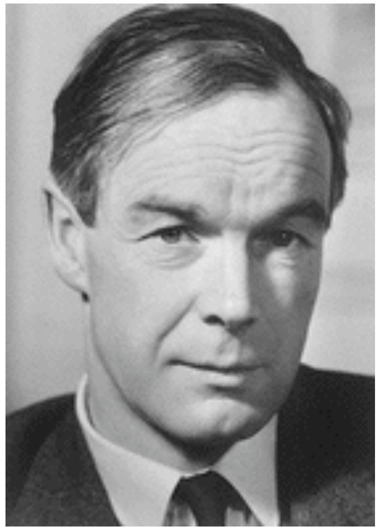
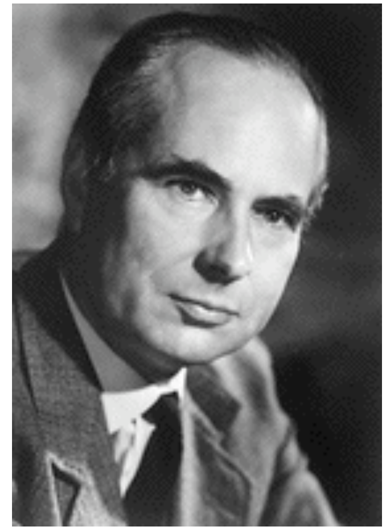
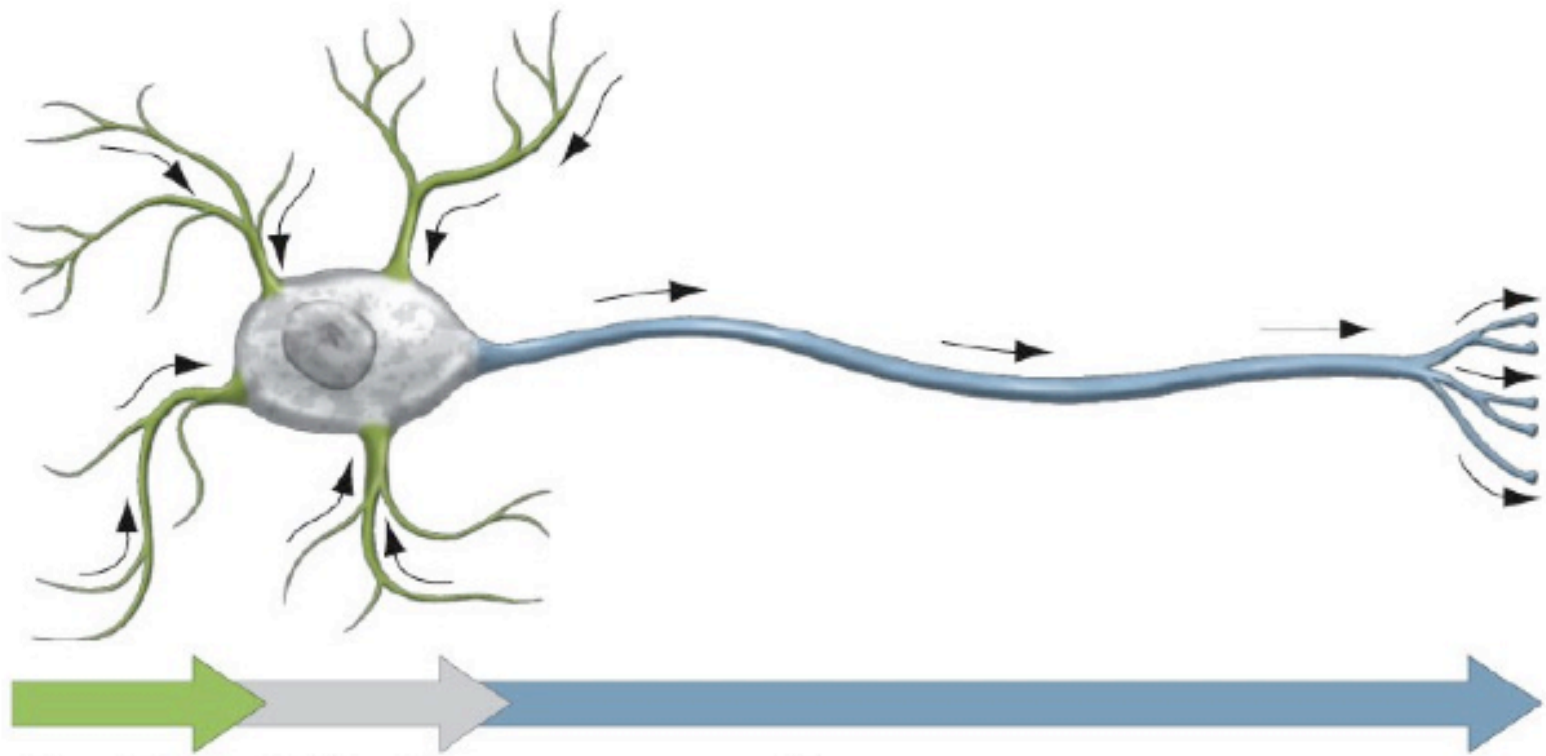




Hodgkin-Huxley Model of Action Potentials

Differential Equations
Math 210

Neuron

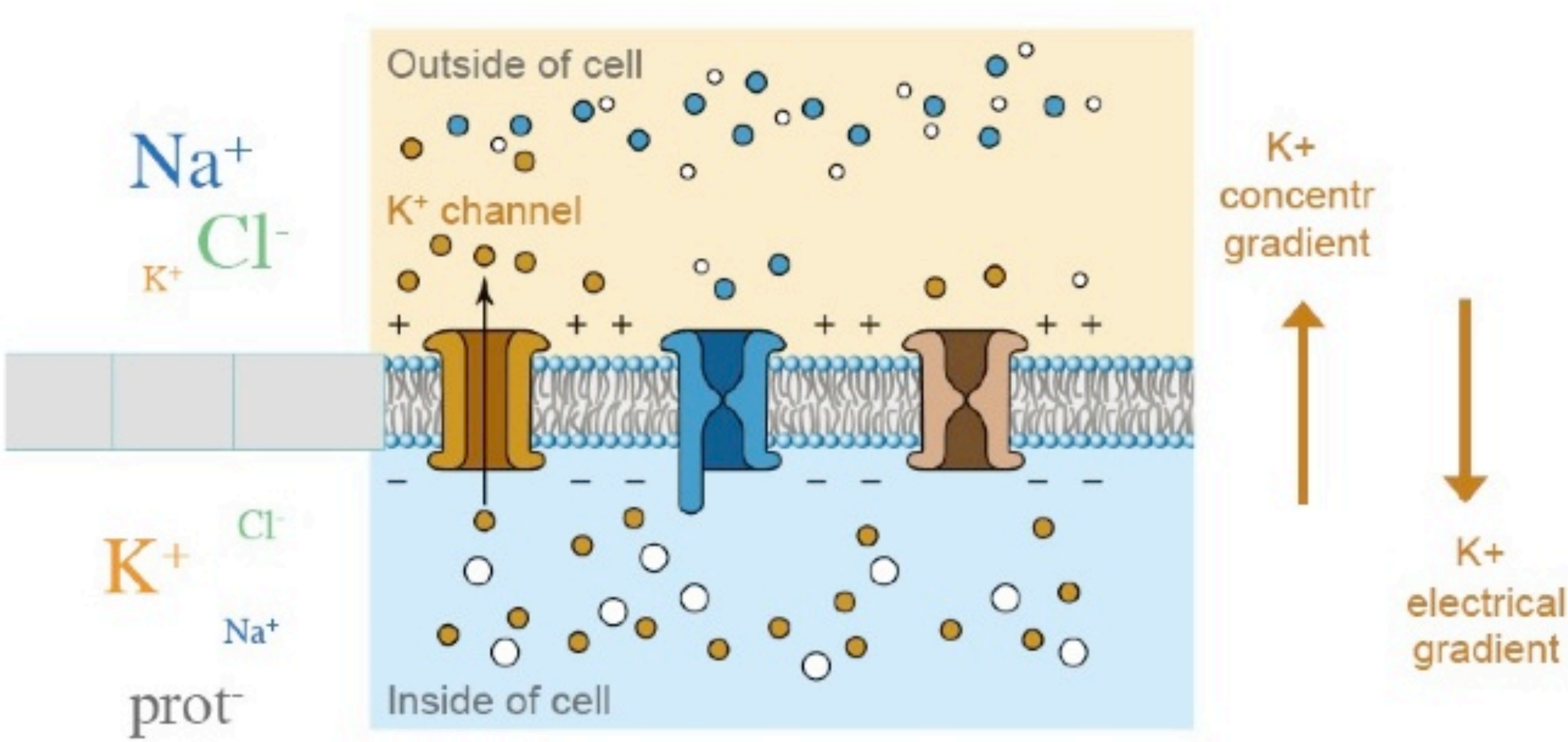


Dendrites
Collect electrical signals

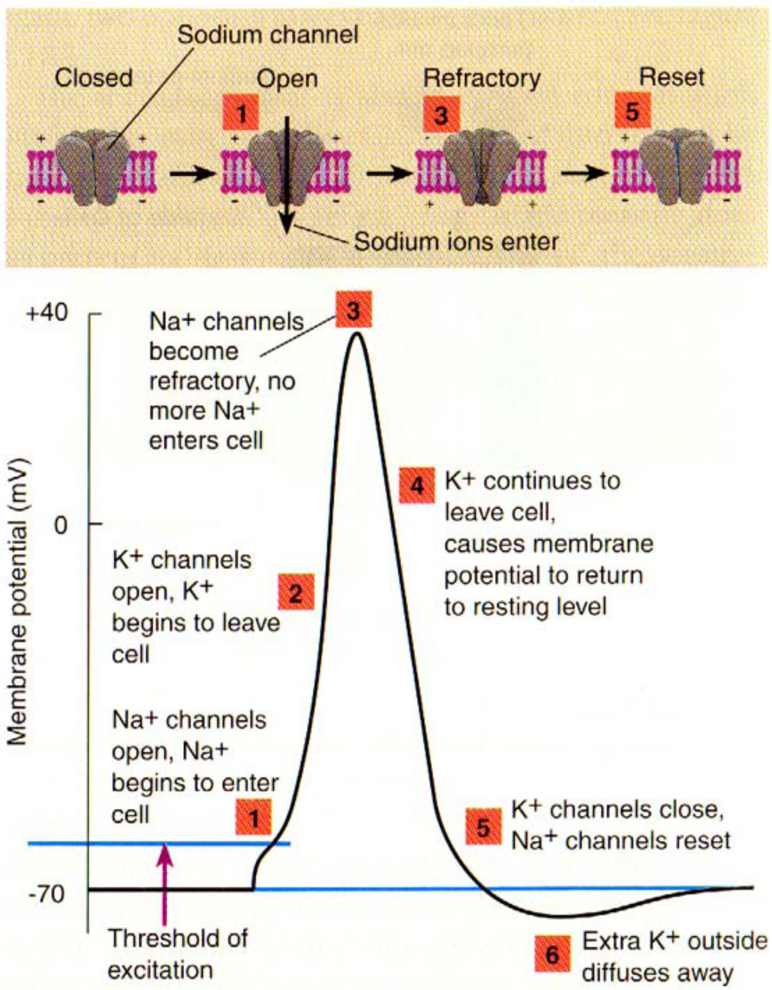
Cell body
Contains nucleus and organelles

Axon
Passes electrical signals on to dendrites of another cell or to an effector cell

Electrochemical Equilibrium



Action Potential

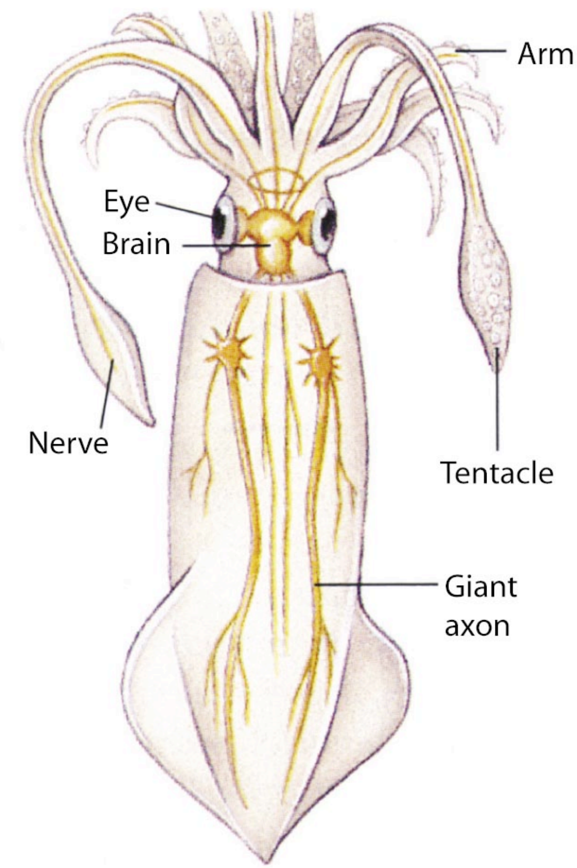


- Axon membrane potential difference

  $V = V_{in} - V_{out}$
- When the axon is excited, V spikes because sodium Na^+ and potassium K^+ ions flow through the membrane

Modeling the dynamics of an action potential

- Alan Lloyd Hodgkin and Andrew Huxley
  - Proposed model in 1952
  - Explains ionic mechanisms underlying the initiation and propagation of action potential in the squid giant axon
  - Received the 1963 Nobel Prize in Physiology or Medicine



Circuit model for axon membrane

$q(t)$ = the charge carried by particles in circuit at time t

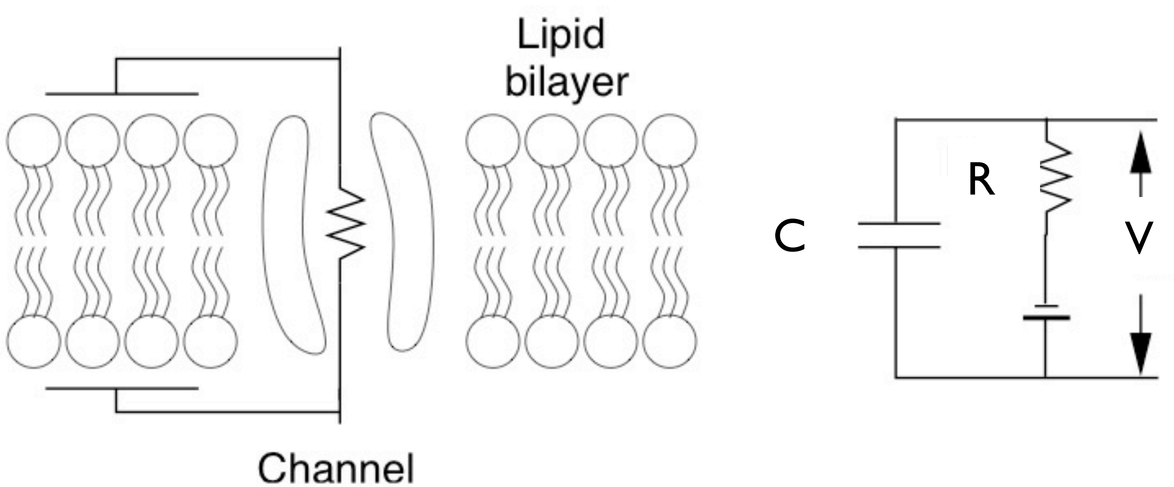
$I(t)$ = the current (rate of flow of charge in the circuit) = dq/dt

$V(t)$ = the voltage difference in the electrical potential at time t

R = resistance (property of a material that impedes flow of charge particles)

$g(V)$ = conductance = $1/R$

C = capacitance (property of an element that physically separates charge)



Conductors or resistors represent the ion channels.
Capacitors represent the ability of the membrane to store charge.

Physical relationships in a circuit

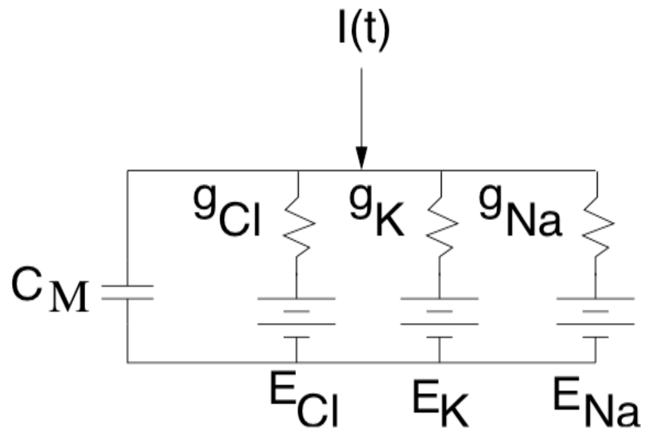
- *Ohm's law*: the voltage drop across a resistor is proportional to the current through the resistor; R (or 1/g) is the factor or proportionality

$$V(t) = I(t)R = \frac{I(t)}{g}$$

- *Faraday's law*: the voltage drop across a capacitor is proportional to the electric charge; 1/C is the factor of proportionality

$$V(t) = \frac{q(t)}{C}$$

Elements in parallel



- For elements in parallel, the total current is equal to the sum of currents in each branch; the voltage across each branch is then the same.

$$I(t) = I_1(t) + I_2(t) + I_3(t)$$

Differentiate Faraday's Law ($V(t) = \frac{q(t)}{C}$) leads to

$$\frac{dV}{dt} = \frac{1}{C}\frac{dq}{dt} = \frac{I(t)}{C} = \frac{1}{C}\left(I_1(t) + I_2(t) + I_3(t)\right)$$

Hodgkin-Huxley Model

$$\frac{dV}{dt} = -\frac{1}{C}\left(I_{Na}(t) + I_K(t) + I_L(t)\right)$$

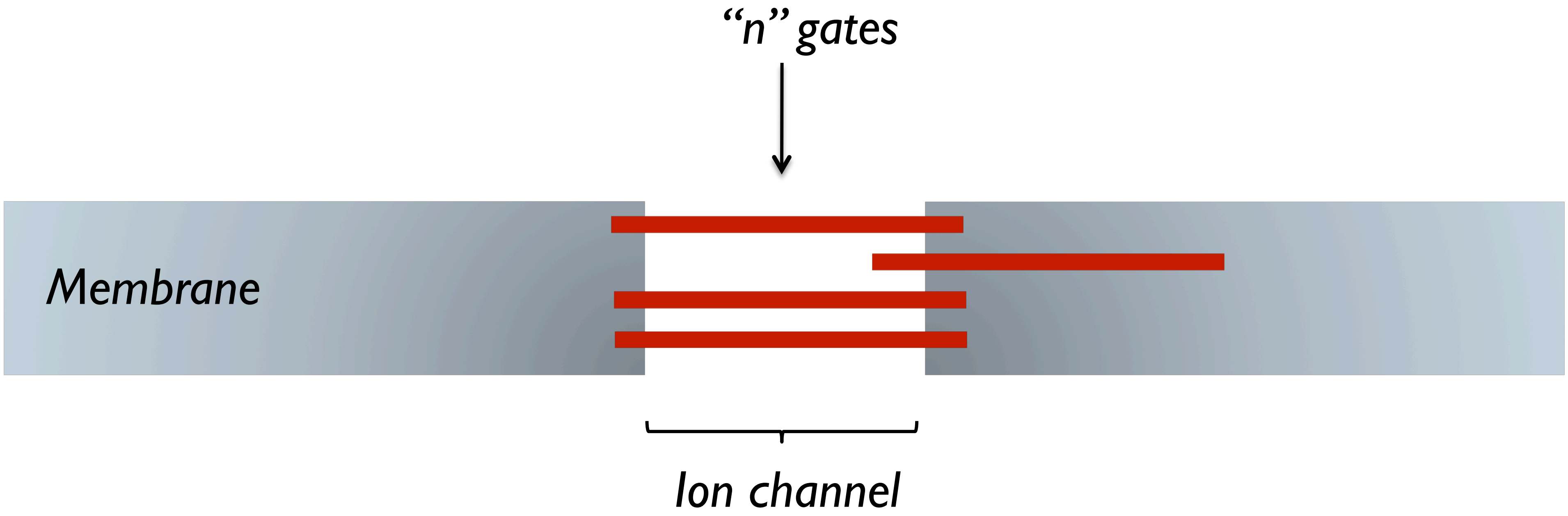
$$I_{Na} = g_{Na}\left(V - E_{Na}\right)$$

$$I_K = g_K\left(V - E_K\right)$$

$$I_L = g_L\left(V - E_L\right)$$

- g_L is constant
- g_{Na} and g_K are voltage-dependent

Ion channel gates



Voltage dependency of gate position

$$n \;\underset{\beta_n}{\overset{\alpha_n}{\rightleftharpoons}}\; \cancel{n - 1}\ \ 1 - n$$

n (proportion in the ~~open~~ shut state)

$\cancel{n - 1}$ $1 - n$ (proportion in the open state)

α_n, β_n are *transition rate constants* (voltage-dependent)

α_n = the # of times per second that a gate which is in the shut state opens

β_n = the # of times per second that a gate which is in the open state shuts

Fraction of gates opening per second = $\alpha_n(1 - n)$

Fraction of gates shutting per second = $\beta_n n$

The rate at which n changes: $\dfrac{dn}{dt} = \alpha_n(1 - n) - \beta_n n$

Equilibrium: $n_\infty = \dfrac{\alpha_n}{\alpha_n + \beta_n}$

What is the behavior of *n?*

Gating variable

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n, \qquad n(0) = n_0$$

- Solve initial value problem by separation of variables:

$$n(t) = \frac{\alpha_n}{\alpha_n + \beta_n} - \left(\frac{\alpha_n}{\alpha_n + \beta_n} - n_0 \right) e^{-(\alpha_n + \beta_n)t}$$

$$= n_\infty - (n_\infty - n_0)e^{-t/\tau}, \qquad \text{where } \tau_n = \frac{1}{\alpha_n + \beta_n}$$

time constant

- If α_n or β_n is large $\rightarrow$ time constant is short $\rightarrow$ n approaches n_∞ rapidly
- If α_n or β_n is small $\rightarrow$ time constant is long $\rightarrow$ n approaches n_∞ slowly

Gating Variables

- K^+ channel is controlled by 4 n activation gates:

$$\frac{dn}{dt} = \frac{1}{\tau_n}(n_\infty - n) \quad \Rightarrow \quad g_K = n^4 \overline{g_K}$$

maximum K^+ conductance

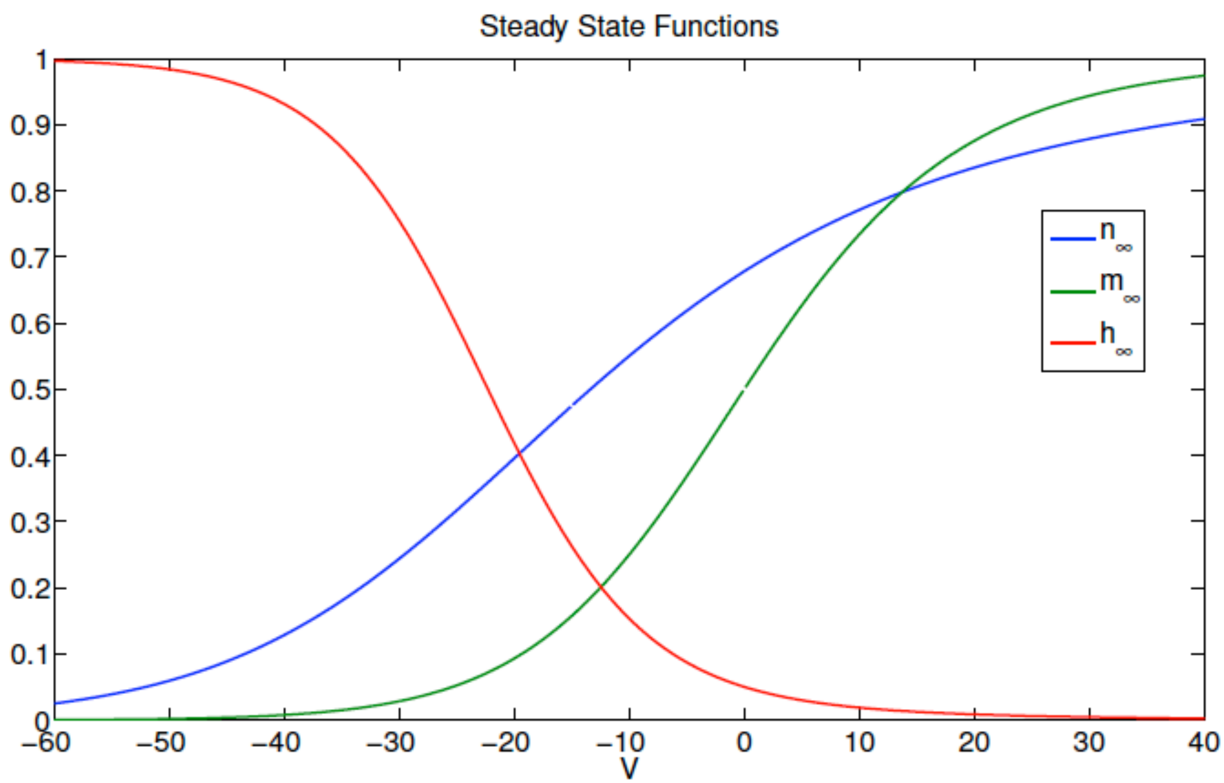
- Na^+ channel is controlled by 3 m activation gates and 1 h inactivation gate:

$$\frac{dm}{dt} = \frac{1}{\tau_m}(m_\infty - m)$$

$$\frac{dh}{dt} = \frac{1}{\tau_h}(h_\infty - h)$$

- Activation gate: open probability increases with depolarization
- Inactivation gate: open probability decreases with depolarization

Steady state values



Time constants