Synapses & Dendritic Computation

Lecture 8
Neural Communication

- Synapse
  - Communication of information between neurons is accomplished by movement of chemicals across a small gap called the **synapse**
  - Synapses play a role in all the operations of the nervous system

- Flavors of synaptic transmission
  - Electrical Synapses or Gap Junctions
  - Chemical Synapses
Loewi’s Experiment - 1921

- Chemical transmission at synapses
  - Vagus nerve stimulation slowed heart1
  - Allowing fluid flow from chamber #1 into chamber #2 also slowed heart2 with some delay
  - Loewi hypothesized that electrical stimulation of the vagus nerve released a chemical "Vagusstoff" into the fluid of chamber #1 that flowed into chamber #2
Chemical Synapses

- **Direction of Information Flow**
  - In one direction: Neuron to target cell
  - First neuron = Presynaptic neuron
  - Target cell = Postsynaptic neuron
Types of Synapses

Axodendritic

Axosomatic

A xoaxonic

Dendrodendritic (not shown)
A Chemical Synapse
Sequence of events in chemical transmission (duration 0.5 – 2 ms)

- action potential conducted down the axon
- action potential invades terminal, opening of Ca\(^{2+}\) channels
- fusion of vesicle to membrane, exocytotic release of vesicle contents (time between influx of Ca\(^{2+}\) and transmitter release: 100 - 200 μs)
- diffusion of transmitter (~30 nm in 0.6 μs)
- gating of ion channels
- recycling of vesicles
Principles of Chemical Syntaptic Transmission

- Synaptic Vesicle (~50 nm)
- Voltage-dependent $Ca^{2+}$ channel
- Post-synaptic terminal

Axon Terminal

Synaptic Cleft (~20-40 nm)

Dendrite

Wikipedia, Synapses
Quantal Release of Neurotransmitters

1. Synaptic transmission is Stochastic

2. Each successful event is some product of a some unit event (or quanta)

Del Castillo and Katz; 1954
Quantal Release of Neurotransmitters

- If the probability of a single unit responding is ‘$p$’, and if each unit has an independent and equal ‘$p$’, then the mean number of units responding to each stimulus is given by: ‘$np$’

- Probability that $x$-units successfully contributing is given by the binomial distribution:

$$P(success = x) = \binom{n}{x} p^x (1 - p)^x$$

Problem: $n$ and $p$ are not known
Quantal Release of Neurotransmitters

If \( n \) is large (or \( p \) is small), then approximate the binomial distribution with Poisson distribution

\[
P(success = x) = \frac{\lambda^x e^{-\lambda}}{x!} \quad [\lambda = np]
\]

\( \lambda \) can be estimated as follows:

- mean amplitude of synaptic potential/mean amplitude of minimal synaptic potential, or,
- Count for failures (\( x=0 \))

\[
\lambda = \ln \frac{N}{P(success = 0; trials = N)}
\]
Quantal Release of Neurotransmitters

Neurotransmitters are released in small pockets called vesicles.

Del Castillo and Katz; 1954
Neurotransmitters

- **Amino acids**: Small organic molecules
  - e.g., Glutamate, Glycine, GABA

- **Amines**: Small organic molecules
  - e.g., Dopamine, Acetylcholine, Histamine

- **Peptides**: Short amino acid chains (i.e. proteins) stored in and released from secretory granules
  - e.g., Dynorphin, Enkephalins
**Post-synaptic Receptors**

- Neurotransmitters cross synaptic-cleft and can bind to two types of receptors:
  - Ionotropic (Ligand-gated ion channels; LGIC)
  - Metabotropic (G-protein coupled receptors; GPCR)
Post-synaptic Receptors

**Ionotropic**

- Contains a ligand-binding site
- A normally-closed ion channel that opens after binding with the neurotransmitter
- Contribute to fast changes in the membrane potential
Post-synaptic Receptors

- **Metabotropic**
  - G-protein coupled receptor
  - Secondary messenger involved
  - Slow postsynaptic processes (plays a role in synaptic plasticity)
NMDA Receptor
Synapses types

The potential change produced in the post-synaptic cell is called a "Post-Synaptic Potential" (PSP)

- when the influence of this potential is to increase firing, it is called an "Excitatory Post-Synaptic Potential" (EPSP)
- when the influence of this potential is to decrease firing, it is called an "Inhibitory Post-Synaptic Potential" (IPSP)
Excitatory Synapse
Inhibitory Synapse
Synapses types

- **Type I** – glutamergic synapses – usually on dendrites
- **Type II** – GABAergic synapses – usually on cell bodies
Temporal Summation

- A single nerve cell may receive up to 100,000 synapses
  - some of excitatory
  - some inhibitory

- Summation
  - the process whereby these inputs are added up by the cell body

- Temporal -summation of input from a single synapse over time
Spatial Summation

- A single nerve cell may receive up to 100,000 synapses
  - some of excitatory
  - some inhibitory

- Summation
  - the process whereby these inputs are added up by the cell body

- Spatial -summation of input from multiple synapses
**Electrical Synapses**

- **Gap junction**
  - Channel: Connexon- formed by six connexins
  - Cells are said to be “electrically coupled” when ions flow from cytoplasm to cytoplasm

*Neuroscience: Exploring the Brain, 3rd Ed, Bear, Connors, and Paradiso Copyright © 2007 Lippincott Williams & Wilkins*
Electrical Synapses
Electrical Synapse

Galarreta & Hestrin, 2001
# Electrical vs. Chemical Synapse

<table>
<thead>
<tr>
<th>Electrical Synapse</th>
<th>Chemical Synapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>simple primitive system</td>
<td>highly developed structure</td>
</tr>
<tr>
<td>often symmetrical, bidirectional</td>
<td>polarized, structurally and functionally</td>
</tr>
<tr>
<td>gap junction (connexins)</td>
<td>pre: active zone</td>
</tr>
<tr>
<td></td>
<td>post: postsynaptic density</td>
</tr>
<tr>
<td>very fast, no synaptic delay</td>
<td>slower, synaptic delay (~ 0.5 ms)</td>
</tr>
<tr>
<td>Ca2+-independent</td>
<td>transmitter release</td>
</tr>
<tr>
<td></td>
<td>requires Ca2+ influx</td>
</tr>
<tr>
<td>temperature-insensitive</td>
<td>temperature-sensitive</td>
</tr>
<tr>
<td>large synapse</td>
<td>thousands of small synapses</td>
</tr>
<tr>
<td>limited functions, usually excitatory</td>
<td>versatile: excitatory and Inhibitory</td>
</tr>
<tr>
<td>synchronized activity</td>
<td>specificity: point to point communication</td>
</tr>
</tbody>
</table>
Modeling Synapses

Voltage clamp data

I-V curve

What do these plots tell you?
Modeling Synapses

Voltage clamp data (Excitatory Synapse)

What do these plots tell you?
Synaptic input well capture by Ohm’s law
Equivalent circuit of a fast chemical synapse

\[ I_{\text{syn}} = g_{\text{syn}}(t)(V_m(t) - E_{\text{syn}}) \]

\[ g_{\text{syn}}(t) \quad C \quad R \quad V_m \]

Modified membrane patch equation with a synapse:

\[ C \frac{dV_m}{dt} + g_{\text{syn}}(t)(V_m - E_{\text{syn}}) + \frac{V_m - V_{\text{rest}}}{R} = 0 \]

Koch, Biophysics of Computation, Chapter 1
Equivalent circuit of a fast chemical synapse

Rewriting, we get:

\[ \tau \frac{dV_m}{dt} = -(1 + R g_{syn}(t)) V_m + R g_{syn}(t) E_{syn} + V_{rest} \]

\[ [\tau = RC] \]
Alpha Function

Synaptic input is usually approximated by an ‘alpha function’ of the form

\[ g_{syn}(t) = g_{peak} \cdot t \cdot \exp \left( \frac{-t}{t_{peak}} \right) \]
Multiple Synaptic Input

You will need to add synapses in parallel with the RC circuit to create additional synaptic components.

Since current add:

\[
C \frac{dV_m}{dt} = \sum_{i=0}^{n} g_{syn,i}(t)(E_{syn,i} - V_m) + \frac{V_{rest} - V_m}{R}
\]
Synaptic input is non-linear

- If we consider synaptic input to be slowly varying, we can approximate $g_{syn}(t) \sim g_{syn}$;
- Further, if $V_m \ll E_{syn}$, we can approximate synaptic input as a constant current source ($g_{syn}E_{syn}$)

Original:

$$\tau \frac{dV_m}{dt} = -(1 + Rg_{syn}(t))V_m + Rg_{syn}(t)E_{syn} + V_{rest}$$

New (slightly re-written):

$$\tau' \frac{dV}{dt} = -V + \frac{g_{syn}E_{syn}}{G_{in}}$$

$$\begin{bmatrix}
G_{in} = g_{syn} + \frac{1}{R} \\
\tau' = \frac{C}{G_{in}}
\end{bmatrix}$$
**Synaptic input is non-linear**

Solving ODE:

\[
\tau \frac{dV}{dt} = -V + \frac{g_{syn} E_{syn}}{G_{in}}
\]

\[
V_\infty = \frac{R_{g_{syn}} E_{syn}}{1 + R_{g_{syn}}}.
\]

**Case 1: Small synaptic input**

\[
R_{g_{syn}} \ll 1
\]

\[
V_\infty = R_{g_{syn}} E_{syn}
\]

*Scales linearly with synaptic input*

**Case 2: Large synaptic input**

\[
R_{g_{syn}} \gg 1
\]

\[
V_\infty = E_{syn}
\]

*Saturates at Synaptic reversal potential*
Shunting Inhibition

- Special case, when the synaptic reversal potential is equivalent to the resting membrane potential

\[ C \frac{dV}{dt} = g_e (E_e - V) - g_i V - \frac{V}{R} \]

Rewrite this to:

\[ \tau' \frac{dV}{dt} = -V + \frac{g_e E_{\text{syn}}}{G_{\text{in}}} \]

\[ G_{\text{in}} = g_e + g_i + \frac{1}{R} \]

\[ \tau' = \frac{C}{G_{\text{in}}} \]
Shunting Inhibition

Solving ODE:

\[ \tau' \frac{dV}{dt} = -V + \frac{g_e E_{syn}}{G_{in}} \]

\[ V(t) = \frac{g_e E_e}{G_{in}} (1 - e^{-t/\tau'}) \]

\[ V_{\infty} = \frac{g_e E_e}{g_e + \frac{1}{R} + g_i} \]

Notice \( g_i \) only appears in the denominator

This is reason why shunting inhibition is often referred to as ‘divisive inhibition’
Shunting Inhibition

Solving ODE:

\[ \tau' \frac{dV}{dt} = -V + \frac{g_e E_{syn}}{G_{in}} \]

\[ V(t) = \frac{g_e E_e}{G_{in}} (1 - e^{-t/\tau'}) \]

\[ V_\infty = \frac{g_e E_e}{g_e + \frac{1}{R} + g_i} \]
Non-synaptic interactions

Su et al, 2012
**Ephaptic Coupling**

Su et al, 2012
Ephaptic Coupling

Su et al, 2012
Ephaptic Coupling
Plasticity

- Hebb’s law:
  - Neurons that fire together wire together
Spike-time Dependent Plasticity

- **LTP**

- **neocortex-layer 5**
  - Xenopus tectum
  - hippocampus

- **neocortex-layer 2/3**
  - hippocampus

- **ELL of electric fish**

- **GABA-ergic neurons**
  - in hippocampal culture

- **neocortex-layer 4 spiny stellates**

- $t_{pre} - t_{post}$ (ms)
London and Hauser, Dendritic Computation, 2005
Passive Properties of Dendrites

- Amplitude

- Time course
Passive Properties of Dendrites

Linear filtering:

→ Inputs from dendrites are broadened and delayed

→ Alters summation properties...
  coincidence detection to temporal integration

→ Delay lines

→ Segregation of inputs

→ Nonlinear interactions within a dendrite
  -- sublinear summation
  -- shunting inhibition

→ Dendritic inputs “labelled”
Coincidence Detection – Backpropagating APs
Coincidence Detection – Backpropagating APs
Dendritic Multiplication
Dendritic Multiplication
Active Properties of Dendrites

Mechanisms to deal with the distance dependence of PSP size

→ Subthreshold boosting: inward currents with reversal near rest
  Eg persistent Na⁺

→ Synaptic scaling

→ Dendritic spikes
  Na⁺, Ca²⁺ and NMDA
  Dendritic branches as mini computational units

→ backpropagation:
  feedback circuit
  Hebbian learning through supralinear interaction of backprop spikes with inputs
Sound Localization

Computation: Do the inputs from both ears arrive together?

- left inputs
- right inputs

\[ \sqrt{N_{\text{inputs}}} \]

\[ \Sigma \]

no coincidence \[ \times \] sum > \[ \sqrt{2} \]? \[ \checkmark \] coincidence
Direction Selectivity
Direction Selectivity
Image Processing
Looming object recognition
Looming object recognition