Synaptic Transmission and Integration

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Neural Signal Processing
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Roadmap

Introduction to neuroscience
• Chapter 1 – The brain and behavior
• Chapter 2 – Nerve cells and behavior

How are neural signals generated?
• Chapter 7 – Membrane potential
• Chapter 9 – Propagated signaling: the action potential

How do neurons communicate with each other?
• Chapter 10 – Overview of synaptic transmission
• Chapter 12 – Synaptic integration
Synaptic Transmission

• We will only cover excerpts from Chapters 10 and 12 of *Principles of Neural Science* (PNS).

• You are only responsible for text corresponding to figures shown in these lecture notes.

• The point at which one neuron communications with another is called a synapse.

• The average neuron forms about $10^3$ synaptic connections and receives $> 10^3$ synaptic connections.

• With $>10^{11}$ neurons in the brain, $>10^{14}$ synaptic connections are formed in a single brain – more than then number of stars in our galaxy!

• **Plasticity** – the change in strength of synaptic transmission – is crucial to memory and other higher brain functions.
Electrical vs. Chemical Synapses

- **Electrical synapses** – specialized ion channels (“gap junction channels”) that connect the pre- and postsynaptic cells provide a low-resistance pathway for electrical current to flow between the two cells.

- **Chemical synapses** – action potential in the presynaptic neuron leads to the release of a chemical substance (“neurotransmitter”) that in turn initiates current flow in the postsynaptic cell.
Electrical vs. Chemical Synapses

- **Electrical synapses** – *any* amount of current (even subthreshold) in the presynaptic cell triggers a response in the postsynaptic cell.

- **Chemical synapses** – the presynaptic current *must* reach threshold for an action potential before the cell can release neurotransmitter and affect the postsynaptic cell.
Electrical vs. Chemical Synapses

- **Electrical synapses** – largely excitatory
- **Chemical synapses** – can be excitatory or inhibitory
Electrical vs. Chemical Synapses

<table>
<thead>
<tr>
<th>Type of synapse</th>
<th>Distance between pre- and postsynaptic cell membranes</th>
<th>Cytoplasmic continuity between pre- and postsynaptic cells</th>
<th>Ultrastructural components</th>
<th>Agent of transmission</th>
<th>Synaptic delay</th>
<th>Direction of transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrical</td>
<td>3.5 nm</td>
<td>Yes</td>
<td>Gap-junction channels</td>
<td>Ion current</td>
<td>Virtually absent</td>
<td>Usually bidirectional</td>
</tr>
<tr>
<td>Chemical</td>
<td>20–40 nm</td>
<td>No</td>
<td>Presynaptic vesicles and active zones; postsynaptic receptors</td>
<td>Chemical transmitter</td>
<td>Significant: at least 0.3 ms, usually 1–5 ms or longer</td>
<td>Unidirectional</td>
</tr>
</tbody>
</table>
Electrical vs. Chemical Synapses

• Most synapses are chemical.

• Chemical synapses are capable of more variable signaling than electrical synapses (vis-à-vis excitatory / inhibitory effects, synaptic plasticity, signal amplification).

• Chemical synapses are central to most brain functions we know and love.

• Thus, we will focus on chemical synapses.

• If you want to learn more about electrical synapses, you can read about it in PNS Chapter 10 (p. 177-182), but it’s beyond the scope of this course.
1) Action potential arriving at *presynaptic terminal* (swelling of axon) causes voltage-gated Ca$^{2+}$ channels at the *active zone* (membrane specialized for releasing neurotransmitter) to open.

2) Influx of Ca$^{2+}$ causes *synaptic vesicles* containing *neurotransmitter* to fuse with the presynaptic cell membrane.
3) Vesicles release their contents into the synaptic cleft (a process termed “exocytosis”).

4) Released neurotransmitter molecules diffuse across synaptic cleft and bind to specific receptors on post-synaptic membrane.
5) Receptors cause ion channels to open (or close), thereby changing the membrane potential of the post-synaptic cell.

6) If membrane of post-synaptic cell crosses threshold, then the action potential is propagated.
Chemical Synapses Can Amplify Signals

- The action of **one** synaptic vesicle can open **thousands** of ion channels in the postsynaptic cell!

- **Reason**: one vesicle contains several thousand molecules of neurotransmitter, but only a couple molecules are typically needed to open an ion channel.

- Thus, even a small presynaptic terminal (with weak electrical current) can depolarize a large postsynaptic cell.
Neurotransmitter release is probabilistic

• Transmitter released in discrete packages called *quanta* (one vesicle contains one quantum of transmitter).

• Each quantum produces a postsynaptic potential of a fixed size, called the *quantal synaptic potential*.

• Probability that a loaded vesicle will dock at a release site and release a quantum of transmitter is directly dependent on the amount of Ca$^{2+}$ influx into the presynaptic terminal.

• Alterations in Ca$^{2+}$ concentration affect the average number of quanta that are released in response to a presynaptic action potential, *not* the size of a quantum.

• The effectiveness of chemical synapses can be modified by Ca$^{2+}$ concentration ⇒ synaptic plasticity
Chemical Synapses Can Mediate Either Excitatory or Inhibitory Effects on Postsynaptic Cells

• There are many kinds of neurotransmitters (e.g., acetylcholine, dopamine, glutamate).

• There are many types of postsynaptic receptors (some gate ion channels directly, others indirectly).

• Whether the effect of a chemical synapse is excitatory or inhibitory depends not on the neurotransmitter, but on the receptor.
Synaptic integration

• Everything that we’ve talked about so far involves just one synapse.
• But, a typical neuron receives $> 10^3$ synaptic connections.
• These synaptic connections may be excitatory or inhibitory.
• Some connections are strong, some are weak.
• How does a neuron integrate its inputs to “decide” whether or not to emit an action potential?
Threshold varies within a cell

- **Recall**: an action potential is generated when the membrane potential exceeds threshold.

- Threshold is lower at the axon hillock than at cell body or dendrites.

- **Reason**: The axon hillock has a high density of voltage-dependent Na$^+$ channels. For each increment of membrane depolarization, more inward current flows at the axon hillock than elsewhere in the cell.
Action potential typically generated at axon hillock

- Difference between threshold and resting membrane potential is 10 mV at axon hillock, compared to 30 mV in cell body.

- Peak synaptic potential drops with distance from synapse.

- Key crossing point: neuron fires an action potential.

- Membrane potential at axon hillock serves as the readout for the integrative action of a neuron.
Temporal summation

- Consecutive synaptic potentials are added together in the postsynaptic cell.

- Larger time constant => more likely that two consecutive inputs will summate to cross threshold.

- Time constant depends on density of resting ion channels, their conductance, membrane properties.
Spatial summation

- Inputs from presynaptic neurons acting at different sites on postsynaptic neuron are added together.
- Larger length constant => signals do not rapidly decay with distance, thus 2 different inputs are more likely to bring postsynaptic neuron to threshold.
- Length constant depends on size of axons and dendrites, resistive properties of cytoplasm, density of resting ion channels, their conductance.