Basics of Computational Neuroscience: Neurons and Synapses to Networks

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Useful Book

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

Neural Networks

- Networks of complex neurons
- Pulse train signals (action potentials or spikes)
- Dynamic connection weights
Complicated Neural Circuits

- CA1 region of hippocampus

(Klausberger & Somogyi, 2008)

Neurons

- Neurons come in many shapes and sizes

(Dendrites, Hausser et al (eds))
Why Model a Neuron?

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

Compartmental Modelling

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

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

A Model of Passive Membrane

- A resistor and a capacitor
- Kirchhoff’s current law
A Length of Membrane

- Membrane *compartments* connected by intracellular resistance

![Diagram of membrane compartments](image)

- Compartamental modelling equation

\[
C_m \frac{dV_i}{dt} = \frac{E_m - V_i}{R_m} + \frac{d}{4Ra} \left( \frac{V_{j+1} - V_j}{I^2} + \frac{V_j - V_{j-1}}{I^2} \right) + I_{ext}. \quad (2.23)
\]

(Fig. 2.15 pg 36)

The Action Potential

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

![Diagram of action potential](image)

(Fig. 3.1 pg 47)
**Action Potential Model**

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

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

(Fig. 3.1 pg 47)

**Time Varying Conductances**

- K conductance: \( n \) a function of time and voltage

\[
I_K = g_R n^4 (V-E_K),
\]

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

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

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

(Fig. 3.12 pg 63)
Complete Action Potential Model

Box 3.5 pg 61

Propagating Action Potential

(Fig. 3.10 pg 60)

(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.

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**Potassium A-current: \(K_A\)**

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

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

\[
I_A = g_A(V-E_A),
\]

\[
a = \left( \frac{0.0761 \exp \left( \frac{V-60.62}{20.35} \right)}{1 + \exp \left( \frac{V-60.62}{20.35} \right)} \right),
\]

\[
g_A = \bar{g}_A a b.
\]

\[
\tau_a = 0.3632 + \frac{1.158}{1 + \exp \left( \frac{V-60.62}{26.02} \right)}
\]

\[
b = \left( 1 + \exp \left( \frac{V-60.62}{26.02} \right) \right),
\]

\[
\tau_b = 1.24 + \frac{2.678}{1 + \exp \left( \frac{V-60.62}{26.02} \right)}.
\]
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

Pyramidal Cell Model Responses
• Reproduces somatic and dendritic current injection experimental results
  – Sodium spiking with distance

(Poirazzi & Pissadaki, in Hippocampal Microcircuits)
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
Pinsky-Rinzel Model in Action

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

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

\[
C \frac{dV}{dt} = -\frac{V - E_m}{R_m} + I
\]

**I&F Model Response**

- Response to constant current injection
  - No refractory period

(Fig. 8.4 pg 204) (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
  \[
  C_m \frac{dV}{dt} = -\frac{(V - E_m - \Delta T \exp\left(\frac{V - V_T}{\Delta T}\right))}{R_m} + I,
  \]
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 \( V \) is reset to \( c \)

\( u \) is reset to \( u + d \)

Neural Connections: Synapses

(Fig. 7.1 pg 173)
**Synaptic Conductance**

- 3 commonly used simple waveforms
  a) Single exponential
     \[ g_{syn}(t) = g_{syn} \exp \left( \frac{t - t_i}{\tau} \right) \]
  b) Alpha function
     \[ g_{syn}(t) = g_{syn} \frac{t - t_i}{\tau} \exp \left( \frac{t - t_i}{\tau} \right) \exp \left( -\frac{t - t_i}{\tau} \right) \]
  c) Dual exponential

- 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

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**Computing Science & Maths, Stirling U.K.**

3rd Baltic-Nordic Summer School on Neuroinformatics, June 2015
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

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

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

  ![Diagram](image)

- Decrease synaptic strength when the pre- or postsynaptic neuron is active alone: LTD

  ![Diagram](image)

**Example: Associative Memory**

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

![Images](image)
**Heteroassociative Memory**

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

**Memory Recall**

- Weighted synaptic input from memory cue
- Threshold setting on output
Multistep Memory Recall

- Autoassociative recurrent network

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)
To Follow…

• PRACTICAL WORK: Simulating neurons and neural networks with NEURON
• Plasticity in the nervous system
  – Spike-time-dependent plasticity (STDP)
• Other scales (spatial and temporal) to model
• Other signals
  – Extracellular field potentials