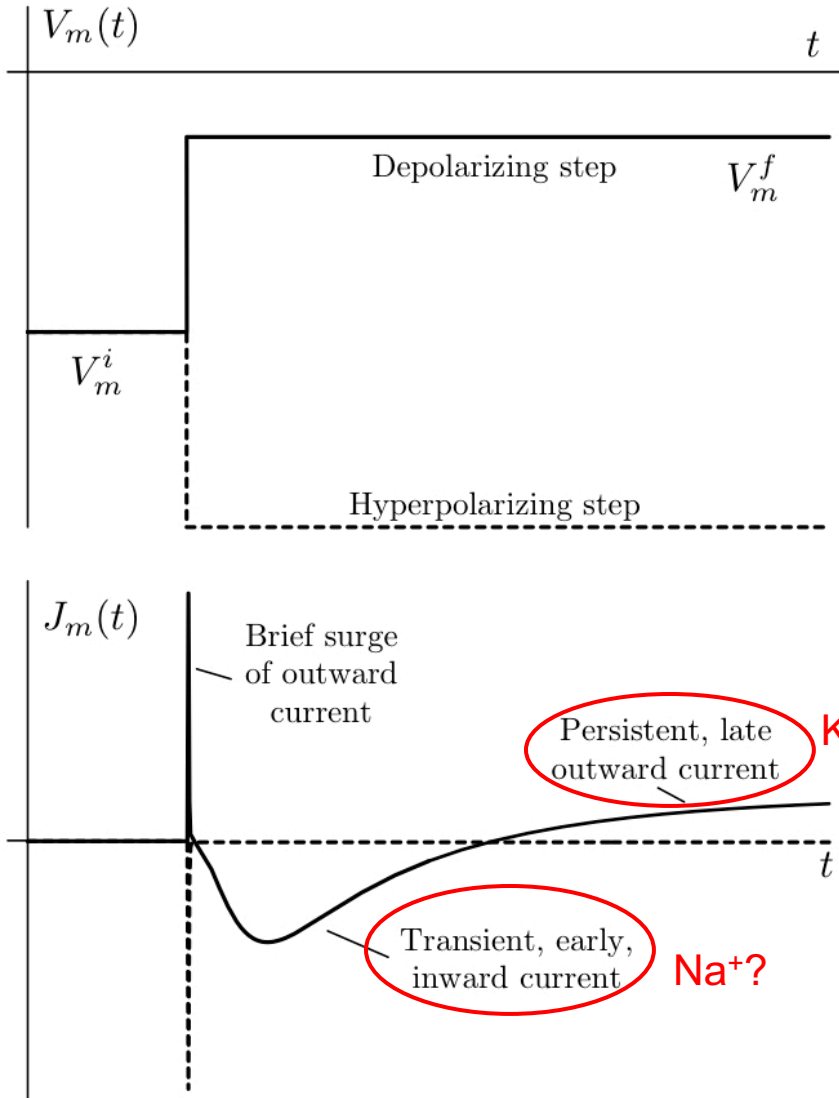


Figure 4.12

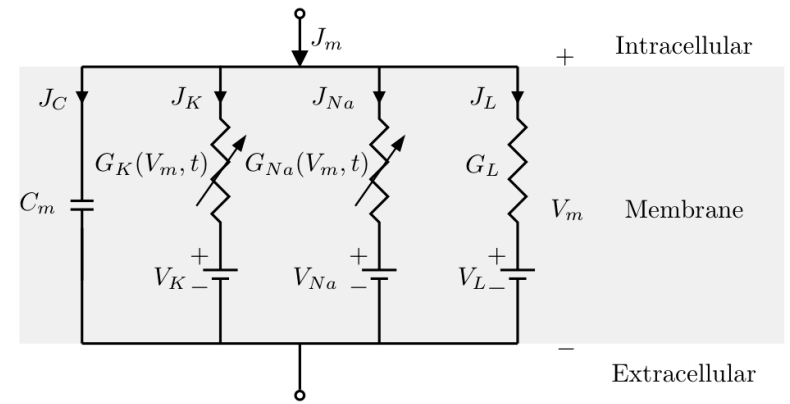
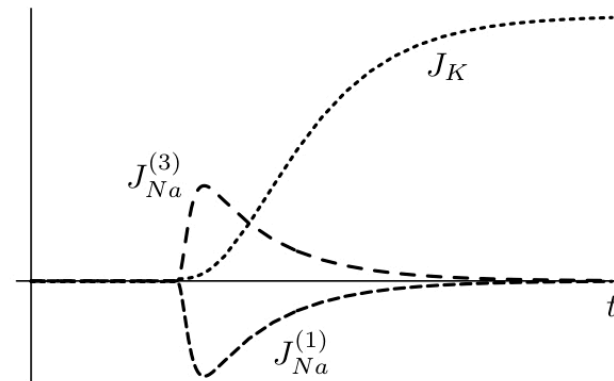
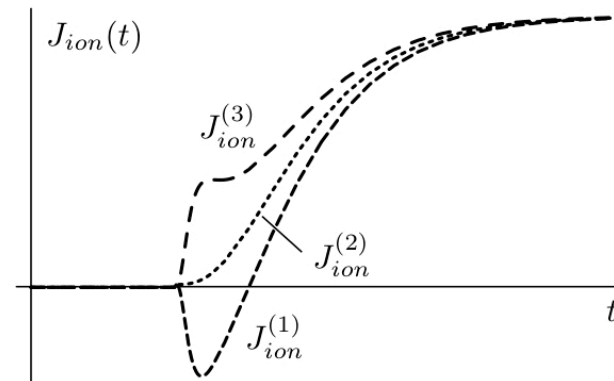
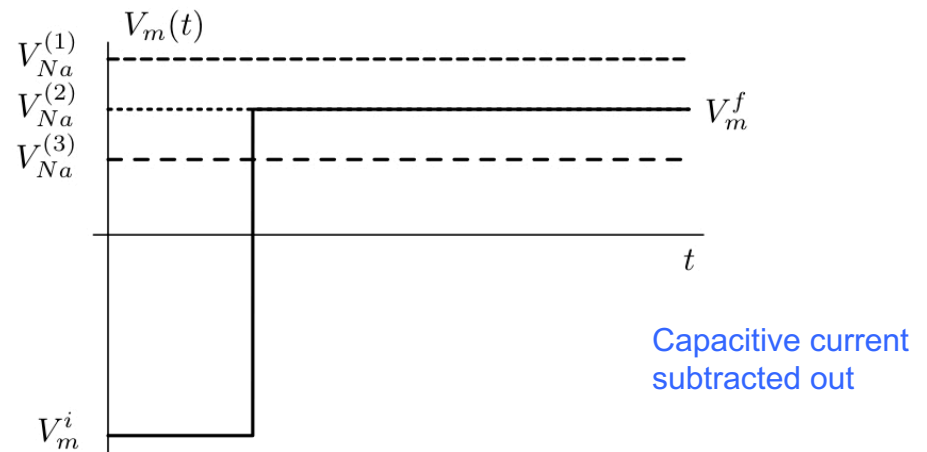


Figure 4.6

Changing $[Na^+]$

$$V_{Na} = \frac{RT}{F} \log \frac{C_{Na}^o}{C_{Na}^i}$$



→ Separating ionic currents by subtraction
(assumes J_K unaffected by changes in $[Na^+]$)

Figure 4.17

Reversal Potential?

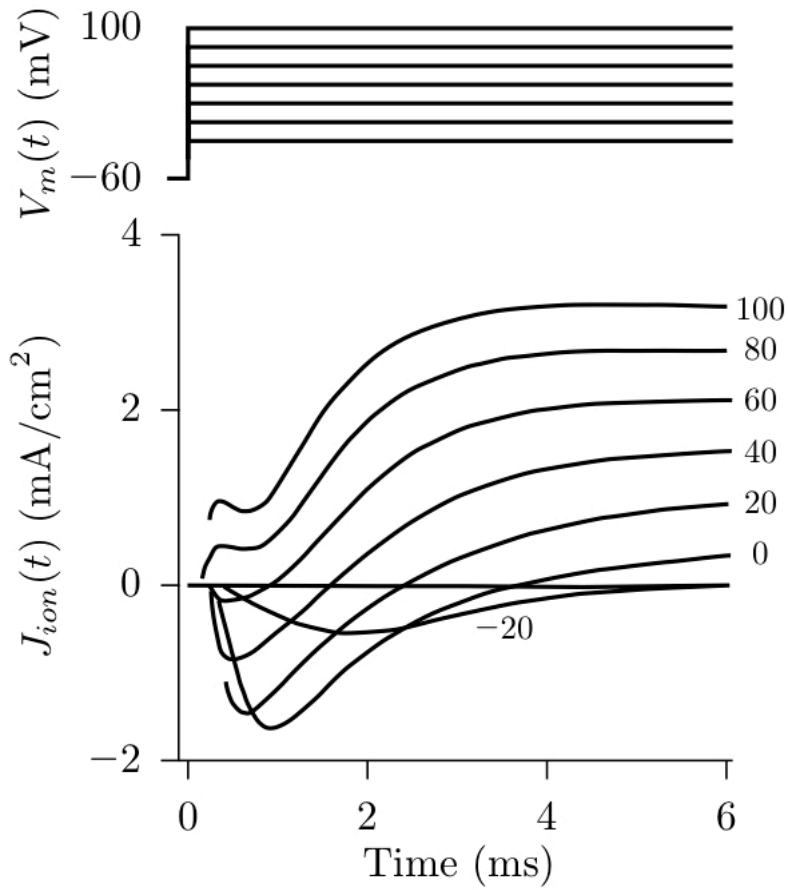


Figure 4.14

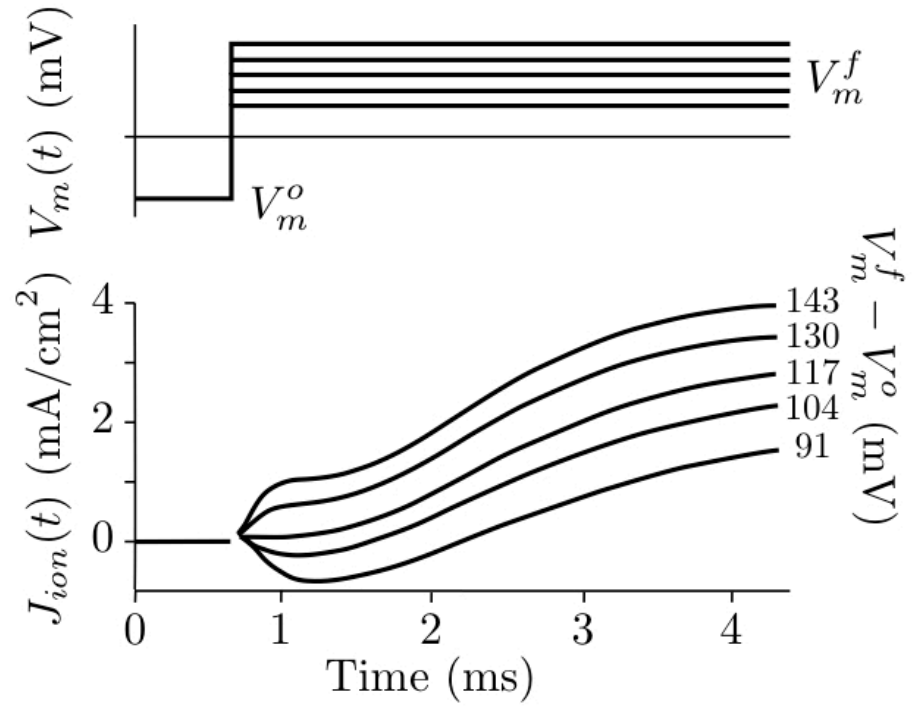


Figure 4.15

→ Close to Na⁺ Nernst potential!

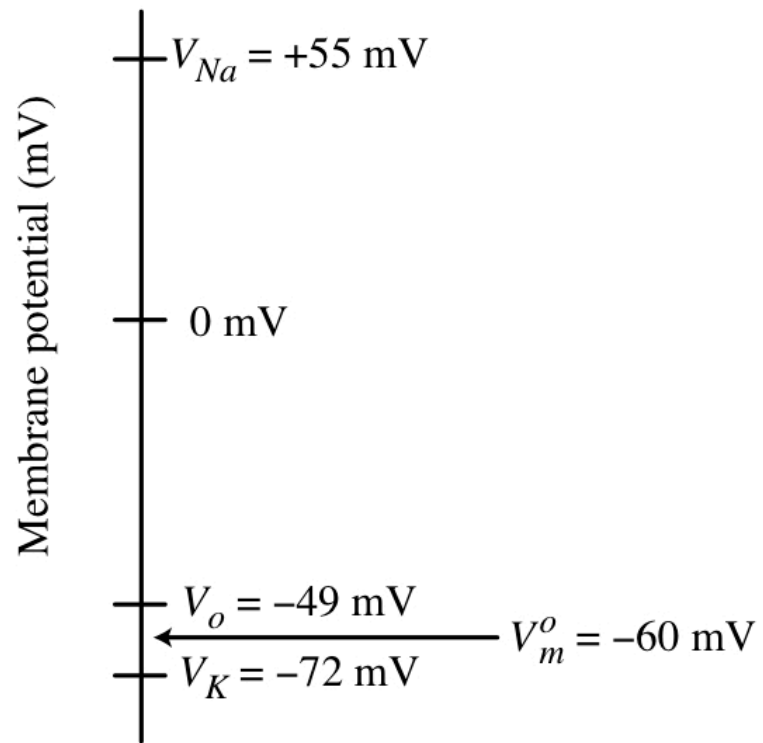
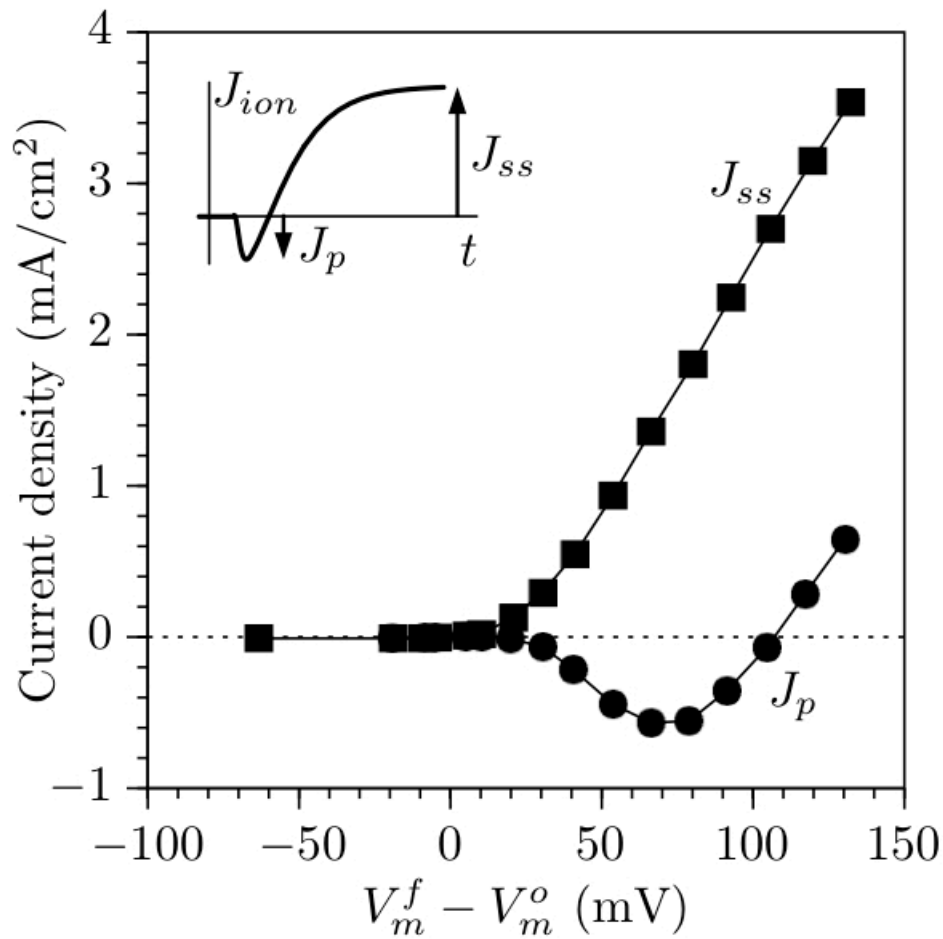
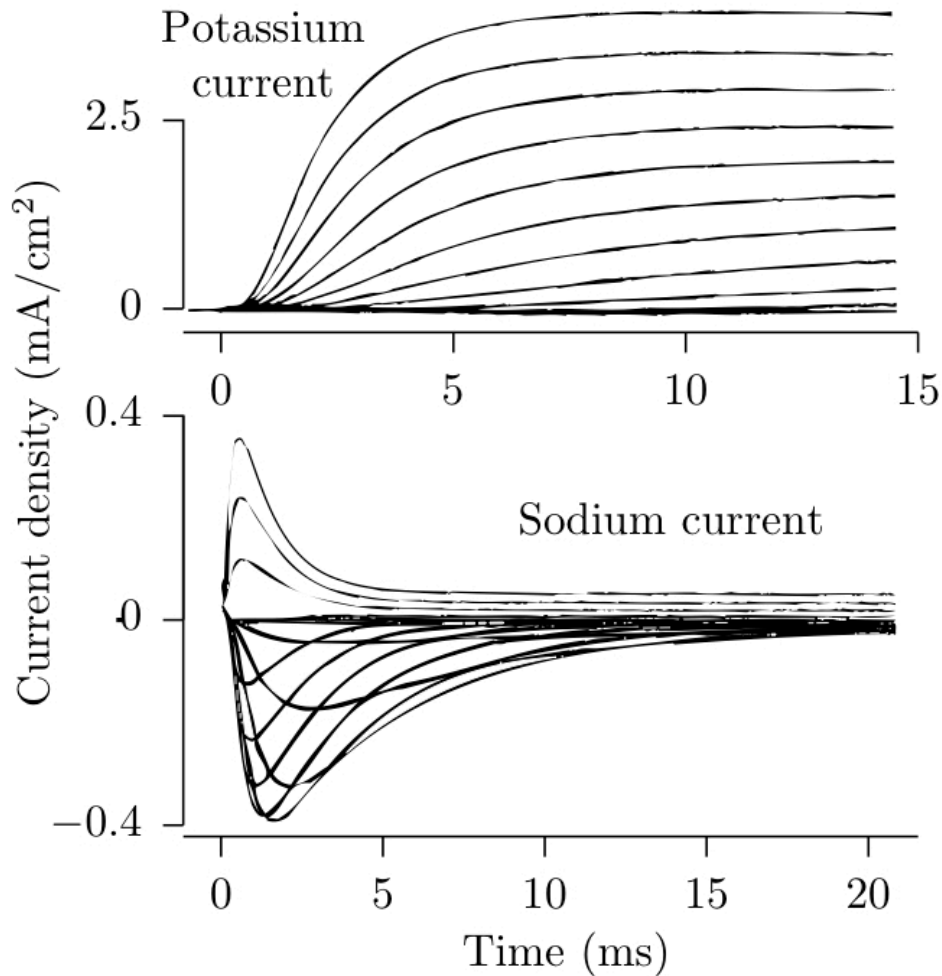


Figure 4.16

Separating Ionic Currents



NOTE: Other methods besides subtraction (e.g., TTX to block Na⁺ current, replace K⁺ w/ Cs⁺, etc...)

→ K⁺ simply turns on
(with a bit of a slow start)

→ Na⁺ more complex
(early 'activation', followed by 'inactivation')

Figure 4.20

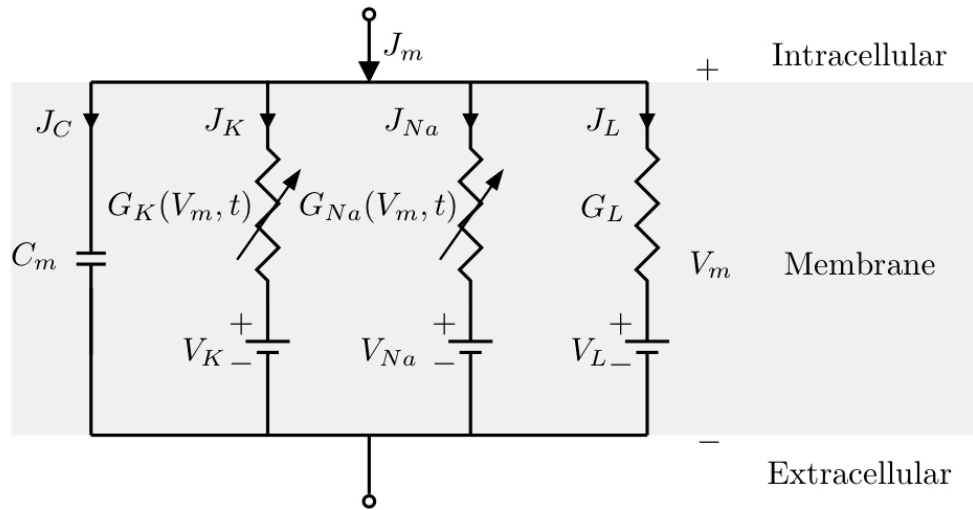


Figure 4.6

What are $G_K(V_m, t)$ and $G_{Na}(V_m, t)$?

→ Physiological data suggests Na^+ *activates* and then *inactivates* while K^+ simply *activates* (based upon V_m)

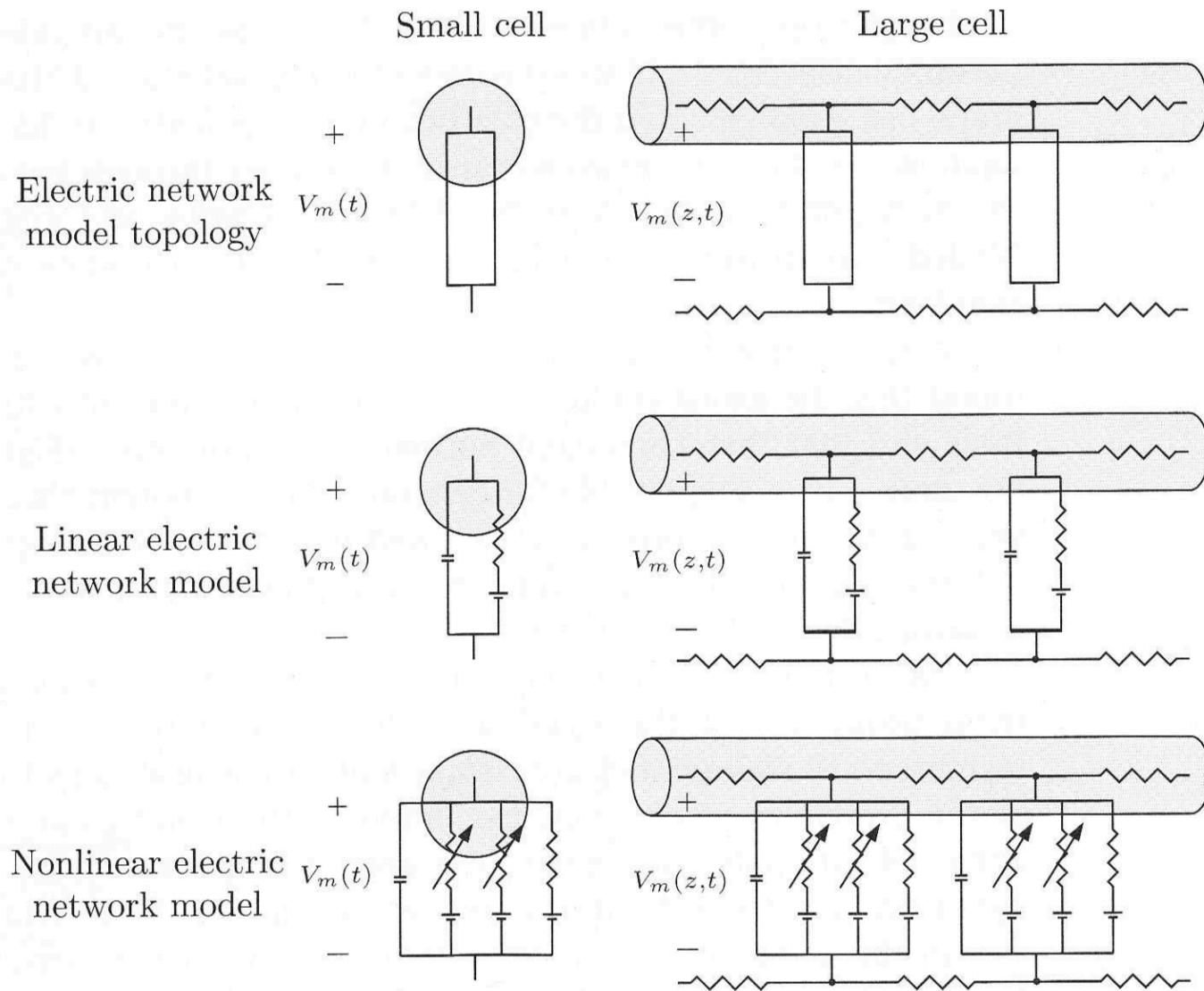


Figure 1.32

→ Electrically 'small' cell can still fire action potentials

Model for $G_K(V_m, t)$ and $G_{Na}(V_m, t)$?

1. Use voltage-clamp to obtain suitable data

$$G_K(V_m, t) = \frac{J_K(V_m, t)}{V_m - V_K}$$

$$G_{Na}(V_m, t) = \frac{J_{Na}(V_m, t)}{V_m - V_{Na}}$$

2. Devise sufficient model to describe

→ First-order kinetics variables

$$\frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x$$

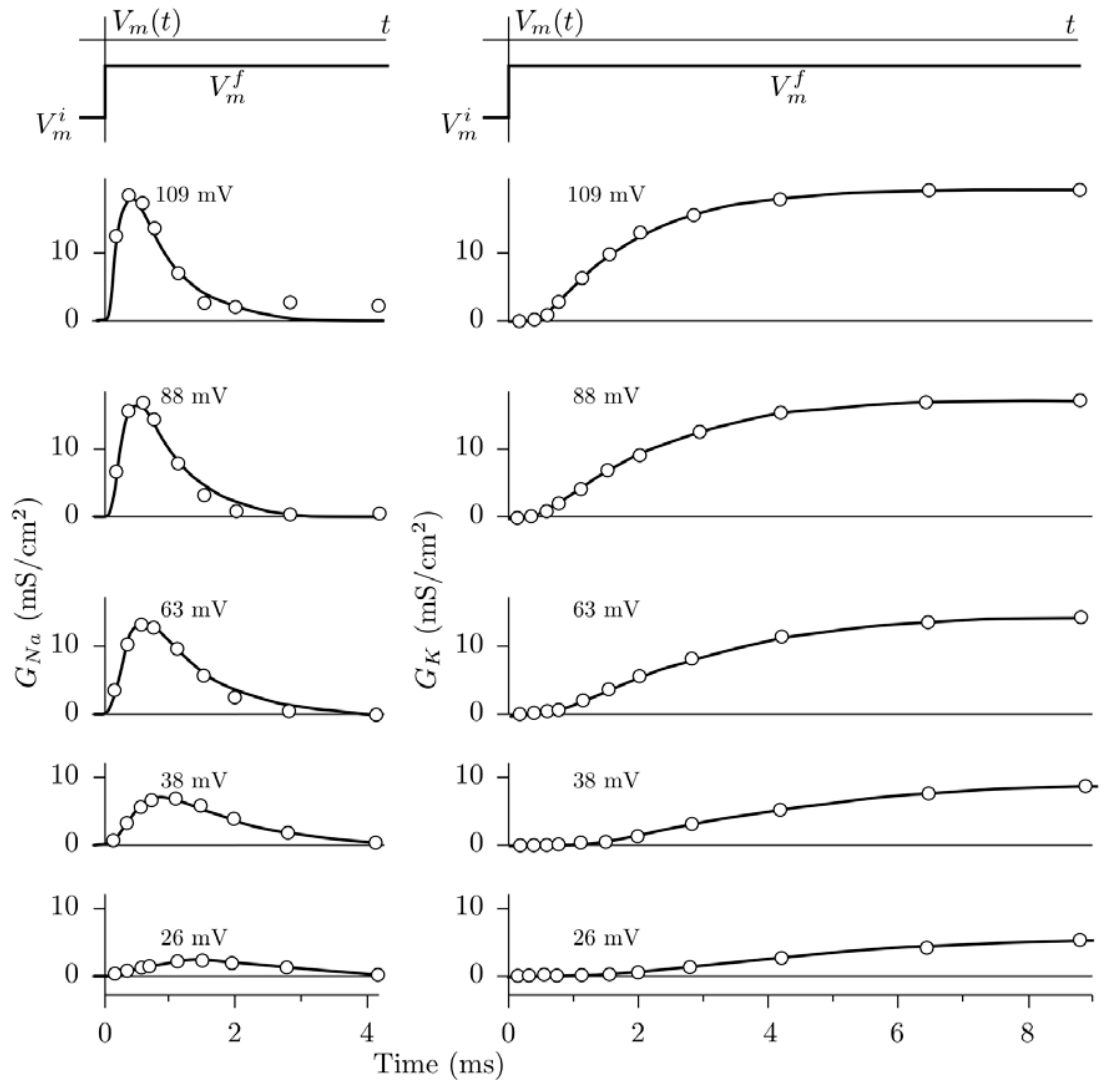
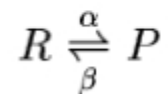


Figure 4.23

Review: First-Order Chemical Kinetics

First-order, reversible reaction



$$\frac{dc_R(t)}{dt} = \beta c_P(t) - \alpha c_R(t) \quad \text{AND} \quad \frac{dc_P(t)}{dt} = \alpha c_R(t) - \beta c_P(t)$$

Equilibrium:

$$\frac{dc_R(t)}{dt} = \frac{dc_P(t)}{dt} = 0 \quad \rightarrow \quad \beta c_P(\infty) = \alpha c_R(\infty)$$
$$\frac{c_P(\infty)}{c_R(\infty)} = \frac{\alpha}{\beta} = K_a \quad \left(\begin{array}{l} \text{association, equilibrium, affinity,} \\ \text{stability, binding, formation constant} \end{array} \right)$$

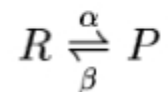
Kinetics: assume total amount of reactant and product is conserved

$$c_R(t) + c_P(t) = C$$

$$\frac{dc_R(t)}{dt} = \beta \left(C - c_R(t) \right) - \alpha c_R(t)$$
$$\frac{dc_R(t)}{dt} + (\alpha + \beta)c_R(t) = \beta C$$

Review: First-Order Chemical Kinetics

First-order, reversible reaction

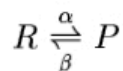


First-order linear differential equation with constant coefficients

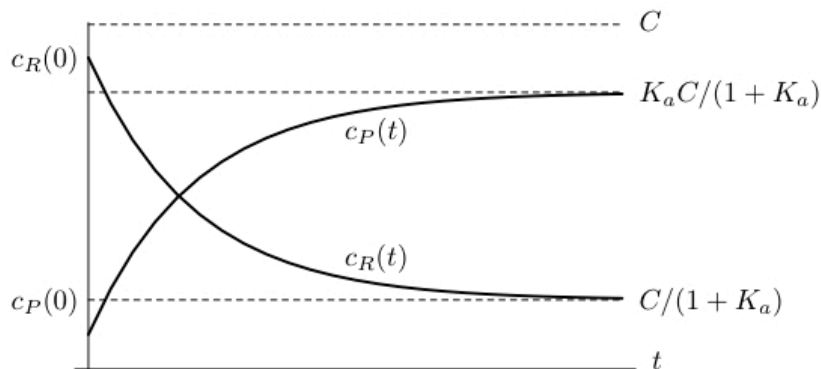
$$c_R(t) = c_R(\infty) - \left(c_R(\infty) - c_R(0) \right) e^{-t/\tau}, \text{ for } t > 0$$

$$c_R(\infty) = \frac{\beta}{\alpha + \beta} C = \frac{1}{1 + K_a} C \quad \text{AND} \quad \tau = \frac{1}{\alpha + \beta}$$

First-order, reversible reaction



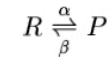
$$c_P(t) = C - c_R(t)$$



$$\tau = \frac{1}{\alpha + \beta}$$

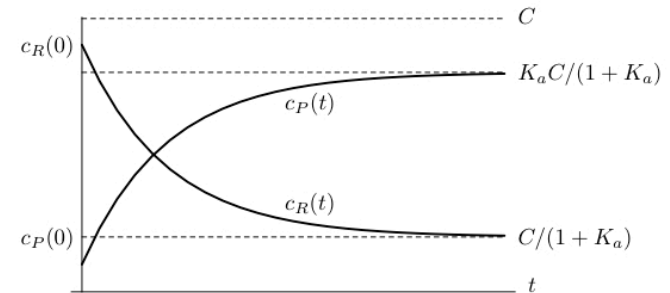
HH: First-Order Kinetics

First-order, reversible reaction



$$\frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x$$

$$\tau_x \frac{dx}{dt} + x = x_\infty$$



$$\tau = \frac{1}{\alpha + \beta}$$

$$x_\infty = \alpha_x / (\alpha_x + \beta_x) \text{ and } \tau_x = 1 / (\alpha_x + \beta_x)$$

functions of V_m only

$$x(t) = x_\infty - (x_\infty - x_0)e^{-t/\tau_x} \quad t \geq 0$$

- Dynamics (i.e., depend. upon t) captured by chemical kinetics
- Voltage depend. (i.e., V_m) captured by how kinetic's parameters affected by membrane potential

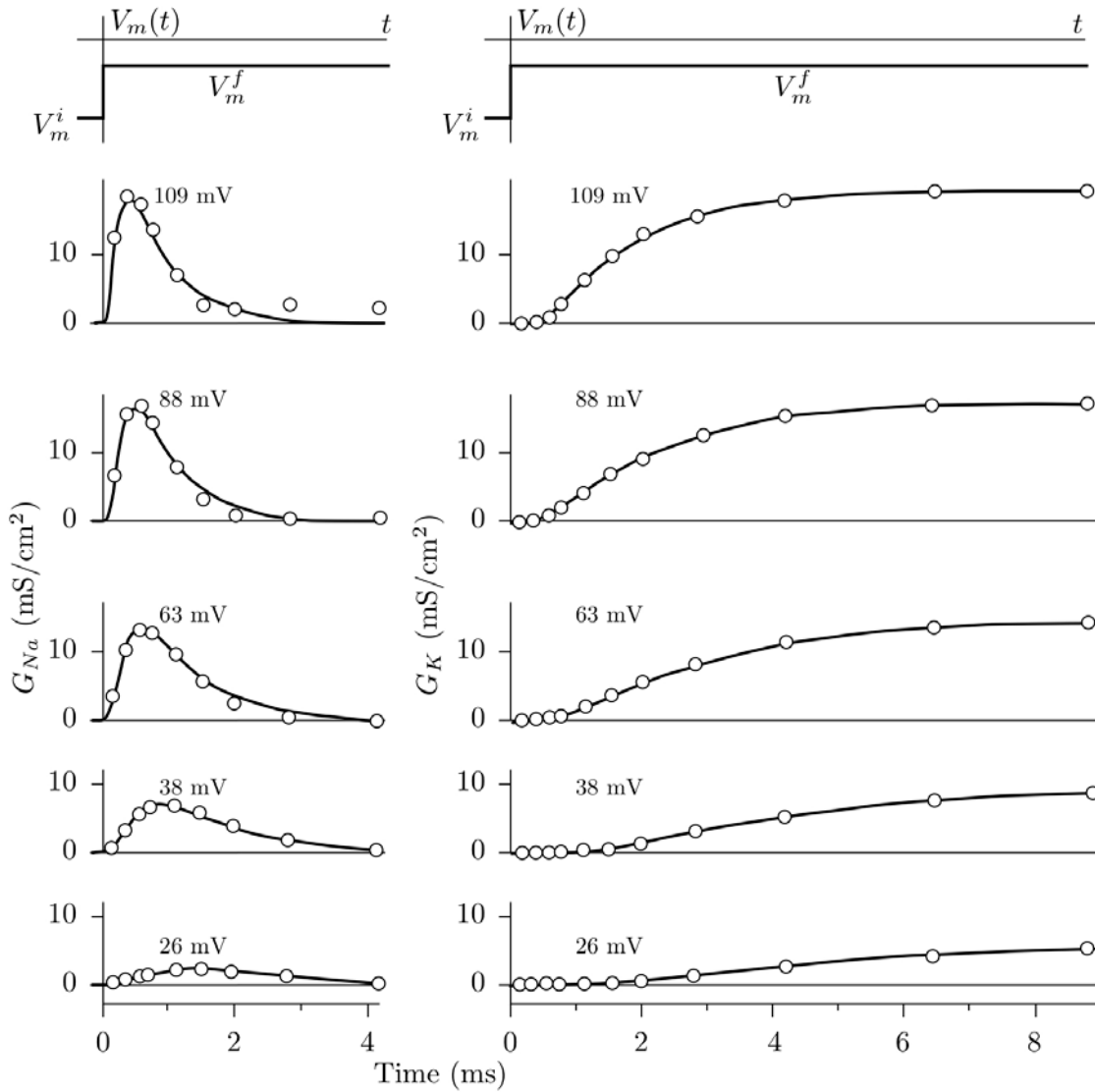


Figure 4.23

$$n(V_m, t) + \tau_n(V_m) \frac{dn(V_m, t)}{dt} = n_\infty(V_m)$$

$$m(V_m, t) + \tau_m(V_m) \frac{dm(V_m, t)}{dt} = m_\infty(V_m)$$

$$h(V_m, t) + \tau_h(V_m) \frac{dh(V_m, t)}{dt} = h_\infty(V_m)$$

$$\tau_m = \frac{1}{\alpha_m + \beta_m}, \quad \text{and} \quad m_\infty = \frac{\alpha_m}{\alpha_m + \beta_m},$$

$$\tau_h = \frac{1}{\alpha_h + \beta_h}, \quad \text{and} \quad h_\infty = \frac{\alpha_h}{\alpha_h + \beta_h},$$

$$\tau_n = \frac{1}{\alpha_n + \beta_n}, \quad \text{and} \quad n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n}.$$

m – sodium activation

h – sodium inactivation

n – potassium activation

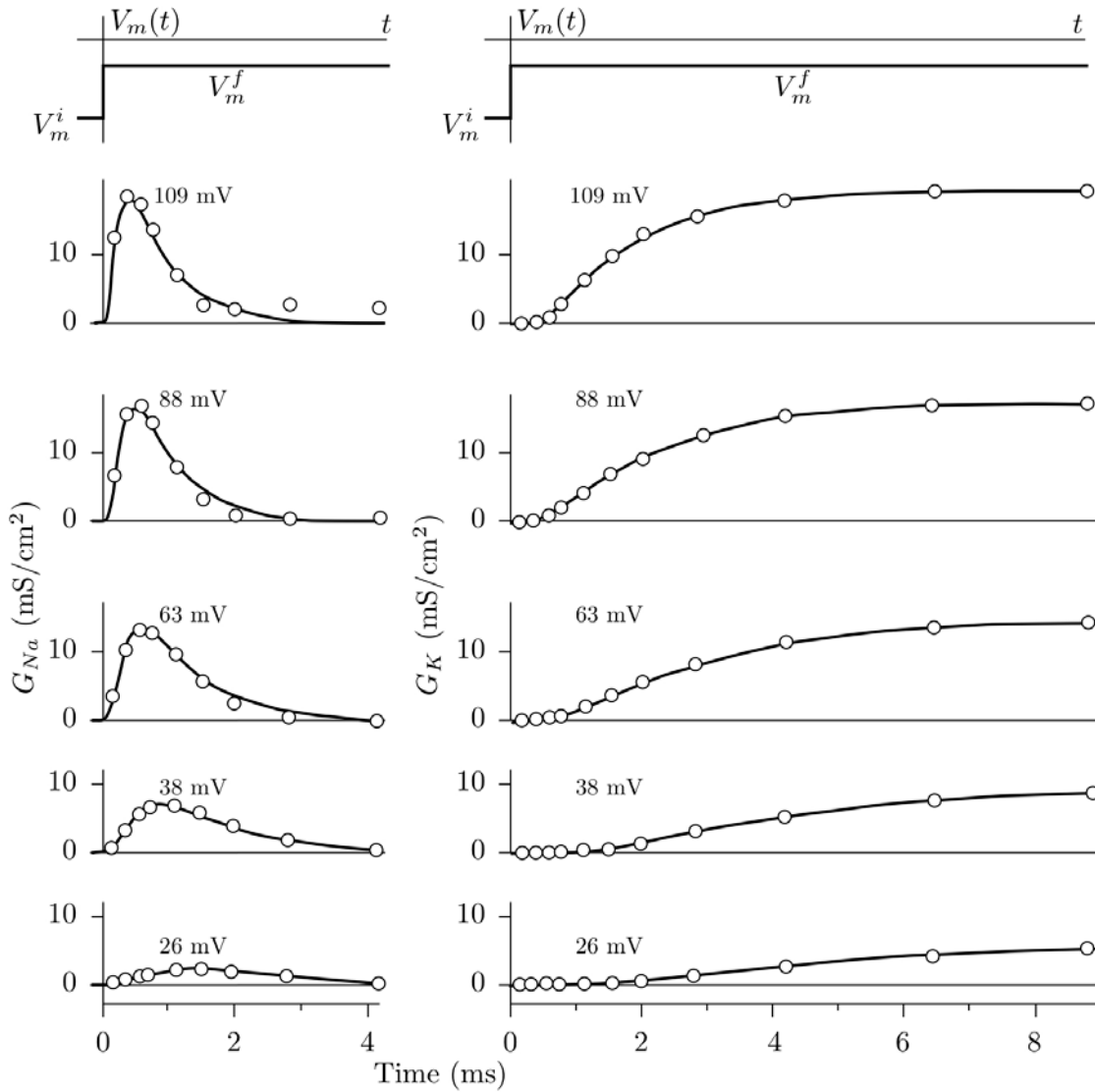


Figure 4.23

$$G_K(V_m, t) = \bar{G}_K n^4(V_m, t)$$

$$G_{Na}(V_m, t) = \bar{G}_{Na} m^3(V_m, t) h(V_m, t)$$

→ Functional form to best fit the data
(e.g., exponentiating yields sigmoids)

$$\alpha_m = \frac{-0.1(V_m + 35)}{e^{-0.1(V_m + 35)} - 1},$$

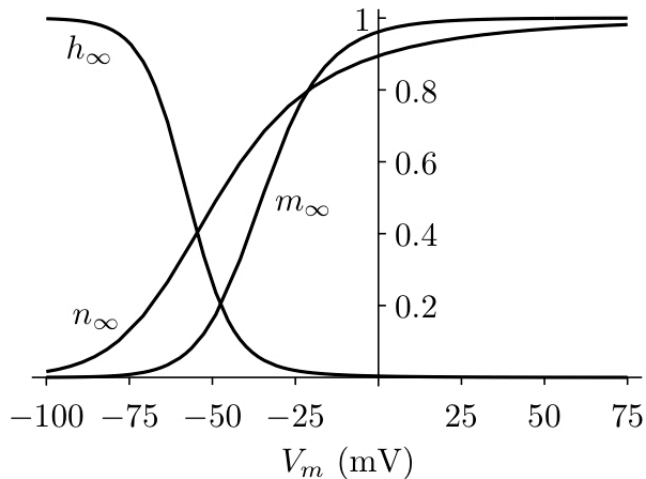
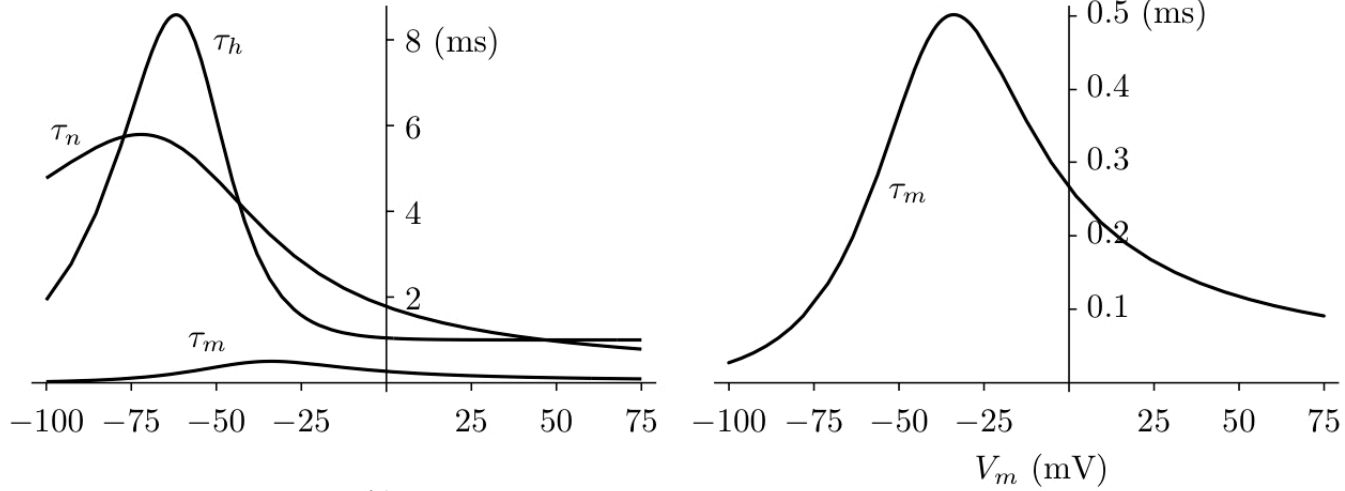
$$\beta_m = 4e^{-(V_m + 60)/18},$$

$$\alpha_h = 0.07e^{-0.05(V_m + 60)},$$

$$\beta_h = \frac{1}{1 + e^{-0.1(V_m + 30)}},$$

$$\alpha_n = \frac{-0.01(V_m + 50)}{e^{-0.1(V_m + 50)} - 1},$$

$$\beta_n = 0.125e^{-0.0125(V_m + 60)},$$



→ Fast Na⁺ activation

→ Slower Na⁺ deactivation and K⁺ activation

$\bar{G}_{Na} = 120$, $\bar{G}_K = 36$, and $G_L = 0.3$ mS/cm²; $C_m = 1$ μ F/cm²; $c_{Na}^o = 491$, $c_{Na}^i = 50$,
 $c_K^o = 20.11$, $c_K^i = 400$ mmol/L; $V_L = -49$ mV; temperature is 6.3°C.

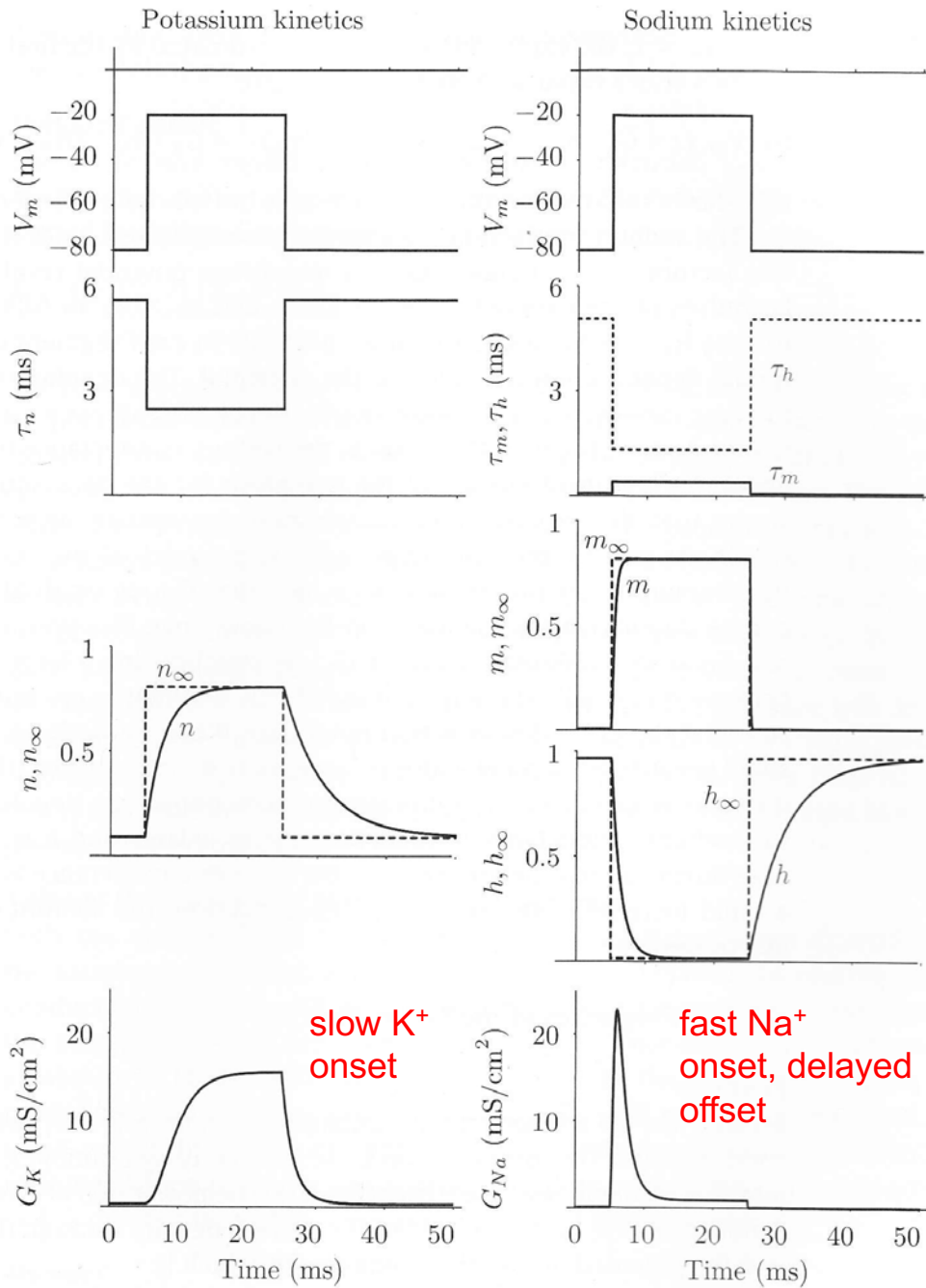


Figure 4.26

