Computational Neuroscience Group

Calcium Enhanced Spiking Models

Nathan Crock
Motivation
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- Ask what is memory? How do we learn?
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- **Identify** neuron/synapse as the functional unit of the brain
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- **Ask** what is memory? How do we learn?
- **Identify** neuron/synapse as the functional unit of the brain
- **Understand** that astrocytes modulate synaptic activity
- **Hypothesize** answers may be found in tripartite dynamics
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 neurotransmitters 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.
Goals
Explore... Mathematical techniques for model reduction
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Explore... The role of calcium in neuronal dynamics
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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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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

4 Equations

18 Parameters

\[
\begin{align*}
C \frac{dv}{dt} &= I - g_{Na} m^3 h (V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) \\
\frac{dm}{dt} &= a_m(V)(1 - m) - b_m(V) m \\
\frac{dh}{dt} &= a_h(V)(1 - h) - b_h(V) h \\
\frac{dn}{dt} &= a_n(V)(1 - n) - b_n(V) n \\
a_m(V) &= 0.1 \frac{(V + 40)}{(1 - \exp(-(V + 40)/10))} \\
b_m(V) &= 4 \exp(-(V + 65)/18) \\
a_h(V) &= 0.07 \exp(-(V + 65)/20) \\
b_h(V) &= 1/(1 + \exp(-(V + 35)/10)) \\
a_n(V) &= 0.01 \frac{(V + 55)}{(1 - \exp(-(V + 55)/10))} \\
b_n(V) &= 0.125 \exp(-(V + 65)/80)
\end{align*}
\]
Hodgkin-Huxley Dynamics
Hodgkin-Huxley Dynamics

4 ODES and 18 Parameters
Hodgkin-Huxley Dynamics

4 ODES and 18 Parameters

Too much going on to tractably intuit dynamics
Hodgkin-Huxley Dynamics

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Need to reduce the model...
Hodgkin-Huxley Dynamics

4 ODES and 18 Parameters

Too much going on to tractably intuit dynamics

Need to reduce the model...

How?
Hodgkin-Huxley Reduction
Hodgkin-Huxley Reduction

Model reduction requires mathematical “tricks” which leverage details about its dynamics.
Hodgkin-Huxley Reduction

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

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

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...
First we observe...

m is faster than both \( h \) and \( n \)
First we observe...

\[ \frac{dn}{dt} = \alpha_n (1-n) - \beta_n n \]
\[ \frac{dm}{dt} = \alpha_m (1-m) - \beta_m m \]
\[ \frac{dh}{dt} = \alpha_h (1-h) - \beta_h h \]

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

\[ j_\infty (V) \equiv \frac{\alpha_j (V)}{\alpha_j (V) + \beta_j (V)} \]
\[ \tau_j (V) \equiv \frac{1}{\alpha_j (V) + \beta_j (V)} \]
Timescale Analysis

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

Now we deal with $h$ and $n$
Correlation of Variables

Now we deal with $h$ and $n$
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
Hodgkin-Huxley + Calcium

Calcium plays a critical role in neuronal processes
Hodgkin-Huxley + Calcium

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

\[
\begin{align*}
\dot{V} &= -g_K n^4 (V - V_K) - g_Na m^3 h (V - V_{Na}) - g_l (V - V_l) + I_{app} + I_{Ca} + I_{pump} \\
n &= \alpha_n(V)(1-n) - \beta_n(V)n \\
m &= \alpha_m(V)(1-m) - \beta_m(V)m \\
h &= \alpha_h(V)(1-h) - \beta_h(V)h,
\end{align*}
\]
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.

\[
C\dot{V} = -g_K n^4 (V - V_K) - g_{Na} m^3 h (V - V_{Na}) - g_l (V - V_l) + I_{app} + I_{Ca} + I_{pump}
\]

\[
\dot{n} = \alpha_n(V)(1-n) - \beta_n(V)n
\]

\[
\dot{m} = \alpha_m(V)(1-m) - \beta_m(V)m
\]

\[
\dot{h} = \alpha_h(V)(1-h) - \beta_h(V)h,
\]

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

\[
I_{Ca} = -g_{Ca}d^a (V - V_{Ca})
\]
The standard reduction techniques are used

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

Magically choose $d=3$

\[
\begin{align*}
C\dot{V} & = -\tilde{g}_K n^4 (V - V_K) - \tilde{g}_{Na} m_\infty(V)^3 (0.89 - 1.1n) (V - V_{Na}) - g_l(V - V_i) + I_{app} \\
& - \tilde{g}_{Ca} n^3 (V - V_{Ca}) + I_{pump} \\
\dot{n} & = \alpha_n(V)(1 - n) - \beta_n(V)n
\end{align*}
\]
Reduced HH+Ca Dynamics

Back to XPP