Computing in carbon

Basic elements of neuroelectronics

-- membranes
-- ion channels
-- wiring

Elementary neuron models

-- conductance based
-- modelers’ alternatives

Wiring neurons together

-- synapses
-- long term plasticity
-- short term plasticity

Wires

-- signal propagation
-- processing in dendrites
Equivalent circuit model of a neuron
Closeup of a patch on the surface of a neuron
The passive membrane

Ohm’s law: $V = I_R R$

Capacitor: $C = \frac{Q}{V}$

Kirchhoff: $I_R + I_C + I_{ext} = 0$

$C \frac{dV}{dt} = -\frac{V}{R} - I_{ext}$
Movement of ions through ion channels

Energetics: $qV \sim k_B T$

$V \sim 25\text{mV}$
Ions move down their concentration gradient until opposed by electrostatic forces.

Nernst: \( E = \frac{k_B T}{zq} \ln \frac{[\text{inside}]}{[\text{outside}]} \)
Each ion has an independent circuit path

Different ion channels have associated conductances.

A given conductance tends to move the membrane potential toward the equilibrium potential for that ion

\[ \begin{align*}
E_{Na} & \sim 50 \text{mV} \quad \text{depolarizing} \\
E_{Ca} & \sim 150 \text{mV} \quad \text{depolarizing} \\
E_{K} & \sim -80 \text{mV} \quad \text{hyperpolarizing} \\
E_{Cl} & \sim -60 \text{mV} \quad \text{shunting}
\end{align*} \]

\[ V > E \rightarrow \text{positive current will flow outward} \]

\[ V < E \rightarrow \text{positive current will flow inward} \]

\[ V \rightarrow \text{more polarized} \]
Parallel paths for ions to cross membrane

Several $I-V$ curves in parallel:

New equivalent circuit:
Neurons are excitable
Excitability arises from nonlinearity in ion channels

- Voltage dependent
- Transmitter dependent (synaptic)
- Ca dependent
The ion channel is a complex molecular machine

K channel: open probability increases when depolarized

\[ n \text{ describes a subunit} \]
\[ n \text{ is open probability} \]
\[ 1 - n \text{ is closed probability} \]

Transitions between states occur at voltage dependent rates

\[ \alpha_n(V) \quad C \rightarrow O \]
\[ \beta_n(V) \quad O \rightarrow C \]

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

Persistent conductance
Transient conductances

Gate acts as in previous case

Additional gate can block channel when open

\[ P_{Na} \sim m^3h \]

*m* is activation variable

*h* is inactivation variable

*m* and *h* have opposite voltage dependences:
- Depolarization increases *m*, activation
- Hyperpolarization increases *h*, deactivation
We can rewrite:

\[ \tau_n(V) \frac{dn}{dt} = n_\infty(V) - n \]

where

\[ \tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)} \]

\[ n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)} \]
Activation and inactivation dynamics
Putting it together

Ohm’s law:  \( V = I R \)  
and Kirchhoff’s law

\[
-C_m \frac{dV}{dt} = \sum_i g_i (V - E_i) + I_e
\]

- Capacitative current
- Ionic currents
- Externally applied current
The Hodgkin-Huxley equation

\[ C_m \frac{dV}{dt} = - \sum_i g_i (V - E_i) - I_e \]

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

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

\[ \frac{dm}{dt} = \alpha_m (V)(1 - m) - \beta_m (V)m \]

\[ \frac{dh}{dt} = \alpha_h (V)(1 - h) - \beta_h (V)h \]
Activation and inactivation dynamics
Dynamics of a spike

\[ V \text{ (mV)} \]

\[ h_\infty, m_\infty, n_\infty \]

\[ E_K, E_Na \]

\[ V_{m}(\mu A/\text{mm}^2) \]

\[ t (\text{ms}) \]
Ion channel stochasticity
A microscopic stochastic model for ion channel function

approach to macroscopic description
Different from the continuous model:
interdependence between inactivation and activation
transitions to inactivation state 5 can occur only from 2, 3 and 4
$k_1$, $k_2$, $k_3$ are constant, not voltage dependent
The integrate-and-fire model

Like a passive membrane:

\[ C_m \frac{dV}{dt} = -g_L(V - E_i) - I_e \]

but with the additional rule that

when \( V \rightarrow V_T \), a spike is fired

and \( V \rightarrow V_{\text{reset}} \).

\( E_L \) is the resting potential of the “cell”.

![Graph showing integrate-and-fire model output](image)
The spike response model

Kernel $f$ for subthreshold response $\leftarrow$ replaces leaky integrator
Kernel for spikes $\leftarrow$ replaces “line”

- determine $f$ from the linearized HH equations
- fit a threshold
- paste in the spike shape and AHP

Gerstner and Kistler
The generalized linear model

- general definitions for $k$ and $h$
- robust maximum likelihood fitting procedure

Truccolo and Brown, Paninski, Pillow, Simoncelli
Building circuits

Eickholt lab, Kings College London
Synapses

Signal is carried chemically across the synaptic cleft
Synaptic signalling
Synaptic signalling
Synaptic signalling
Synaptic signalling
Synaptic signalling
Synaptic signalling
Synaptic signalling
Synaptic signalling

Neurotransmitter: glutamate
AMPA receptor
NMDA receptor
Cation (Na)
Ca
Requires pre- and post-synaptic depolarization
Connection strength

\[ w = npq \]
Long-term potentiation

Wiki commons
Long-term depression

Ronesi and Lovinger, J Physiol 2005
Empirical model

\[
\frac{dW_i(t)}{dt} = \frac{1}{\tau([Ca^{2+}]_i)} \left( \Omega([Ca^{2+}]_i) - W_i \right)
\]

Shouval, .., Cooper, Biological Cybernetics 2002
Hebbian plasticity

\[ \Delta w_{ij} = \eta x_i x_j \]

Hebb, 1949
Requires pre- and post-synaptic depolarization

Coincidence detection, Hebbian
Spike-timing dependent plasticity

A. LTP  
   LTD  
   $t_{post} - t_{pre}$

B. LTP  
   LTD  
   $t_{post} - t_{pre}$

C. LTP  
   LTD  
   $t_{post} - t_{pre}$

D. LTP  
   LTD  
   $t_{post} - t_{pre}$

E. LTP  
   LTD  
   $t_{post} - t_{pre}$
Short-term synaptic plasticity

Depression

Facilitation
Modeling short-term synaptic plasticity

\[ \frac{dR}{dt} = \frac{I}{\tau_{rec}} \]

\[ \frac{dE}{dt} = -\frac{E}{\tau_{\text{inact}}} + U_{SE}R \delta(t - t_{AP}) \]

\[ I = 1 - R - E, \]

Tsodyks and Markram, 1997
Modeling short-term synaptic plasticity

Tsodyks and Markram, 1997
Gap junctions

Echevaria and Nathanson