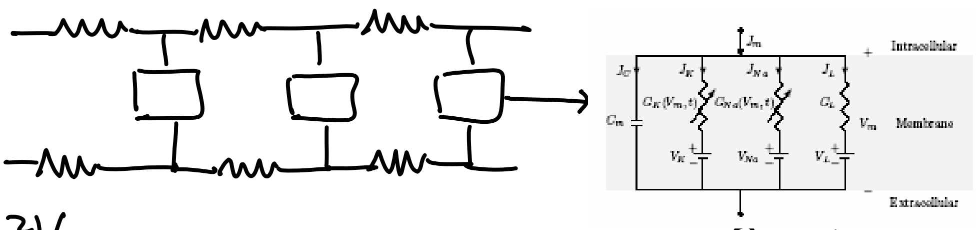
HH model = Core Conductor + nonlinear G_K / G_{Na}



$$\left.\begin{aligned} \frac{\partial^2 V_m}{\partial z^2} &= 2\pi a (r_o + r_i) J_m \\ J_m &= J_c + J_K + J_{Na} + J_L \end{aligned}\right\} \text{ eliminate } J_m$$

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

space clamp : prevent the propagation of AP
$V_m \neq f(z)$

current clamp : a space-clamped axon driven by a current
(can generate AP)
(V_m is changing → m.n.h coupled)

Voltage clamp : a space-clamped by a voltage
CANNOT generate AP
V_m is known → m.n.h decoupled

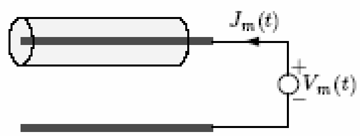


Figure 4.10

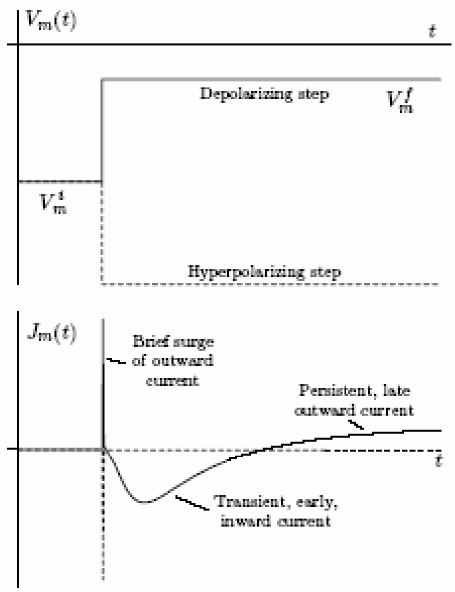


Figure 4.12

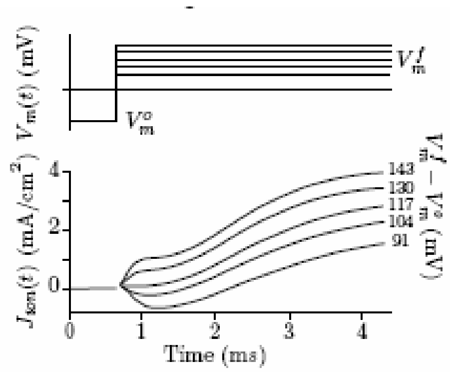


Figure 4.15

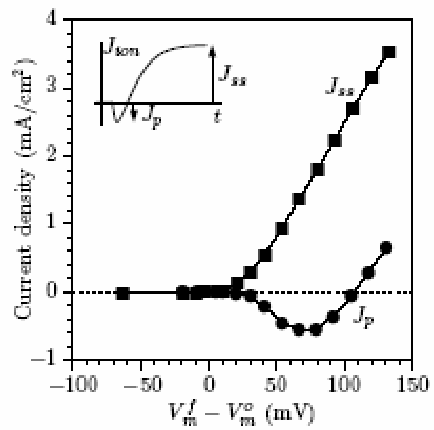


Figure 4.16

Which feature in Figure 4.12 is J_C?

Which feature in Figure 4.12 is J_{Na}?

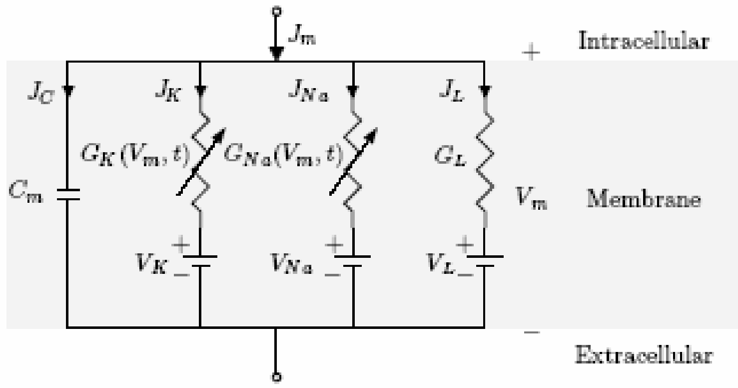
Which feature in Figure 4.12 is J_K?

How do we separate J_C from J_{ion}?

How do we separate J_{Na} from J_{ion}?

How do we separate J_k from J_{ion}?

Hodgkin Huxley model



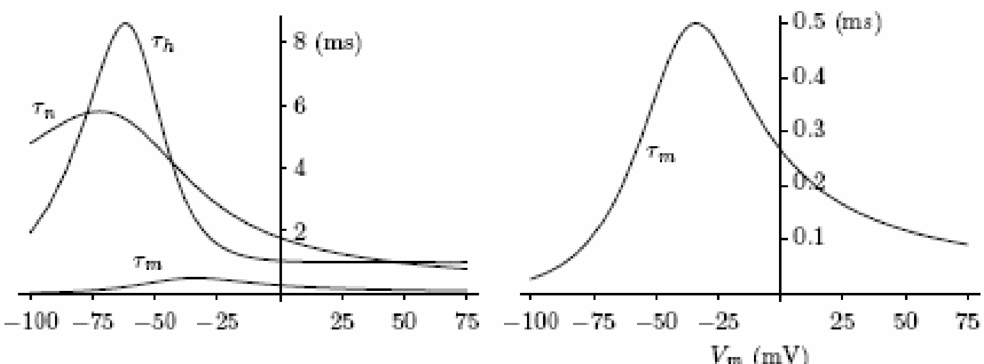
$$G_K(V_m,t) = \overline{G}_K n^4(V_m,t)$$

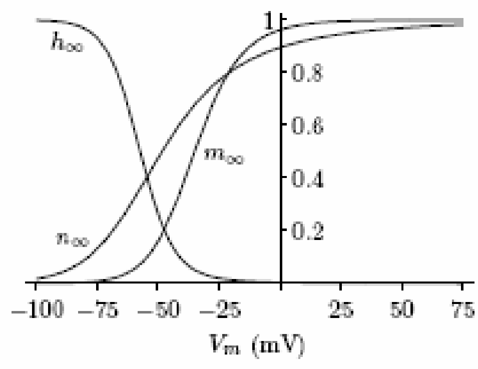
$$G_{Na}(V_m,t) = \overline{G}_{Na} m^3(V_m,t) h(V_m,t)$$

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

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

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





4 state variables
n, m, h, V_m
τ_x, x_∞: function of V_m only

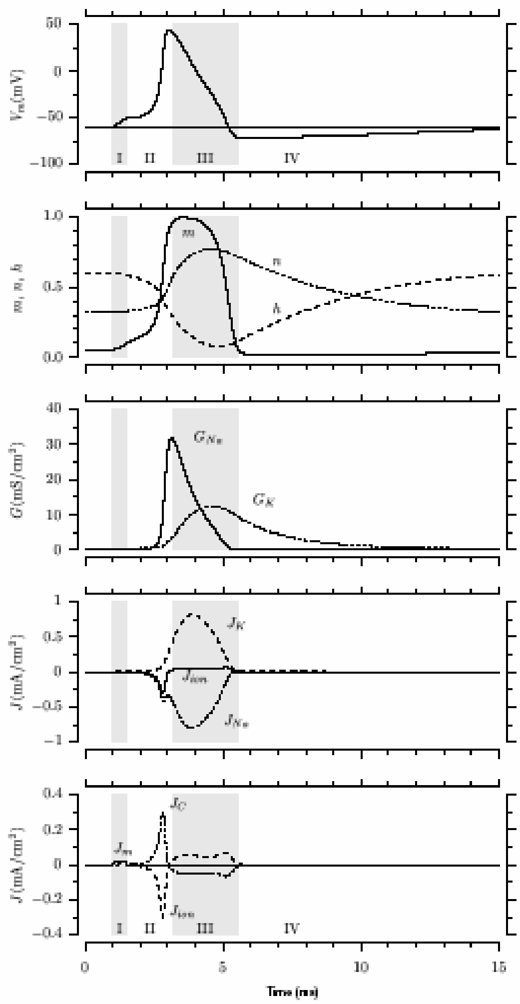
$\overline{G}_{Na} = 120$, $\overline{G}_K = 36$, and $G_L = 0.3$ mS/cm²; $C_m = 1$ μF/cm²; $c^o_{Na} = 491$, $c^i_{Na} = 50$, $c^o_K = 20.11$, $c^i_K = 400$ mmol/L; $V_L = -49$ mV; temperature is 6.3°C.

Membrane Action Potential (space clamped axon, current injected)

$$\text{space clamp}: \quad \frac{\partial V_m}{\partial z} = \frac{\partial^2 V_m}{\partial z^2} = 0$$

$$\therefore \; J_m = 0 = J_c + J_{ion}$$

$$= C_m \frac{\partial V_m}{\partial t} + J_K + J_{Na} + J_L$$



Phase I : stimulation by injection of current
Why does V_m go up here?

Phase II: positive feedback
Why does V_m go up here?

Why is J_{ion} inward here?

Phase III : negative feedback
Why does V_m goes down here?

Why is J_{ion} outward here?

Why does G_{Na} go down here?

Phase IV : Refractory
Why is it hard to stimulate another action potential here? (Why is it refractory?)

Propagated Action Potential (not space clamped, AP propagating in space)

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

wave equation : $\frac{\partial^2 V_m}{\partial z^2} = \frac{1}{\nu^2}\frac{\partial^2 V_m}{\partial t^2}$

$\Rightarrow$ Becomes 2nd order nonlinear D.E in t only

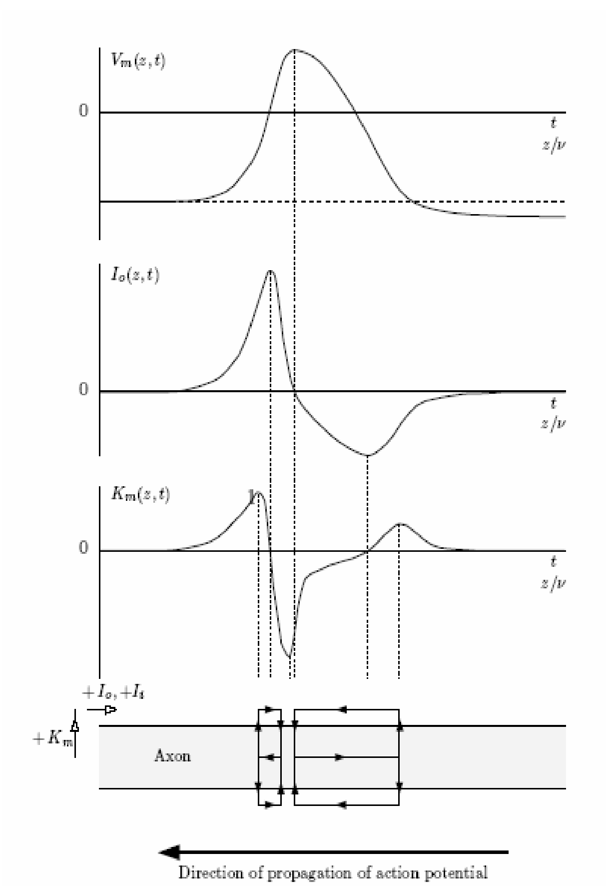


Figure 2.12

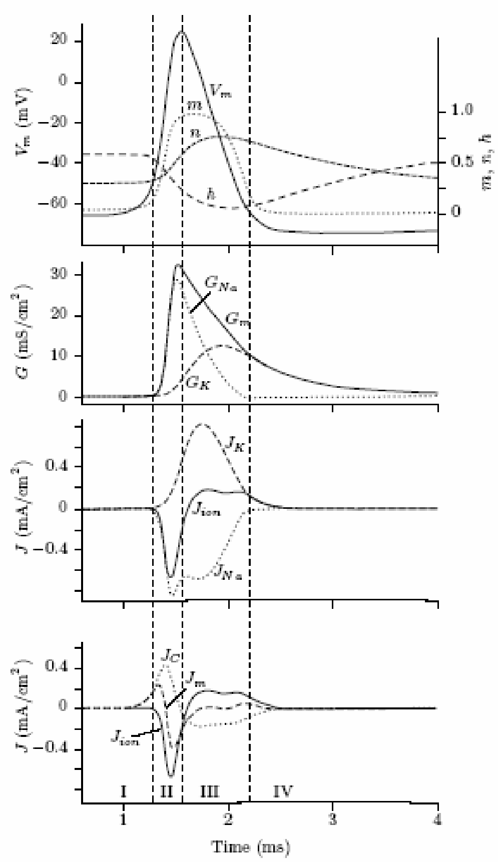


Figure 4.32

Why does J_m reverse the direction twice?

Problem 2. This problem deals with the Hodgkin-Huxley model under space-clamp conditions in response to a pulse of membrane potential (upper left panel in Figure 1). Figure 1 shows a

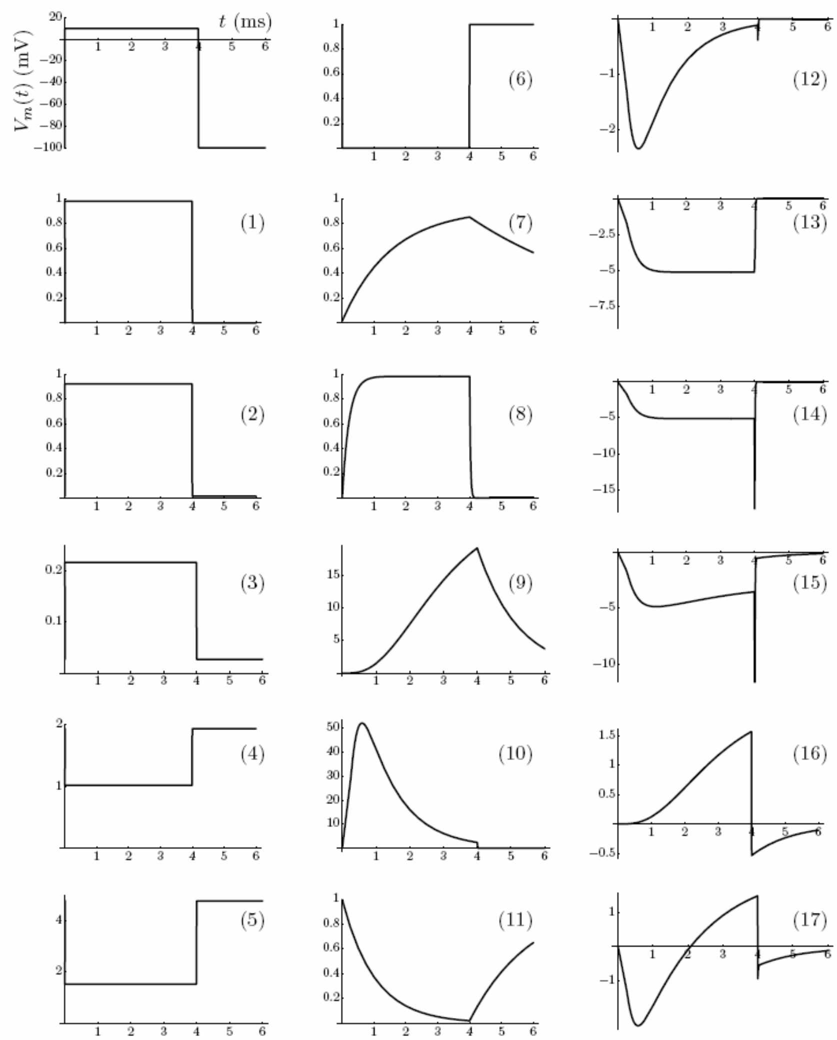


Figure 1: Waveforms purported to be responses to a pulse of membrane potential (upper left panel). The pulse consists of a depolarization of 110 mV lasting for 4 ms superimposed on a dc potential of -100 mV.

collection of waveforms purported to be responses of variables in the Hodgkin-Huxley model to the voltage pulse. The variable is not identified but the numerical values have the units: mS/cm^2 for conductance, mA/cm^2 for current, mV for potential, ms for time constants. The [in]activation factors are dimensionless.

For each of the following variables choose the appropriate waveform that represents its response to the voltage pulse and briefly justify your choice:

a) $m(V_m, t)$;

b) $m_\infty(V_m)$;

c) $\tau_m(V_m)$;

d) $G_K(V_m, t)$;

e) $G_{Na}(V_m, t)$;

f) $J_{Na}(V_m, t)$;

g) $J_K(V_m, t)$.

Answer

Problem 2.

a. **Ans. (8).** From Figure 4.25 in volume 2 of the text, $m_\infty(-100) \approx 0$, $m_\infty(10) \approx 1$, $\tau_m(-100) \approx 0.03$ ms, and $\tau_m(10) \approx 0.23$ ms. Therefore, at the onset of the pulse m rises exponentially from 0 to 1 with a time constant of about 0.23 ms. At the offset of the pulse m falls exponentially from 1 to 0 with a time constant of 0.03 ms.

b. **Ans. (1).** From the analysis in part a, m_∞ is a rectangular pulse that goes from 0 to 1 at the onset and from 1 to 0 at the offset.

c. **Ans. (3).** From the analysis in part a, τ_m is a rectangular pulse that goes from 0.03 to 0.23 ms at the onset and from 0.23 to 0.03 ms at the offset.

d. **Ans. (9).** From Figure 4.25 of volume 2 of the text, $n_\infty(-100) \approx 0$, $n_\infty(10) \approx 0.9$, $\tau_n(-100) \approx 5$ ms, and $\tau_n(10) \approx 1.7$ ms. Therefore, in 4 ms $n(4) \approx 0.9(1 - e^{-4/1.7}) = 0.81$, and $G_K(4) \approx 36(0.81)^4 \approx 16$ mS/cm^2. Therefore, the potassium conductance rises with an S-shaped onset to a value of about 16 mS/cm^2 with a time constant of the underlying factor n of 1.7 ms. Thus, the transient response will not be completed at the offset of the 4 ms pulse. After the offset, the conductance declines exponentially to ≈ 0 with a time constant that is about $5/4 = 1.25$ ms.

e. **Ans. (10).** From Figure 4.25 of volume 2 of the text, $h_\infty(-100) \approx 1$, $h_\infty(10) \approx 0$, $\tau_h(-100) \approx 2$ ms, and $\tau_h(10) \approx 1$ ms. Therefore, at the onset of the pulse h falls exponentially from 1 to 0 with a time constant of about 1 ms. At the offset of the pulse h rises exponentially from 0 to 1 with a time constant of 2 ms. Therefore, the sodium conductance has an S-shaped onset to a peak value of roughly $120(1)^3e^{-0.8/1} = 54$ mS/cm^2. The conductance then declines exponentially to approximately 0. At the offset, the conductance goes to zero with a time constant of $0.03/3 = 0.01$ ms.

f. **Ans. (12).** $J_{Na} = G_{Na}(V_m - V_{Na})$, i.e., the current is the product of the two terms. During the pulse $V_m - V_{Na} \approx 10 - 55 = -45$ mV. Thus, at the peak of the conductance, the current is $50 \times -45 = -2250$ μA/cm^2 which is -2.25 mA/cm^2. At the voltage offset there will be a discontinuity in the current.

g. **Ans. (16).** $J_K = G_K(V_m - V_K)$, i.e., the current is the product of the two terms. During the pulse $V_m - V_K \approx 10 + 70 = 80$ mV. Thus, at the peak of the conductance, the current is $18 \times 80 = 1440$ μA/cm^2 which is 1.44 mA/cm^2. At the voltage offset the direction of current flow will reverse.