Computations in single Nerve cells I

• Nerve cells
• Ion transport and membrane potential
• Action Potential
• Ion currents, voltage and time dependent conductance
Nerve cells (Neurons)

- separate entities (Ramon y Cajal, Nobel Laureate 1906)
- connected by synapses (Sherington and Adrian, Nobel Laureates, 1932)
- different types of neurons with different functionality

Optic tectum (sparrow), drawing by Cajal
Neurons

• building blocks of nervous system

• central nervous system (CNS) contains about $10^{11} = 100$ billion neurons

• information processing within a neuron: electrical.

• information processing between neurons: (mostly) chemical (exception: gap junctions)
Sketch of a neuron

http://www.usm.maine.edu/psy/broida/101/neuron.JPG
Information processing in a neuron

Squid Giant Axon

- A membrane separates intracellular space from extracellular space.
Membrane Potential

- Membrane: Lipid bilayer (good insulator)
- Ion-channels (passive) and Ion-pumps (active transport)
- Concentration of ions is different on the inside and on the outside

Electrical potential across membrane

http://speakeasies.bizgraphics/membrane_as.jpg
Ion pump

• Na+, K+ - ATPase. Enzyme.
  (J. Skou, Nobel Laureate 1997)

• sodium (Na+) out; potassium (K+) in.

• driven by phosphorylation


Nernst equation

- Probability that a molecule has a state of energy $E$ (Boltzmann):

$$p(E) \sim e^{-E/kT}$$

- Energy of charged particle (charge $q$, potential $u$, location $x$)

$$E(x) = qu(x)$$

- Lots of ions -> interpret probability as ion density, $n(x)$
Nernst Equation

- relation between ion density at point $x_1$ and $x_2$:

$$\frac{n(x_1)}{n(x_2)} = e^{-\frac{q}{kT}[u(x_1) - u(x_2)]}$$

- therefore a difference in ion concentration generates a difference in potential:

$$u(x_1) - u(x_2) = \frac{kT}{q} \ln \left[ \frac{n(x_2)}{n(x_1)} \right]$$
Resting potential $E_{\text{rest}}$

Reversal potential of sodium: $E_{\text{Na}}$
Reversal potential of potassium: $E_{\text{K}}$

$E_{\text{K}} = -82 \text{ mV}$  $E_{\text{Na}} = +45 \text{ mV}$

http://www.genesis-sim.org/GENESIS/cnslecs/HHcompt.gif
(A) Capillary tube filled with sea water inside axon -- electrode used to measure potential difference across membrane (after Hille 1984)

(B) Membrane voltage $V_m$ (in mV) during action potential. Time indicated by 500 Hz sine wave on oscilloscope screen. (Adapted from Hodgkin and Huxley (1939))

(From: “The Book of GENESIS”, Internet edition (C) 2003 James M. Bower and David Beeman)
Ionic currents

- Voltage clamp experiment: Hold voltage at constant value -- measure ionic currents.

- Ohm’s Law: \( I = g \cdot V \) (\( I \): current, \( g \): conductance, \( V \): voltage)

- \( V = V_{\text{membrane}} - V_{\text{reversal}} \)

\[
I_{Na} = g_{Na}(V_{m} - E_{Na})
\]

\[
I_{K} = g_{K}(V_{m} - E_{K})
\]

http://physioweb.med.uvm.edu/cardiacep/EP/handh.htm
Ionic currents identified:

- Sodium (Na+): inward movement of positive ions -- “inward” or negative current
- Potassium (K+): outward current
- Conductance is a function of time and of the voltage
- “Leak” current (voltage independent)
Membrane acts as capacitor

http://www.genesis-sim.org/GENESIS/cnslecs/HHcompt.gif
Homework

• Read: http://diwww.epfl.ch/~gerstner/SPNM/
• Chapter 2
Computations in single Nerve cells II

- Biophysical model due to Hodgkin and Huxley
- Action Potential
- Computer simulations of neurons
Modeling the time and voltage dependence

- “Gating” variables describe the probability that an ion-channel is open
- Two gates for Na+ channel:
  - activation gate $m$ (opens fast)
  - inactivation gate $h$ (closes slowly)

http://physioweb.med.uvm.edu/cardiac.ep/EP/handh.htm
Probability of channel being open: $m^3h$
Conductance when channel is open: $G_{Na}$
Total conductance: $g_{Na} = m^3h \cdot G_{Na}$
Putting all currents together

- One gating variable $n$ for potassium $K^+$
- $Na^+$ current: $I_{Na} = m^3 h G_{Na}(V_m - E_{Na})$
- $K^+$ current: $I_K = n^4 G_K(V_m - E_K)$
- Leak current: $I_L = G_L(V_m - E_L)$
- Capacitive current: $I_C$ Input current: $I_{in}$

Conservation of charge gives us altogether:

$$I_{in}(t) = I_C(t) + I_{Na}(t) + I_K(t) + I_L(t)$$
Dynamics

- The gating variables are time dependent:

\[
\frac{dx}{dt} = -\frac{1}{\tau_x(V_m)} (x - x_0(V_m))
\]

- for fixed voltage, they approach the value \(x_0(V_m)\) with time constant \(\tau_x(V_m)\)

- \(x\) stands for either \(m\), \(h\), or \(n\).

[Diagram A and B showing the gating variables as functions of voltage with different curves for \(m\), \(h\), and \(n\).]
**Voltage dynamics**

- Capacitive current
  \[ I_C = C \frac{dV_m}{dt} \]
- Total current
  \[ I_{in}(t) = I_C(t) + I_{Na}(t) + I_K(t) + I_L(t) \]
- Voltage change
  \[ \frac{dV_m}{dt} = \frac{1}{C} [I_{in}(t) - I_{Na}(t) - I_K(t) - I_L(t)] \]
Hodgkin Huxley
MODEL

• Four coupled differential equations:

\[
\frac{dV_m}{dt} = \frac{1}{C} \left[ I_{in}(t) - m^3(t)h(t)G_{Na}(V_m(t) - E_{Na}(t)) \right.
\left. - n^4(t)G_{K}(V_m(t) - E_{K}(t)) - G_{L}(V_m(t) - E_{L}(t)) \right]
\]

\[
\frac{dm}{dt} = -\frac{1}{\tau_m} \left( m - m_0(V_m(t)) \right)
\]

\[
\frac{dh}{dt} = -\frac{1}{\tau_h} \left( h - h_0(V_m(t)) \right)
\]

\[
\frac{dn}{dt} = -\frac{1}{\tau_n} \left( n - n_0(V_m(t)) \right)
\]
Input current

- Effects from other neurons add up in the dendritic arbor of the neuron. Another neuron fires an action potential - synaptic events - evoked post synaptic potentials (EPSPs)
Spike Generation

- Input current pulse depolarizes cell
- Conductance of sodium channel increases, because m increases
- Sodium ions flow into cell -> more depolarization
**Refractory period**

- the same input that causes a spike will not cause another spike for some time after the first spike
- cell is hyperpolarized -> need stronger current
- large proportion of ion channels is open right after spike -> membrane resistance reduced -> input current decays faster
The cool thing

- Now we can build computer models of neurons (Simulators: NEURON and GENESIS, both implement multi-compartmental models)

Movie: Effect of an input (NEURON) [http://www.neuron.yale.edu/neuron/demos/sizzle/distal.html](http://www.neuron.yale.edu/neuron/demos/sizzle/distal.html)
...and we can build silicon neurons (micro-chips)!

http://www.ini.unizh.ch/~giacomo/
We can build neural networks...

...we can even put many silicon neurons onto one micro chip, connect them with artificial synapses, and make this neural network, this “micro-brain” learn something!

To be continued...
Homework

• Next lecture: simplifications of H-H model

• Read: [http://diwww.epfl.ch/~gerstner/SPNM/](http://diwww.epfl.ch/~gerstner/SPNM/)
  • Chapter 4
  • What is an integrate-and-fire model?