

COMS30127: Computational Neuroscience

The Hodgkin-Huxley model

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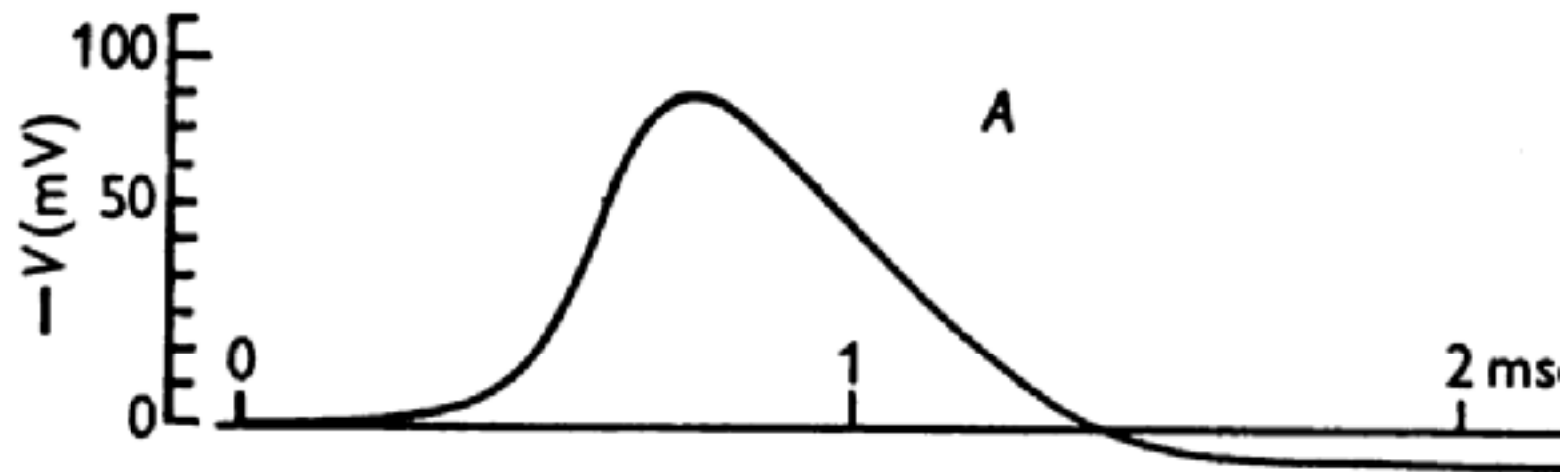
Questions you may have that we will answer today

- “What is the Hodgkin-Huxley model and why do I need to know about it?”
- “Who were Hodgkin and Huxley?”
- “What does the model consist of?”
- “What does it do?”
- “What does it *not* do?”

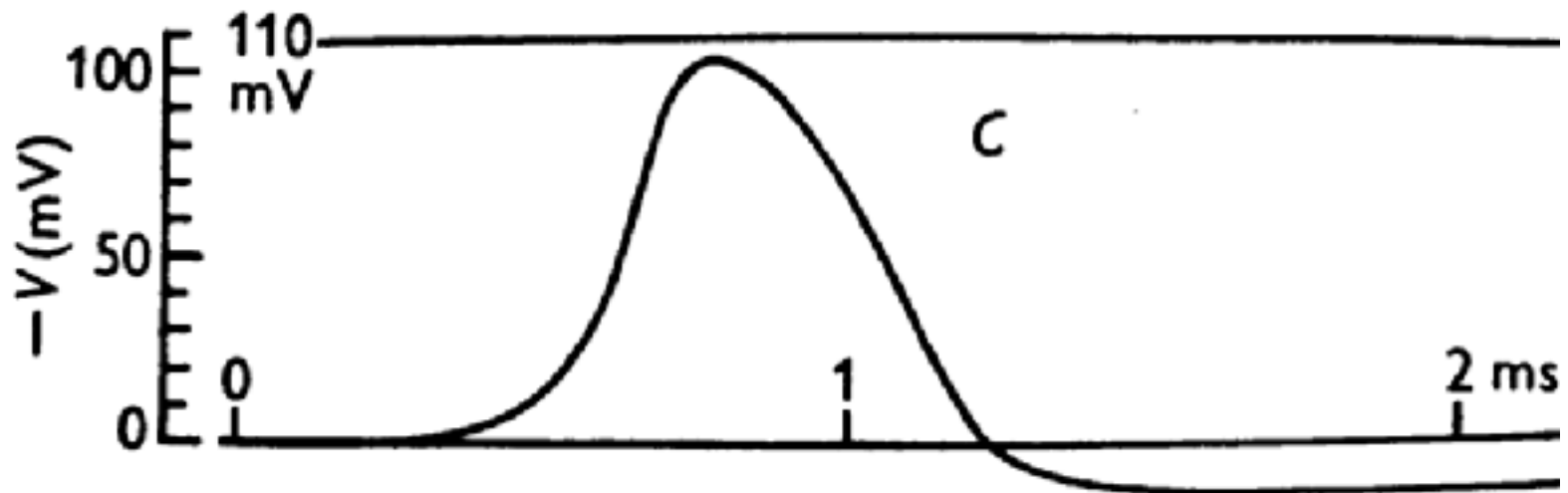
What is the Hodgkin-Huxley model?

- The original Hodgkin-Huxley model is a mathematical model of the electrical dynamics of the 'giant' axon of the squid *Loligo forbesi*.
- Its key success was to demonstrate that **two voltage-gated membrane conductances** were sufficient to explain the **action potential**.
- These days people often use the term "Hodgkin-Huxley style model" more loosely to mean any mathematical model of any neuron that is built using **conductance-based** dynamics.
- The Hodgkin-Huxley model stands as one of the outstanding successes of computational neuroscience.

Model



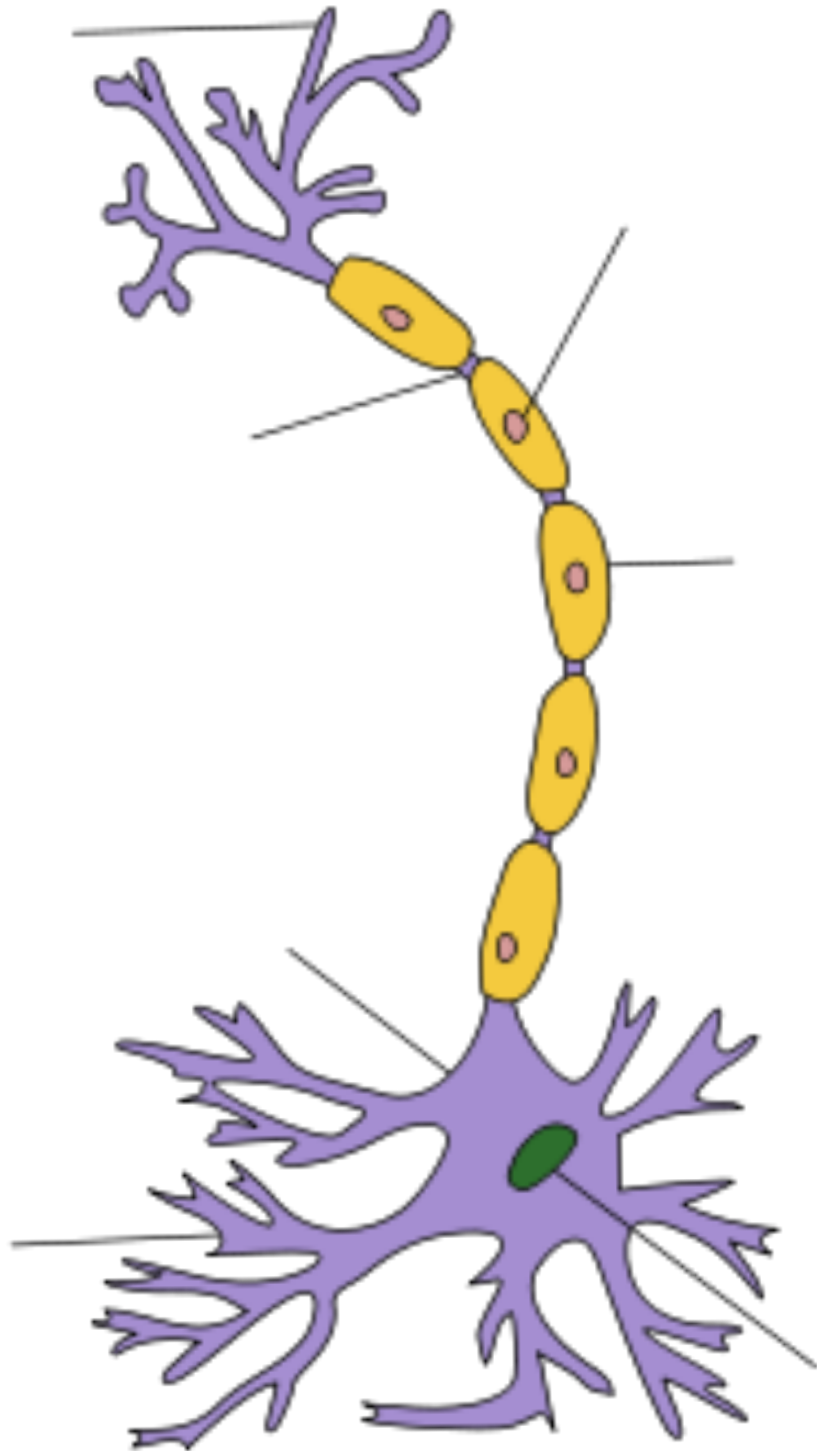
Data



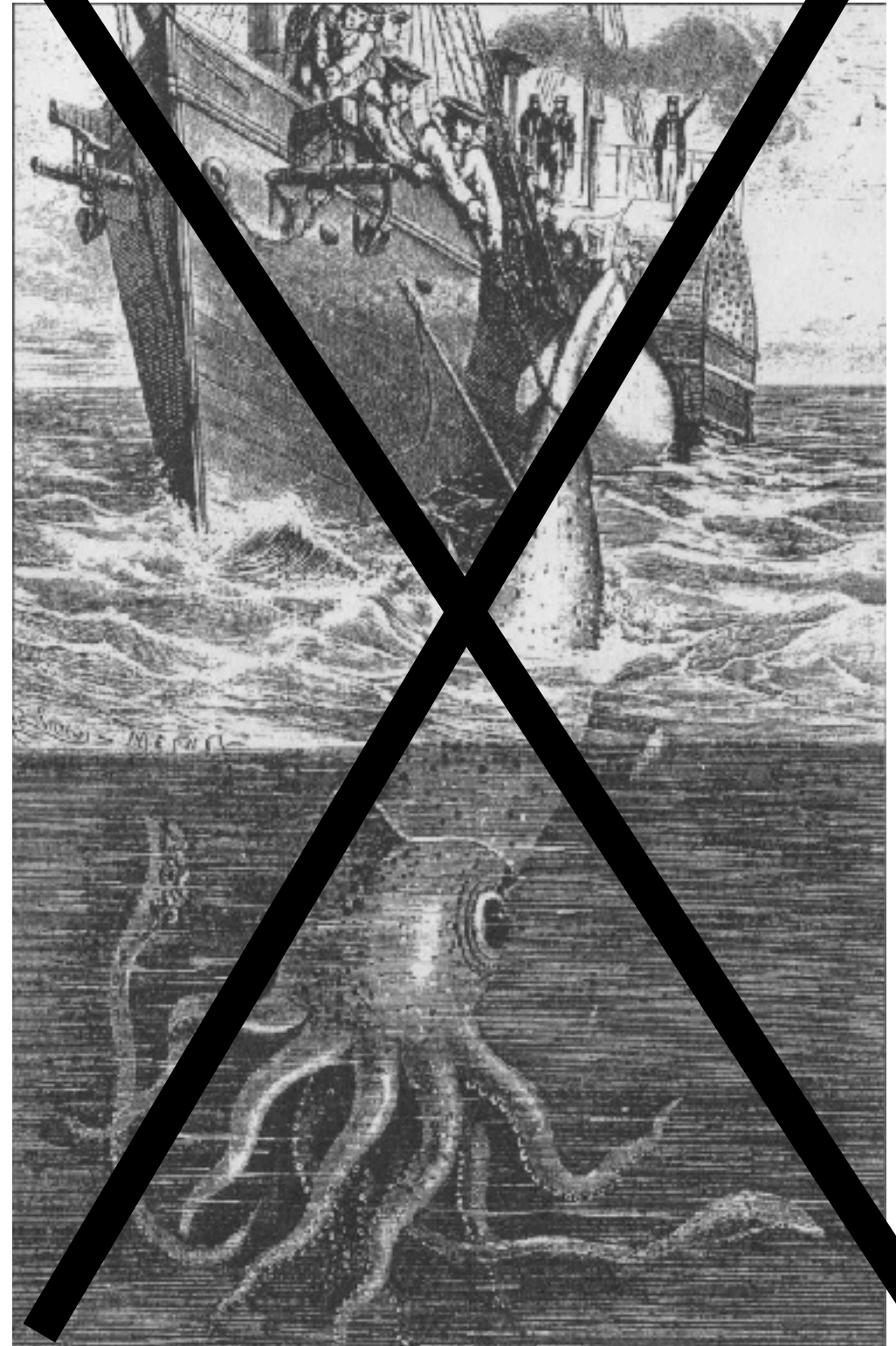
Loligo forbessi



(Squid) giant axon



~~Giant squid (axon)~~



Who were Hodgkin and Huxley?

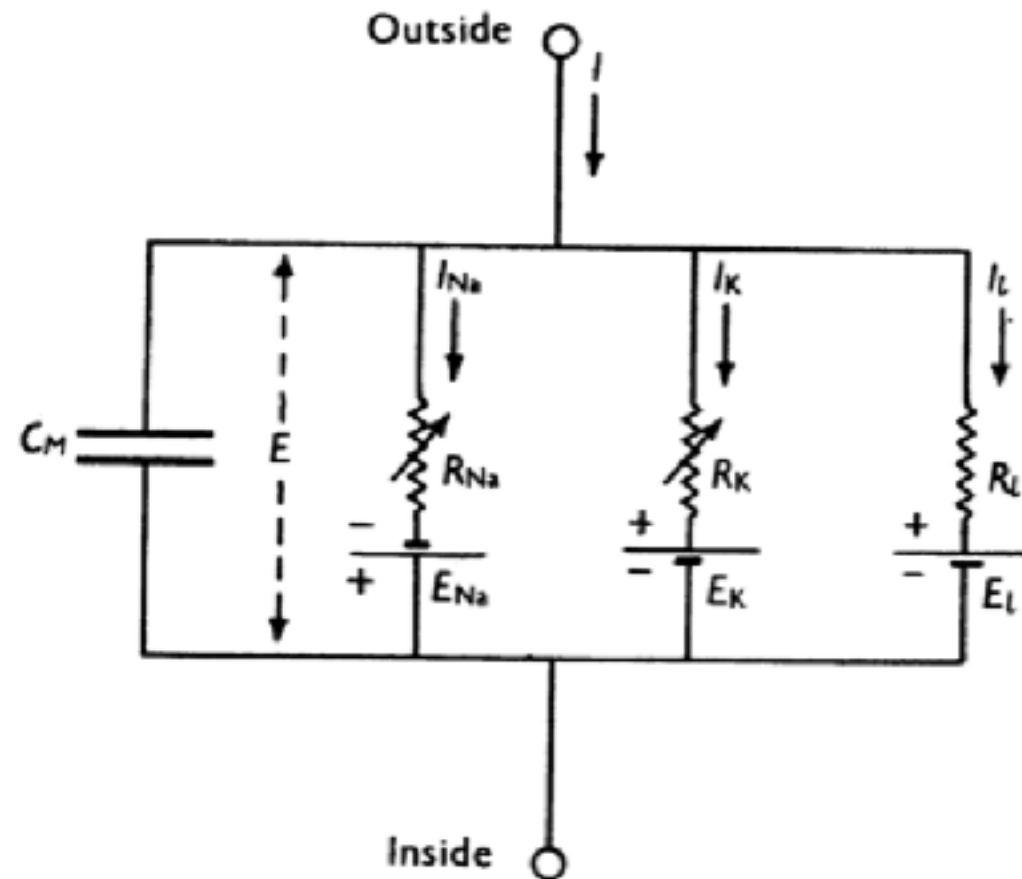
Alan Hodgkin & Andrew Huxley



- Physiologists based at Cambridge and Plymouth.
- Published a series of five landmark papers on the squid axon model of the action potential in 1952.
- Began working together in 1938/9 but were interrupted for seven years by WW2.
- Awarded the 1963 Nobel Prize in Physiology or Medicine (along with John Eccles) "for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane"

What does the model consist of?

The HH model



$$C_M \frac{dV}{dt} = I_{Na} + I_K + I_l$$

$$I_x = g_x (E_x - V) \quad \dots \text{where } x \text{ is } Na, K \text{ or } l$$

$$g_x = ?$$

How do we model the conductances?

How do we model the conductances?

Using time and voltage-dependent gating variables.

$$g_{Na} = \bar{g}_{Na} m^3(V, t) h(V, t)$$

$$g_K = \bar{g}_K n^4(V, t)$$

How do the gating variables evolve in time?

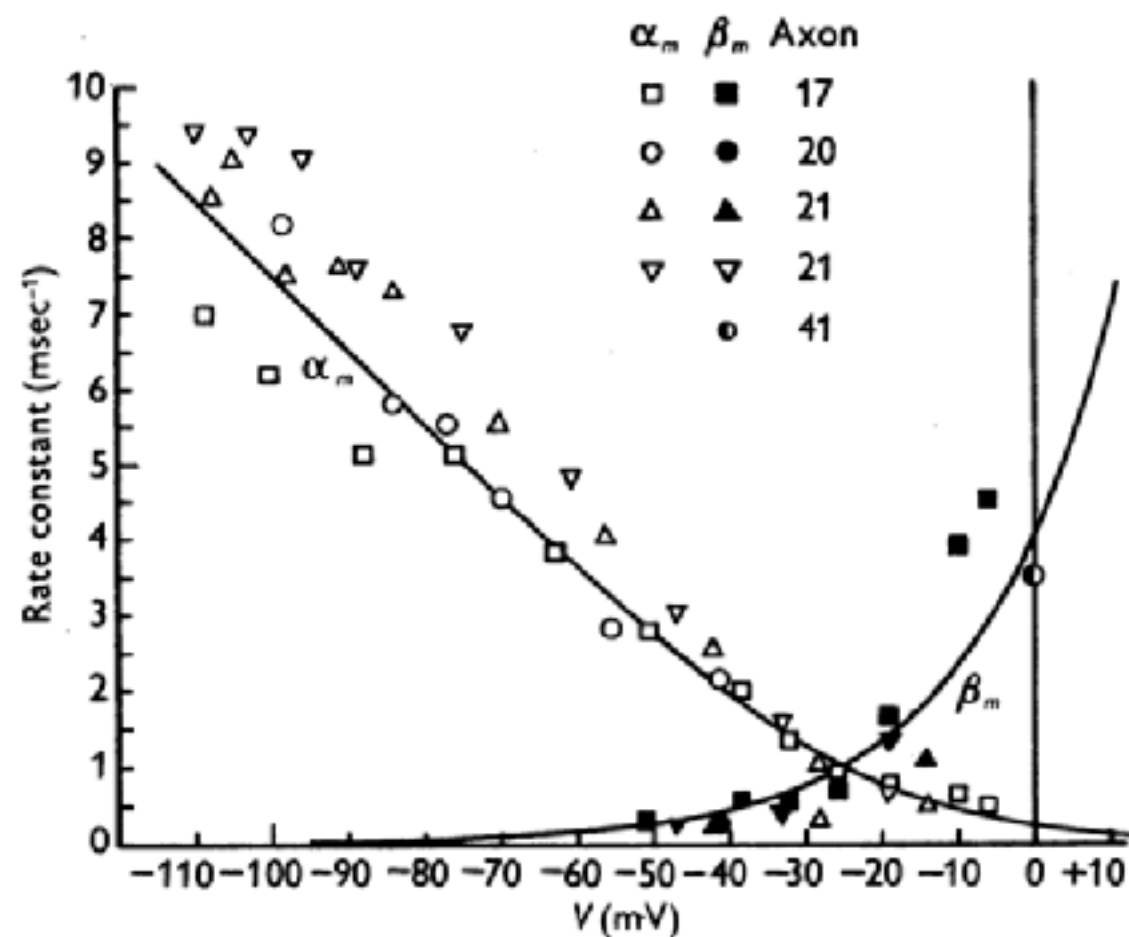
$$\frac{dm}{dt} = \frac{m_{\infty}(V) - m}{\tau_m(V)}$$

How do the steady-state values and time constants depend on voltage?

$$m_{\infty}(V) = \frac{\alpha_m(V)}{\alpha_m(V) + \beta_m(V)}$$

$$\tau_m(V) = \frac{1}{\alpha_m(V) + \beta_m(V)}$$

How do the forward and backward rate constants depend on voltage?
Hodgkin and Huxley fit them to match their voltage-clamp data.



$$\alpha_m(V) = \frac{0.1(V + 40)}{1 - e^{-(V+40)/10}}$$

$$\alpha_h(V) = 0.07e^{-(V+65)/20}$$

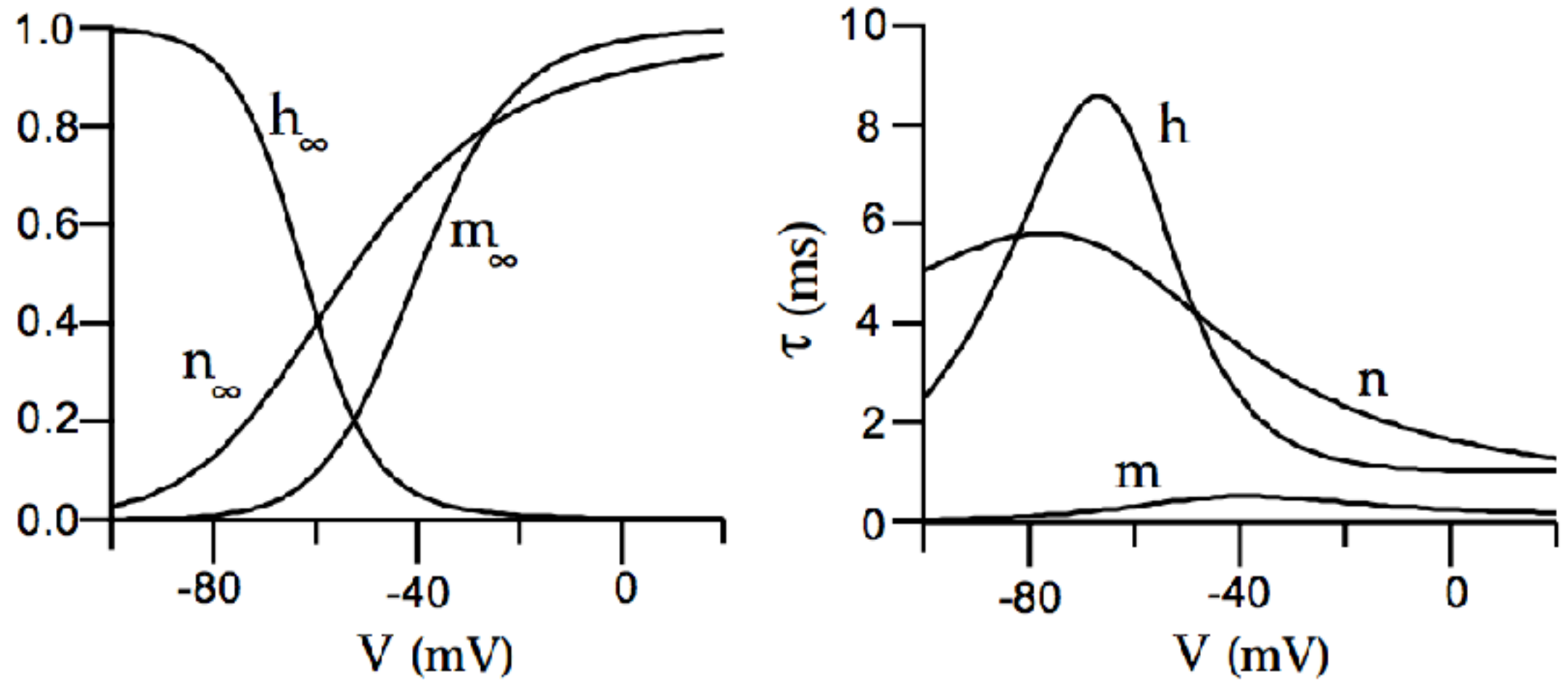
$$\alpha_n(V) = \frac{0.01(V + 55)}{1 - e^{-(V+55)/10}}$$

$$\beta_m(V) = 4e^{-(V+65)/18}$$

$$\beta_h(V) = \frac{1}{1 + e^{-(V+35)/10}}$$

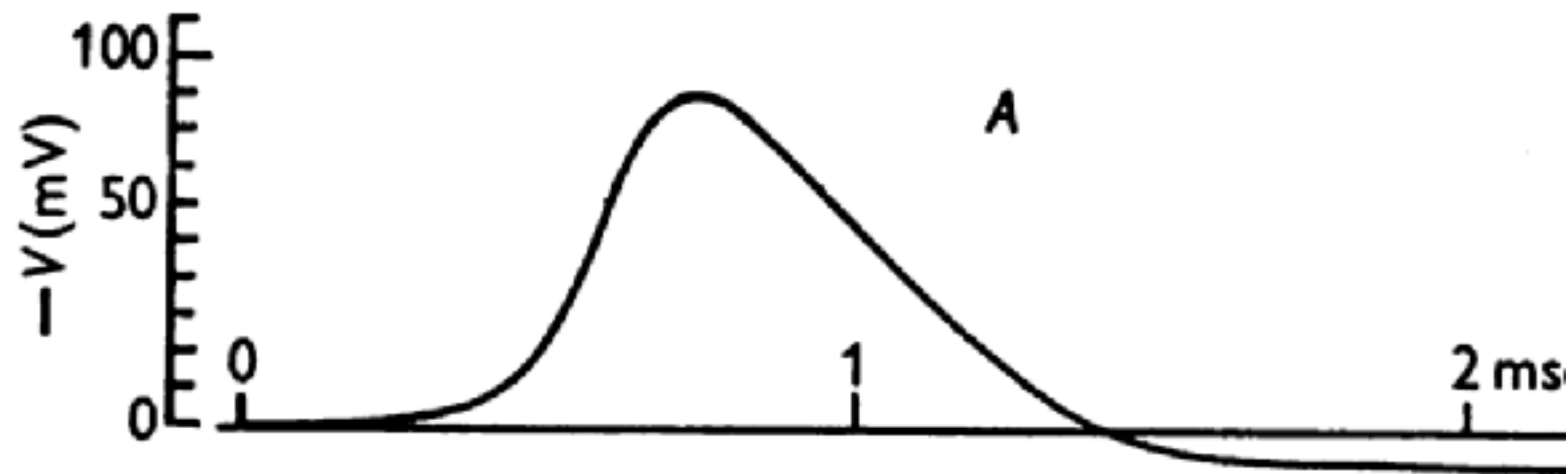
$$\beta_n(V) = 0.125e^{-(V+65)/80}$$

Gating variables steady-state values and time constants as a function of voltage

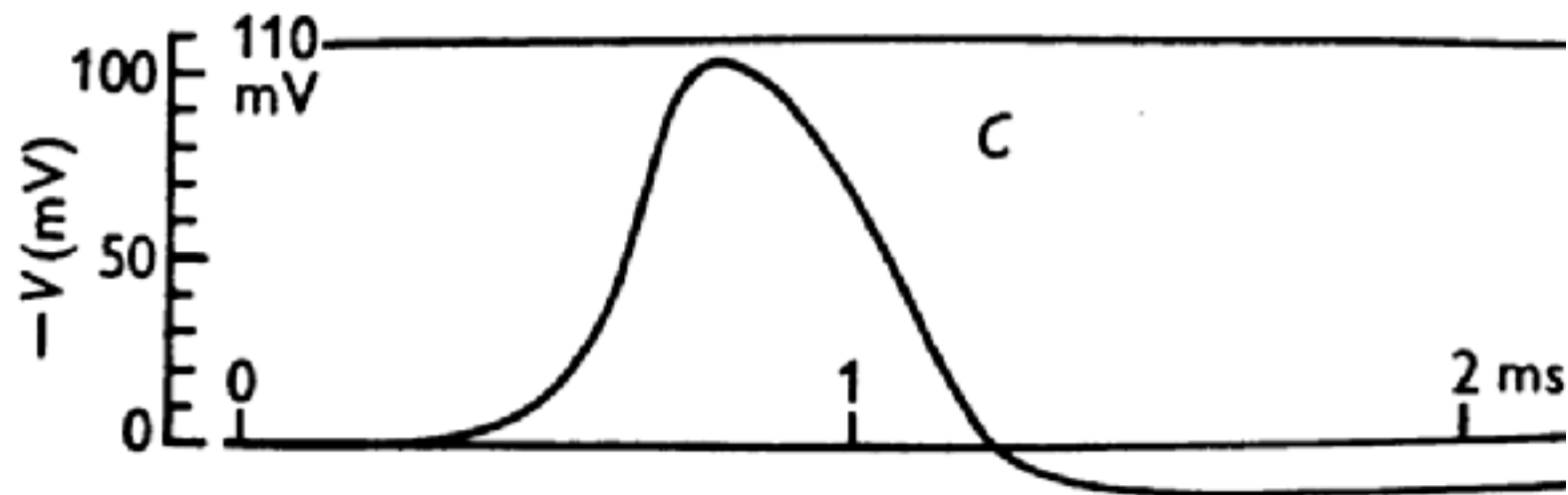


What does the HH model do?

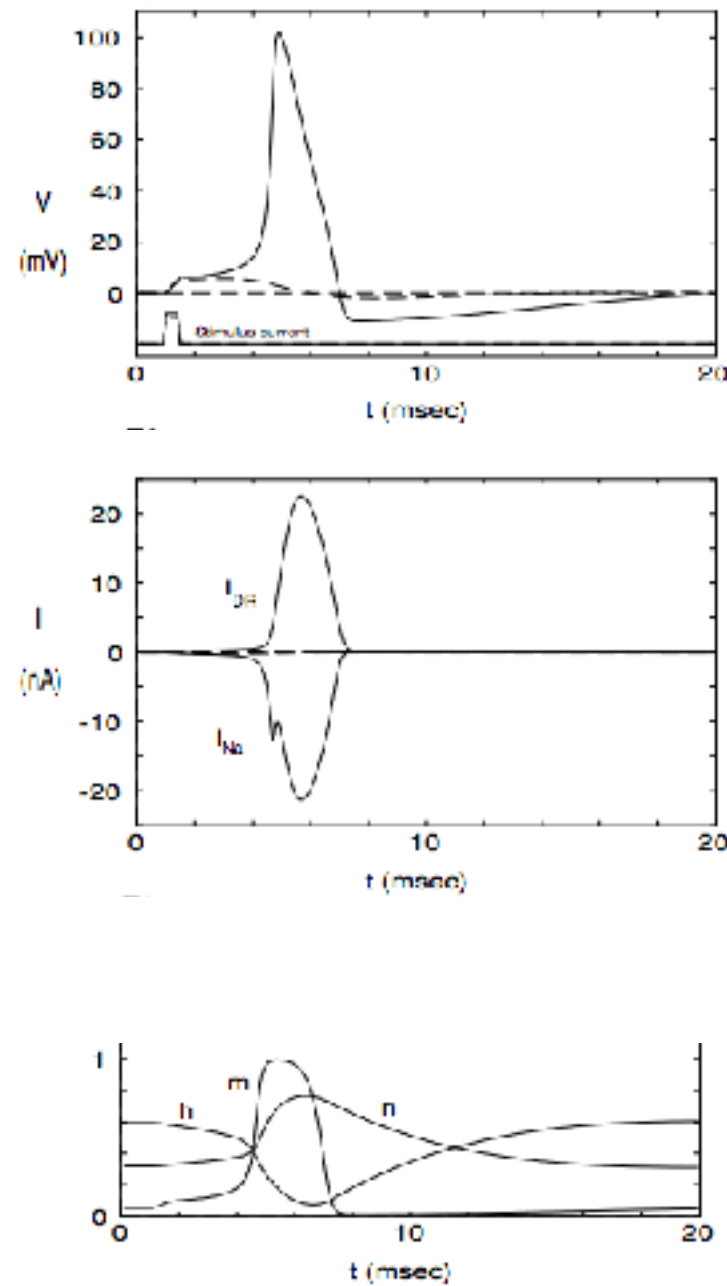
Model



Data



What does the HH model do?



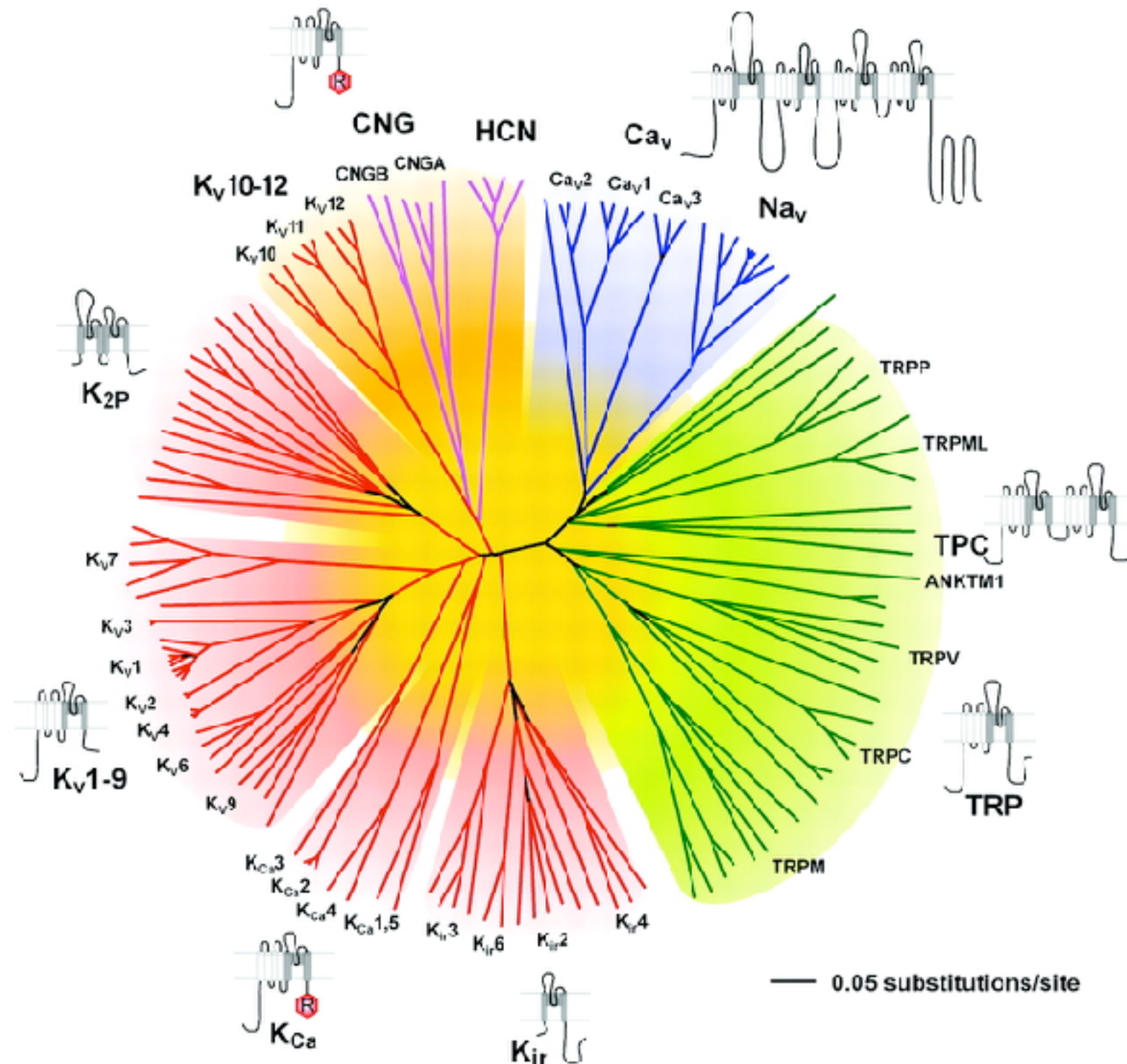
What else does the HH model do?

- It is a "Type 2" model neuron
- Discontinuous fi-curve (unlike the integrate-and-fire model).

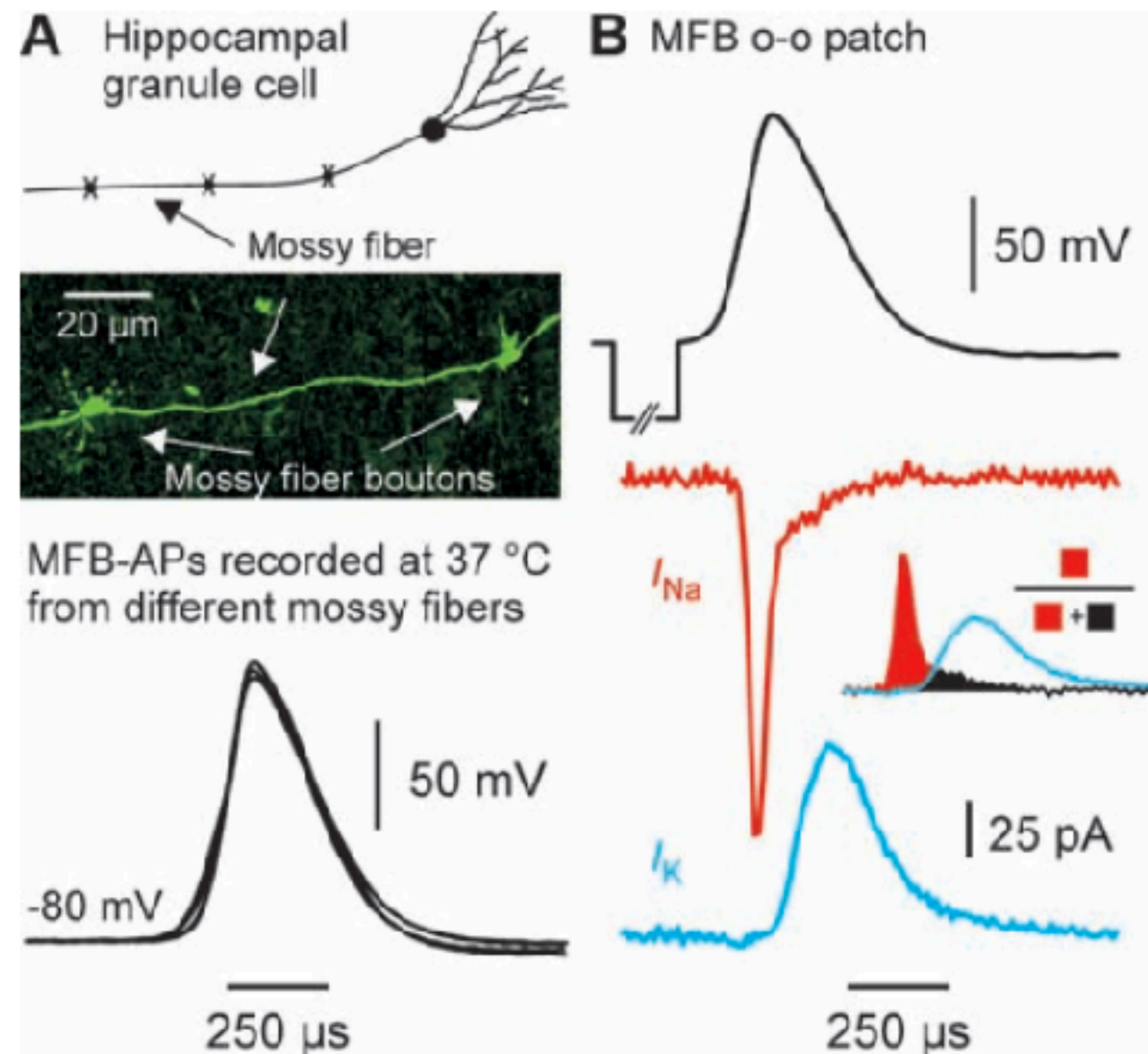
What does the HH model *not* do?

- It is unlike the action potentials in mammalian neurons:
 - different ion channels
 - different waveform
 - energy inefficient
 - extremely leaky resting conductance
- Not a good model for myelinated axons
- It is deterministic.
We now know that ion channels are discrete (Neher and Sakmann) and noisy.
- Description of multiple independent gates per channel type is biophysically unrealistic.

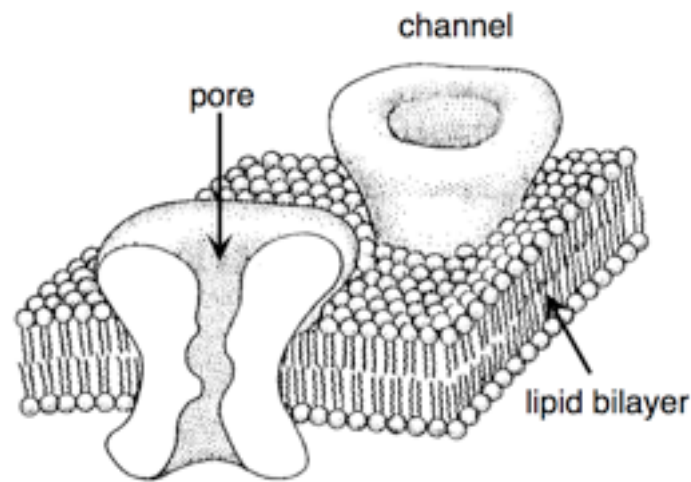
The ion channel zoo



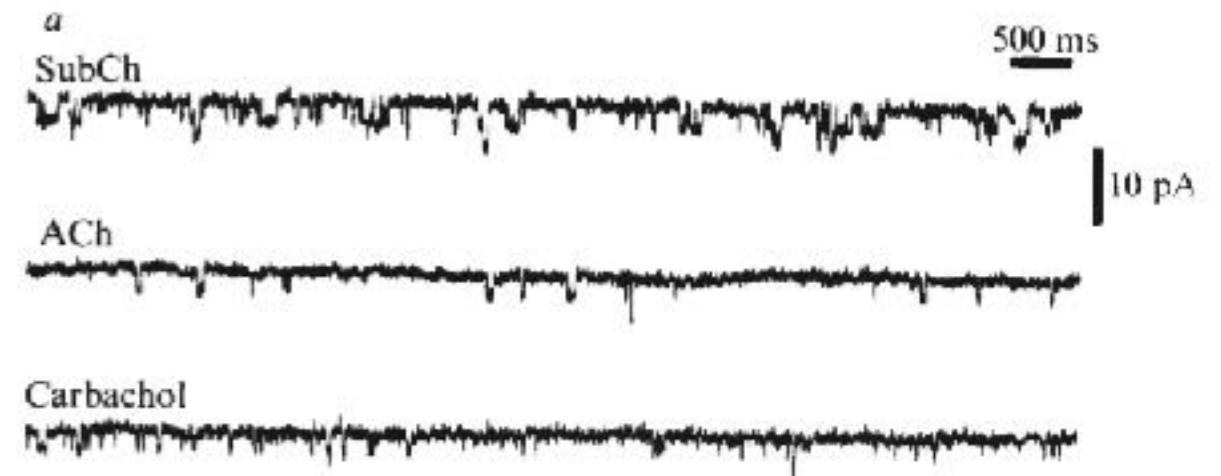
Energy efficiency of mammalian axons



Ion channels are discrete and stochastic

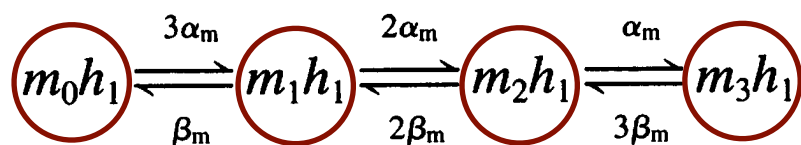
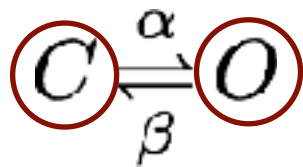


Hille (1992)

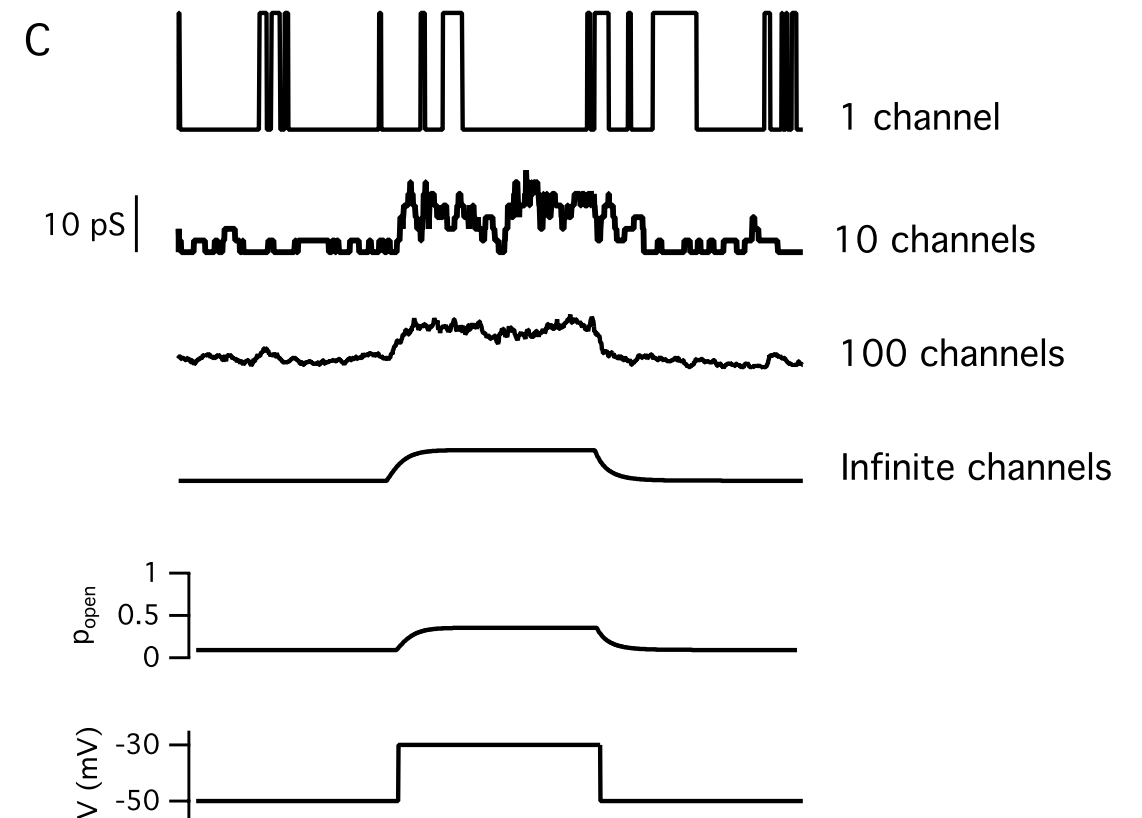
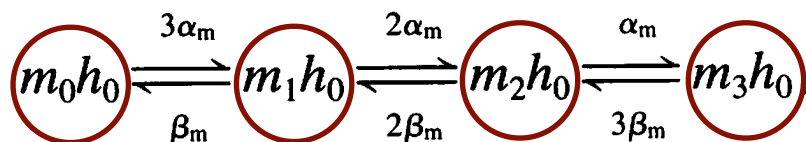


Neher & Sakmann, Nature (1976)

2-state:

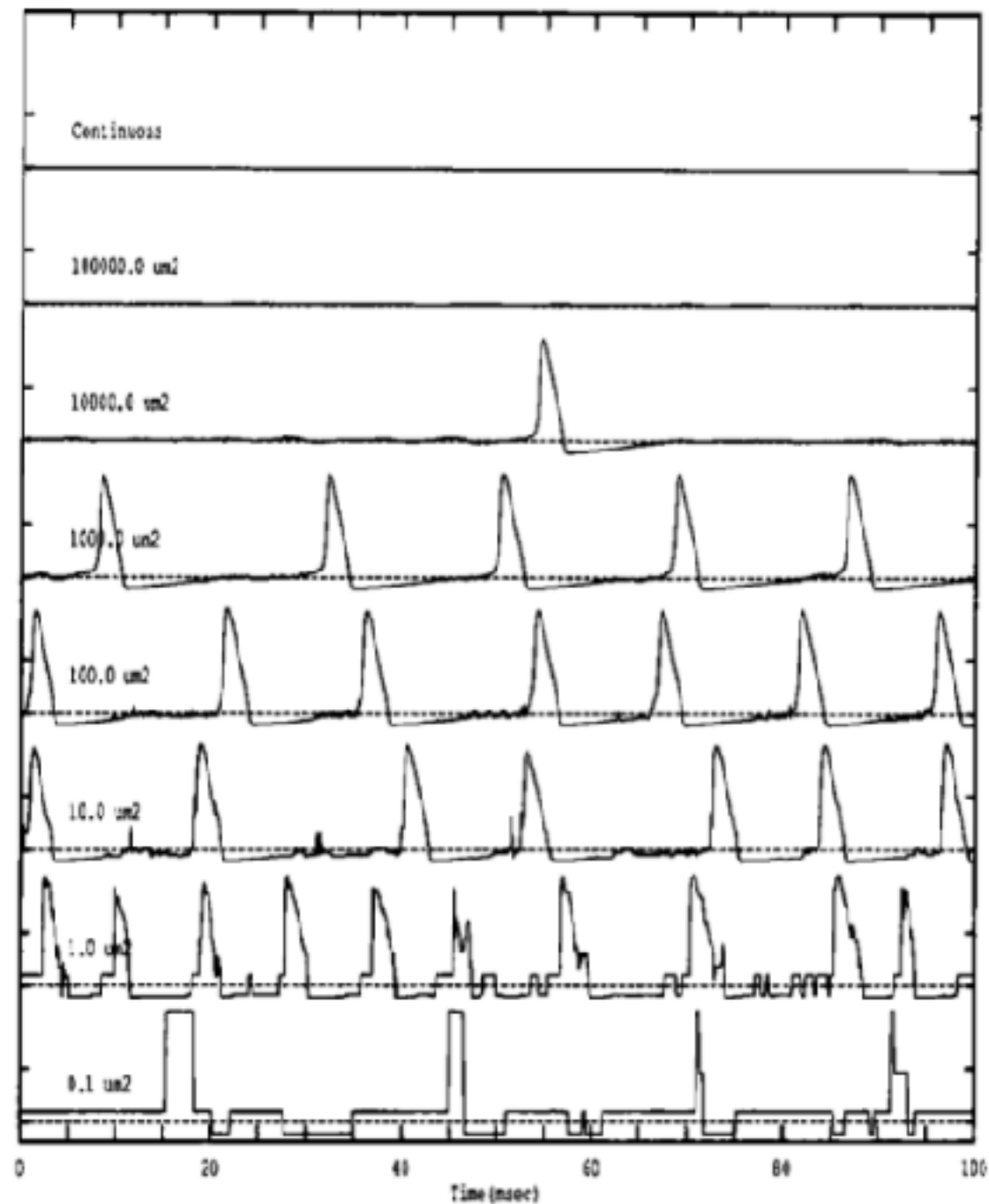


8-state:

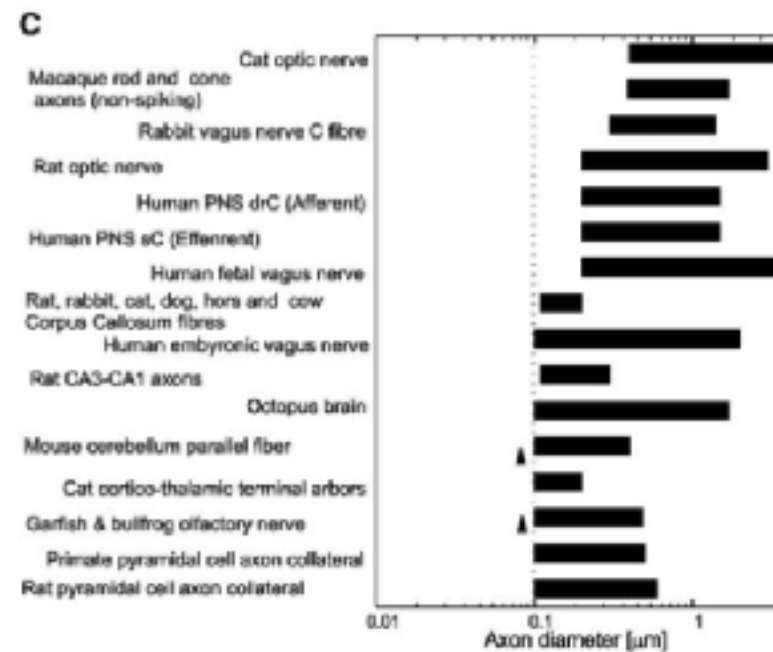
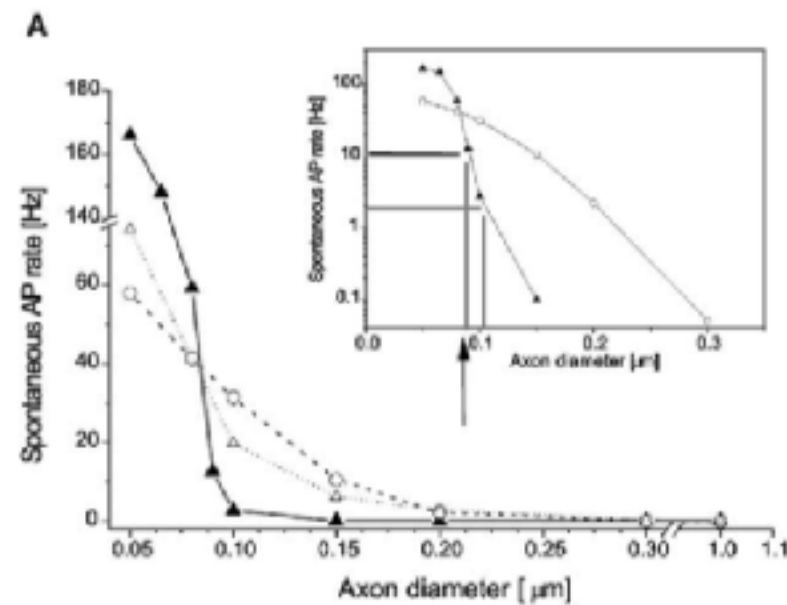


O'Donnell & Nolan (2014)

Spontaneous spikes from ion channel noise



A lower limit on axon diameter



End