Basics of Computational Neuroscience: Neurons and Synapses to Networks

Bruce Graham
Computing Science & Mathematics
Faculty of Natural Sciences
University of Stirling
Scotland, U.K.
Useful Book

PRINCIPLES of COMPUTATIONAL MODELLING in NEUROSCIENCE

Authors: David Sterratt, Bruce Graham, Andrew Gillies, David Willshaw
Cambridge University Press, 2011

Companion website at: compneuroprinciples.org
Levels of Detail

- Whole brain
- Brain nuclei
  - Lumped models
- Networks of neurons
- Single neurons
- Subcellular

(Fig. 1.3 pg 7)
Why Model a Neuron?

• Response to inputs from other neurons?
  – Membrane potential
  – Intrinsic membrane properties
  – Synaptic signal integration

Computing Science & Maths, Stirling U.K.
5th Baltic-Nordic School on Neuroinformatics, Kaunas, 2017
Neurons

- Neurons come in many shapes and sizes

(Dendrites, Hausser et al (eds))
Compartmental Modelling

Membrane potential

(Fig. 4.1 pg 73)
Electrical Potential of a Neuron

- Differences in ionic concentrations
- Transport of ions
  - Sodium (Na)
  - Potassium (K)

(Fig. 2.1 pg 14)

(Fig. 2.13 pg 31)
A Model of Passive Membrane

- A resistor and a capacitor
- Kirchhoff’s current law

\[ C_m \frac{dV}{dt} = \frac{E_m - V}{R_m} + \frac{I_e}{a}. \]

(Fig. 2.14 pg 32)
A Length of Membrane

- Membrane *compartments* connected by intracellular resistance

(Fig. 2.15 pg 36)

- Compartmental modelling equation

\[
C_m \frac{dV_j}{dt} = \frac{E_m - V_j}{R_m} + \frac{d}{4R_a} \left( \frac{V_{j+1} - V_j}{l^2} + \frac{V_{j-1} - V_j}{l^2} \right) + \frac{I_{c,j}}{\pi dl}.
\]  

(2.23)
The Action Potential

• Output signal of a neuron
  – Rapid change in membrane potential
  – Flow of Na and K ions

(Fig. 3.1 pg 47)
Action Potential Model

- Empirical model by Hodgkin and Huxley, 1952
  - Voltage-dependent Na and K channels

\[
\frac{dV}{dt} = \frac{1}{C_m} \left( -g_L(V - E_L) - g_{Na}m^3h(V - E_{Na}) - g_{K}n^4(V - E_{K}) + I \right)
\]

(Fig. 3.1 pg 47)

(Fig. 3.2 pg 50)
Time Varying Conductances

- K conductance: $n$ a function of time and voltage

\[ I_K = \overline{g}_K n^4 (V - E_K) , \]

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

\[ \alpha_n = 0.01 \frac{V + 55}{1 - \exp(-(V + 55)/10)} , \]

\[ \beta_n = 0.125 \exp(-(V + 65)/80) . \]

(Fig. 3.12 pg 63)
Complete Action Potential Model

\[ C_m \frac{dV}{dt} = -g_L(V - E_L) - g_{Na}m^3h(V - E_{Na}) - g_Kn^4(V - E_K). \]

Sodium activation and inactivation gating variables:

\[ \frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m, \quad \frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h, \]

\[ \alpha_m = 0.1 \frac{V + 40}{1 - \exp(-(V + 40)/10)}, \quad \alpha_h = 0.07 \exp(-(V + 65)/20), \]

\[ \beta_m = 4 \exp(-(V + 65)/18), \quad \beta_h = \frac{1}{\exp(-(V + 35)/10) + 1}. \]

Potassium activation gating variable:

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

\[ \alpha_n = 0.01 \frac{V + 55}{1 - \exp(-(V + 55)/10)}, \quad \beta_n = 0.125 \exp(-(V + 65)/80). \]

Parameter values (from Hodgkin and Huxley, 1952d):

\[ C_m = 1.0 \ \mu F cm^{-2} \]

\[ E_{Na} = 50 \ mV \quad g_{Na} = 120 \ mS cm^{-2} \]

\[ E_K = -77 \ mV \quad g_K = 36 \ mS cm^{-2} \]

\[ E_L = -54.4 \ mV \quad g_L = 0.3 \ mS cm^{-2} \]

Box 3.5 pg 61

(Fig. 3.10 pg 60)
Propagating Action Potential

(Fig. 3.15 pg 65)
Families of Ion Channels

- Sodium (Na): fast, persistent
- Potassium (K): delayed rectifier, A, M
- Calcium (Ca): low and high voltage activated
  - L, N, R, T
- Calcium-activated potassium: sAHP, mAHP
- Non-specific cation: H

Around 140 different voltage-gated ion channel types. A neuron may express 10 to 20 types.
Potassium A-current: $K_A$

- Different characteristics from delayed rectifier: $K_{DR}$
- Low threshold activating / inactivating current

\[
\frac{dV}{dt} = -g_{Na}(V-E_{Na}) - g_K(V-E_K) - g_A(V-E_A) - g_L(V-E_L).
\]

\[
I_A = g_A(V-E_A), \quad g_A = \bar{g}_A a^3 b,
\]

\[
a_\infty = \left( \frac{0.0761 \exp \left( \frac{V+99.22}{31.84} \right)}{1 + \exp \left( \frac{V+6.17}{28.93} \right)} \right)^{\frac{1}{3}}, \quad \tau_a = 0.3632 + \frac{1.158}{1 + \exp \left( \frac{V+60.96}{20.12} \right)},
\]

\[
b_\infty = \frac{1}{\left(1 + \exp \left( \frac{V+58.3}{14.54} \right)\right)^4}, \quad \tau_b = 1.24 + \frac{2.678}{1 + \exp \left( \frac{V-55}{16.027} \right)}.
\]
One Effect of A-current

- **Type I:** with $K_A$
  - Steady increase in firing frequency with driving current

- **Type II:** without $K_A$
  - Sudden jump to non-zero firing rate
Large Scale Neuron Model

Hippocampal pyramidal cell (PC)
Detailed Pyramidal Cell Model

- 183 electrical compartments
- Heterogeneous ion channel population

(Poirazzi & Pissadaki, in Hippocampal Microcircuits)
Pyramidal Cell Model Responses

- Reproduces somatic and dendritic current injection experimental results
  - Sodium spiking with distance

(Poirazzi & Pissadaki)
Varying Levels of Detail

- Capture essential features of morphology
Reduced Pyramidal Cell Model

- 2-compartment model
  - Pinsky & Rinzel (1994)

- Captures essence of PC behaviour
  - Single spikes and bursting

\[
\begin{align*}
C_m \frac{dV_s}{dt} &= -g_L(V_s - E_L) - g_{Na}(V_s - E_{Na}) - g_{DR}(V_s - E_K) \\
&\quad + \frac{g_c}{p} (V_d - V_s) + \frac{l_s}{p} \\
C_m \frac{dV_d}{dt} &= -g_L(V_d - E_L) - g_{Ca}(V_d - E_{Ca}) - g_{AHP}(V_d - E_K) - g_C(V_d - E_K) \\
&\quad + \frac{g_c}{1-p} (V_s - V_d) + \frac{l_{syn}}{1-p}.
\end{align*}
\]
Pinsky-Rinzel Model in Action

• Behaviour depends on
  – Compartment coupling strength (g)
  – Magnitude of driving current (I)

(Fig. 8.2 pg 201)
Simple Spiking Neuron Models

- Simplified equations for generating action potentials (APs)
  - FitzHugh-Nagumo; Kepler; Morris-Lecar
  - 2 state variables: voltage plus one other
    - H-H model contains 4 variables: V, m, h, n
- Simple spiking models that DO NOT model the AP waveform
  - Integrate-and-fire models
Integrate-and-Fire Model

- RC circuit with spiking and reset mechanisms
  - When $V$ reaches a threshold
    - A spike (AP) event is “signalled”
    - Switch closes and $V$ is reset to $E_m$
    - Switch remains closed for refractory period

\[
C_m \frac{dV}{dt} = -\frac{V - E_m}{R_m} + I
\]
I&F Model Response

- Response to constant current injection
  - No refractory period

(Fig. 8.5 pg 205)
More Realistic I&F Neurons

• Basic I&F model does not accurately capture the diversity of neuronal firing patterns
  – Adaptation of interspike intervals (ISIs) over time

$$\frac{dg_{\text{adapt}}}{dt} = -\frac{g_{\text{adapt}}}{\tau_{\text{adapt}}} \quad \text{and} \quad I_{\text{adapt}} = g_{\text{adapt}}(V - E_m).$$

– Precise timing of AP initiation
– Noise
Modelling AP Initiation

• Basic I&F is a poor model of the ionic currents near AP threshold

• Quadratic I&F

\[ C_m \frac{dV}{dt} = - \frac{(V - E_m)(V_{\text{thresh}} - V)}{R_m(V_{\text{thresh}} - E_m)} + I. \]

• Exponential I&F

\[ C_m \frac{dV}{dt} = - \left( \frac{V - E_m}{R_m} - \frac{\Delta_T}{R_m} \exp \left( \frac{V - V_T}{\Delta_T} \right) \right) + I, \]

(Fig. 8.9 pg 214)
The Izhikevich Model

- Quadratic I&F plus dynamic recovery variable

\[
\begin{align*}
\frac{dV}{dt} &= k(V - E_m)(V - V_{\text{thresh}}) - u + I \\
\frac{du}{dt} &= a(b(V - E_m) - u)
\end{align*}
\]

if $V \geq 30\text{mV}$, then
\[
\begin{cases}
V \text{ is reset to } c \\
u \text{ is reset to } u + d,
\end{cases}
\]

(Fig. 8.10 pg 215)
Neural Connections: Synapses

(Fig. 7.1 pg 173)
Synaptic Conductance

• 3 commonly used simple waveforms
  a) Single exponential
     \[ g_{syn}(t) = \overline{g}_{syn} \exp \left( -\frac{t-t_s}{\tau} \right) \]
  b) Alpha function
     \[ g_{syn}(t) = \overline{g}_{syn} \frac{t-t_s}{\tau} \exp \left( -\frac{t-t_s}{\tau} \right) \]
  c) Dual exponential
     \[ g_{syn}(t) = \overline{g}_{syn} \frac{\tau_1 \tau_2}{\tau_1 - \tau_2} \left( \exp \left( -\frac{t-t_s}{\tau_1} \right) - \exp \left( -\frac{t-t_s}{\tau_2} \right) \right) \]

– Current: \[ I_{syn}(t) = g_{syn}(t)(V(t)-E_{syn}) \]

(Fig. 7.2 pg 174)
Neuronal Firing Patterns

- Neuronal firing activity is often irregular
- How does this arise?
  - Intrinsic or network property?
  - Balance of excitation and inhibition
Model using I&F Neuron

- I&F neuron driven by 100Hz Poisson spike trains
  - Via excitatory and inhibitory synapses
- Alter balance of excitation and inhibition

300 Excitation + 150 inhibition

18 Excitation only

Irregular firing

More regular

(Fig. 8.6 pg 209)
Network Model with I&F Neurons

- Randomly connected network of 80% excitatory and 20% inhibitory neurons
- External excitatory drive to all neurons
  - Noisy Poisson spike trains
Network Model: Random Firing

(a)  (b)  (c)  (d)  (e)
Rhythm Generation

- E-I oscillator
  - Reciprocally coupled *excitatory* and *inhibitory* neurons
  - Constant drive to excitatory neuron
  - Delay around the loop
Learning in the Nervous System

• ANNs “learn” by adapting the connection weights
  – Different learning rules
• Real chemical synapses do change their strength in response to neural activity
  – Short-term changes
    • Milliseconds to seconds
    • Not classified as “learning”
  – Long term potentiation (LTP) and depression (LTD)
    • Changes that last for hours and possibly lifetime
• Evidence that LTP/LTD corresponds to “learning”
Hebbian Learning

• Hypothesis by Donald Hebb, “The Organization of Behaviour”, 1949
  – “When an axon of cell A excites cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells so that A’s efficiency, as one of the cells firing B, is increased.”
Associative Learning: Hebbian

• Increase synaptic strength if both pre- and postsynaptic neurons are active: LTP

• Decrease synaptic strength when the pre- or postsynaptic neuron is active alone: LTD
Example: Associative Memory

- Autoassociation and heteroassociation
- Hebbian learning of weights
- Content addressable
Heteroassociative Memory

- Associations between binary patterns
- Hebbian learning: $\Delta w_{ij} = p_i \cdot p_j$
- Store multiple patterns
Memory Recall

- Weighted synaptic input from memory cue
- Threshold setting on output

(Fig. 9.5 pg 235)
Multistep Memory Recall

- Autoassociative recurrent network

(Fig. 9.6 pg 236)

Computing Science & Maths, Stirling U.K.

5th Baltic-Nordic School on Neuroinformatics, Kaunas, 2017
Spiking Associative Network

• How could this be implemented by spiking neurons?
  – Sommers and Wennekers (2000, 2001)

• 100 Pyramidal cell recurrent network
  – Pinsky-Rinzel 2-compartment PC model
  – E connections determined by predefined binary Hebbian weight matrix that sets AMPA conductance
  – All-to-all fixed weight inhibitory connections

• Tests autoassociative memory recall
Spiking Associative Network

- Pattern is 10 active neurons out of 100
- 50 random patterns stored
- 4 active neurons as recall cue
Cued Recall in Spiking Network

- **Cue:** 4 of 10 PCs in a stored pattern receive constant excitation
- **Network fires with gamma frequency**
- **Pattern is active cells on each gamma cycle**
- **Timing and strength of inhibition**

(Fig. 9.10 pg 253)
Complicated Neural Circuits

- CA1 region of hippocampus

(Klausberger & Somogyi, 2008)
To Follow…

- **PRACTICAL WORK: Simulating neurons and neural networks with the NEURON software:**
  1. Frequency-Input Current (F-I) Firing Curve of a Neuron
     - 1. F-I curve of a basic neuron
     - 2. F-I curve types I and II
  2. Electrical activity in a CA1 Pyramidal Cell
  3. Simple Excitation-Inhibition (E-I) Oscillator
  4. Excitation-Inhibition Balance
     - 1. Single I&F Neuron
     - 2. Network of I&F Neurons
  5. STDP in Action
     - 1. Phase precession of spike timing
     - 2. Sequence learning
  6. Associative Memory in a Network of Spiking Neurons