COMS30017
Computational Neuroscience

Week 3 / Video 3 / Hodgkin Huxley

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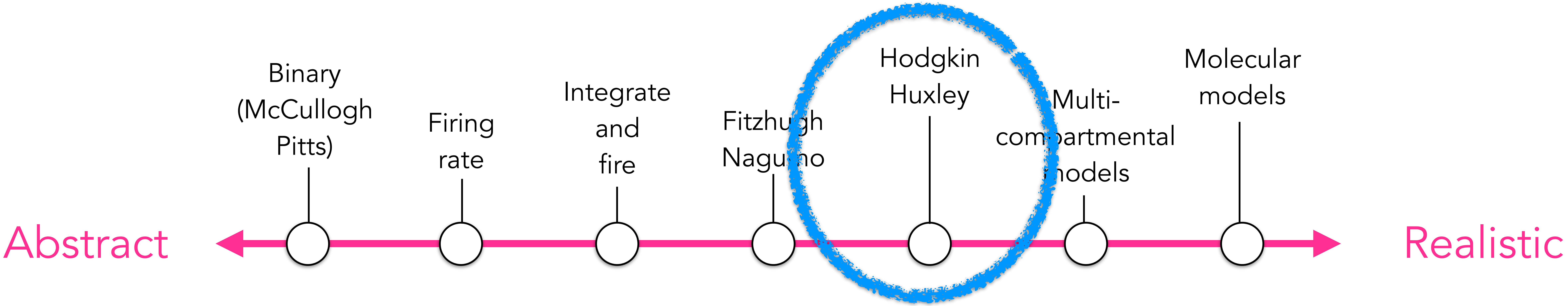
Intended learning outcomes

- Be able to describe the Hodgkin-Huxley model of the action potential.
- Be able to sketch the voltage dependences and reason about the dynamics of the key variables in the model.
- List the limitations of the HH model.

Models of single neurons (recap)



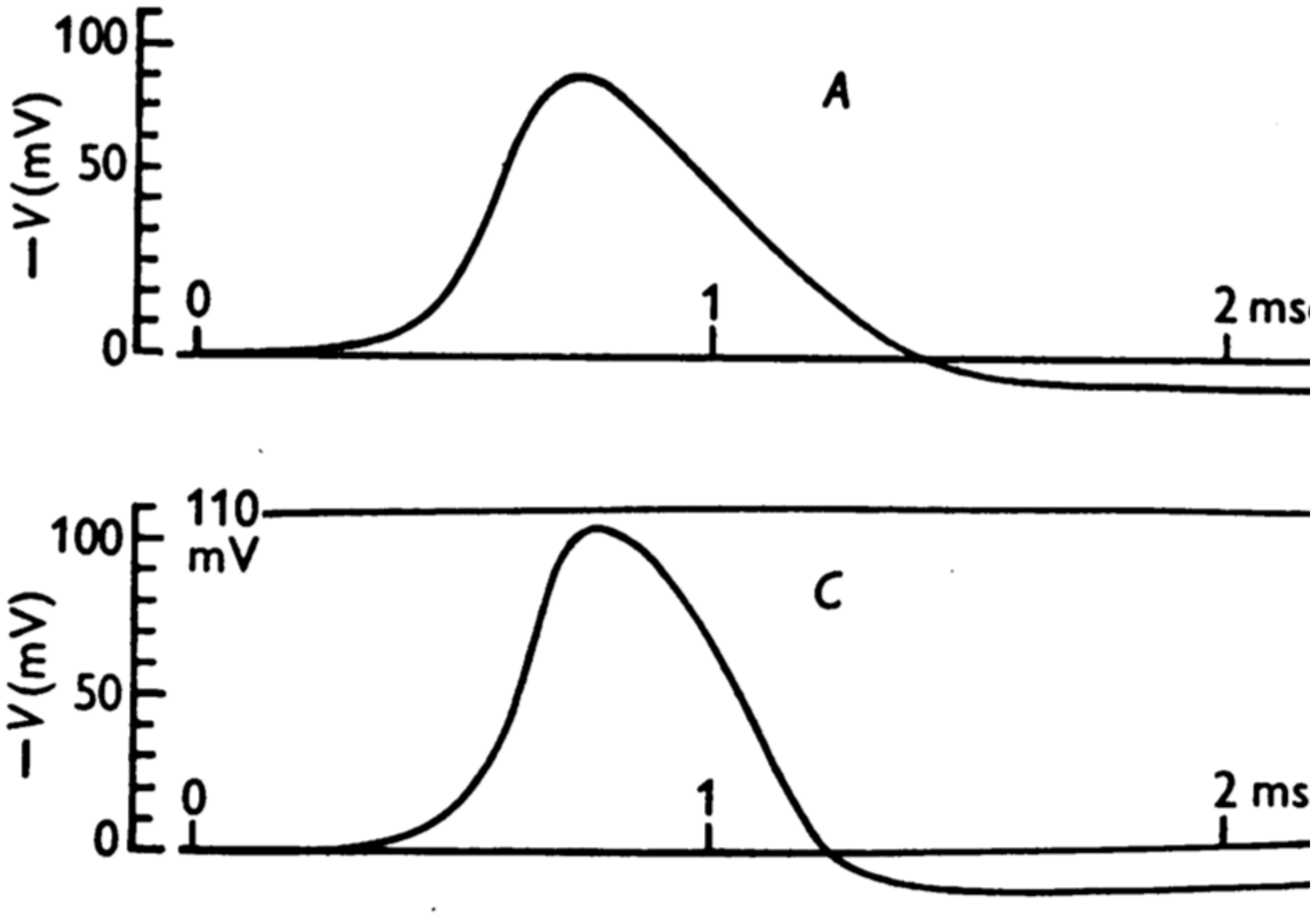
Abstract models		Realistic models
Simple	vs	Detailed
Hard to relate to biology	vs	Contains stuff you could measure
Few parameters	vs	Lots of parameters
Fast simulation	vs	Slow simulation
Mathematical analysis	vs	Intractable
Generic	vs	Specific

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 forbessi*.
- 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

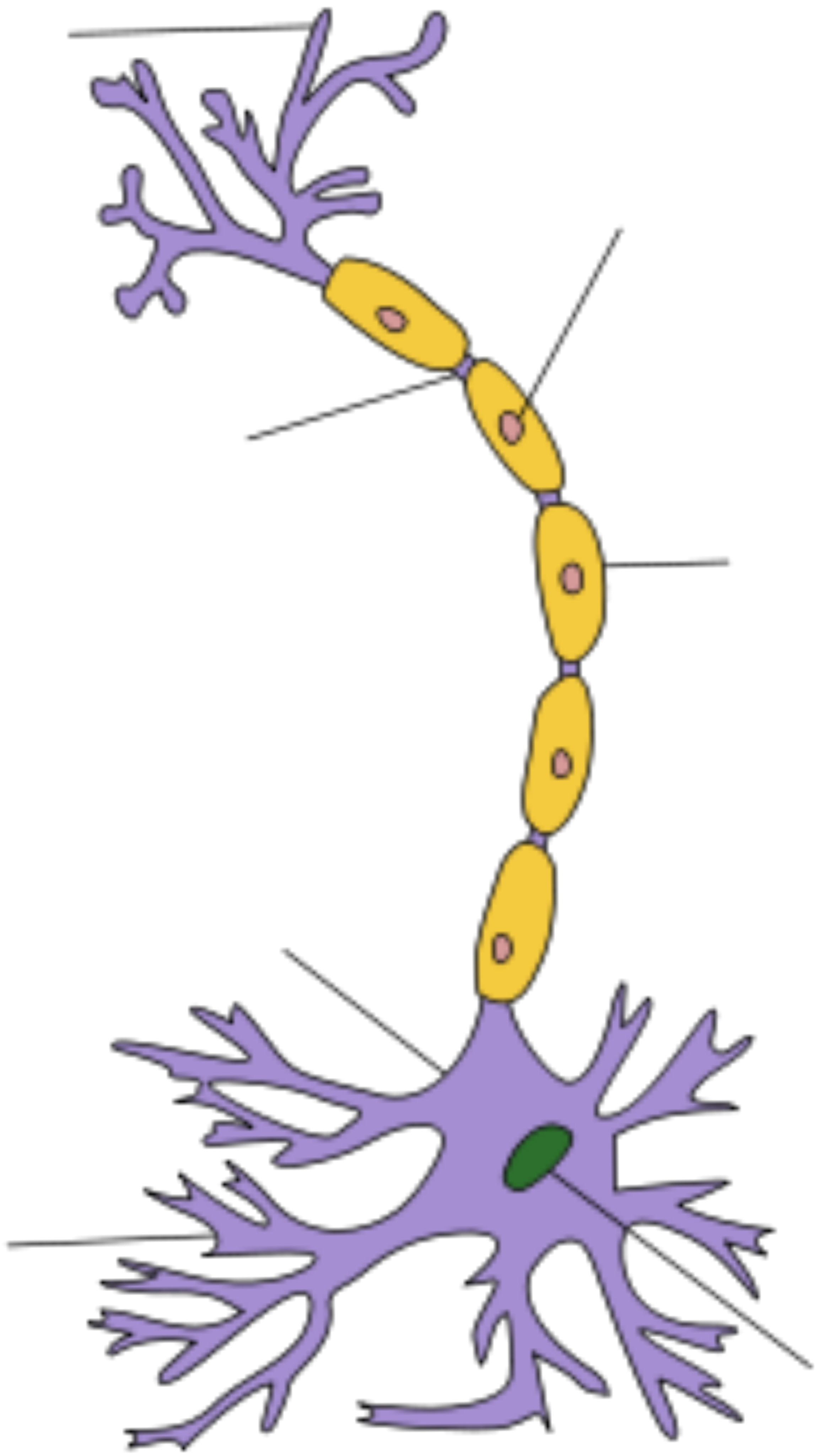
Data



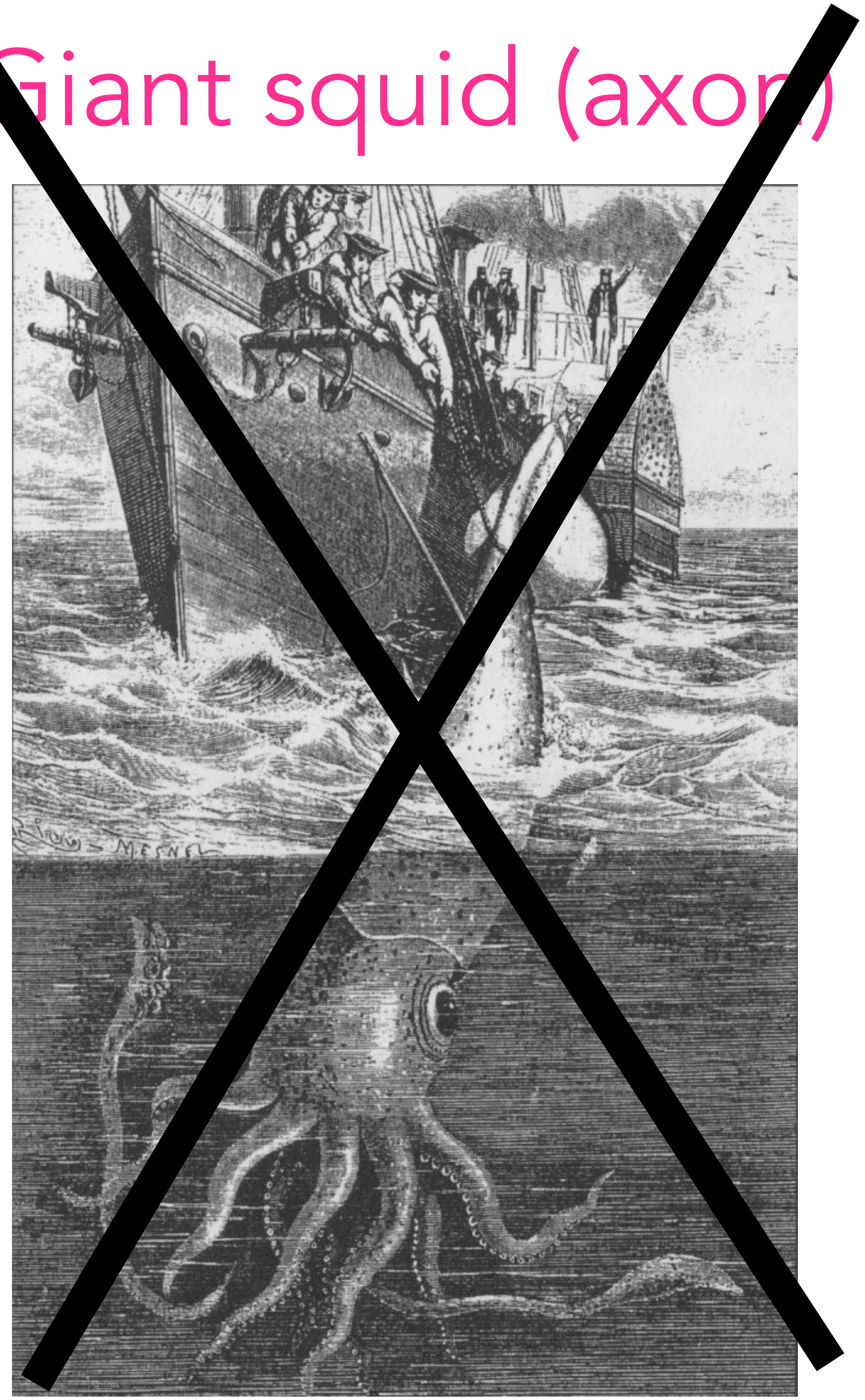
Hodgkin & Huxley, *J Physiol* (1952e)

Loligo forbessi

(Squid) giant axon



Giant squid (axon)



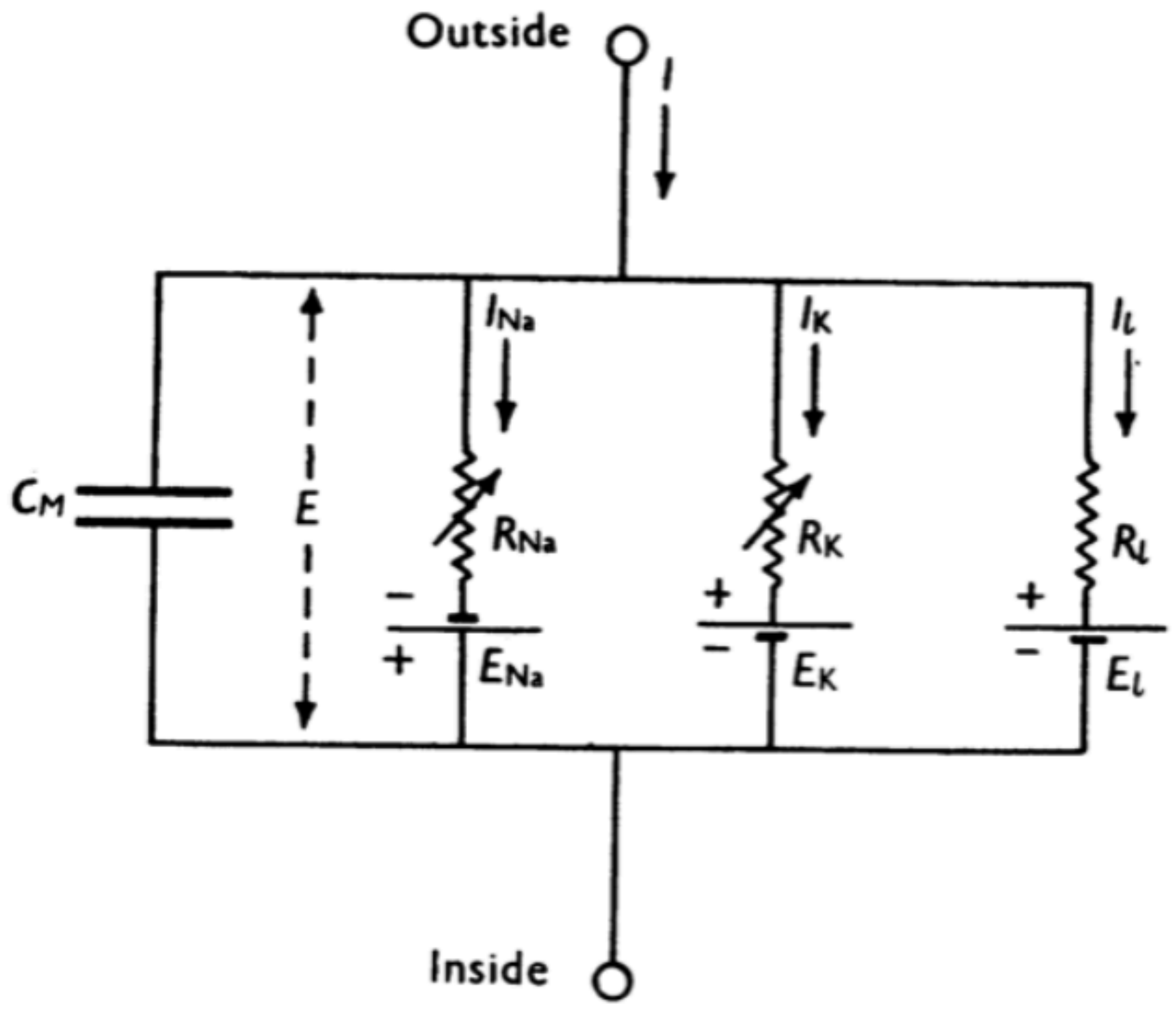
Who were Hodgkin and Huxley?

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



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

$I_x = g_x(E_x - V)$ …where x is *Na*, *K* 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?

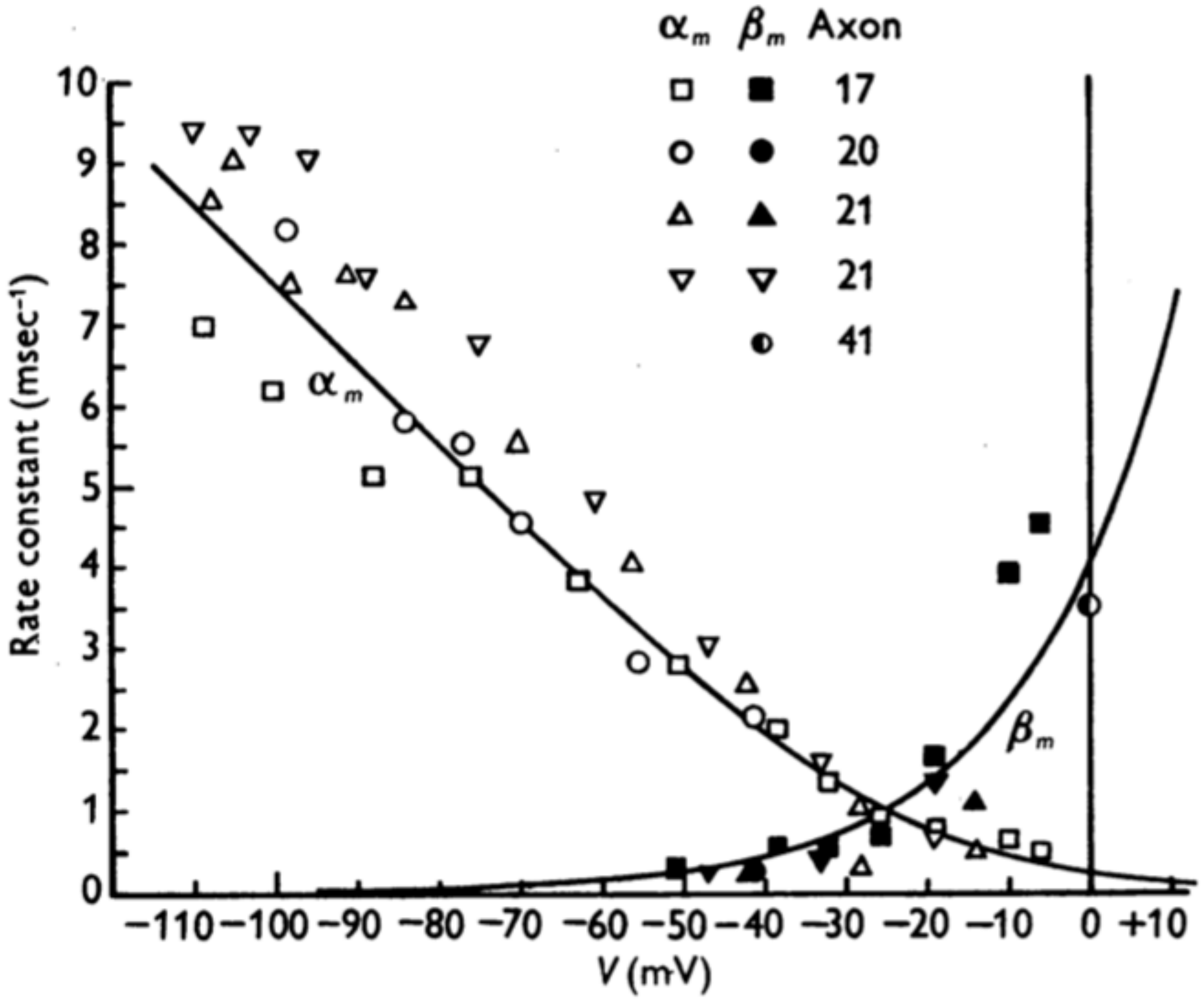
$$\frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)}$$

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

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

How do the forward and backward rate constants depend on voltage?

Hodgkin and Huxley fit them to match their voltage-clamp data.



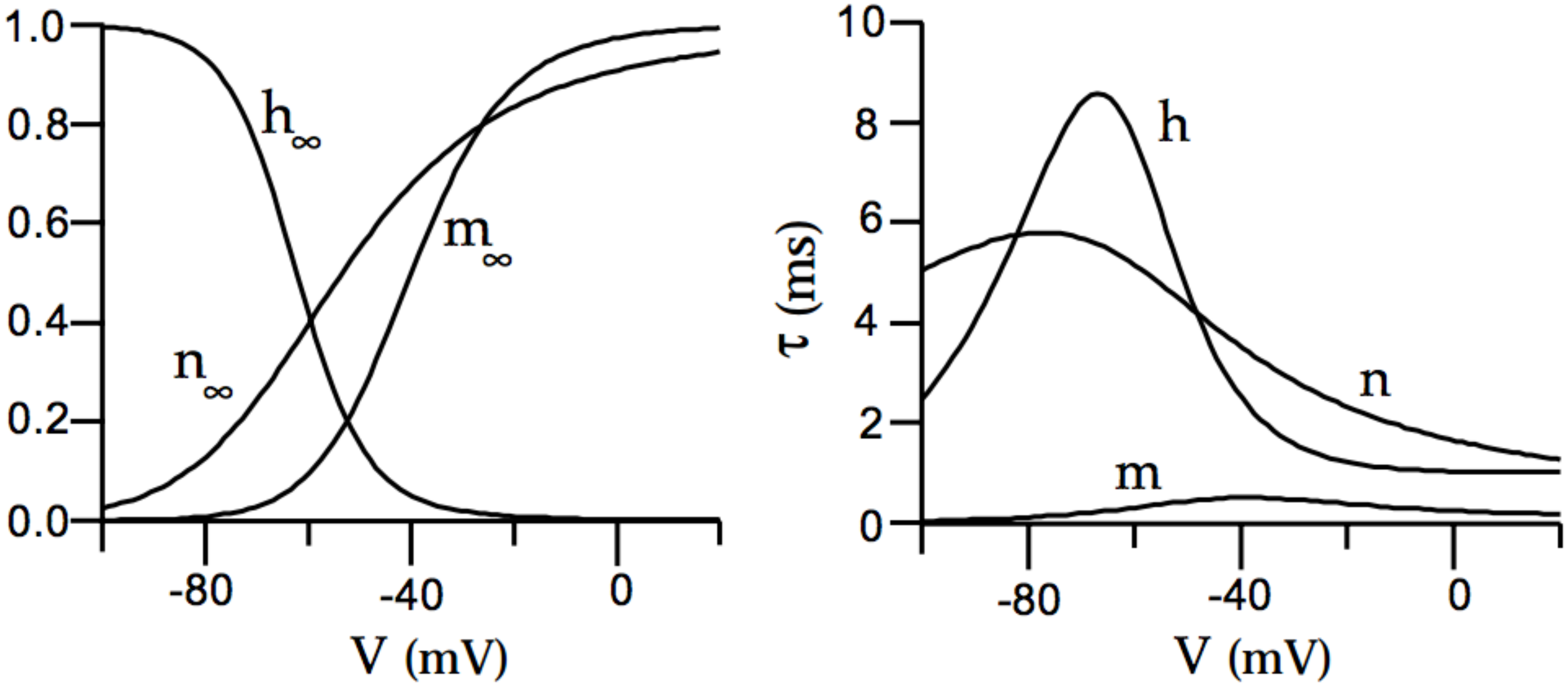
$$\alpha_m(V) = \frac{0.1(V+40)}{1-e^{-(V+40)/10}} \qquad \beta_m(V) = 4e^{-(V+65)/18}$$

$$\alpha_h(V) = 0.07e^{-(V+65)/20} \qquad \beta_h(V) = \frac{1}{1+e^{-(V+35)/10}}$$

$$\alpha_n(V) = \frac{0.01(V+55)}{1-e^{-(V+55)/10}} \qquad \beta_n(V) = 0.125e^{-(V+65)/80}$$

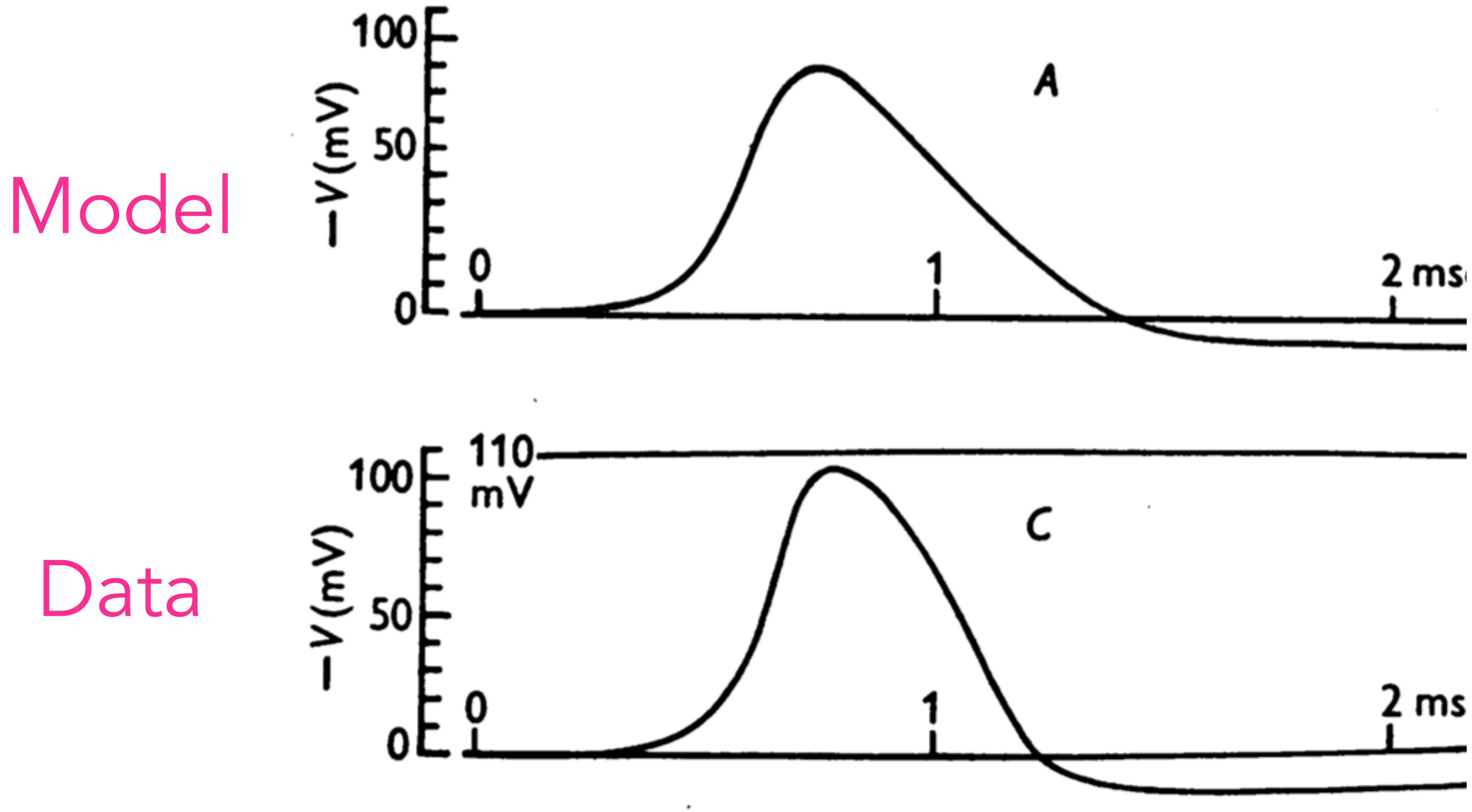
Hodgkin & Huxley, *J Physiol* (1952e)

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



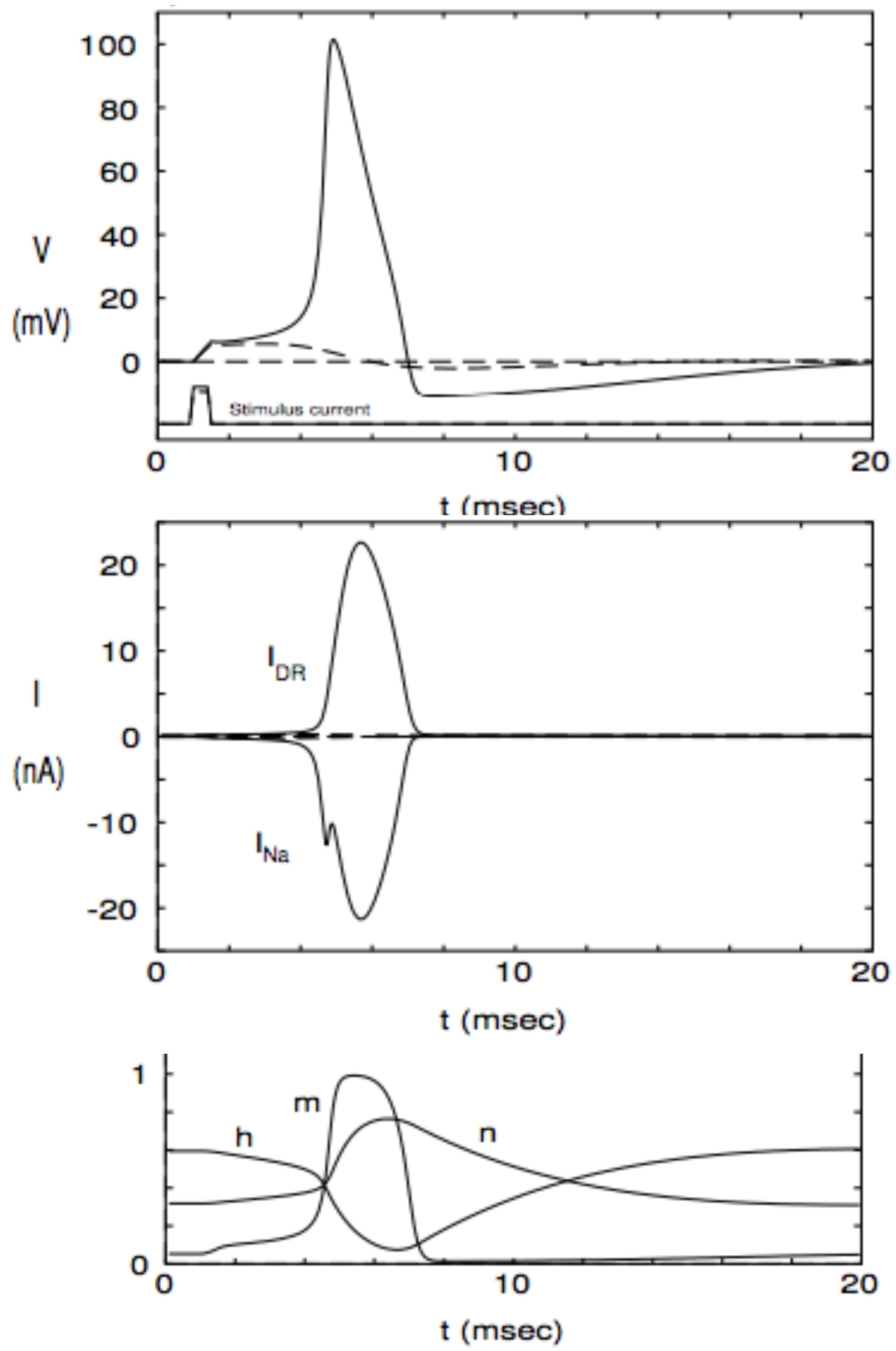
Dayan and Abbott (2001)

What does the HH model do?



Hodgkin & Huxley, *J Physiol* (1952e)

What does the HH model do?



Koch (1999)

What else does the HH model do?

- It is a "Type 2" model neuron:
  - Discontinuous fi-curve (unlike the integrate-and-fire model). The firing rate jumps from 0 Hz to ~50Hz at some threshold value.
  - Has membrane potential oscillations.
- Both of these properties come from its underlying dynamical properties, it undergoes a "Hopf bifurcation" at spike threshold.

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.

- If you want a single-compartment model of spiking, integrate-and-fire can actually be considered *more* realistic by some measures (Brette, *PLoS Comp Biol* 2015).

Summary

- The Hodgkin-Huxley model links the dynamics of sodium and potassium ion channels to the action potential.

- It is probably the most celebrated achievement of computational neuroscience.

- The HH model is still used often today, but it is important to note that it has several properties that are dissimilar to spikes in mammalian neurons.