Biophysics I (BPHS 3090)

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Website: http://www.yorku.ca/cberge/3090W2015.html

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Lecture 26

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

Summary: HH Equations

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

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

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

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

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

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

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

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

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

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

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

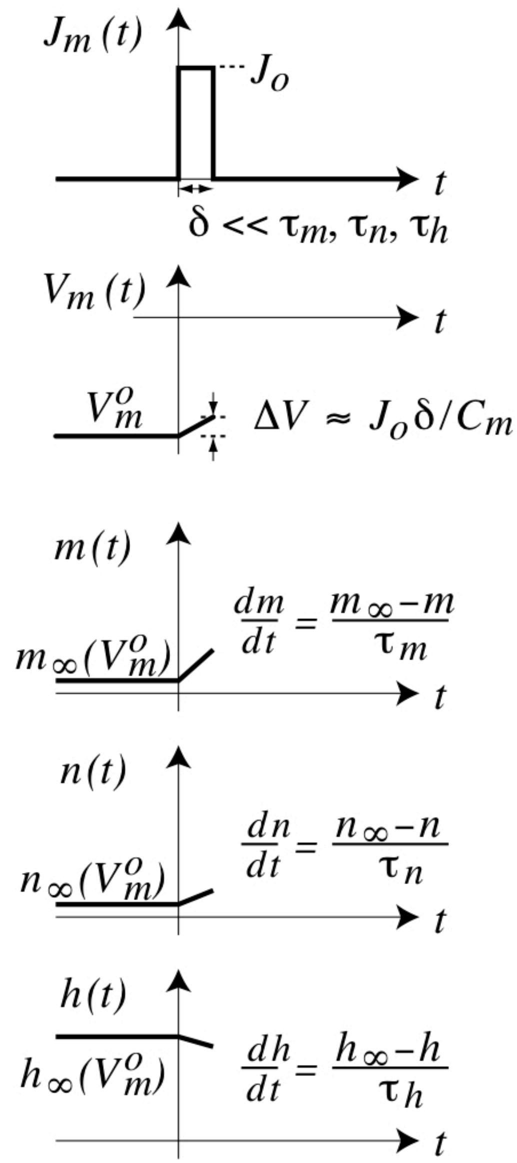
$$\beta_h = \frac{1}{1 + e^{-0.1(V_m+30)}},$$

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

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

(numerically) Solving HH Eqns.

How to run HH model backwards?



SoftCell numerically integrates the ODEs
(e.g., Euler method, Runge-Kutta)

Finally there was the difficulty of computing the action potentials from the equations which we had developed. We had settled all the equations and constants by March 1951 and hoped to get these solved on the Cambridge University computer. However, before anything could be done we learnt that the computer would be off the air for 6 months or so while it underwent a major modification. Andrew Huxley got us out of that difficulty by solving the differential equations numerically using a hand-operated Brunsviga. The propagated action potential took about three weeks to complete and must have been an enormous labour for Andrew. But it was exciting to see it come out with the right shape and velocity and we began to feel that we had not wasted the many months that we had spent in analysing records.

—Hodgkin, 1977

Propagated APs

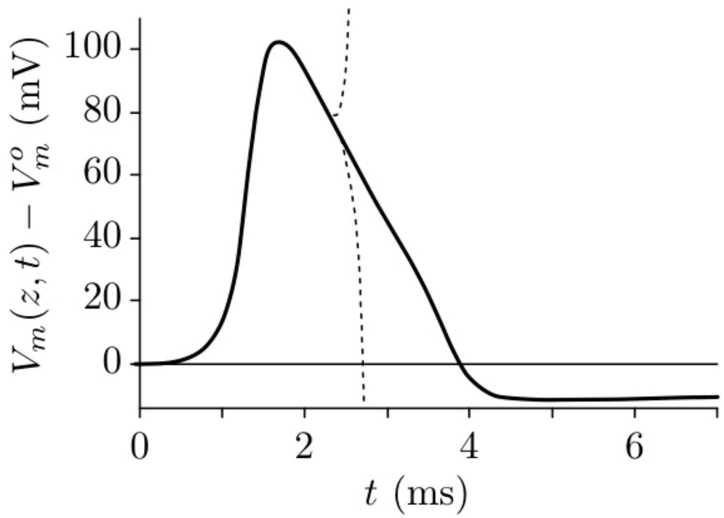


Figure 4.30

→ Solutions only stable for appropriate choice of conduction velocity
(think back to cable model; C_m matters!)

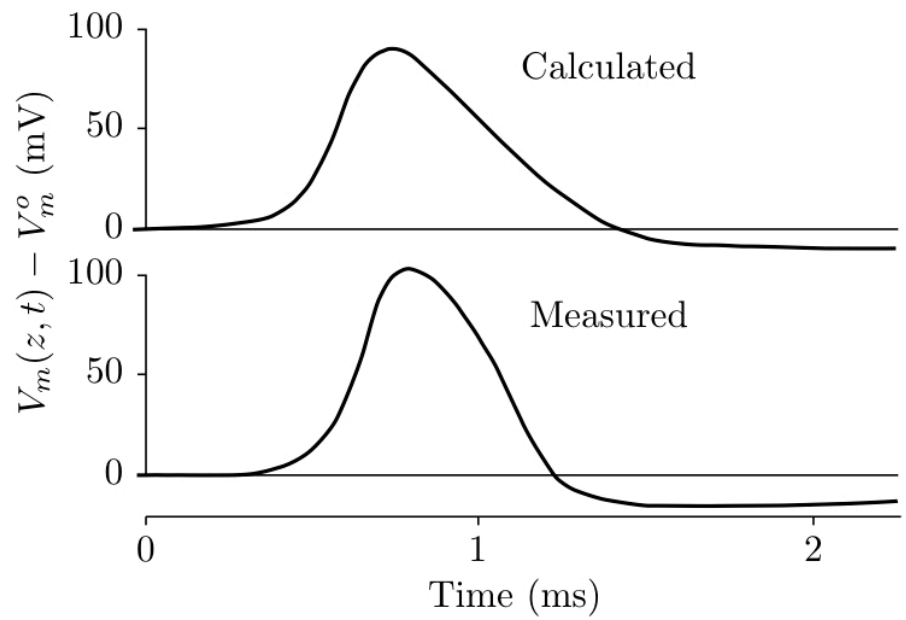


Figure 4.31

Propagated APs

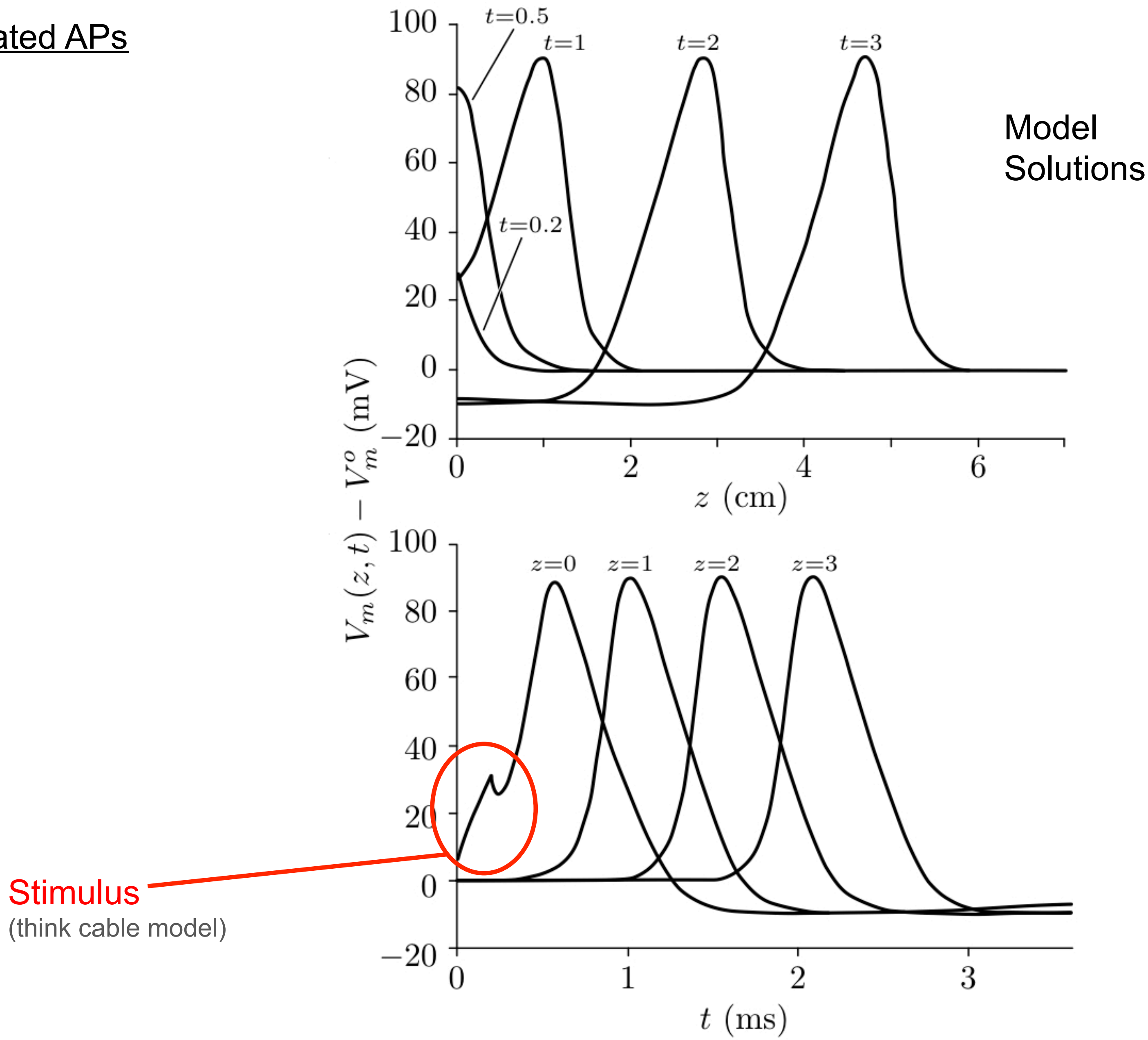
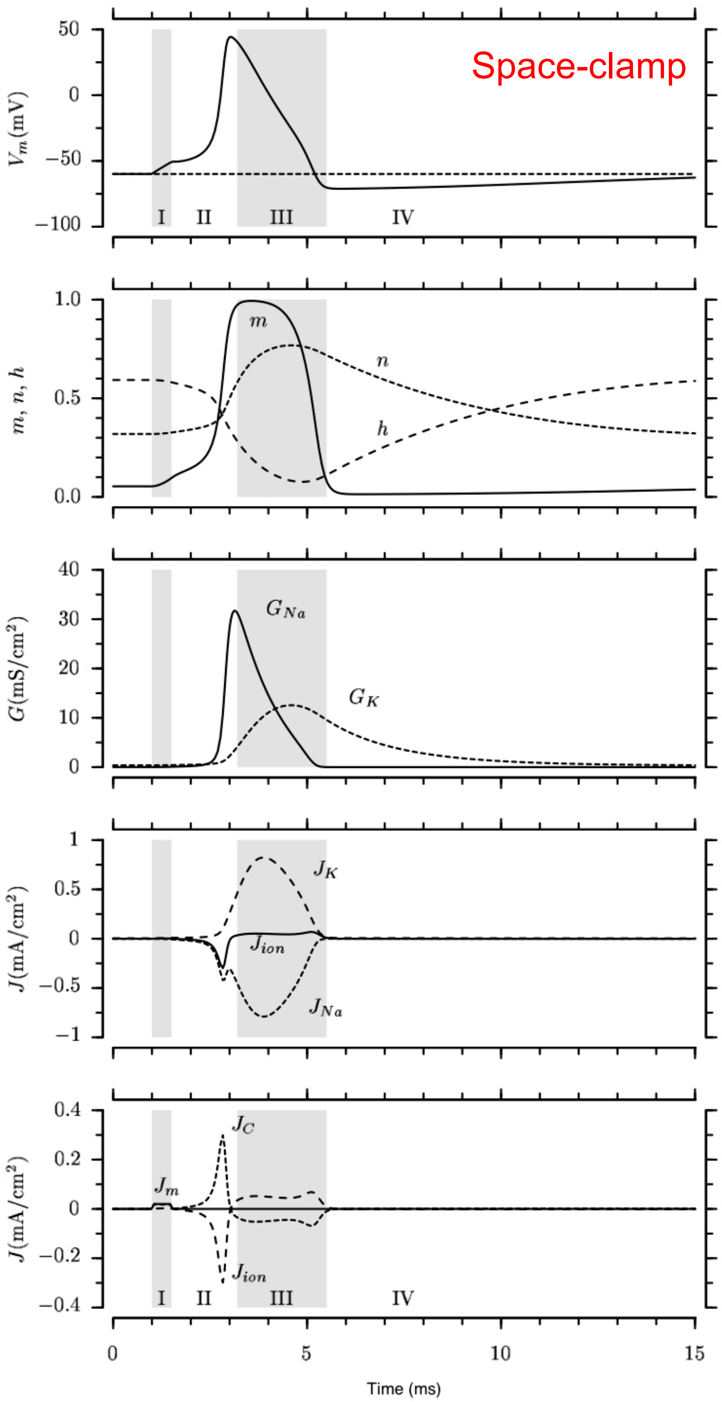


Figure 4.29



Four phases:

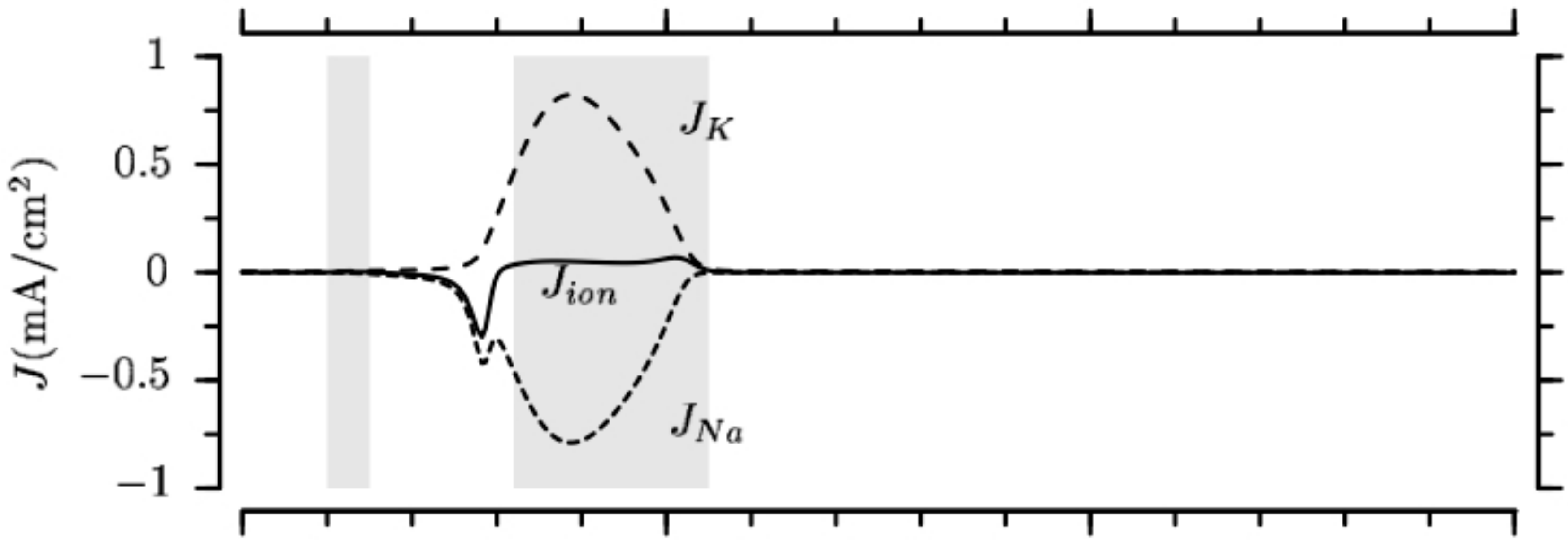
1. Local disturbance due to capacitance
   (behaves like cable model)

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)

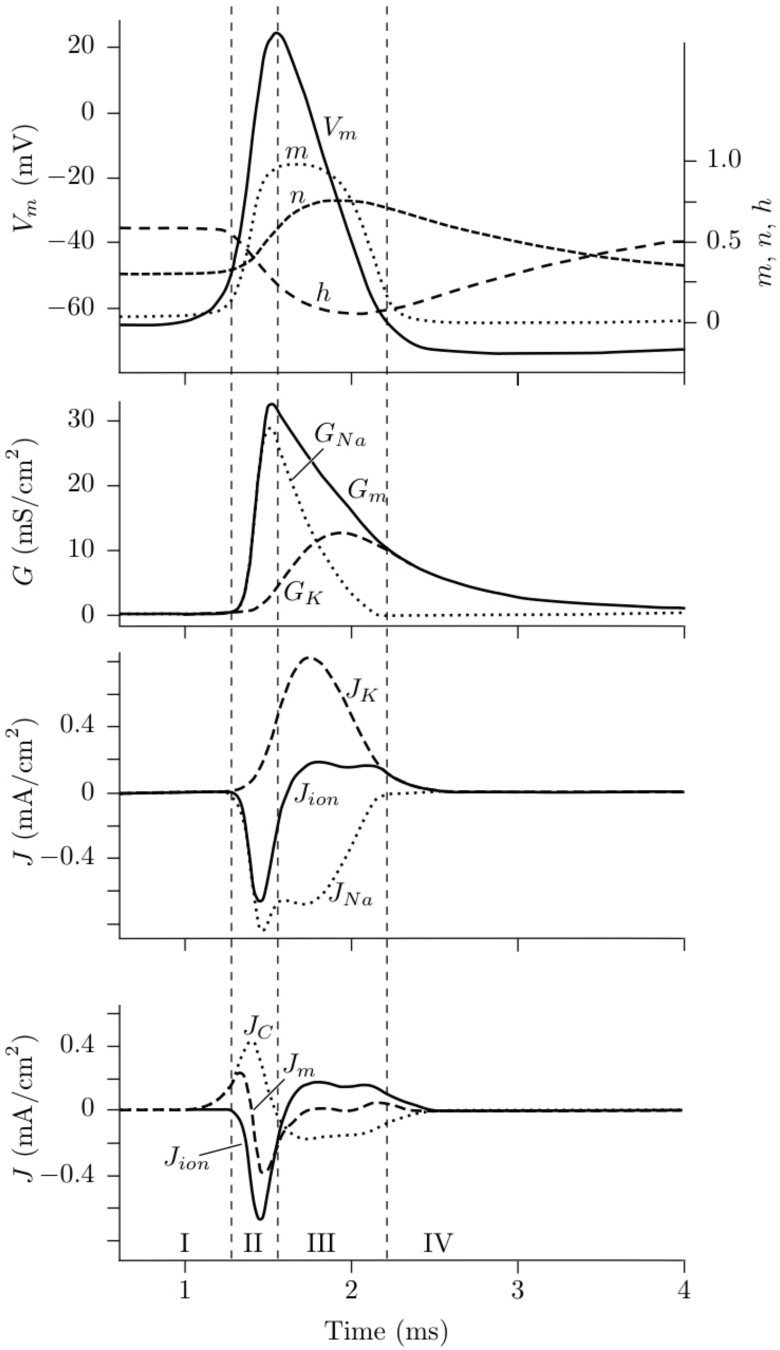
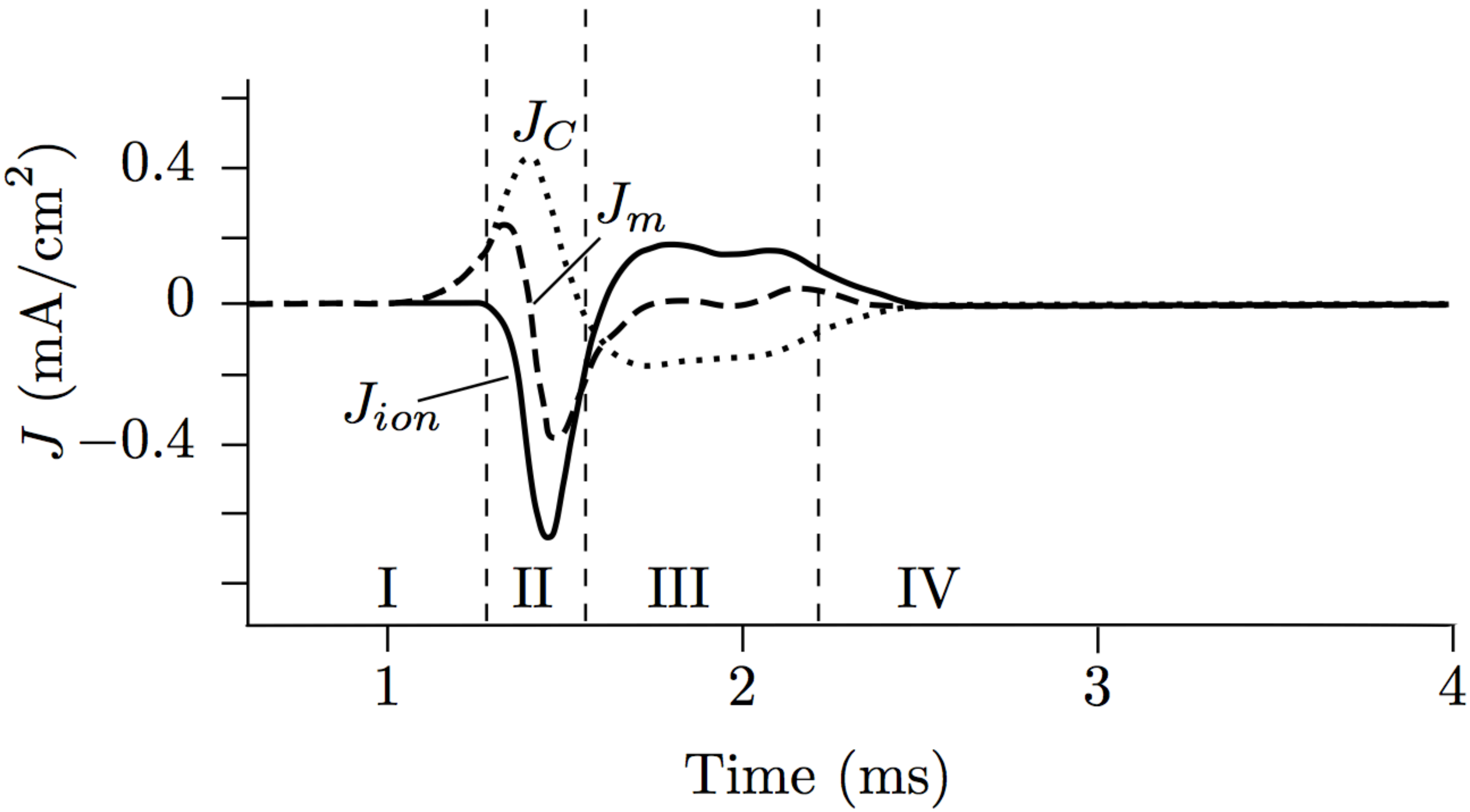


Figure 4.32

Similar picture 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)

Threshold

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

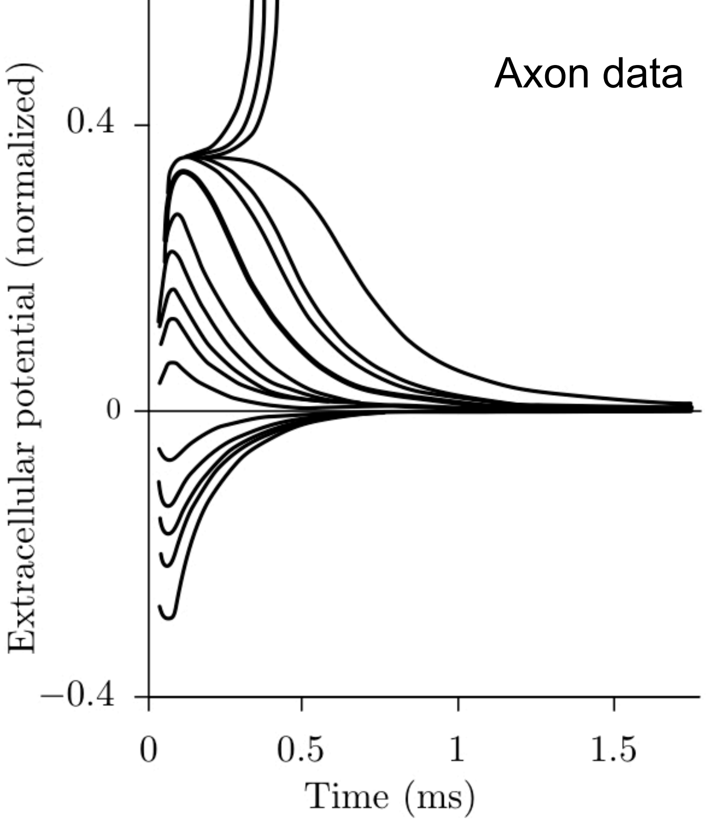


Figure 4.40

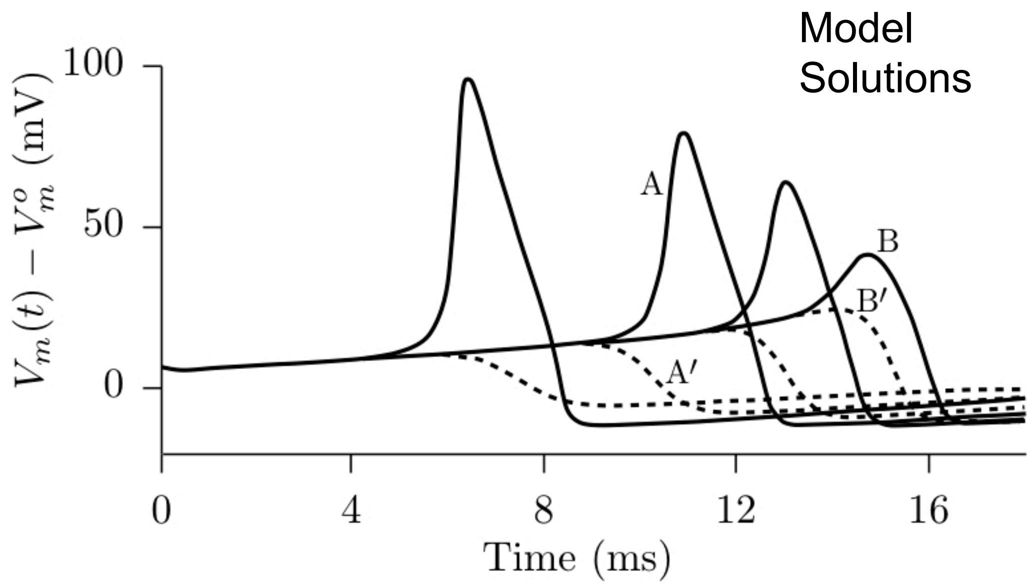


Figure 4.41

→ 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

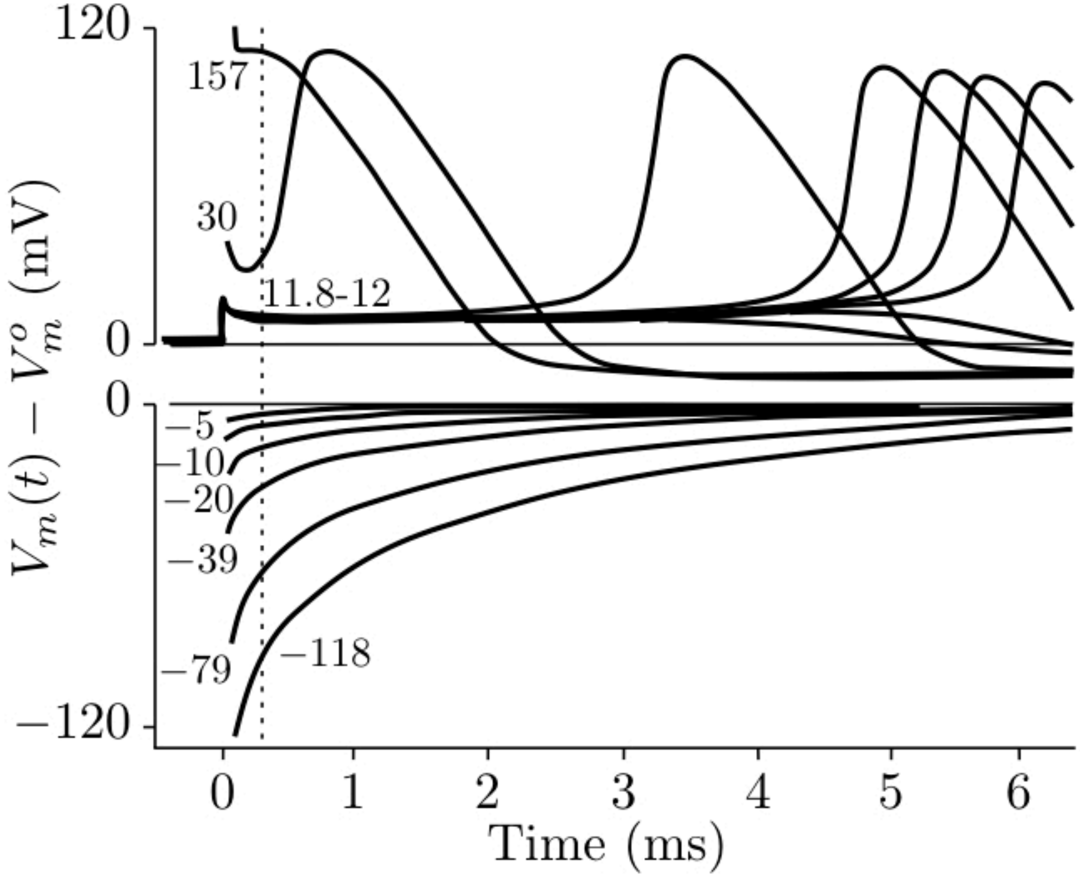


Figure 4.42

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

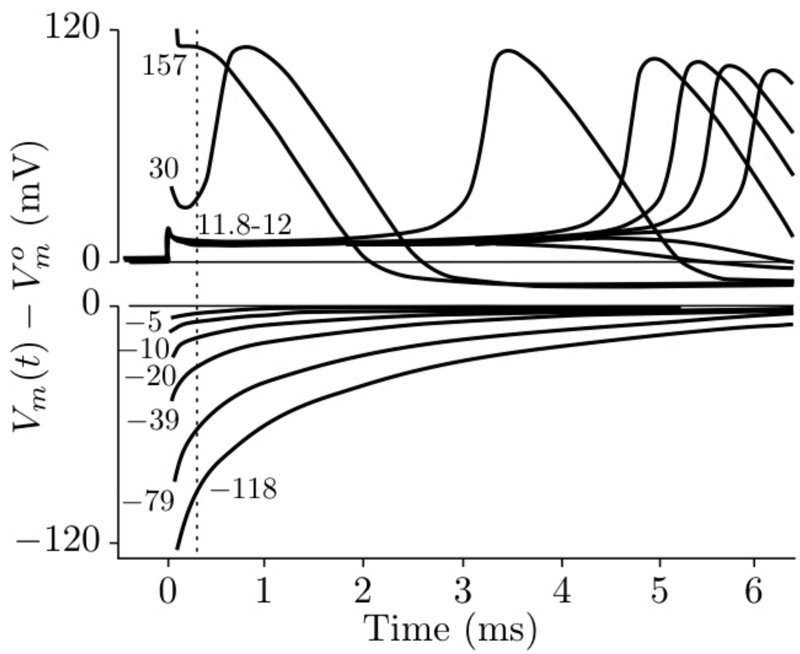


Figure 4.42

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

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

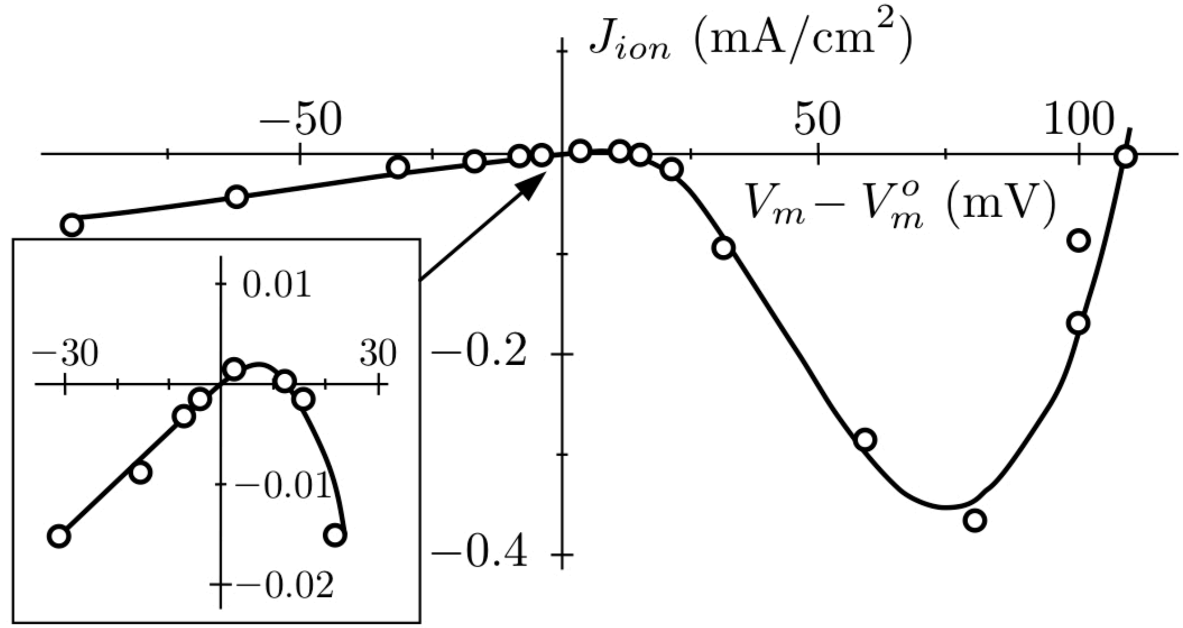


Figure 4.43

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

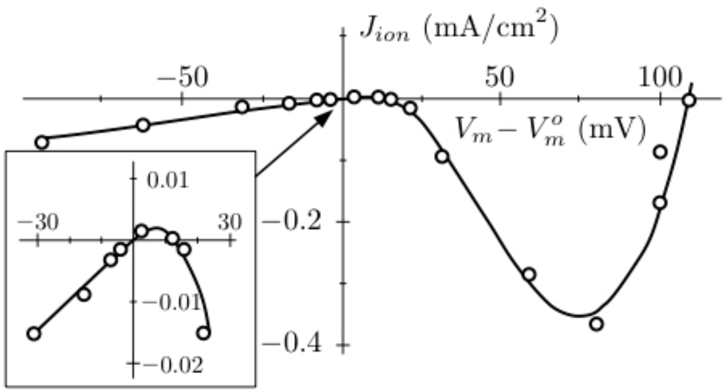
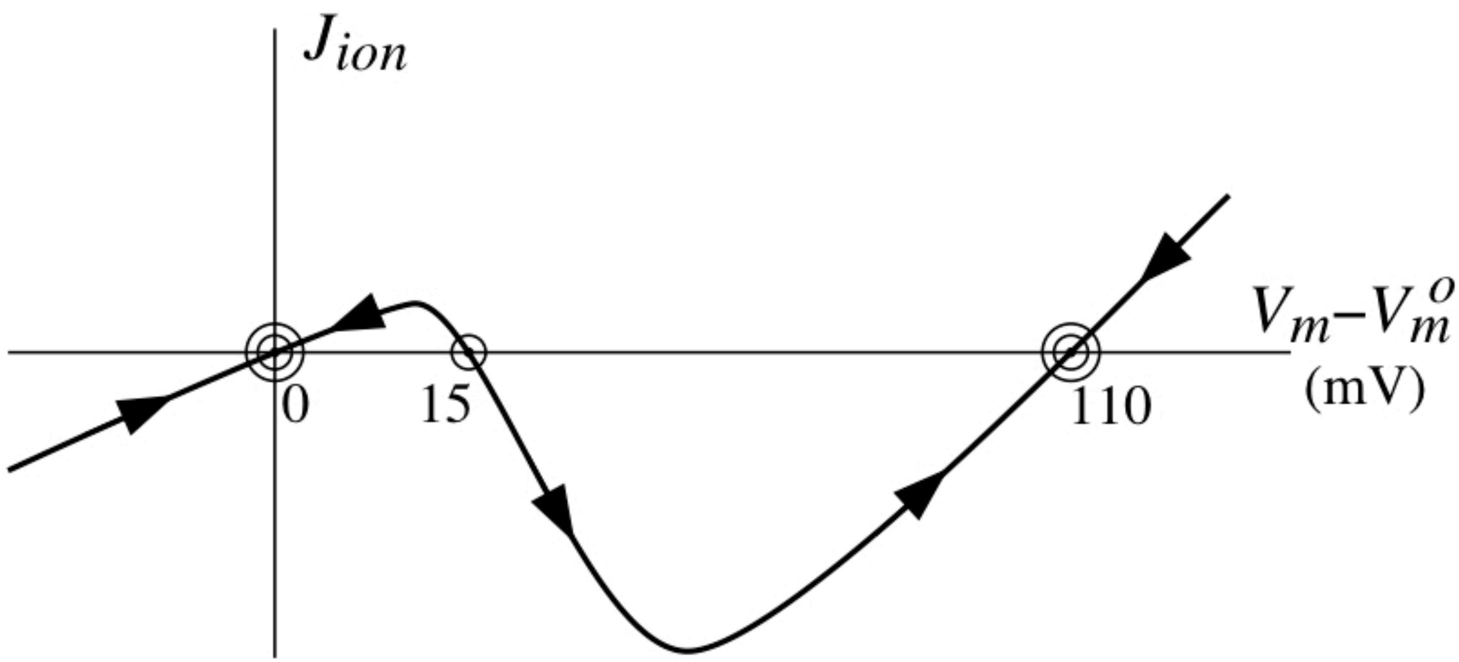


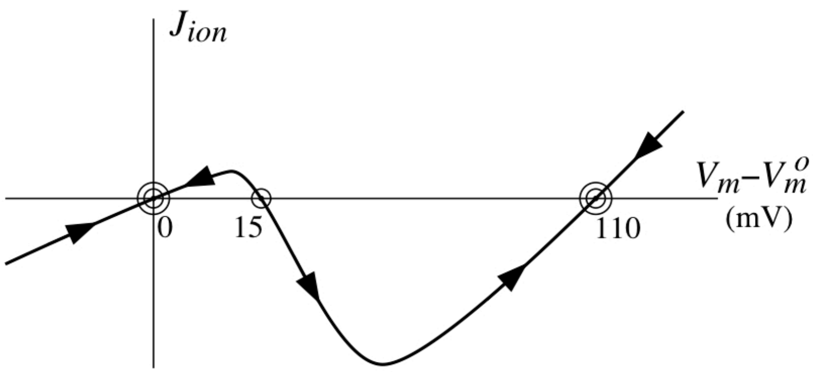
Figure 4.43

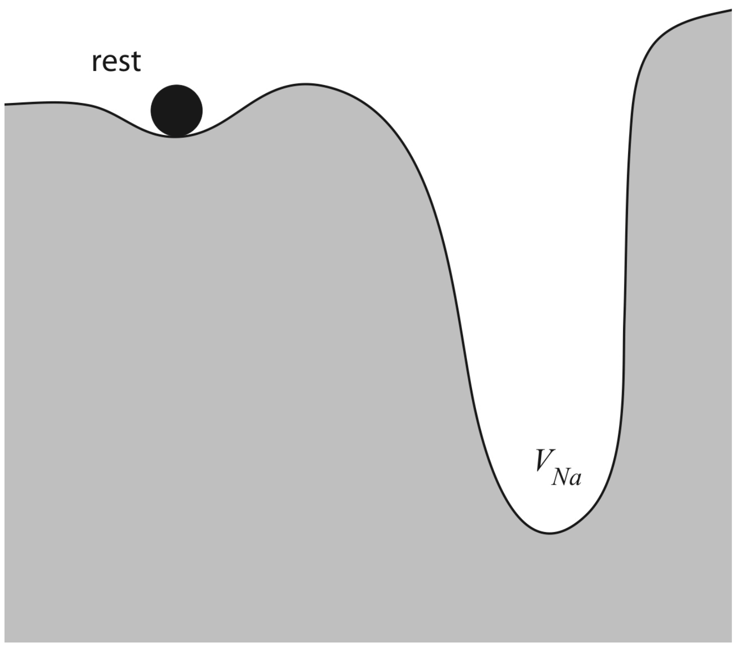
- Equilibrium points
- Stability

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

- Threshold
- Ohm's Law: Negative resistance?







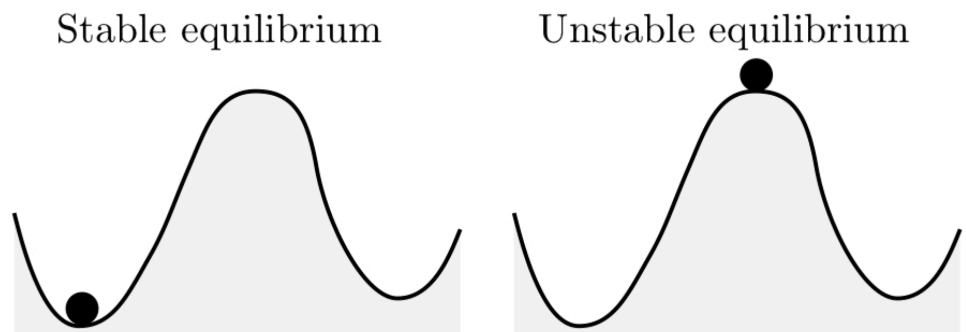


Figure 4.45

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

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

<u>Threshold</u>

assume n and h are constant

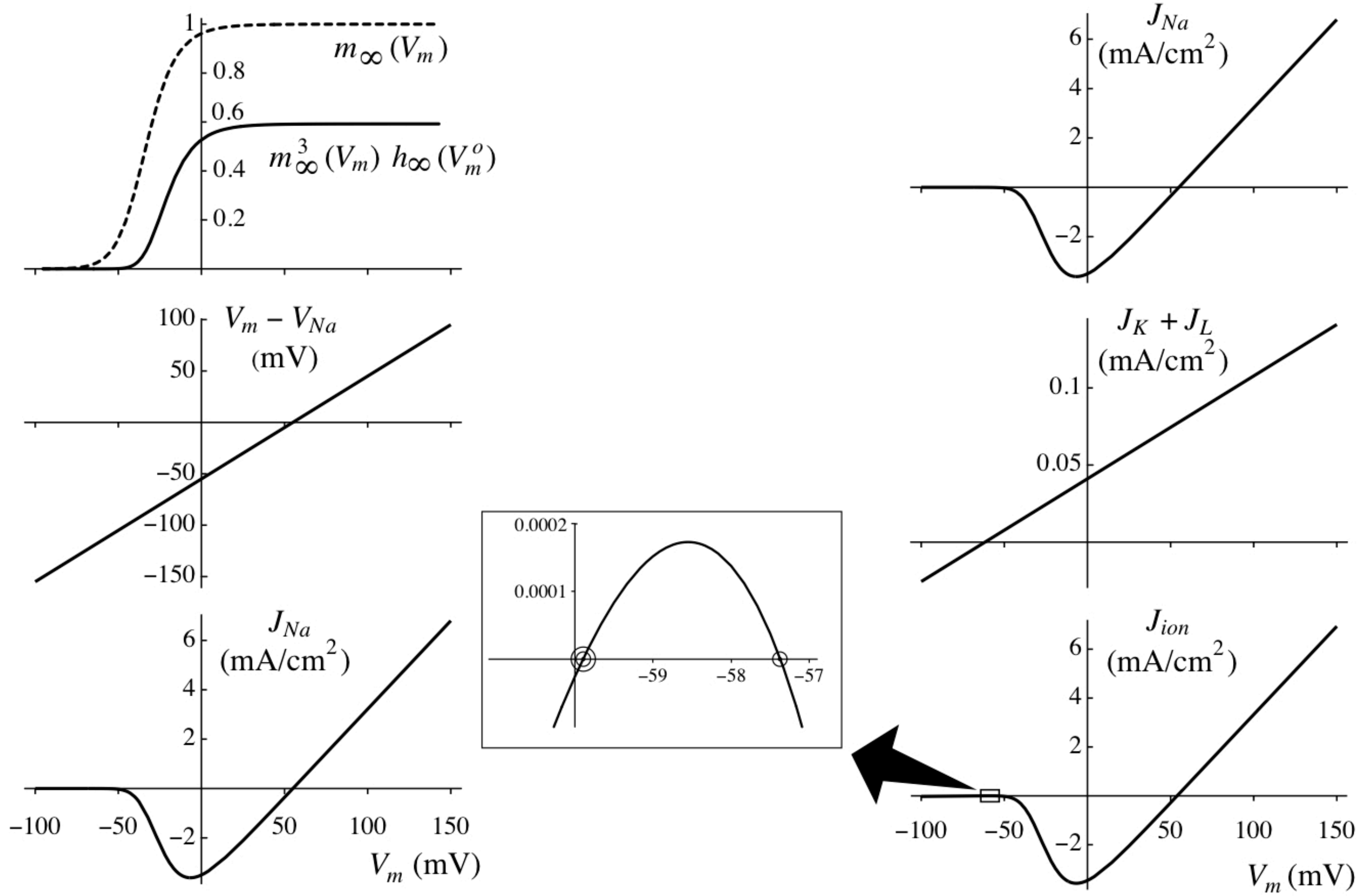
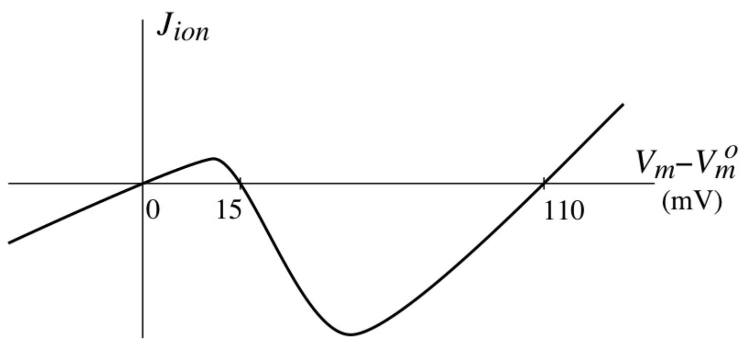
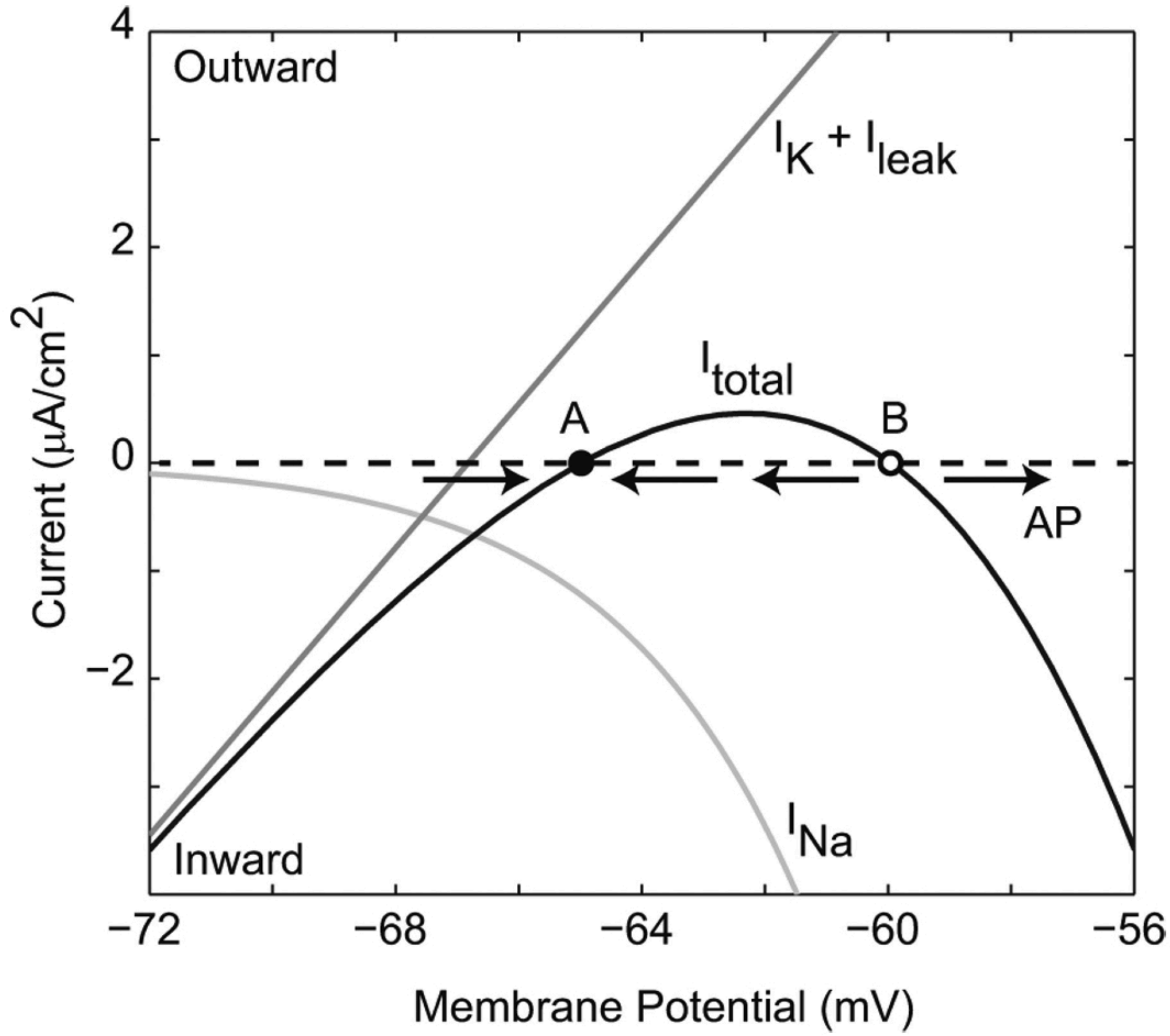


Figure 4.47



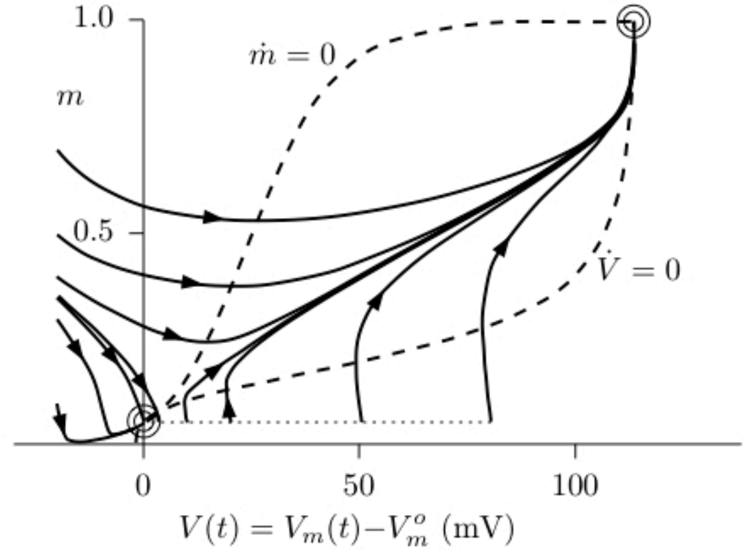
→ Ultimately more than one ion is needed

(Na⁺ alone is insufficient)



Catterall et al. (2012)

<u>Threshold</u>: Phase Plane Portrait



zoomed-in

assumes n and h are constant, but
m varies dynamically

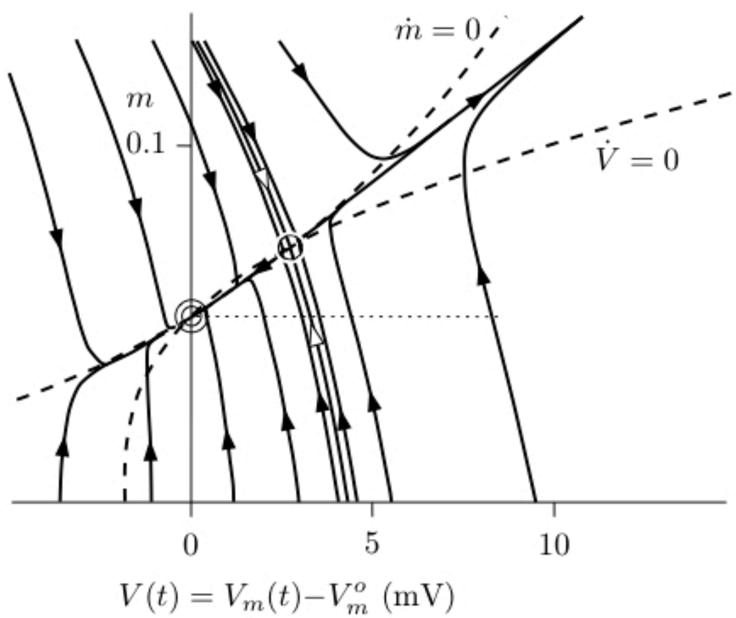


Figure 4.49

Refractory Period

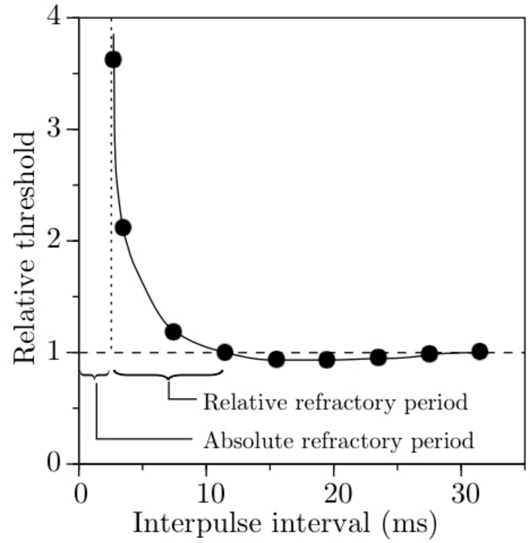


Figure 1.13

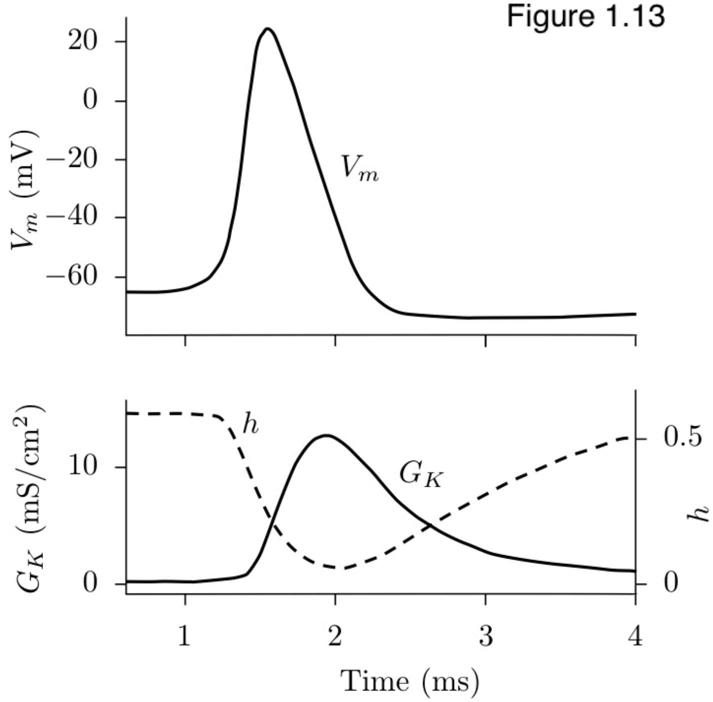


Figure 4.52

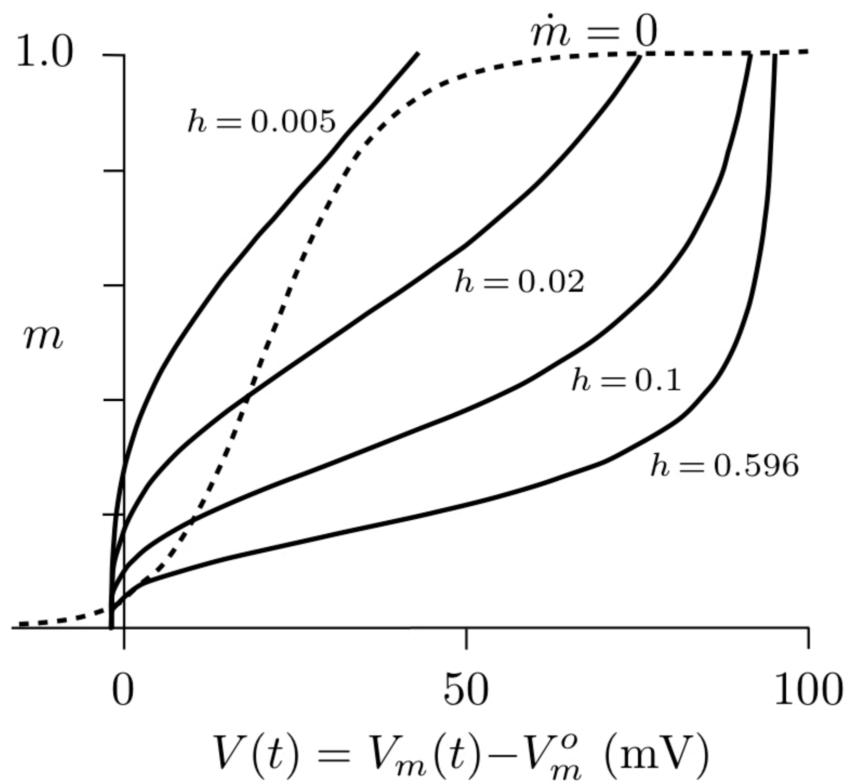


Figure 4.53