Computational Neuroscience Group

Calcium Enhanced Spiking Models

Nathan Crock

Motivation

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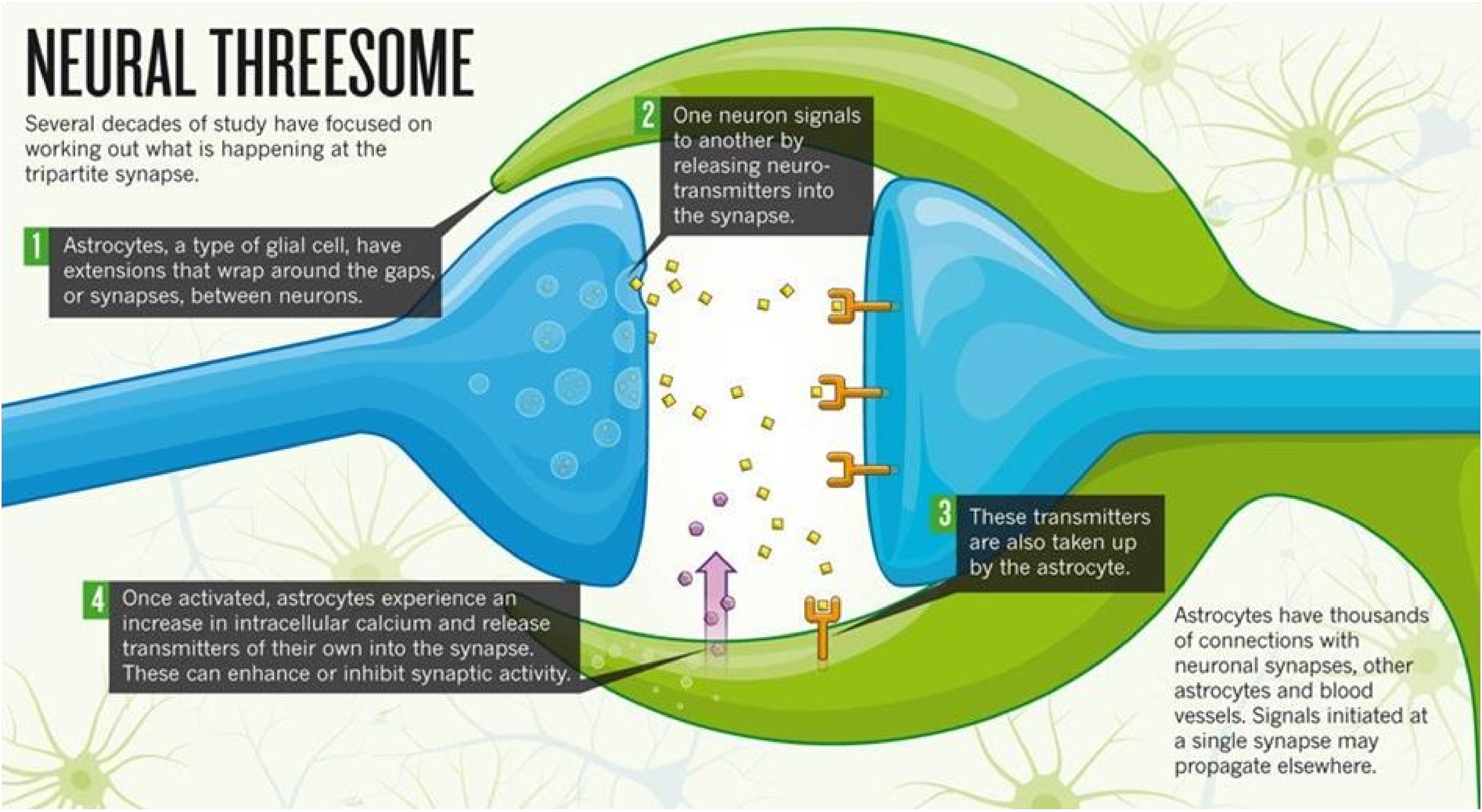
- Identify neuron/synapse as the functional unit of the brain
- Understand that astrocytes modulate synaptic activity
- Hypothesize answers may be found in tripartite dynamics



NEURAL THREESOME
Several decades of study have focused on working out what is happening at the tripartite synapse.
1 Astrocytes, a type of glial cell, have extensions that wrap around the gaps, or synapses, between neurons.
2 One neuron signals to another by releasing neuro-transmitters into the synapse.
3 These transmitters are also taken up by the astrocyte.
4 Once activated, astrocytes experience an increase in intracellular calcium and release transmitters of their own into the synapse. These can enhance or inhibit synaptic activity.
Astrocytes have thousands of connections with neuronal synapses, other astrocytes and blood vessels. Signals initiated at a single synapse may propagate elsewhere.

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Develop a robust model of the tripartite synapse. Reduce the model and construct a large scale simulation of numerous tripartite synapses.

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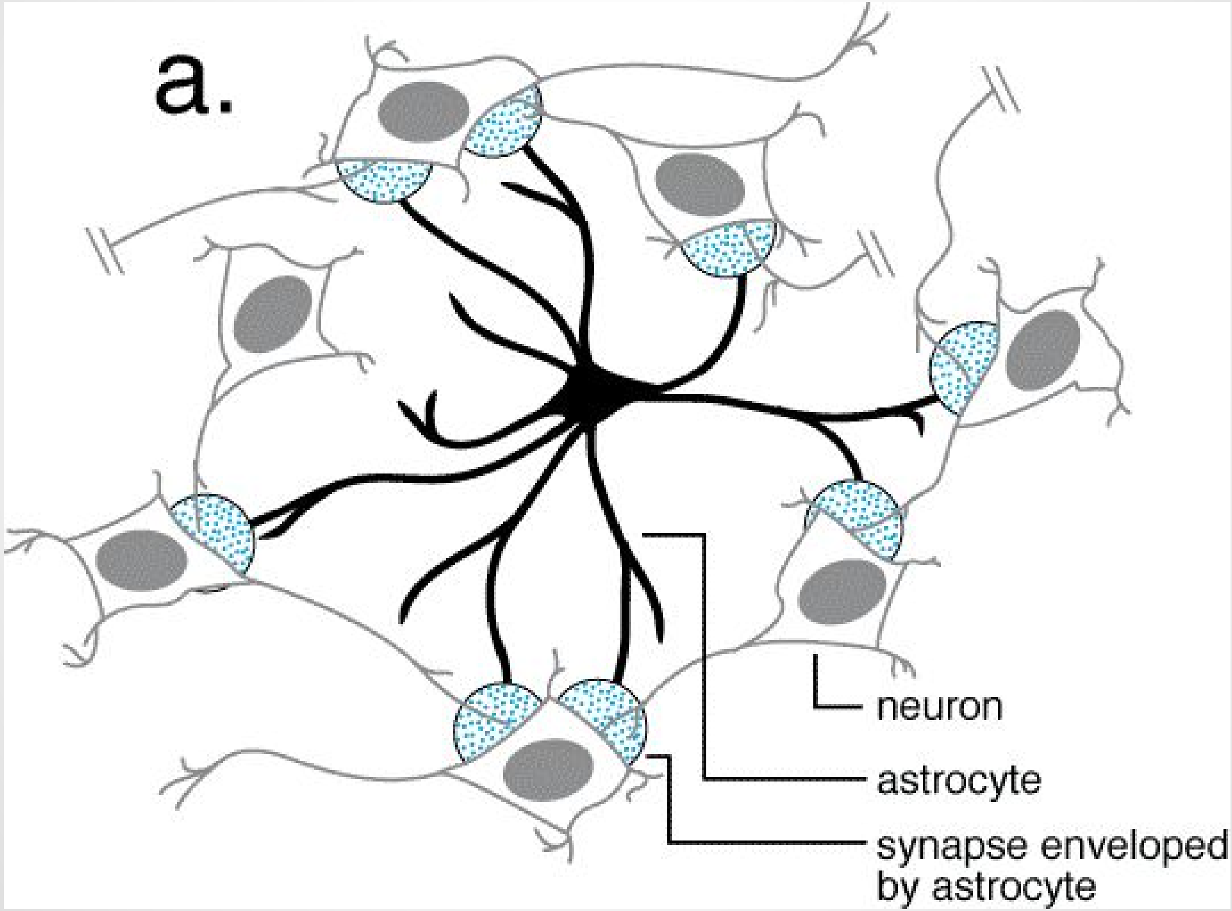
Explore... The dynamics of neuronal and astrocytic interplay

Develop a robust model of the tripartite synapse. Reduce the model and construct a large scale simulation of numerous tripartite synapses. LEARNING? MEMORY?

Network Communication

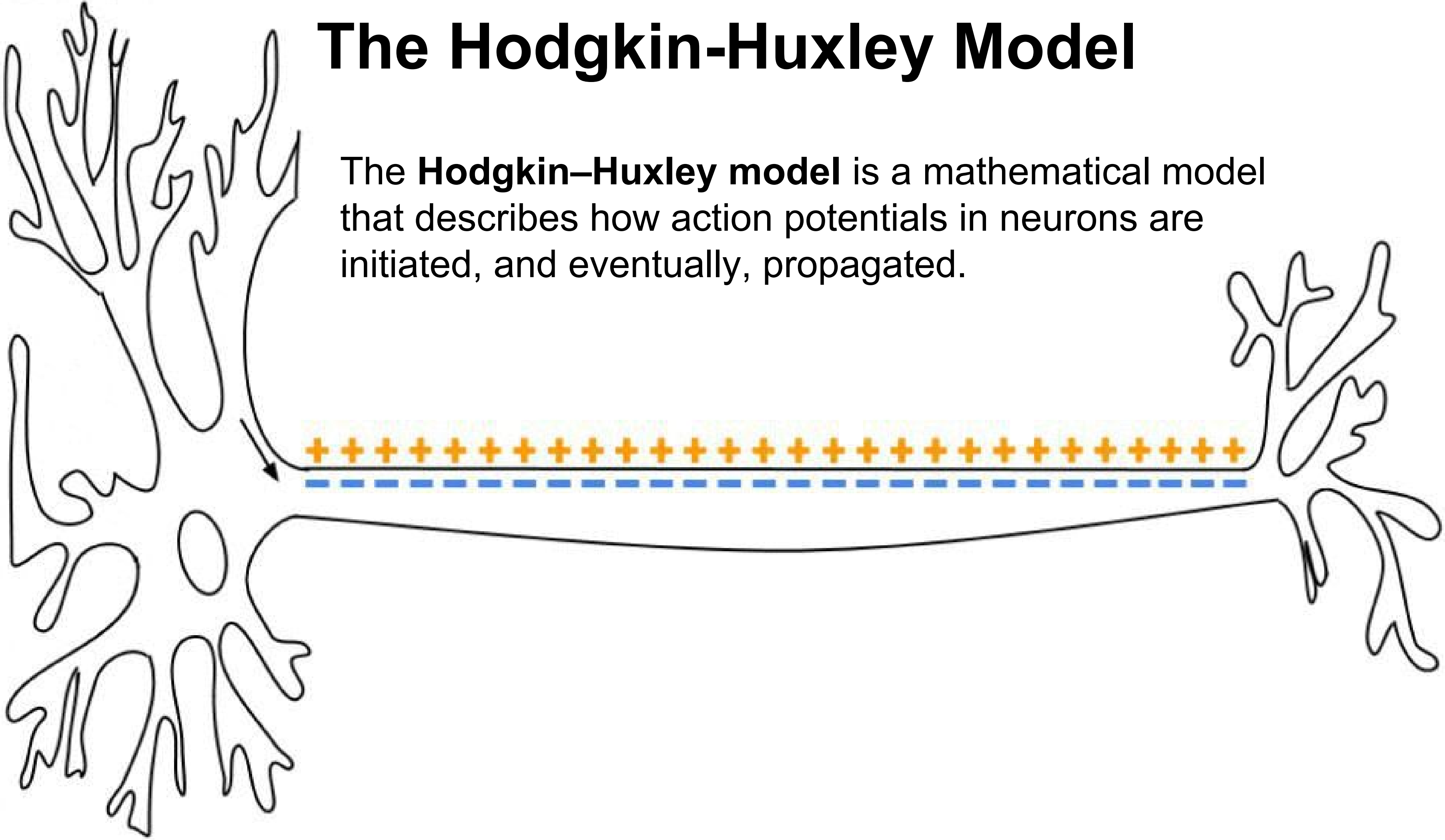


Today's Outline

- Start with the Hodgkin-Huxley equations
- Consider techniques used in reducing the HH equations
- Explore the dynamics of reduced HH model
- Add calcium to the original HH model
- Reduce the calcium enhanced HH equations
- Explore the dynamics of the reduced HH+calcium model

The Hodgkin-Huxley Model

The **Hodgkin–Huxley model** is a mathematical model that describes how action potentials in neurons are initiated, and eventually, propagated.

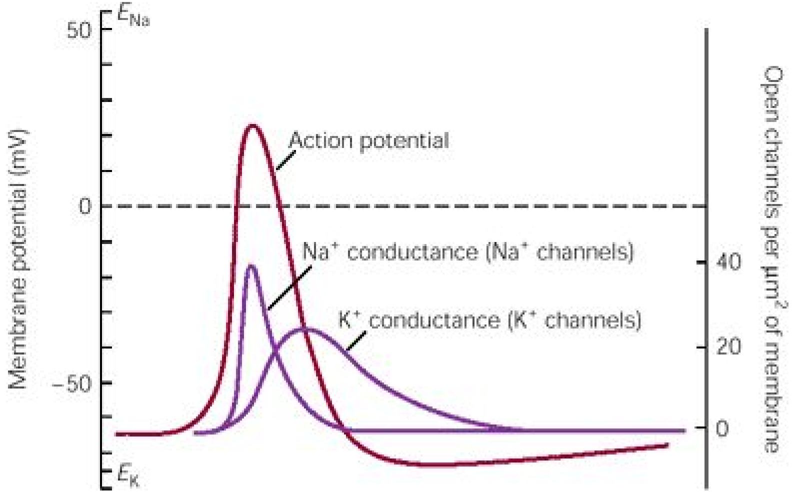


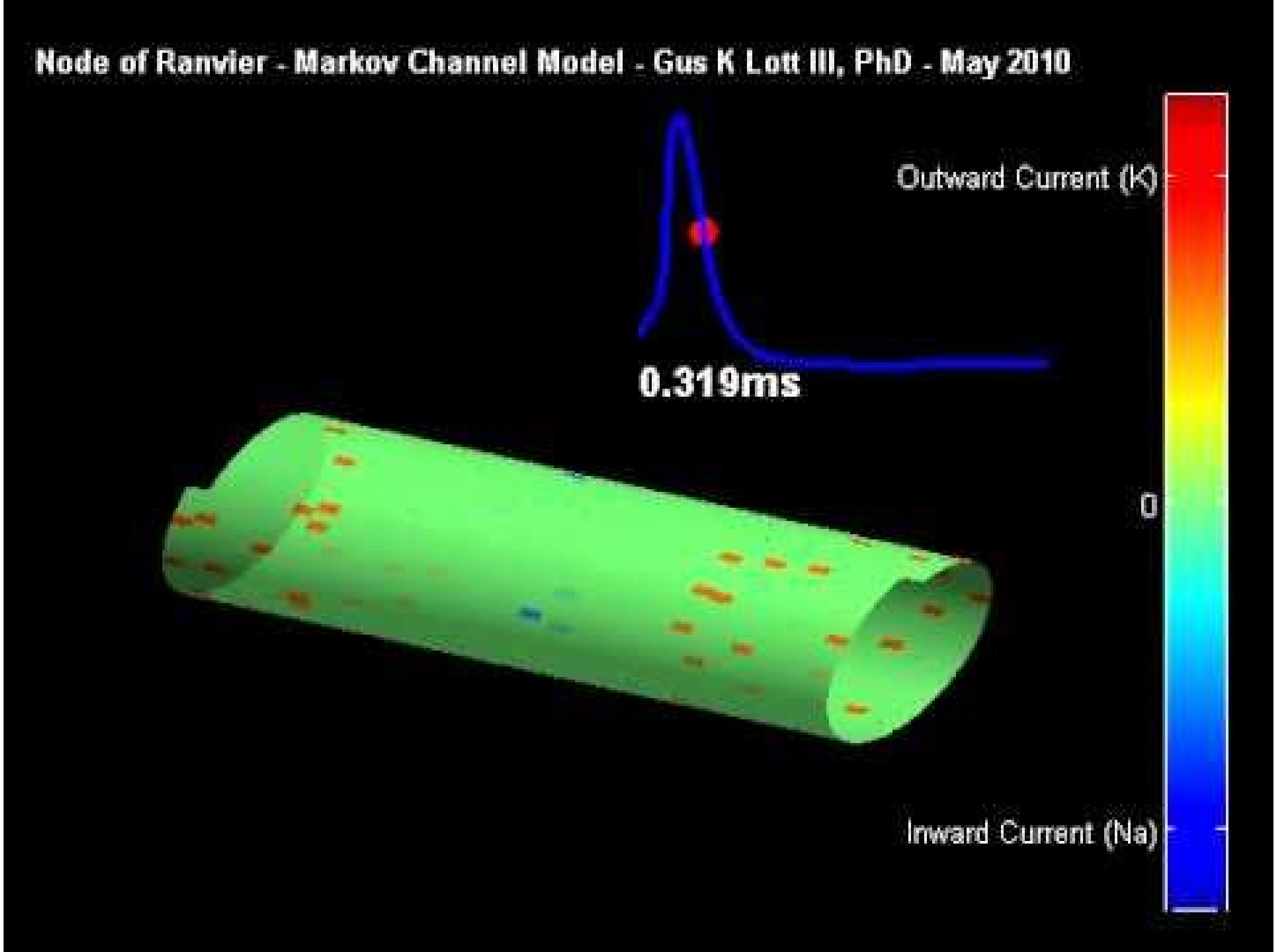
The Hodgkin-Huxley Model

$$
\begin{aligned}
C\frac{dv}{dt} &= I - g_{Na}m^3h(V - V_{Na}) - g_K n^4(V - V_K) - g_L(V - V_L) \\
\frac{dm}{dt} &= a_m(V)(1-m) - b_m(V)m \\
\frac{dh}{dt} &= a_h(V)(1-h) - b_h(V)h \\
\frac{dn}{dt} &= a_n(V)(1-n) - b_n(V)n \\
a_m(V) &= .1(V+40)/(1-\exp(-(V+40)/10)) \\
b_m(V) &= 4\exp(-(V+65)/18) \\
a_h(V) &= .07\exp(-(V+65)/20) \\
b_h(V) &= 1/(1+\exp(-(V+35)/10)) \\
a_n(V) &= .01(V+55)/(1-\exp(-(V+55)/10)) \\
b_n(V) &= .125\exp(-(V+65)/80)
\end{aligned}
$$

4 Equations

18 Parameters




Node of Ranvier - Markov Channel Model - Gus K Lott III, PhD - May 2010
0.319ms
Outward Current (K)
0
Inward Current (Na)

Hodgkin-Huxley Dynamics

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4 ODES and 18 Parameters

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Too much going on to tractably intuit dynamics

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Need to reduce the model...

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How?

Hodgkin-Huxley Reduction

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1. Timescale Analysis

Hodgkin-Huxley Reduction

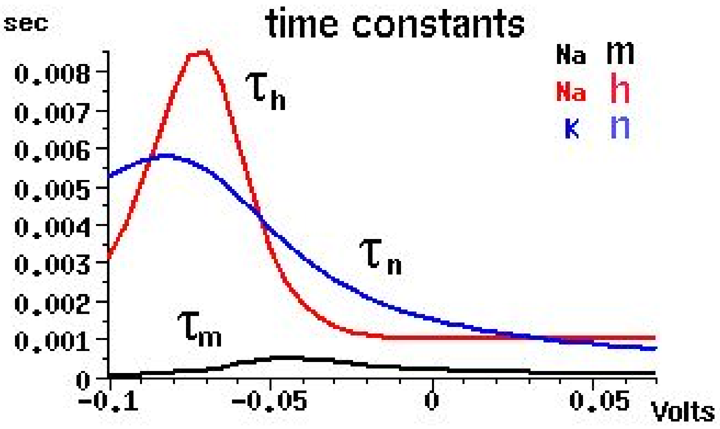
Model reduction requires mathematical “tricks” which leverage details about its dynamics

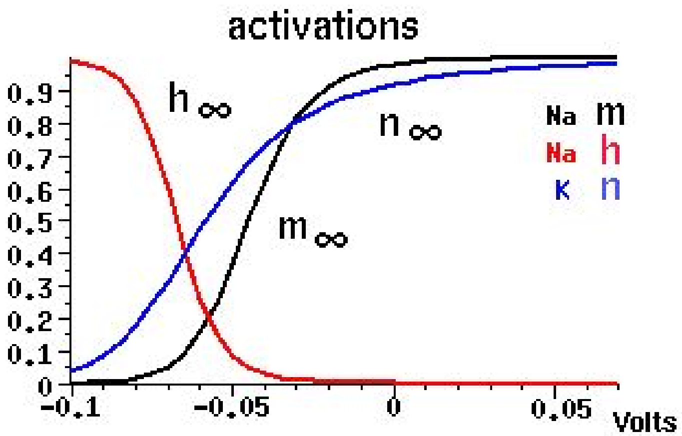
For the Hodgkin-Huxley model we’ll use 2:

1. Timescale Analysis
2. Correlation between Variables

Timescale Analysis

First we observe...

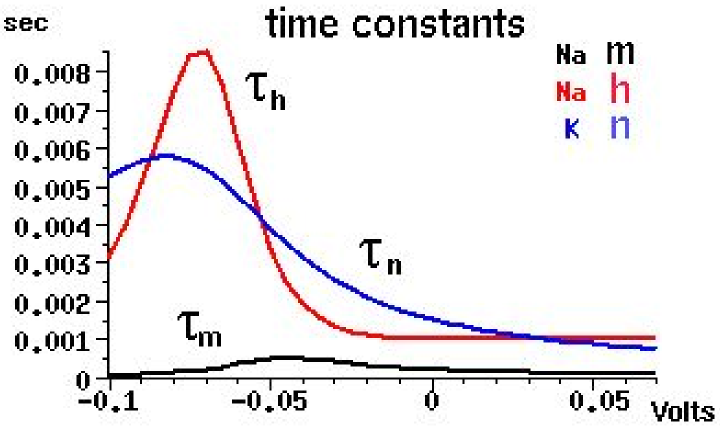


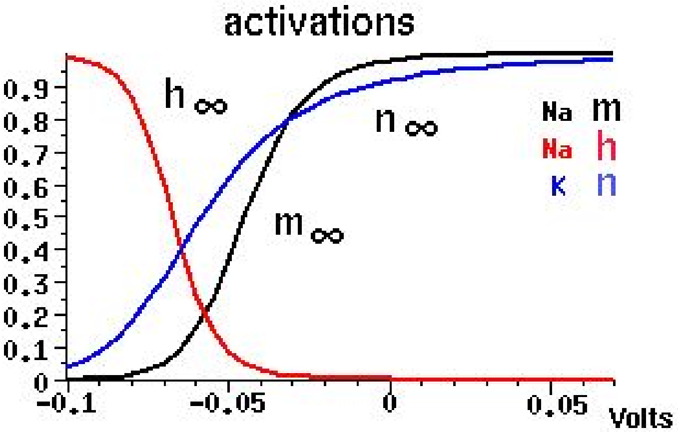


Timescale Analysis

First we observe...

m is faster than both h and n





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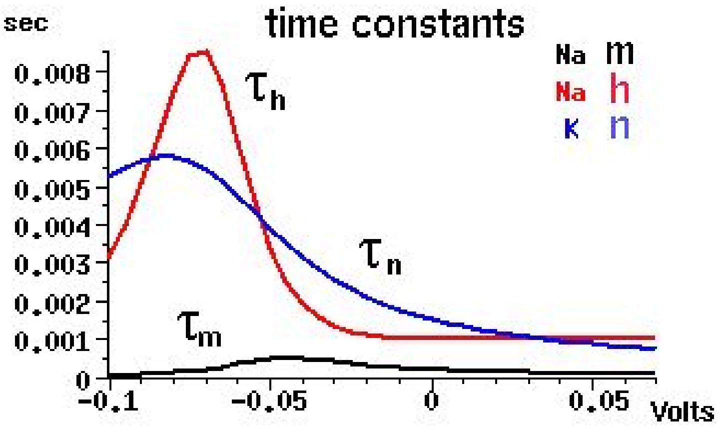

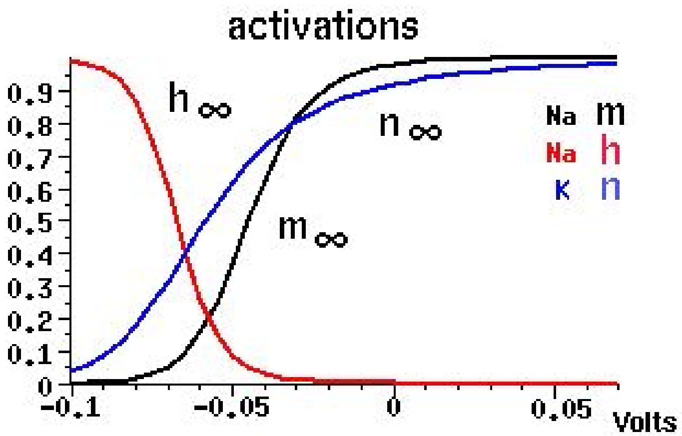

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n$$

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

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

manipulation →

$$\tau_j(V)\frac{dj}{dt} = j_\infty(V) - j$$

$$j_\infty(V) \equiv \frac{\alpha_j(V)}{\alpha_j(V)+\beta_j(V)} \qquad \tau_j(V) \equiv \frac{1}{\alpha_j(V)+\beta_j(V)}$$

Timescale Analysis

$$C\frac{dv}{dt} = I - g_{Na}m^3h(V - V_{Na}) - g_K n^4(V - V_K) - g_L(V - V_L)$$

Correlation of Variables

Now we deal with h and n

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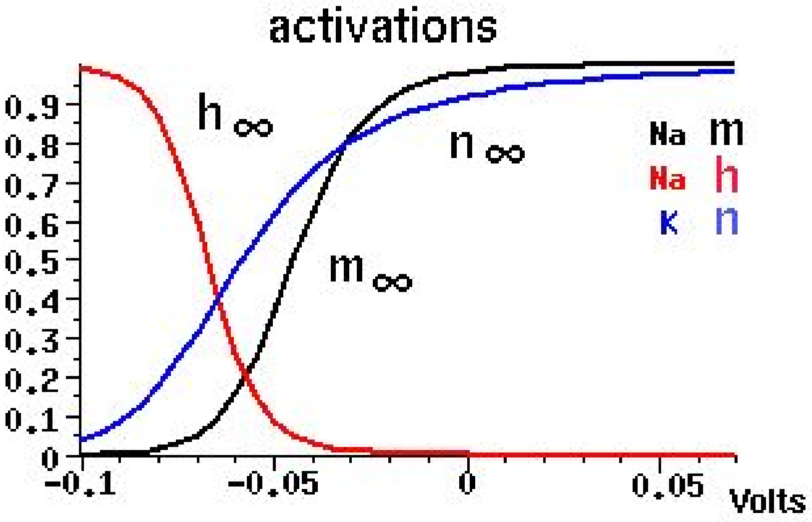

Hodgkin-Huxley Reduction

Now we have finished our argument

1. Dynamics of *m* are fast

2. Dynamics of *n* and *h* are similar

Reduced HH Dynamics

Off to XPP

Hodgkin-Huxley + Calcium

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Calcium plays a critical role in neuronal processes

Hodgkin-Huxley + Calcium

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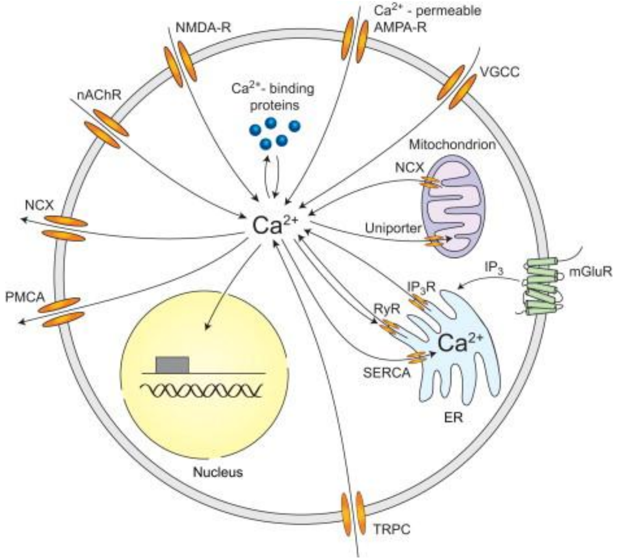
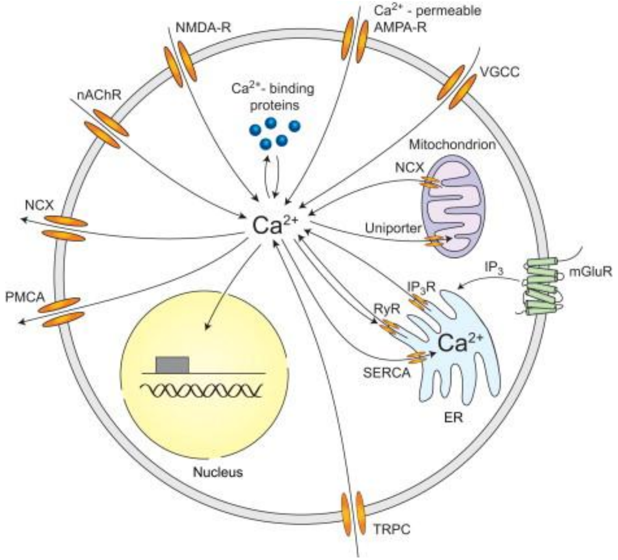


Hodgkin-Huxley + Calcium

Calcium plays a critical role in neuronal processes

Before considering neuron/astrocyte dynamics we should first explore the role of calcium in purely neuronal dynamics



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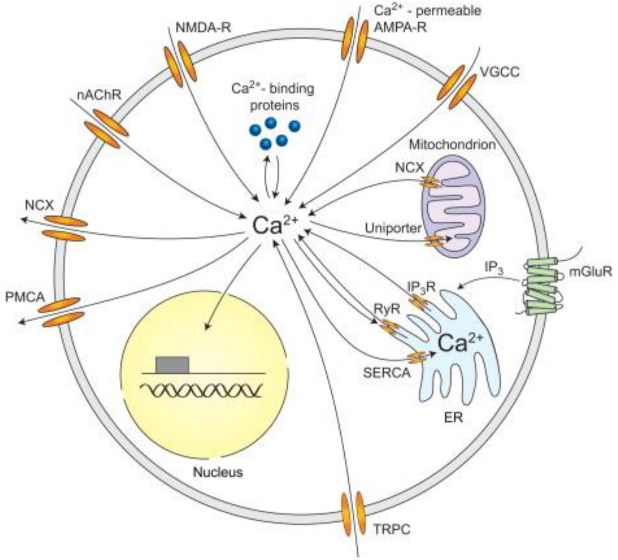
\begin{aligned}
C\dot{V} &= \overbrace{-\bar{g}_K n^4 (V - V_K) - \bar{g}_{Na} m^3 h (V - V_{Na}) - g_l (V - V_l) + I_{app}}^{\text{Hodgkin-Huxley dynamics}} \overbrace{+ I_{Ca} + I_{pump}}^{\text{Calcium currents}} \\
\dot{n} &= \alpha_n(V)(1-n) - \beta_n(V)n \\
\dot{m} &= \alpha_m(V)(1-m) - \beta_m(V)m \\
\dot{h} &= \alpha_h(V)(1-h) - \beta_h(V)h,
\end{aligned}
$$



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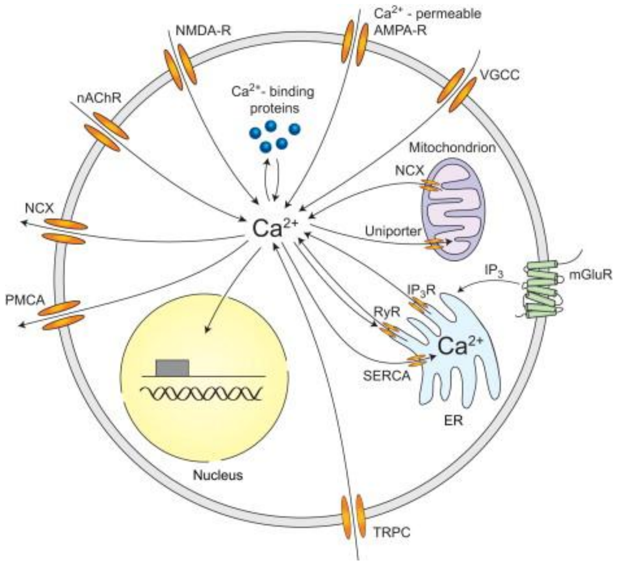
\dot{h} &= \alpha_h(V)(1-h) - \beta_h(V)h,
\end{aligned}$$

Where, like the other currents, the calcium current obeys Ohm's law

$$I_{Ca} = -\bar{g}_{Ca} d^a (V - V_{Ca})$$



Reduced HH+Calcium

The standard reduction techniques are used

The calcium channel dynamics are similar to that of the potassium channel

Magically choose d=3

$$\begin{aligned} C\dot{V} &= -\bar{g}_K n^4 (V - V_K) - \bar{g}_{Na} m_\infty(V)^3 (0.89 - 1.1n)(V - V_{Na}) - g_l(V - V_l) + I_{app} \\ &\quad -\bar{g}_{Ca} n^3 (V - V_{Ca}) + I_{pump} \\ \dot{n} &= \alpha_n(V)(1-n) - \beta_n(V)n \end{aligned}$$

Reduced HH+Ca Dynamics

Back to XPP