Biophysics I (BPHS 4080)

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

York University
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Lecture 25

Reference/Acknowledgement:
- TF Weiss (Cellular Biophysics)
- D Freeman

Summary: HH Equations

$$\frac{1}{2\pi a(r_o + r_i)} \frac{\partial^2 V_m}{\partial z^2} = C_m \frac{\partial V_m}{\partial t} + G_K(V_m, t)\,(V_m - V_K) + G_{Na}(V_m, t)\,(V_m - V_{Na}) + G_L(V_m - V_L)$$

$$\tau_x \frac{dx}{dt} + x = x_\infty \qquad \frac{dx}{dt} = \alpha_x(1 - x) - \beta_x x$$

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

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

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

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

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

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

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

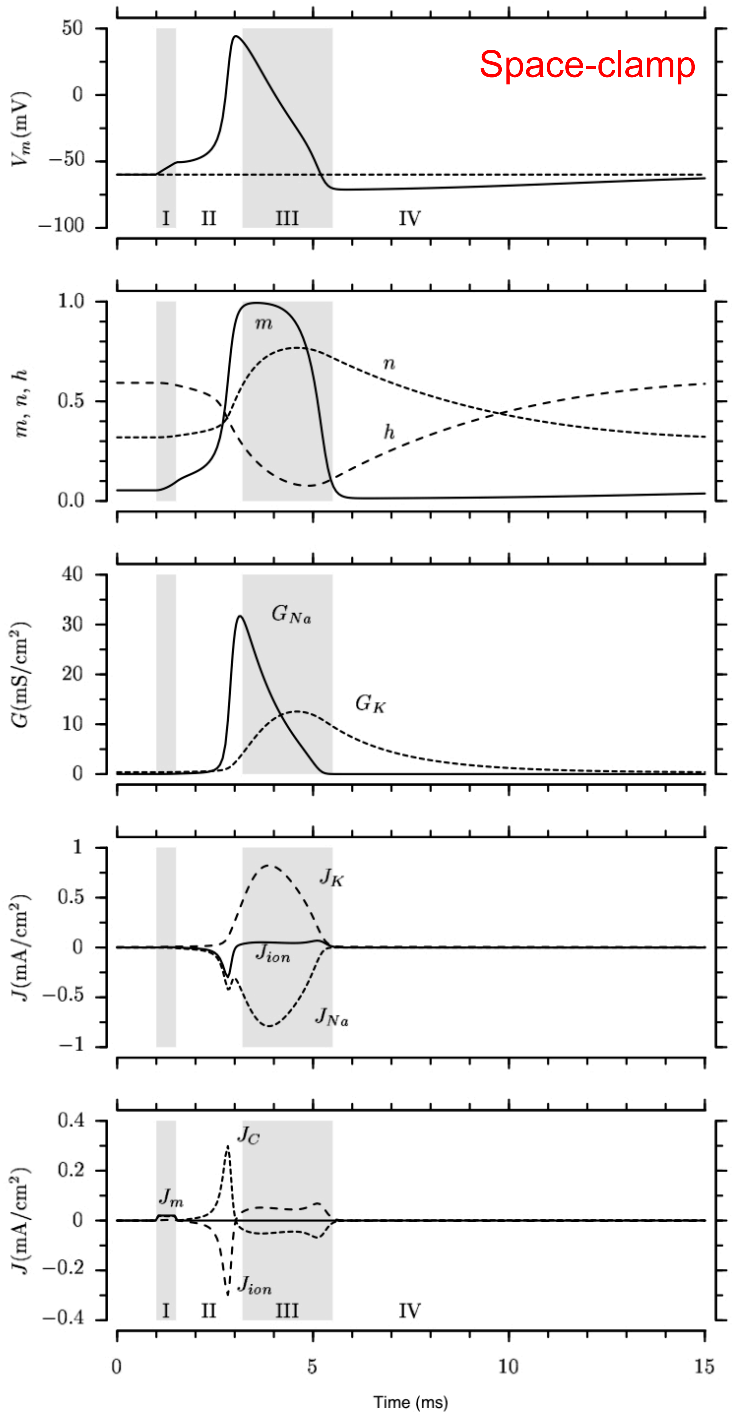
$$\beta_m = 4e^{-(V_m+60)/18},$$

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

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

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

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



Four phases:

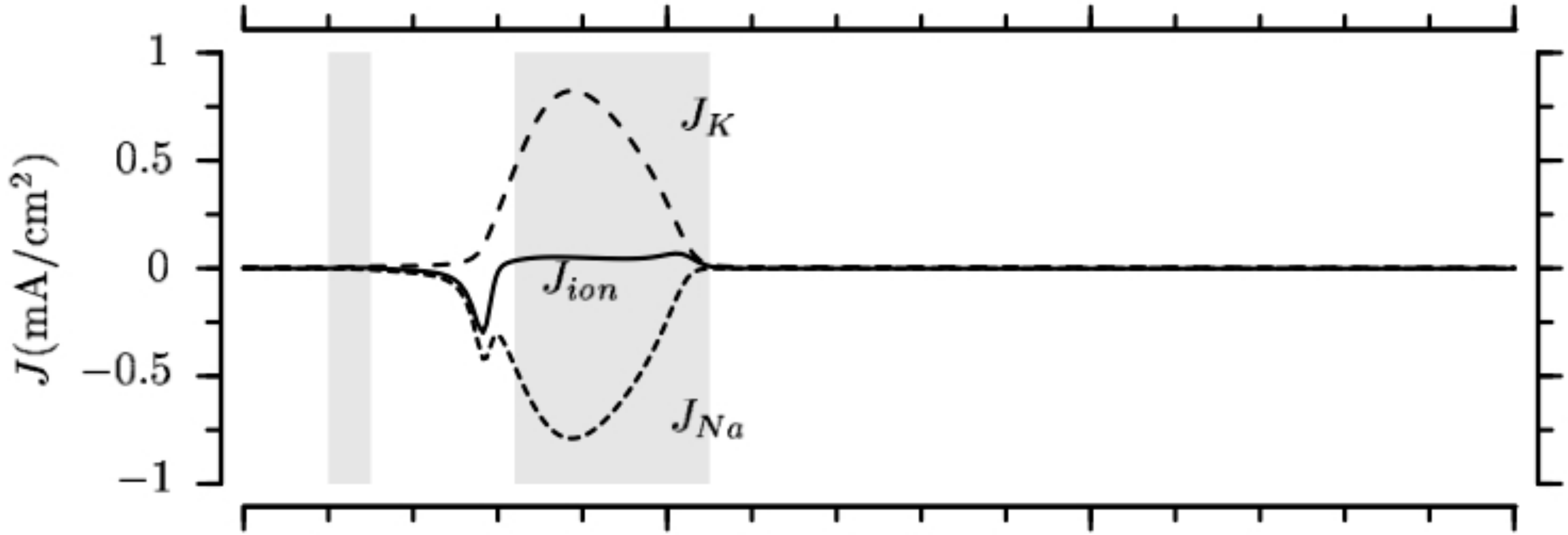
1. Local disturbance due to capacitance
   (behaves like cable model)

2. Onset: V_m change triggers m
   (increased G_{Na} take V_m with it)

3. Falloff: h turns off, n turns on
   (both work to lower V_m back towards V_k , basis for absolute refractory period)

4. Undershoot: increased G_k pushes V_m beyond V^o_m
   (basis for relative refractory period)

Note: Membrane current (J_M) can be parsed up into two components: a capacitive current (J_C) and an ionic current (J_{ion})



Note: Fairly little net current across membrane
(i.e., relatively few net ions transported)

Threshold

In vivo: For the same stimulus, sometimes an AP fires, sometimes it does not

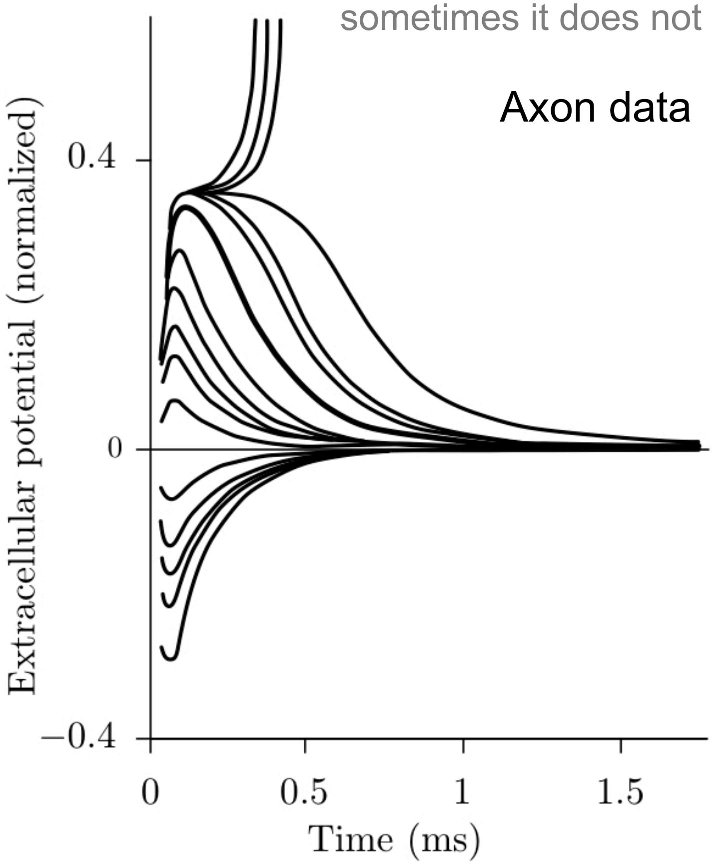


Figure 4.40

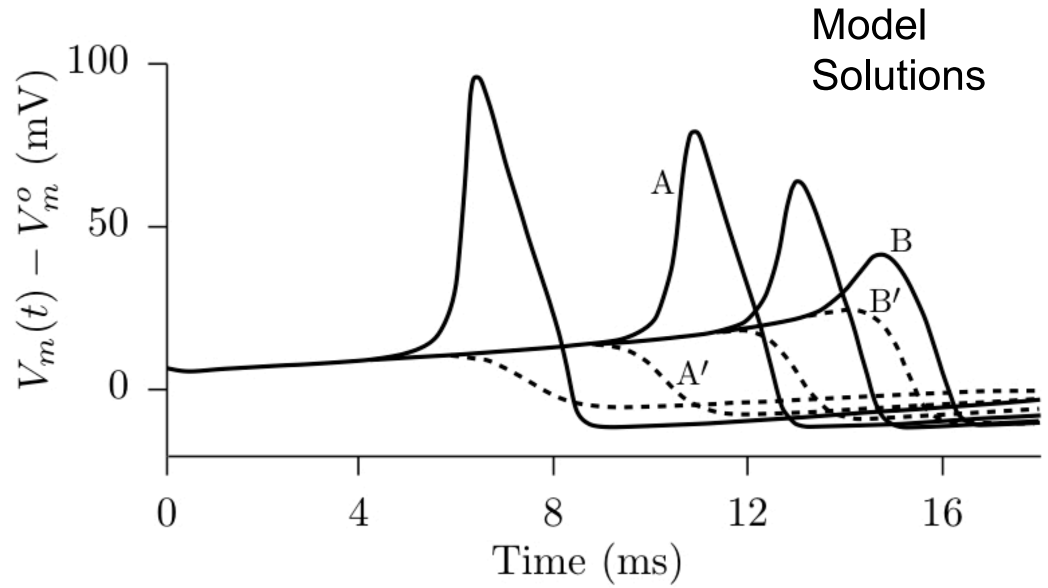


Figure 4.41

→ Model exhibits '*exceedingly narrow threshold region*'

→ What is mechanism for a threshold?

Note: Model is deterministic and does not capture stochastic behaviors manifest in-vivo

Threshold

Space-clamped

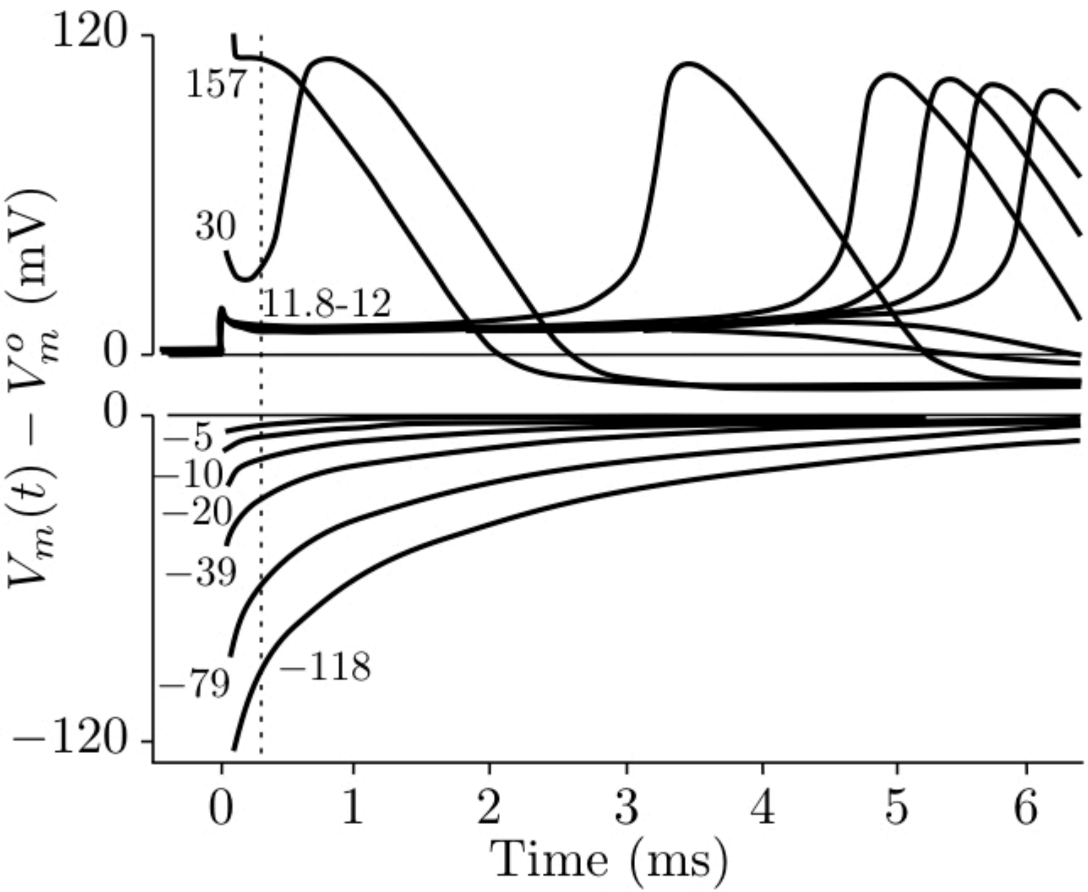


Figure 4.42

→ Note lag for AP to occur (stems from capacitive build-up to threshold)

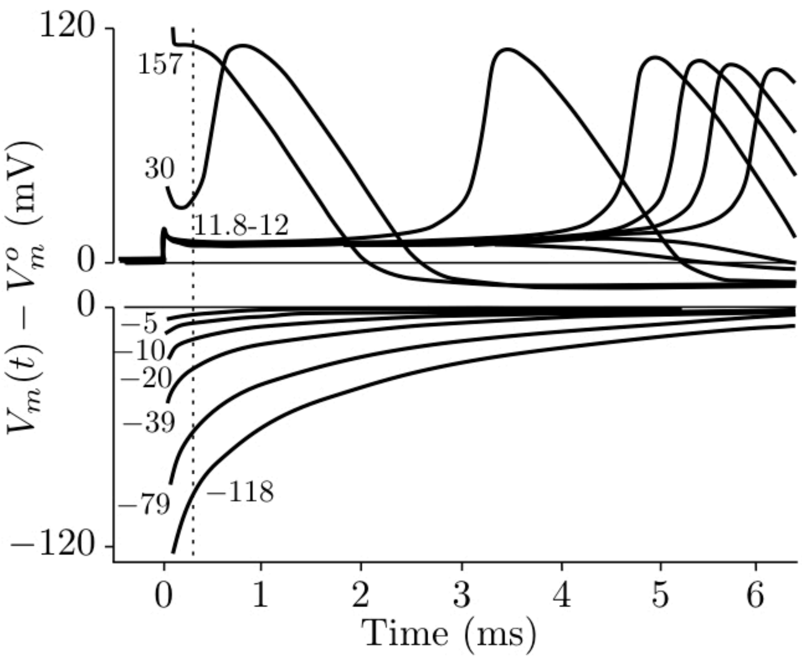


Figure 4.42

Determine J_{ion}-V_m relationship right after shock (dashed line)

- Current purely due to C_m
- Membrane "deciding" whether to fire AP or not

$$J_{ion} = -J_C = -C_m \frac{dV_m}{dt}$$

Note: This picture only holds as a snapshot right after the stimulus

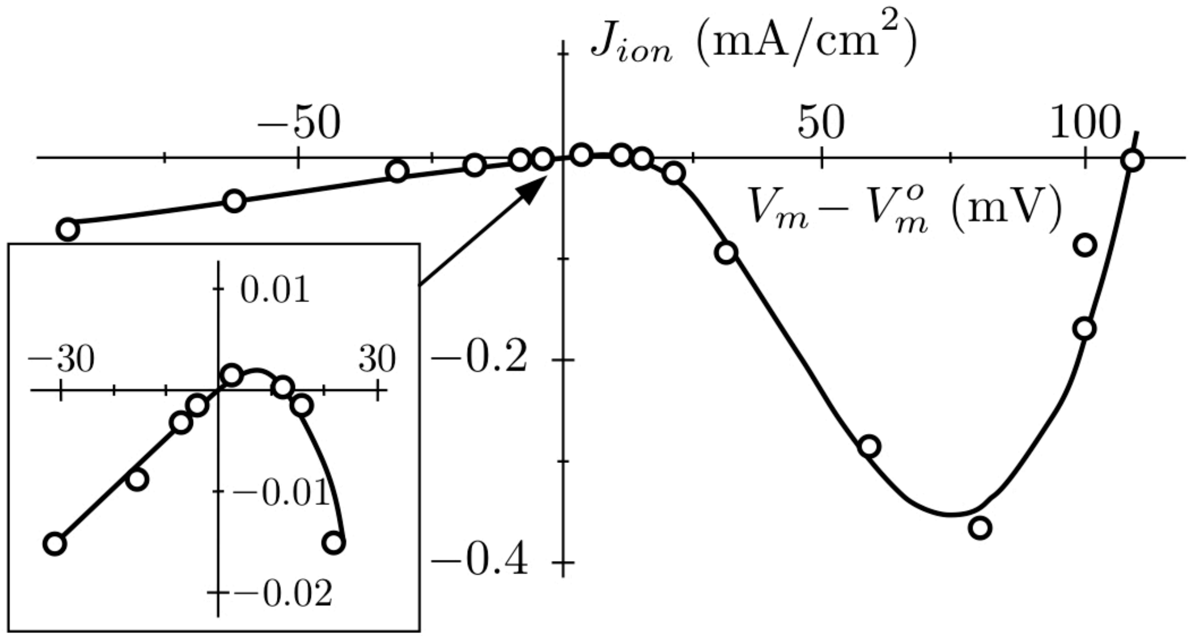


Figure 4.43

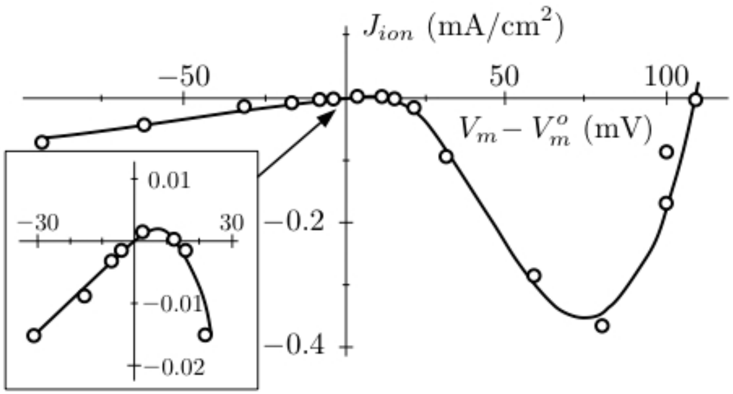
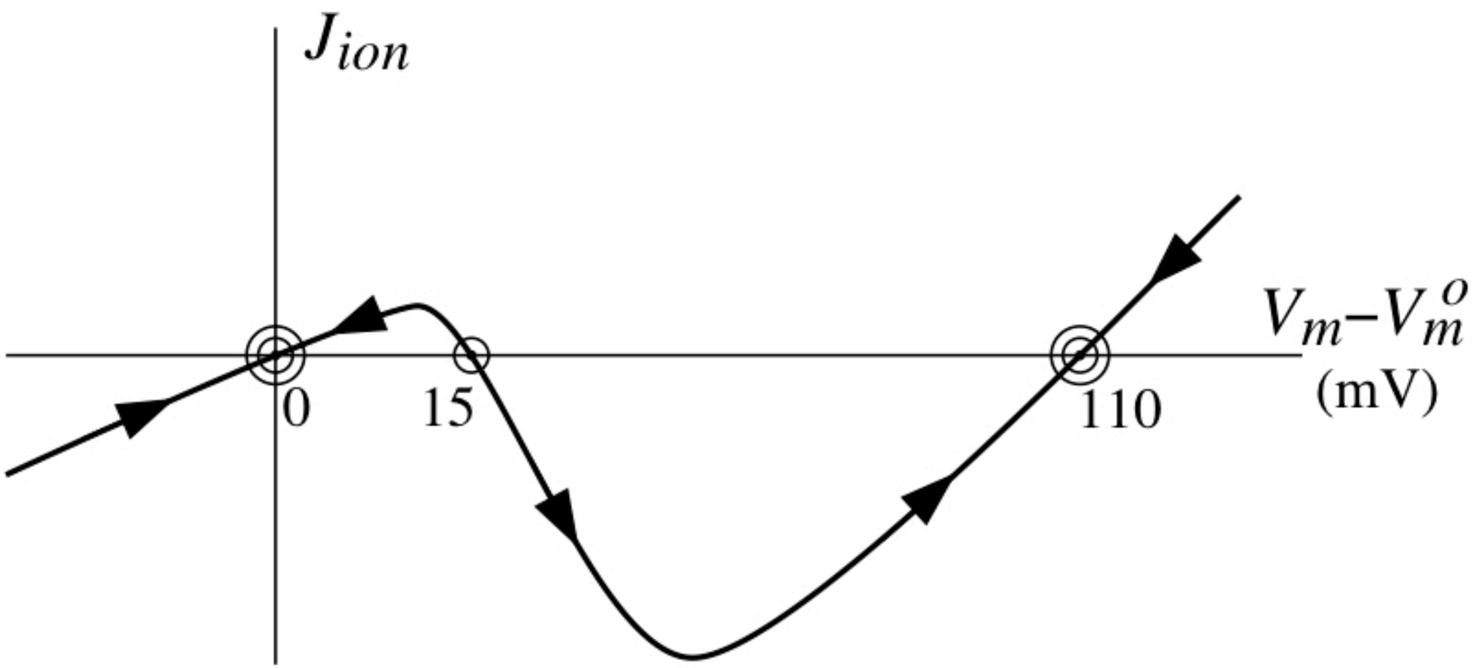


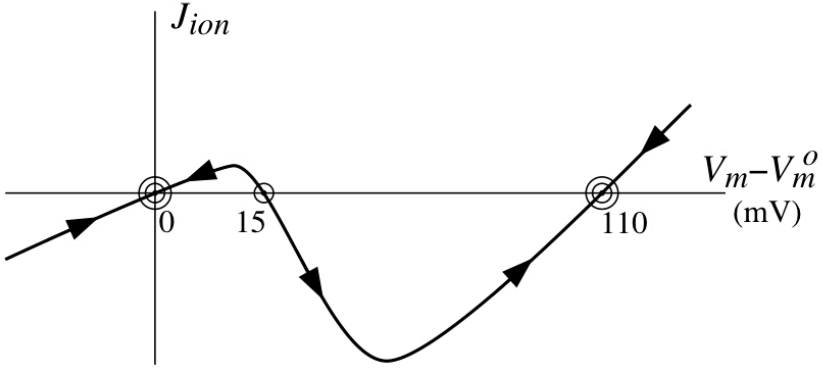
Figure 4.43

- Equilibrium points
- Stability

$$J_{ion} = -J_C = -C_m \frac{dV_m}{dt}$$

- Threshold
- Ohm's Law: Negative resistance?





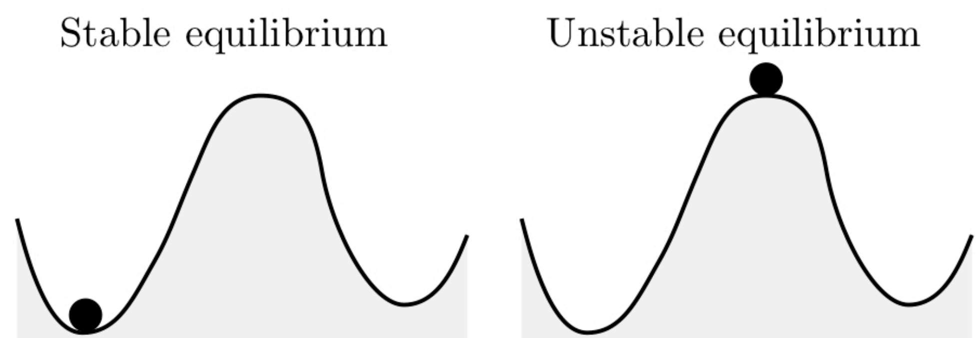
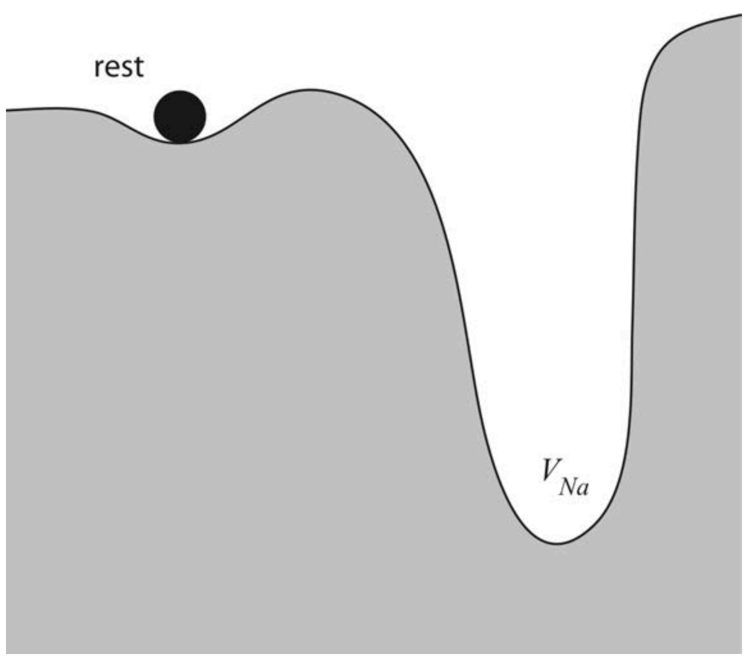


Figure 4.45



→ These pictures make it easy to envision a *stochastic* component too

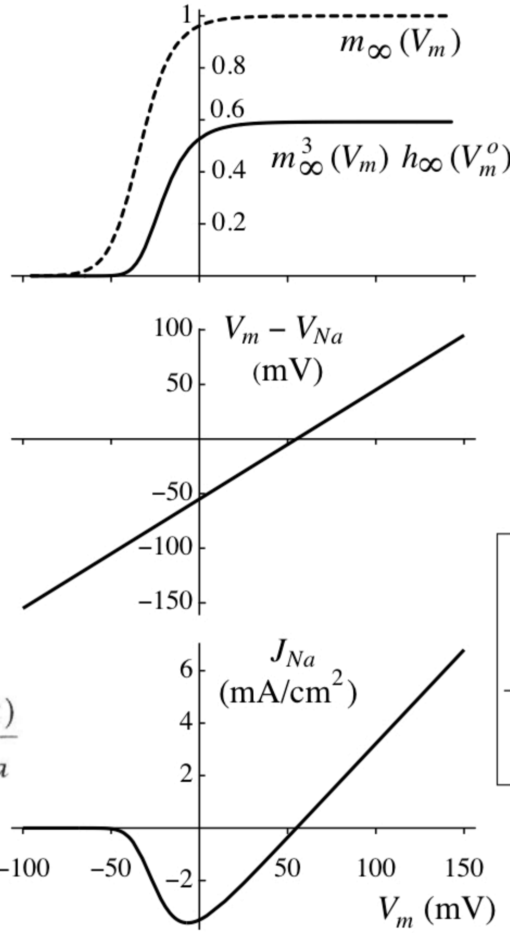
(e.g., consider random force jittering object about)

Threshold

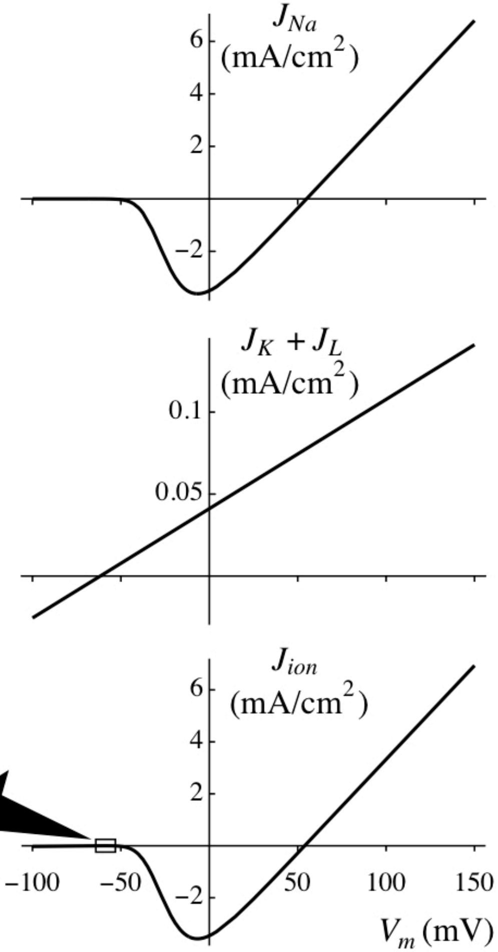
$$G_K(V_m,t) = \overline{G}_K n^4(V_m,t)$$
$$G_{Na}(V_m,t) = \overline{G}_{Na} m^3(V_m,t) h(V_m,t)$$

$$V_{Na} = \frac{RT}{F}\log\frac{c^o_{Na}}{c^i_{Na}}$$

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



- assume n and h are constant



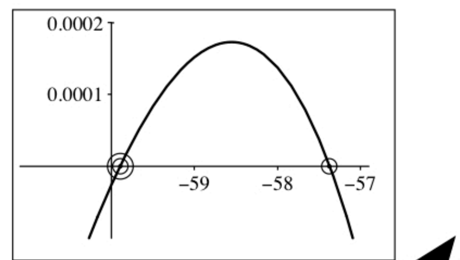
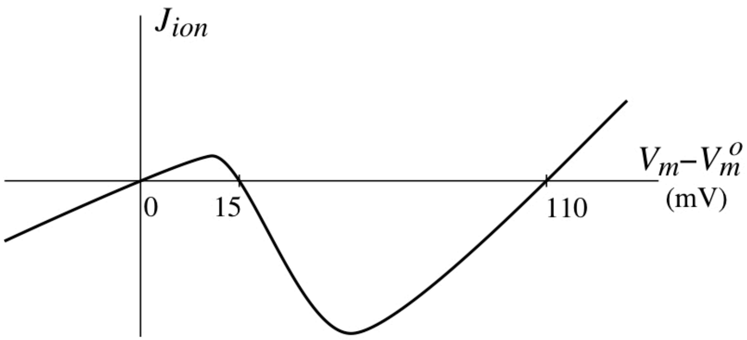
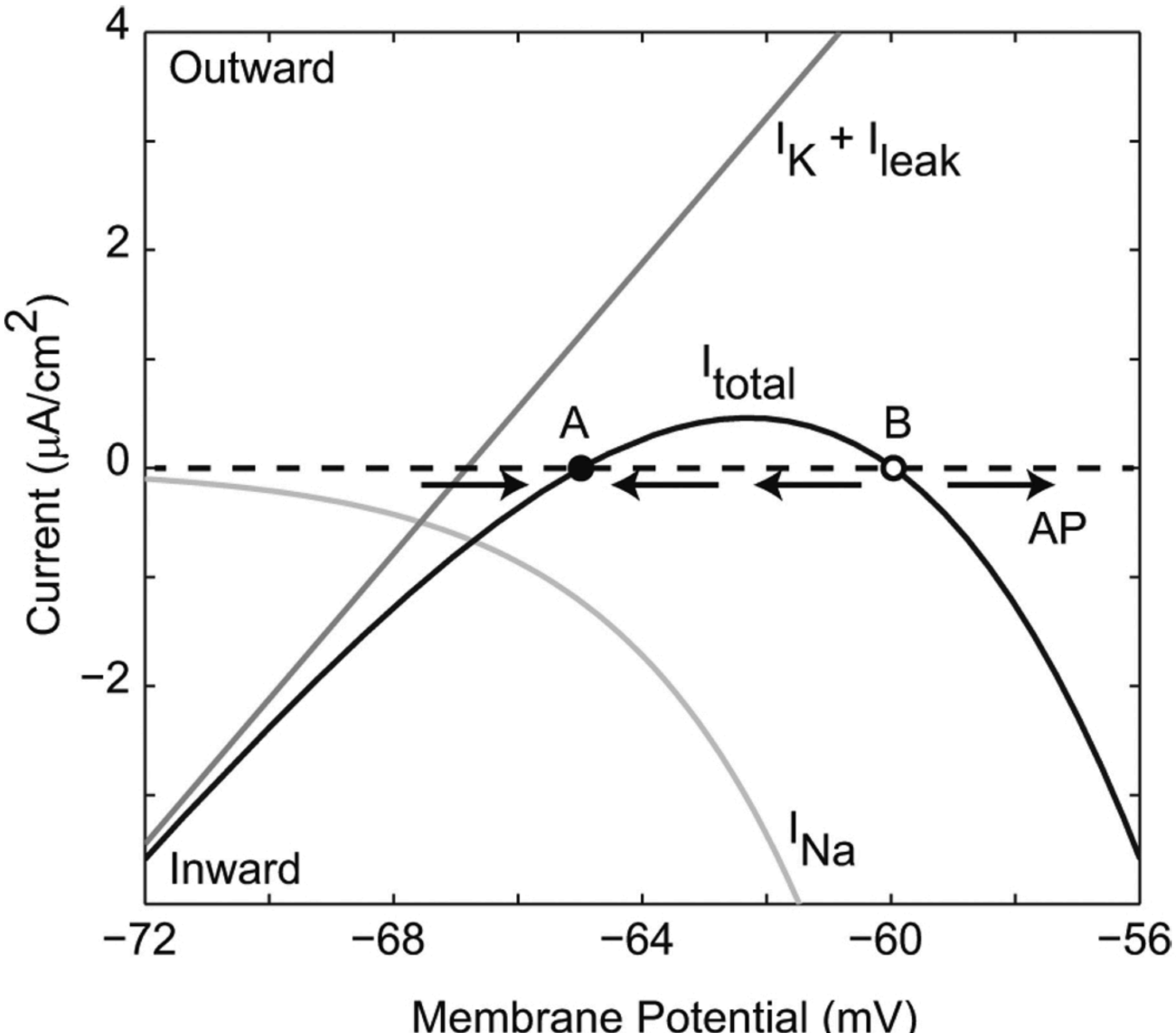


Figure 4.47



→ Ultimately more than one ion is needed

(Na+ alone is insufficient)



Catterall et al. (2012)

Threshold: Phase Plane Portrait

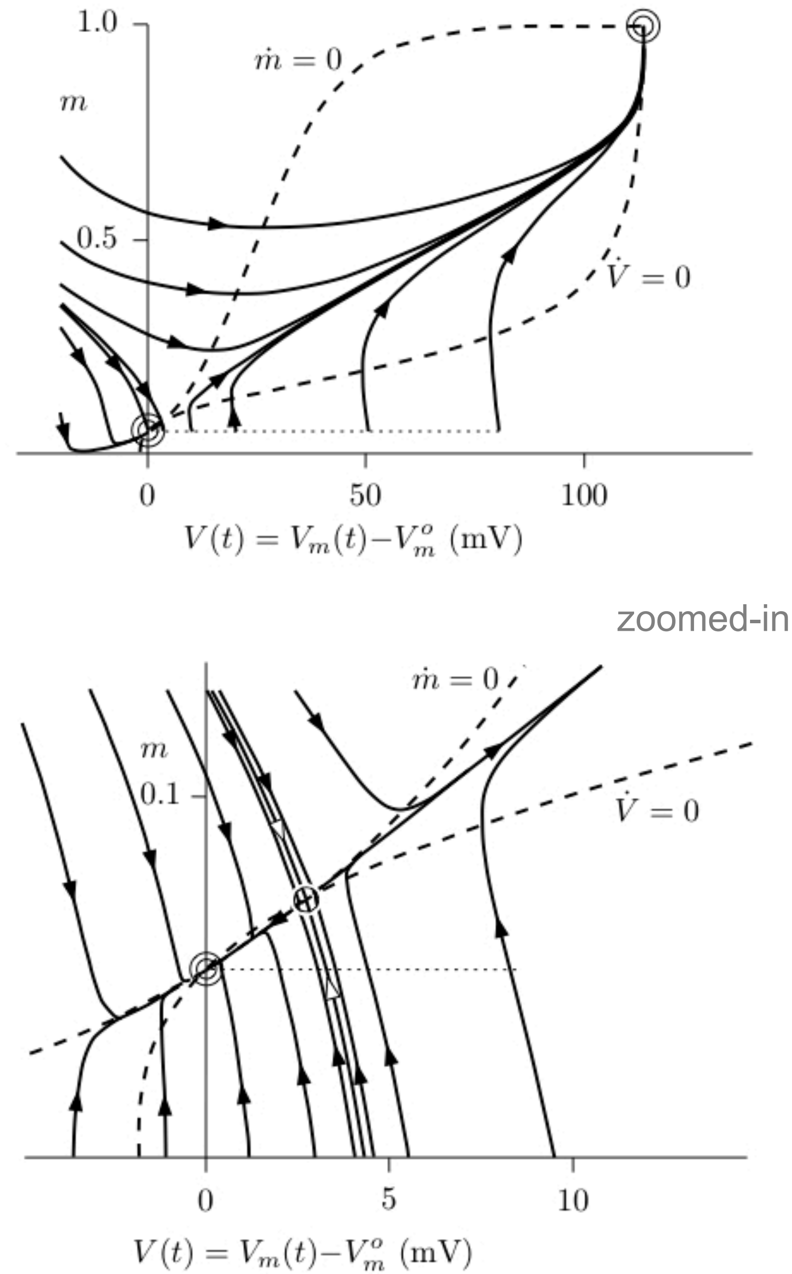


Figure 4.49

assumes n and h are constant, but m varies dynamically

Refractory Period

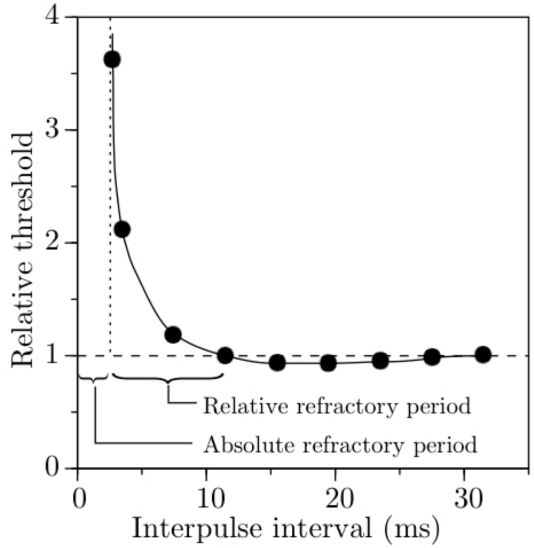


Figure 1.13

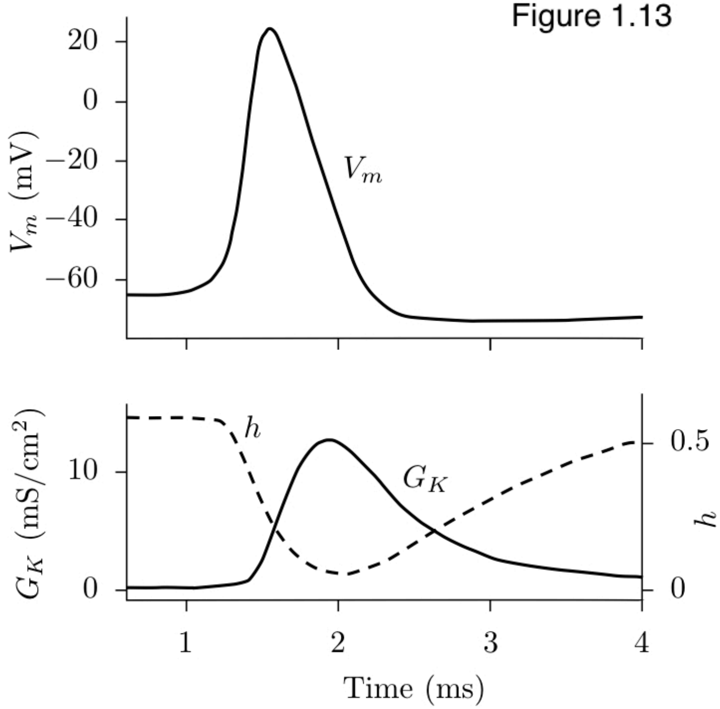


Figure 4.52

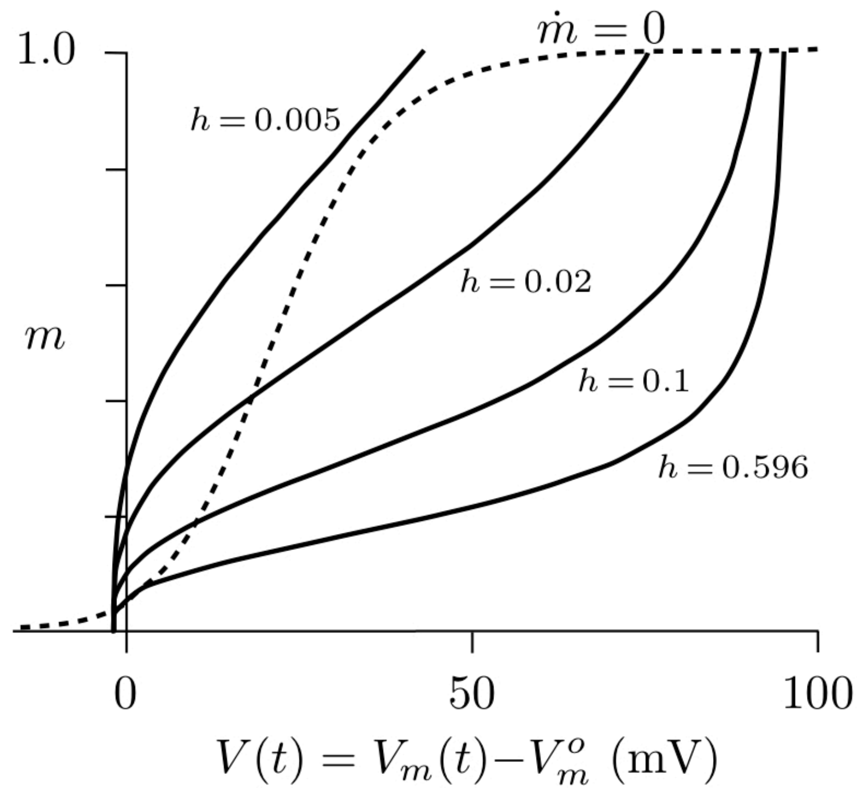


Figure 4.53

Back to the question of spatial propagation...

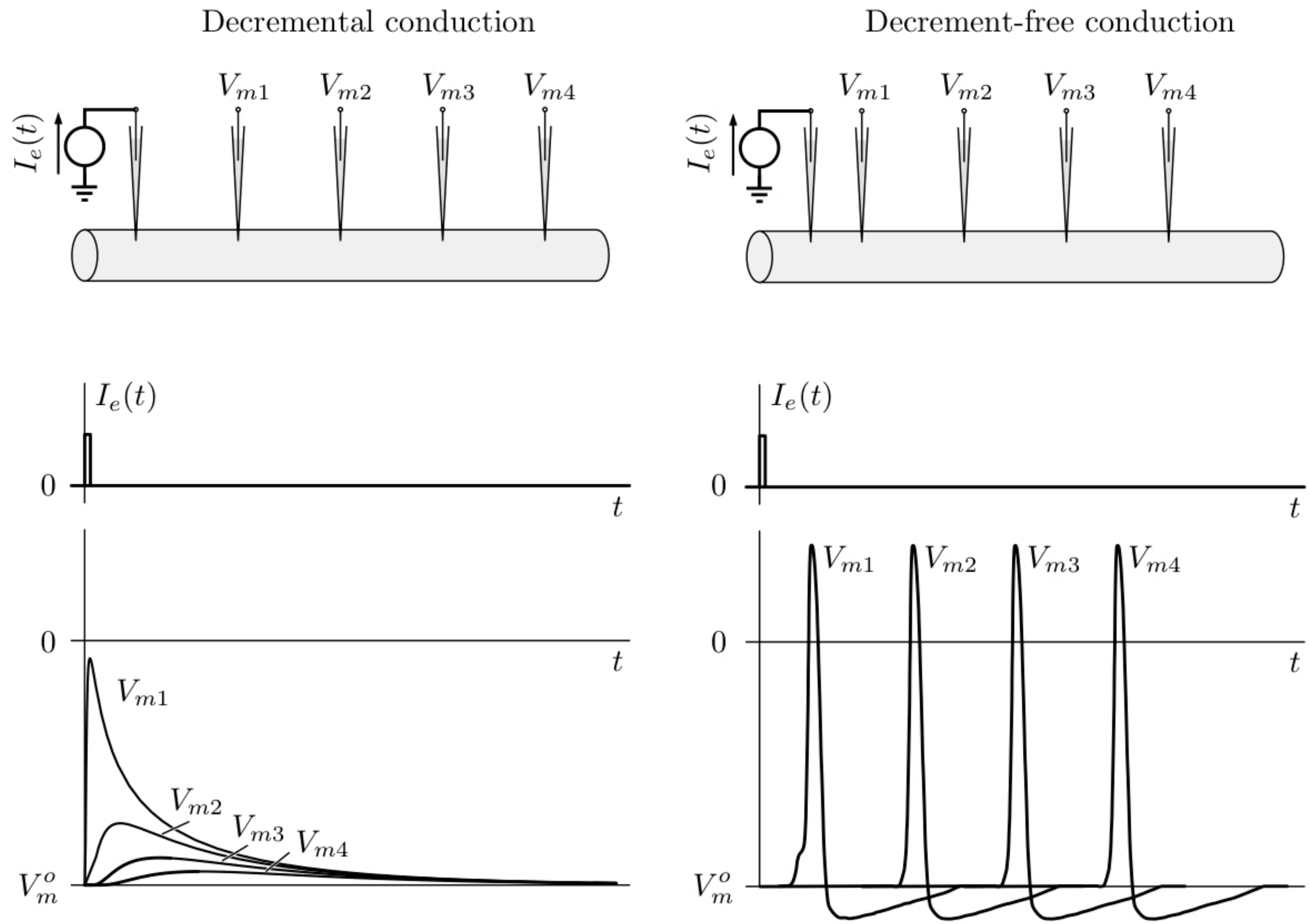
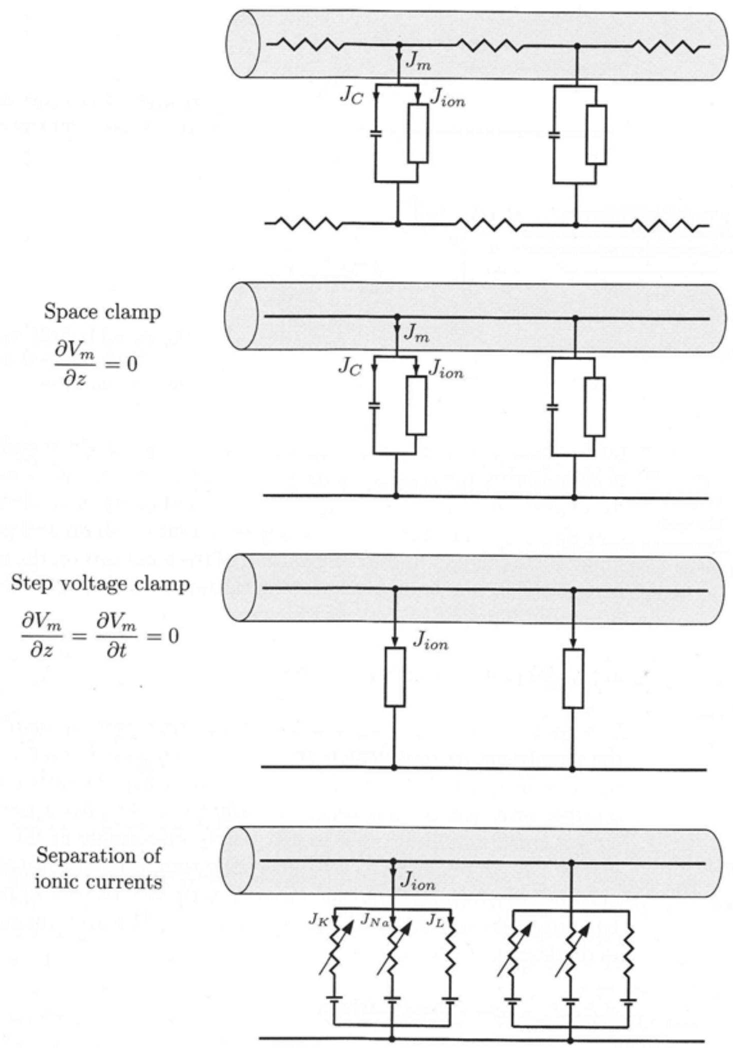


Figure 1.16

Propagated APs



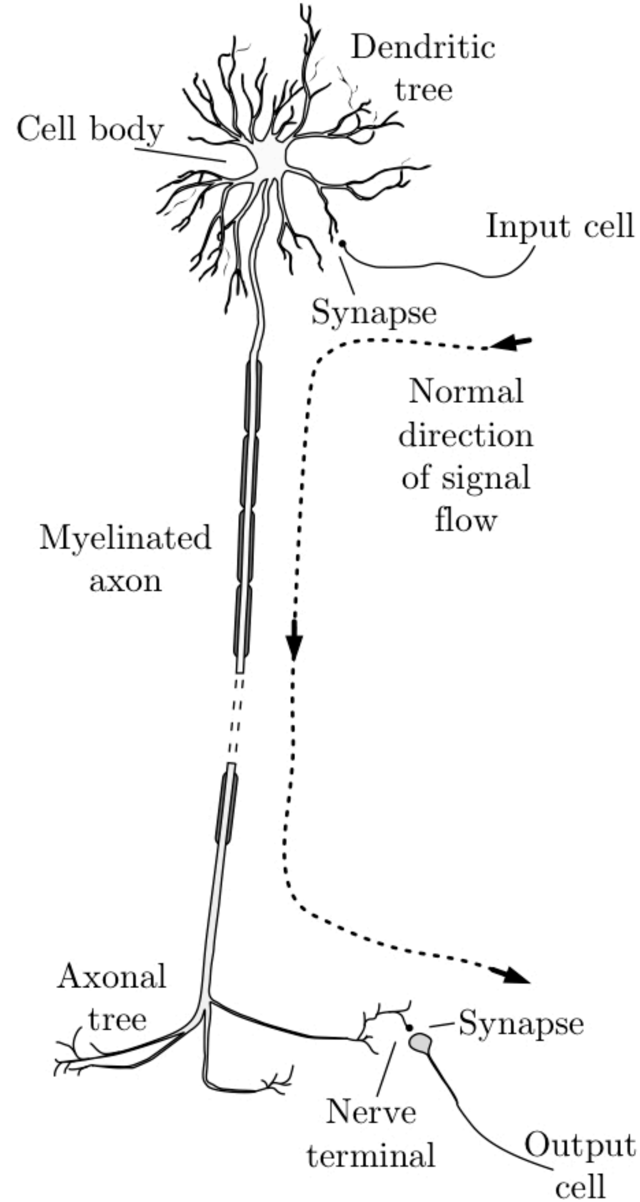


Figure 1.22

Propagated APs

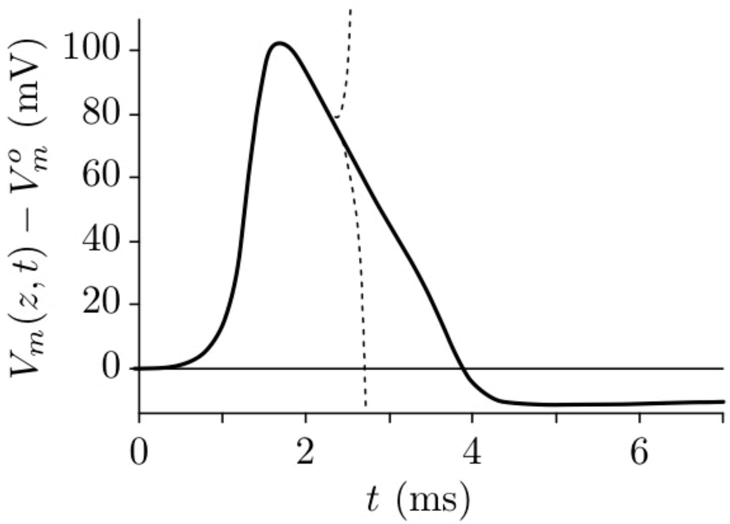


Figure 4.30

→ Solutions only stable for appropriate choice of conduction velocity

(think back to cable model; C_m matters!)

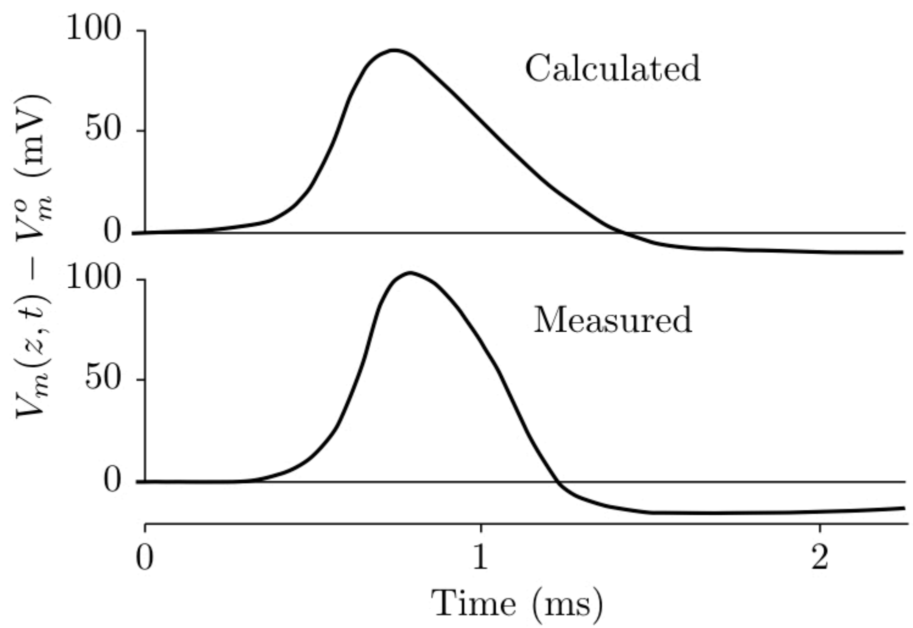


Figure 4.31

Propagated APs

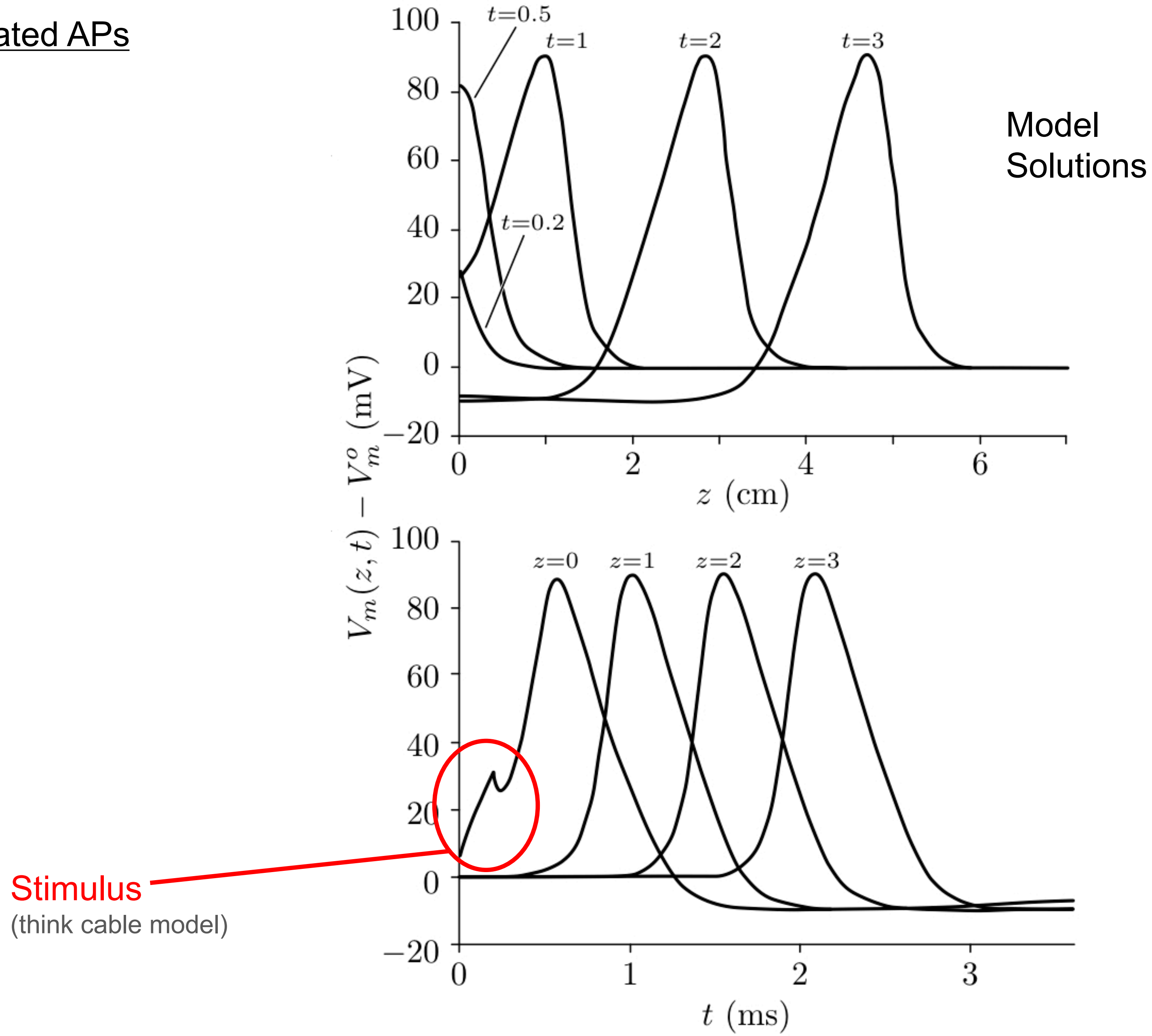


Figure 4.29

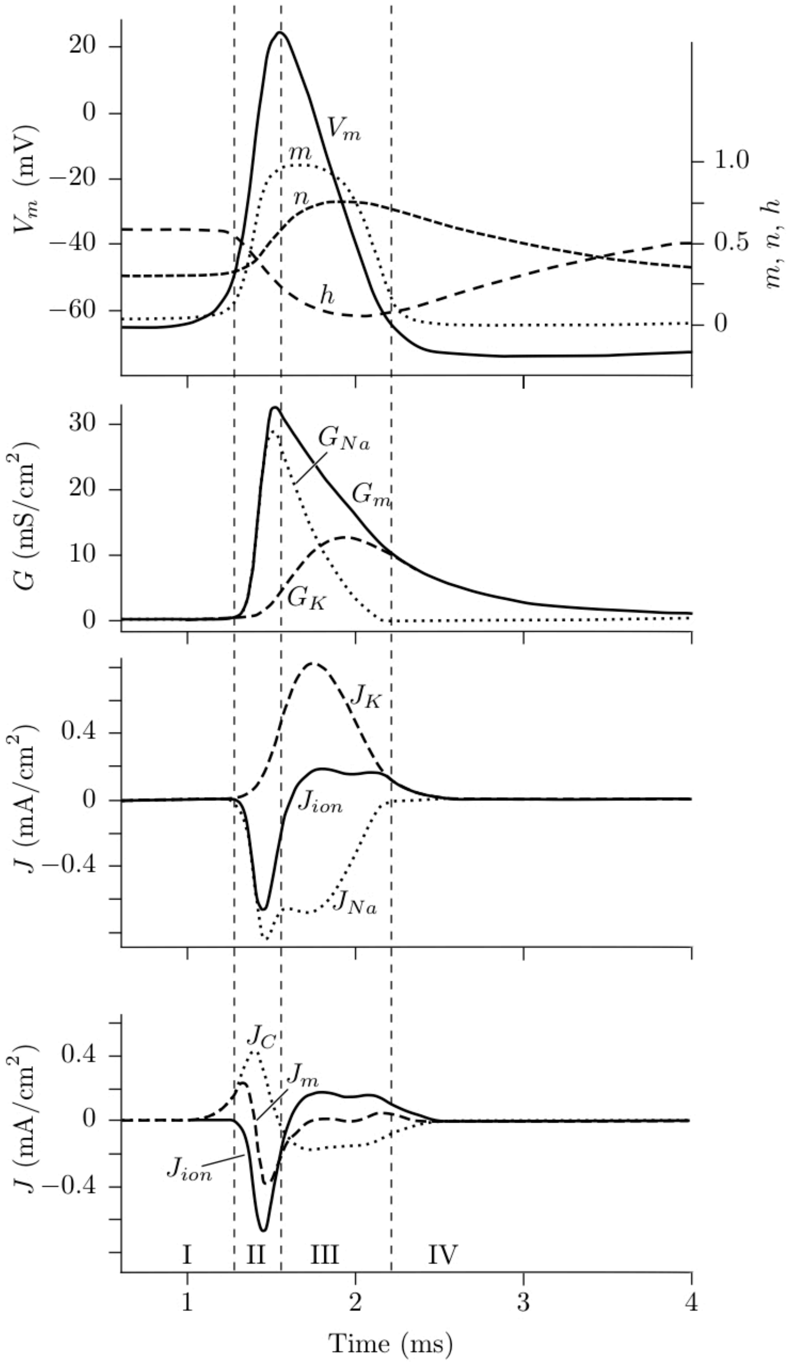
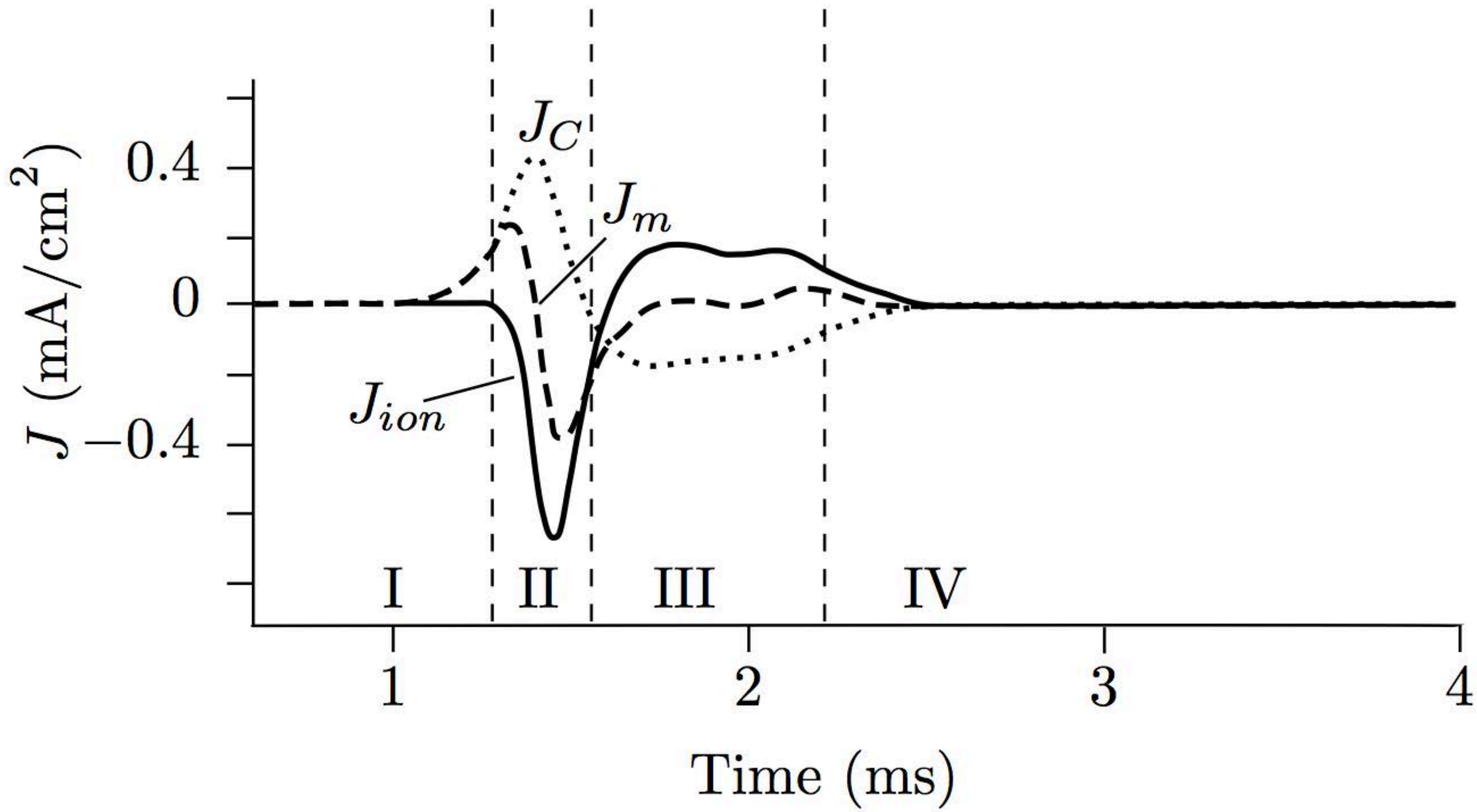


Figure 4.32

Similar picture as before for propagated AP

→ Note lag between V_m and G_m

(stems from capacitive surge)



→ Note lag between V_m and G_m

(stems from capacitive surge)

Myelination

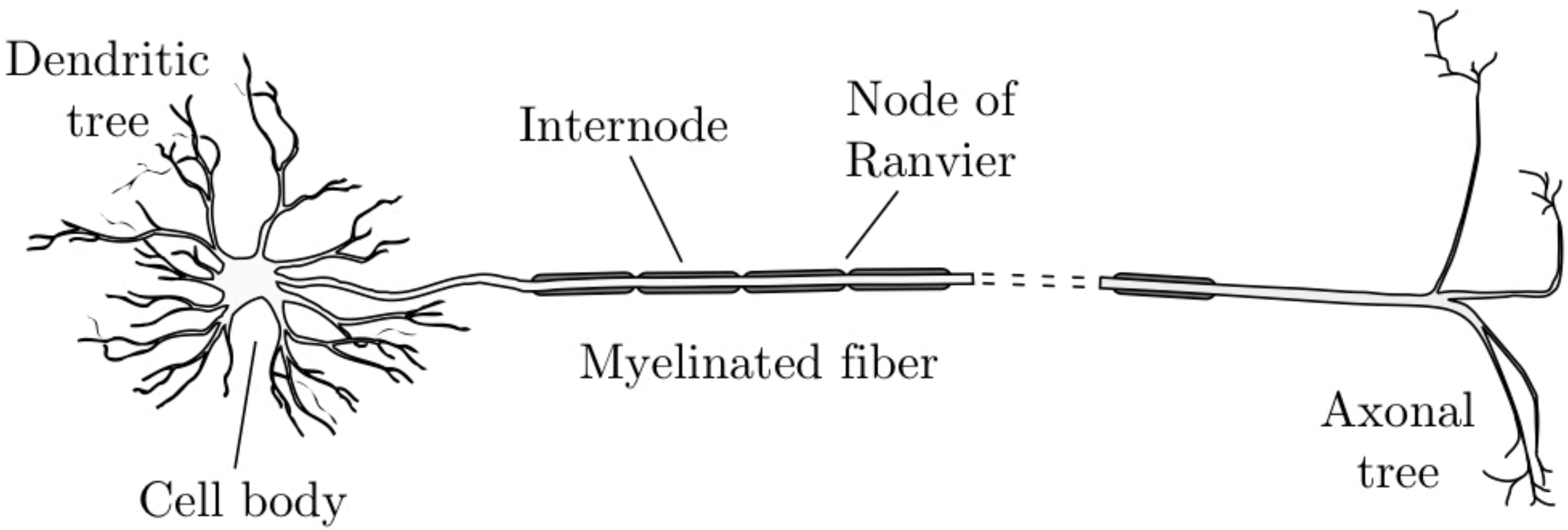


Figure 5.1

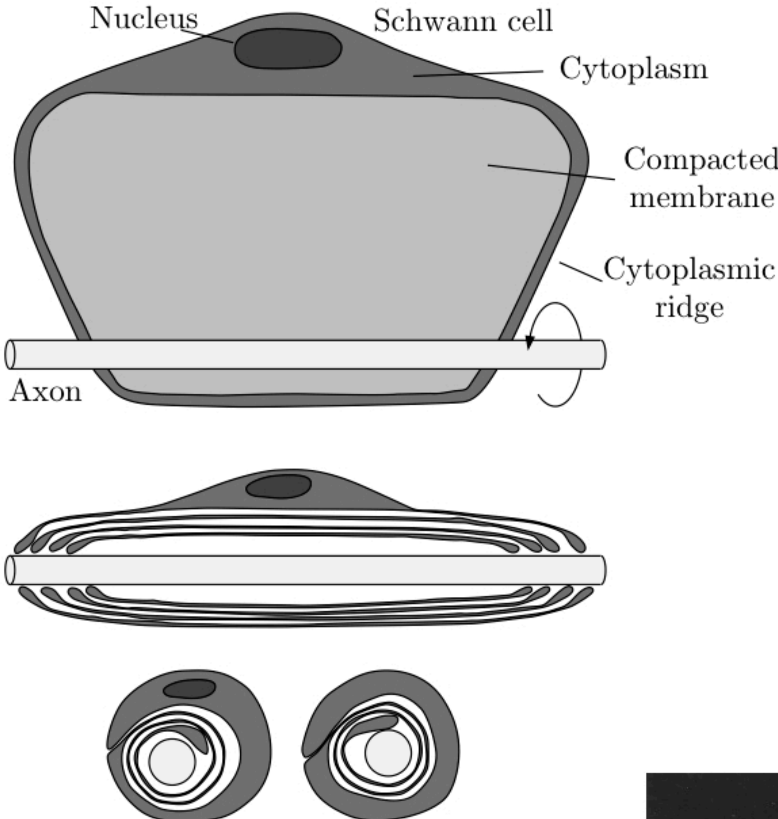


Figure 5.5

Figure 5.6

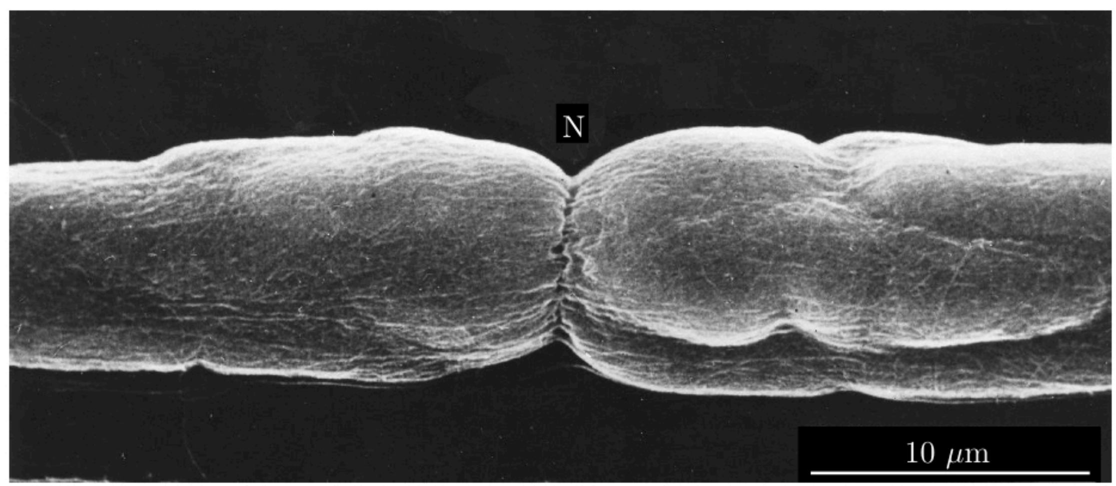


Figure 5.2