Hodgkin-Huxley Model

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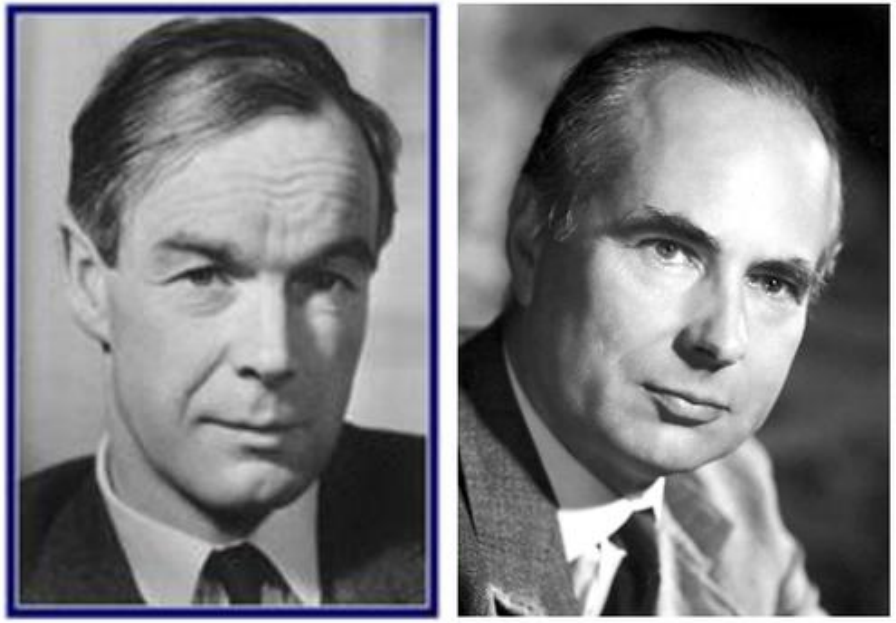
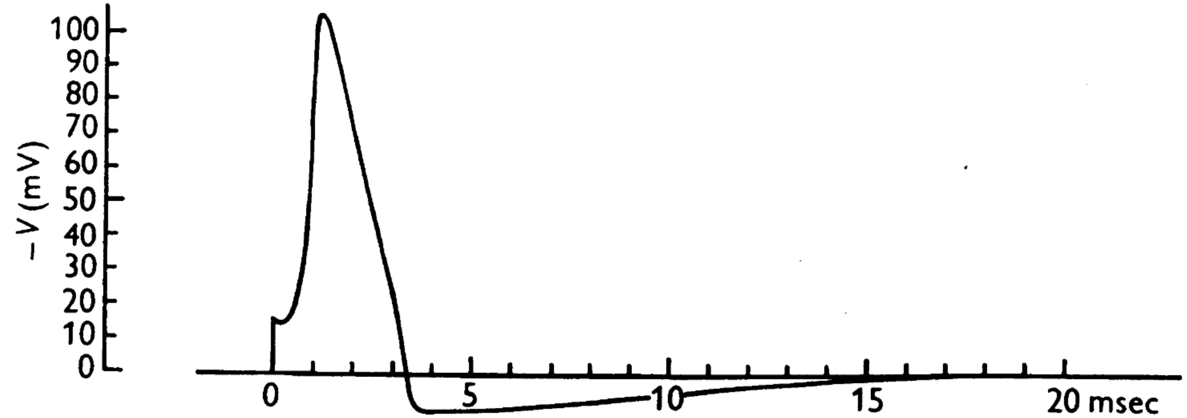
Hodgkin and Huxley

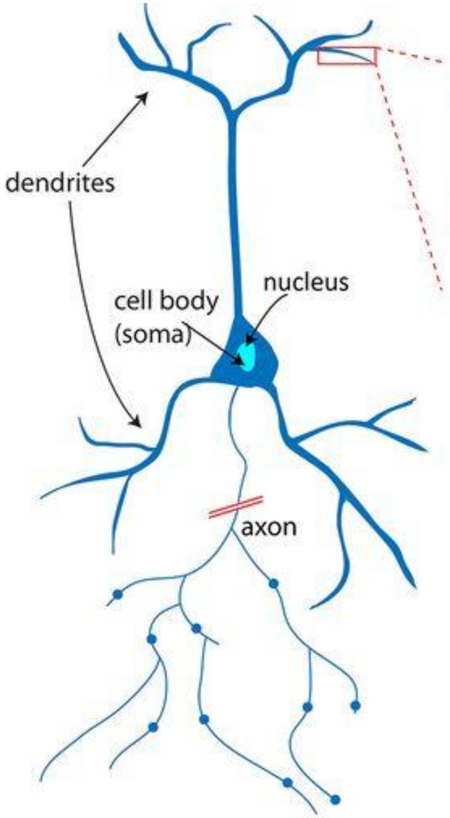


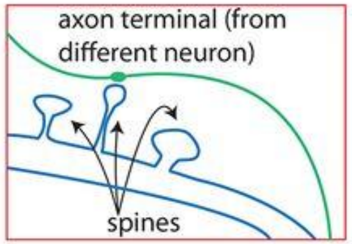
- University of Cambridge
- Published model in 1952
- Set of four coupled ODEs
- Describes the dynamics of the membrane potential of a neuron and the flow of ions across the cell membrane
- Models the action potential

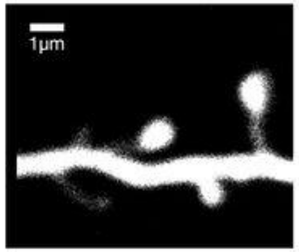


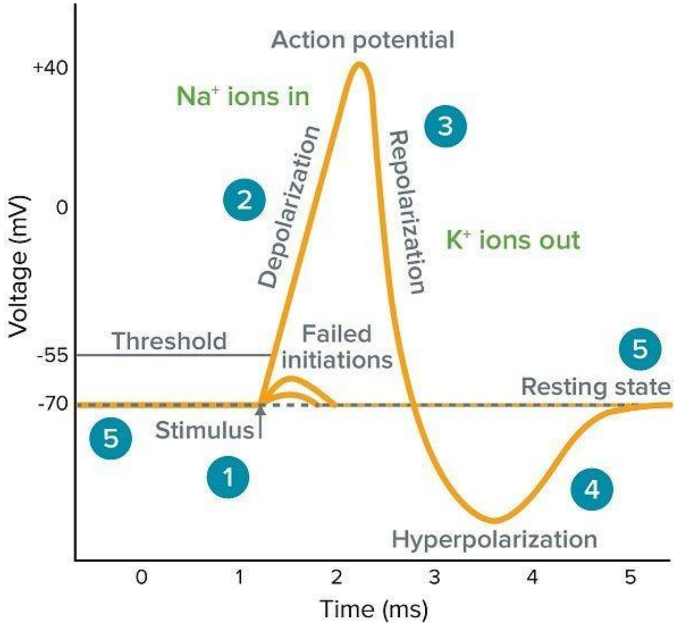
Neurons

- An excitable cell of the nervous system
- ‘Start’ at dendrites
- ‘End’ at axon terminals
- Signal is received from other neurons at the dendrites
- If input signal is larger than the firing threshold, the neuron will fire its own signal down its axon.

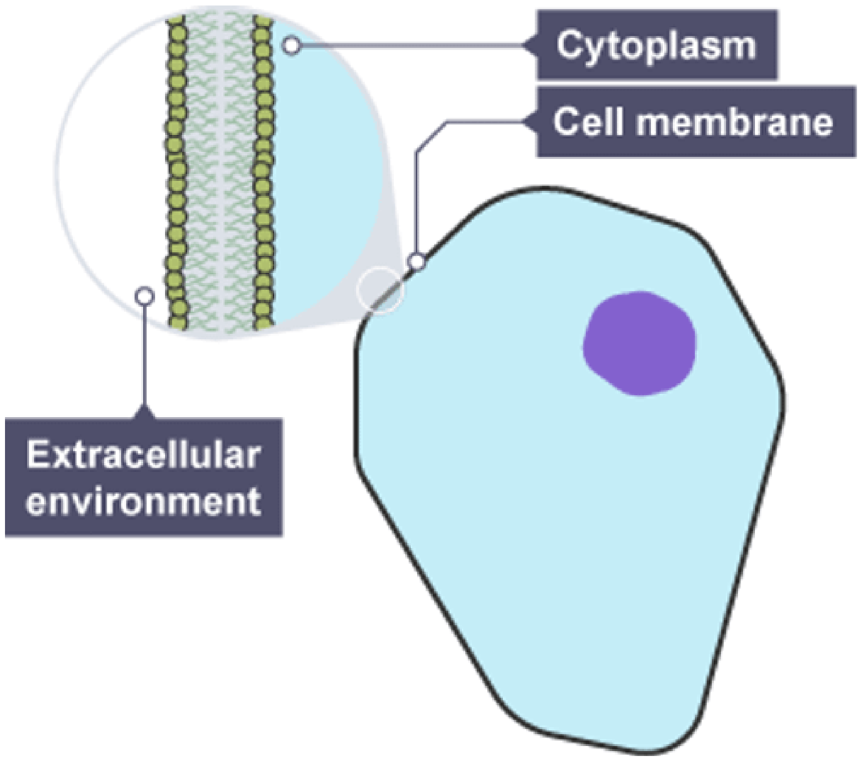


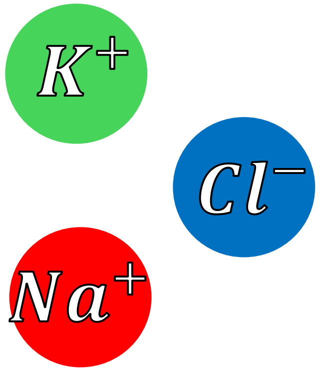


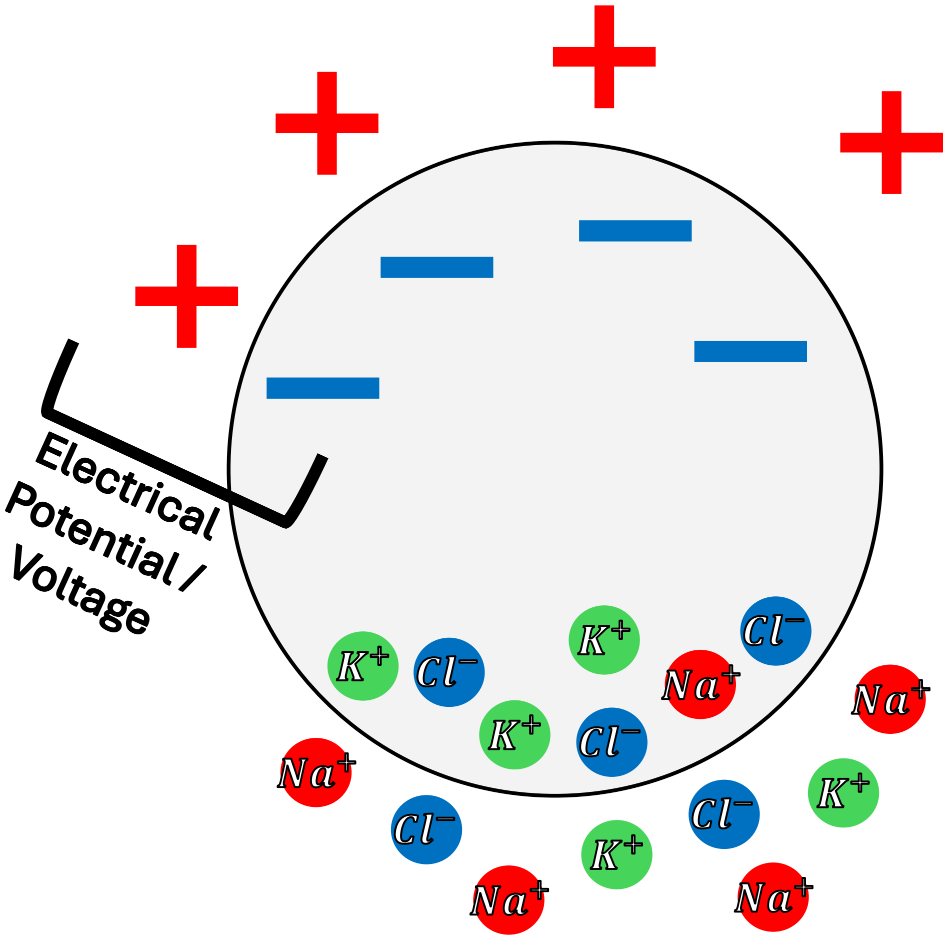




Cell membrane







Capacitance

The ability to store electric charge is called **capacitance.**

$$Q = CV$$

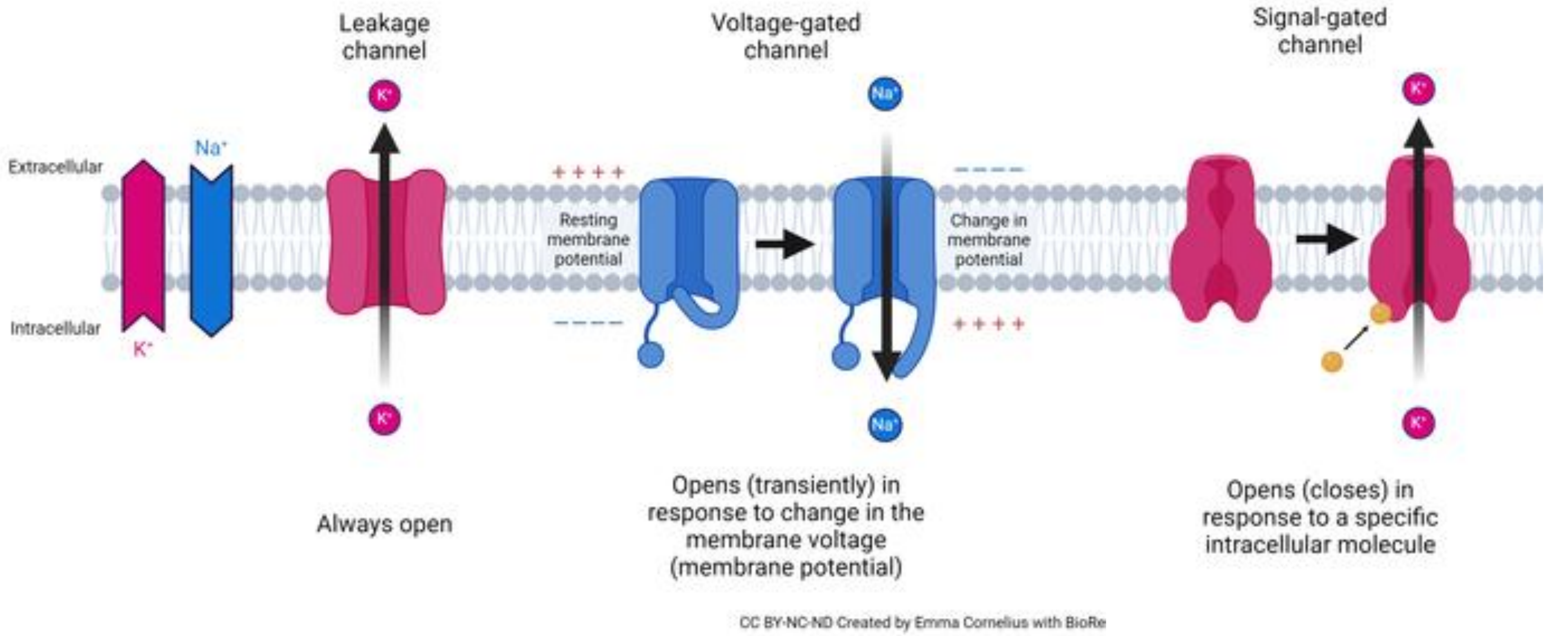
Q is the charge difference

C is capacitance (const)

V is voltage

Time derivative: describes how the voltages changes as charges redistribute across the membrane:

$$\frac{\partial Q}{\partial t} = C\frac{\partial V}{\partial t}$$



Membranes are semi-permeable:

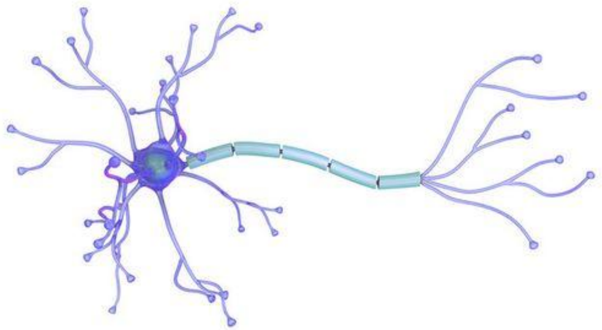
- Sodium and potassium gates that control the flow of ions in and out of the cell

Leak term

$$\frac{\partial Q}{\partial t} = C\frac{\partial V}{\partial t} \quad \rightarrow \quad C\frac{\partial V}{\partial t} = \sum I_{ion} \quad \rightarrow \quad C\frac{\partial V}{\partial t} = I_k + I_{Na} + I_L$$

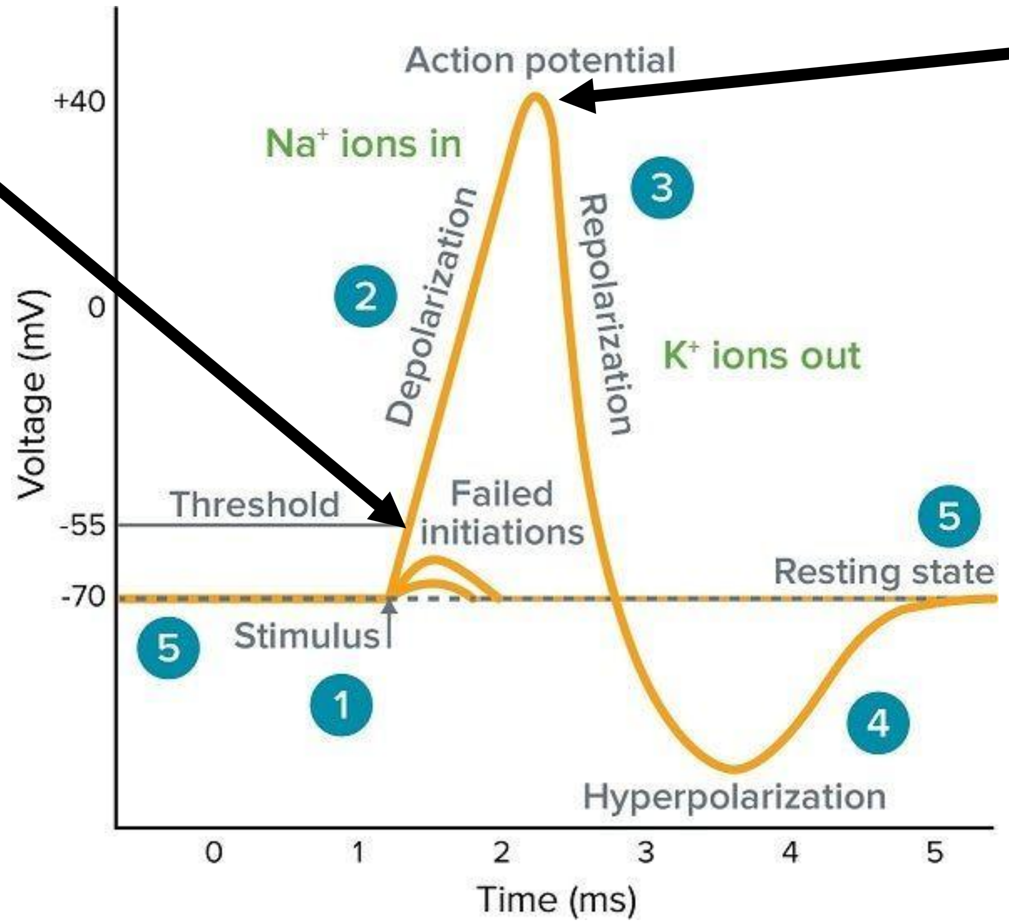
Link between membrane voltage and the ionic currents flowing through ion channels

Action potential



- Brief pulse of increased membrane voltage

Na+ channels open, letting **more + charge into the cell** and increase the voltage

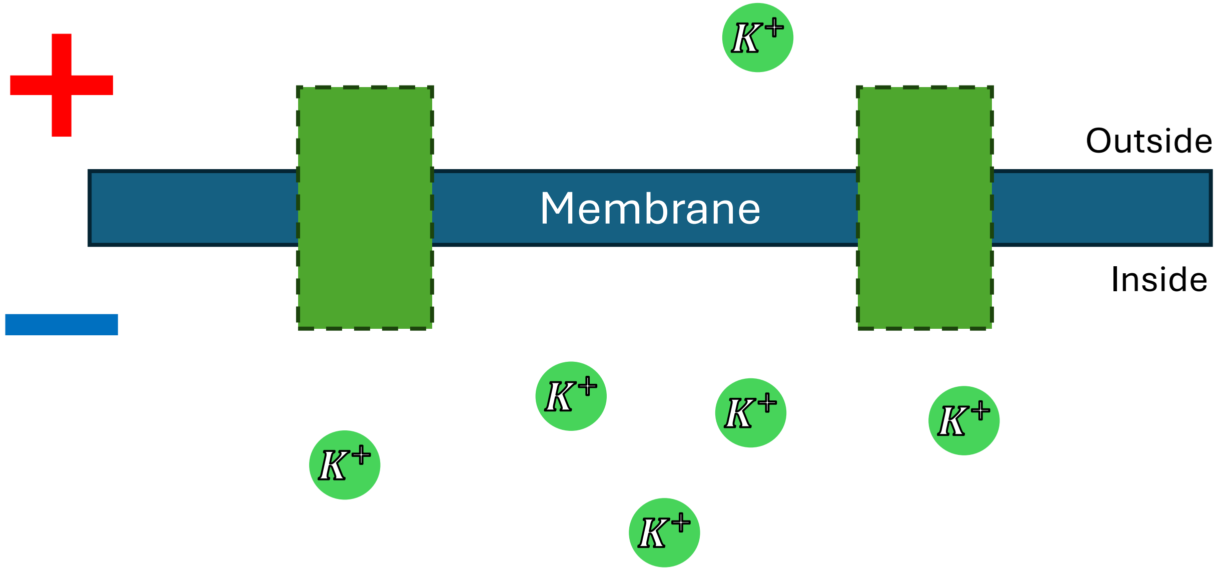


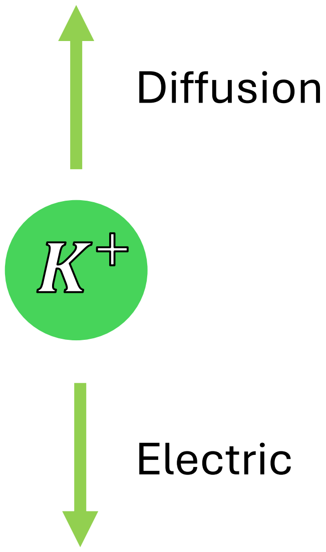
Na+ channels close. K+ channels open, which **+ charge leaves the cell,** decreasing the voltage

How is this all coordinated?

Rate of Ion Flow

- Depends on two factors:
  1. How many channels are open
  2. Driving force
     1. Diffusion
     2. Electrical force





These are competing forces. **Equilibrium potential** of potassium, $\boldsymbol{E_k}$, is the voltage when the two forces are exactly balanced. The current can be modeled as:

$$I_k = \underbrace{g_k}_{\substack{\text{Conductance} \\ \text{(open channels)}}} \underbrace{(E_k - V)}_{\text{Driving force}}$$

Ion channels

- Voltage dependent
  - Conductance term g_{ion} is a function of voltage, $g_{ion}(V)$

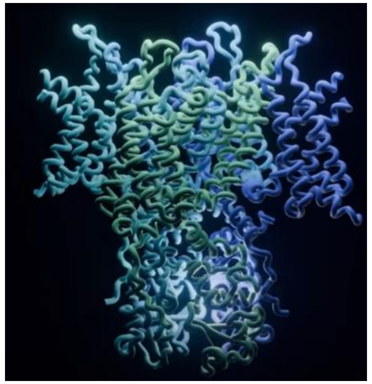
$$I_{ion} = g_{ion}(V)(E_{ion} \ - V)$$

$$g_{ion}(V) = \bar{g}p$$

With $\bar{g}$ being maximal conductance (all channels are open) and p being a probability of a channel being open

$$p = \frac{open}{open + closed}$$

Ion channels



- Potassium Channels: Four gates
  - If all four gates are in a ‘permissive state’, then the channel is open
  - Let n be the probability of a single gate (of the four) being permissive,
    α be the rate of gates moving to a permissible state, and
    β be the rate of gates moving to a non-permissive state :

$$\frac{dn}{dt} = \alpha(1-n) - \beta n$$

The functions of α and β were discovered experimentally and fit from empirical data:

$$\alpha_n(V) = \frac{0.01(V+55)}{1-exp(-0.1(V+55)}$$

$$\beta_n(V) = 0.125exp(-0.0125(\mathrm{V+65}))$$

The probability of the entire channel being permissible is n^4, and the current is now:

$$I_K = \bar{g}n^4(E_K \; - V)$$

Final ODE's

Recall:

- $\frac{\partial Q}{\partial t} = C\,\frac{\partial V}{\partial t} \quad \rightarrow \quad C\,\frac{\partial V}{\partial t} = \sum I_{ion} \quad \rightarrow \quad C\,\frac{\partial V}{\partial t} = I_k + I_{Na} + I_L$

And we have:

- $I_K = \overline{g_K} n^4 (E_K \ - V) \qquad I_{Na} = \overline{g_{Na}} m^3 h (E_{Na} \ - V) \qquad I_L = \overline{g_L}\,(E_L \ - V)$
- $\frac{dn}{dt} = \alpha(1-n) - \beta n \qquad \frac{dm}{dt} = \alpha(1-m) - \beta m \qquad \frac{dh}{dt} = \alpha(1-h) - \beta h$

Final ODE's

$$C\frac{\partial V}{\partial t} = I_{ext} + \left(\overline{g_K}n^4(E_K - V) + \overline{g_{Na}}m^3h(E_{Na} - V) + \overline{g_L}\,(E_L - V)\right),$$

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

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m,$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h,$$

For state variables $\begin{bmatrix} \mathrm{V} \\ n \\ m \\ h \end{bmatrix}$

With constants:

$$\overline{g_{Na}} = 120_{ms/cm^2}$$

$$\overline{g_K} = 36_{ms/cm^2}$$

$$\overline{g_L} = 0.3_{ms/cm^2}$$

$$E_{Na} = 50_{mV}$$

$$E_K = -77_{mV}$$

$$E_L = -54.387_{mV}$$

And equations:

$$\alpha_n(V) = \frac{0.01(V+55)}{1-e^{-0.1(V+55)}}$$

$$\beta_n(V) = 0.125e^{-0.0125(V+65)}$$

$$\alpha_m(V) = \frac{0.1(V+40)}{1-e^{-0.1(V+40)}}$$

$$\beta_m(V) = 4e^{-0.0556(V+65)}$$

$$\alpha_h(V) = 0.07e^{-0.05(V+65)}$$

$$\beta_h(V) = \frac{1}{1+e^{-0.1(V+35)}}$$