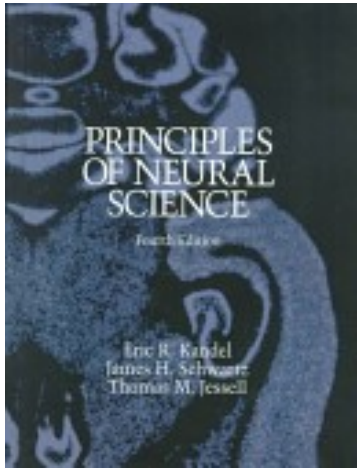
PNS Chapters 10 and 12

Synaptic Transmission and Integration

Carnegie Mellon

18-699 / 42-590
Neural Signal Processing
Spring 2010
Prof. Byron Yu

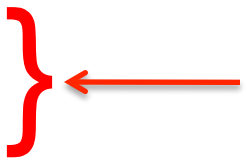
Roadmap



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.

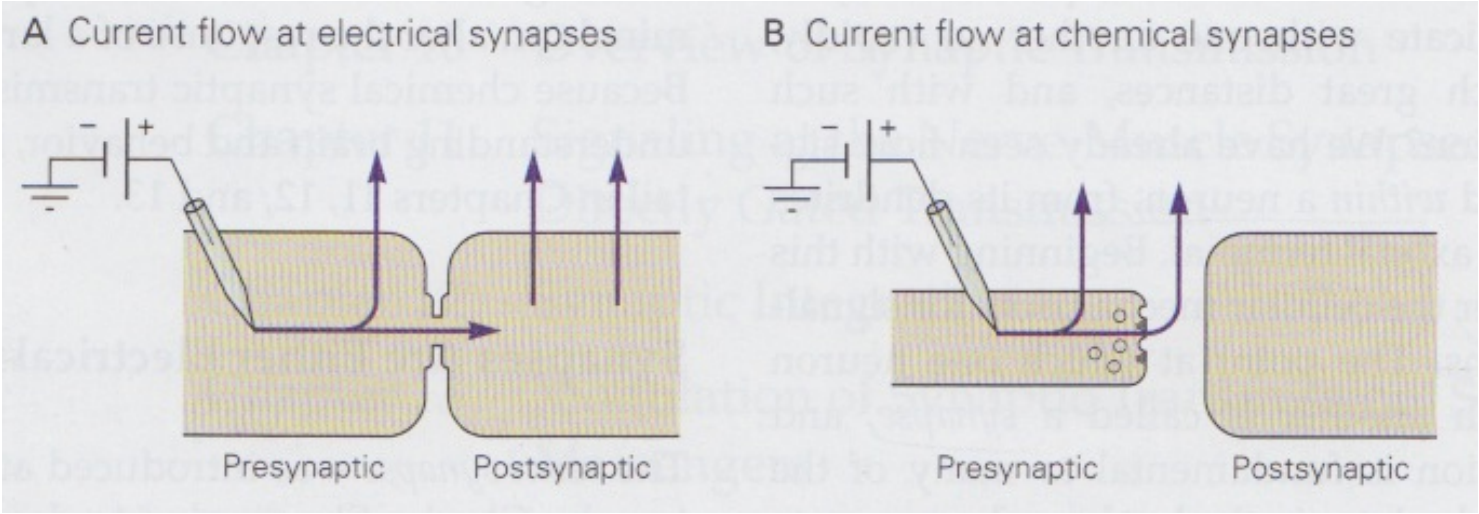
• The point at which one neuron communications with another is called a **synapse**.

• 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.

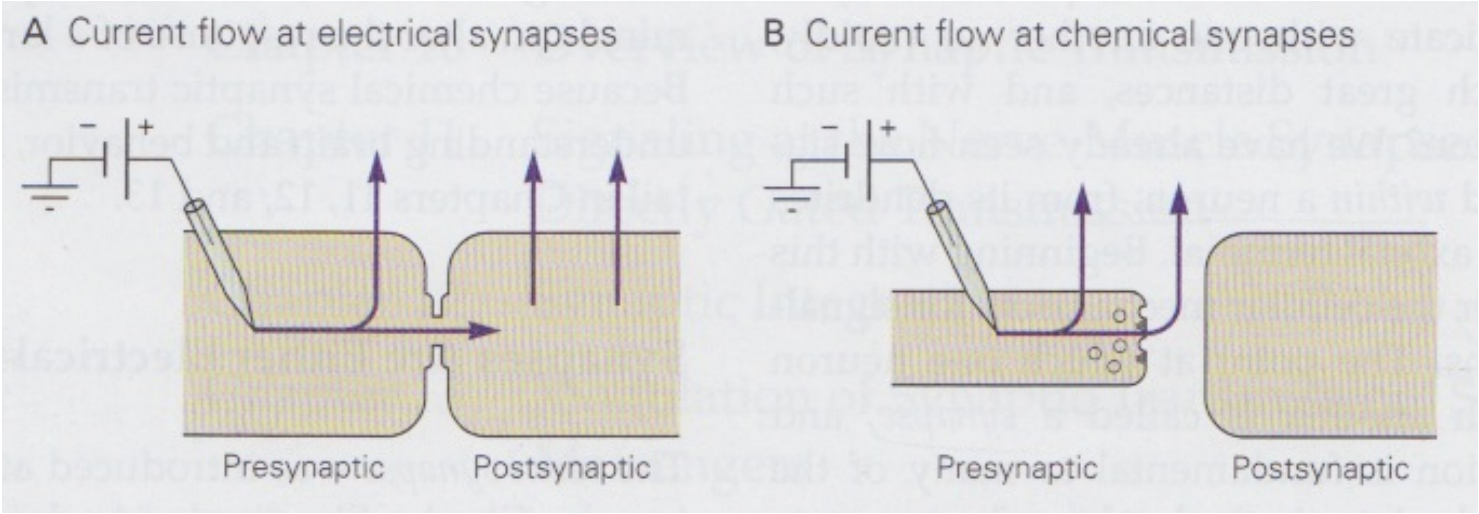
Electrical vs. Chemical Synapses



• 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.

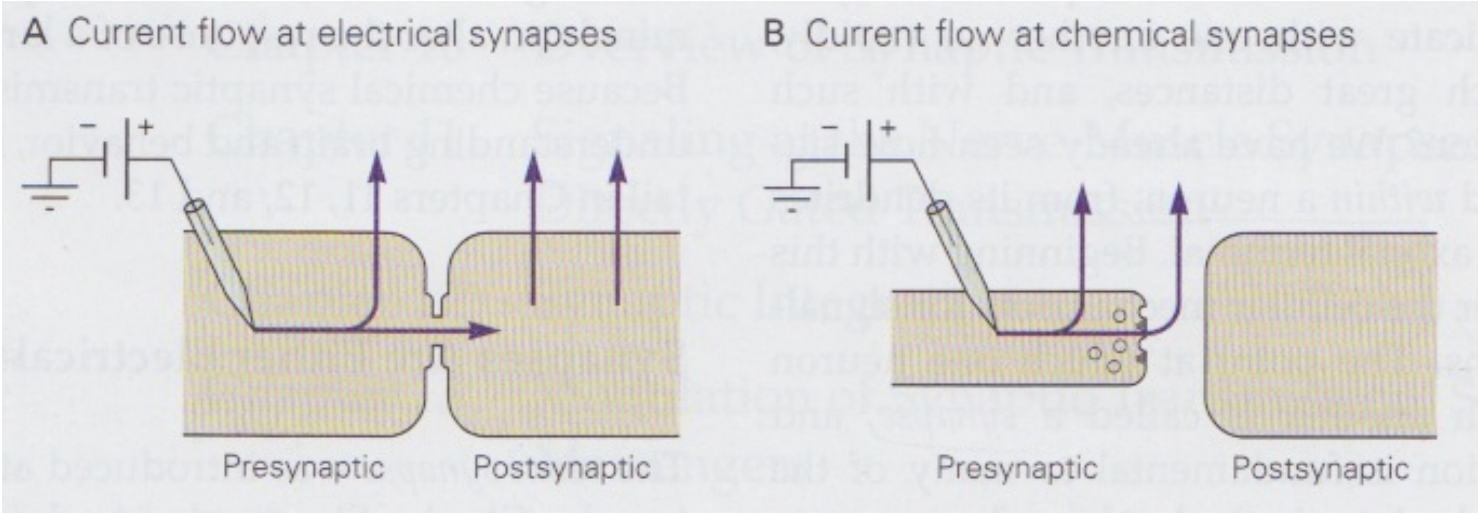
Electrical vs. Chemical Synapses



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

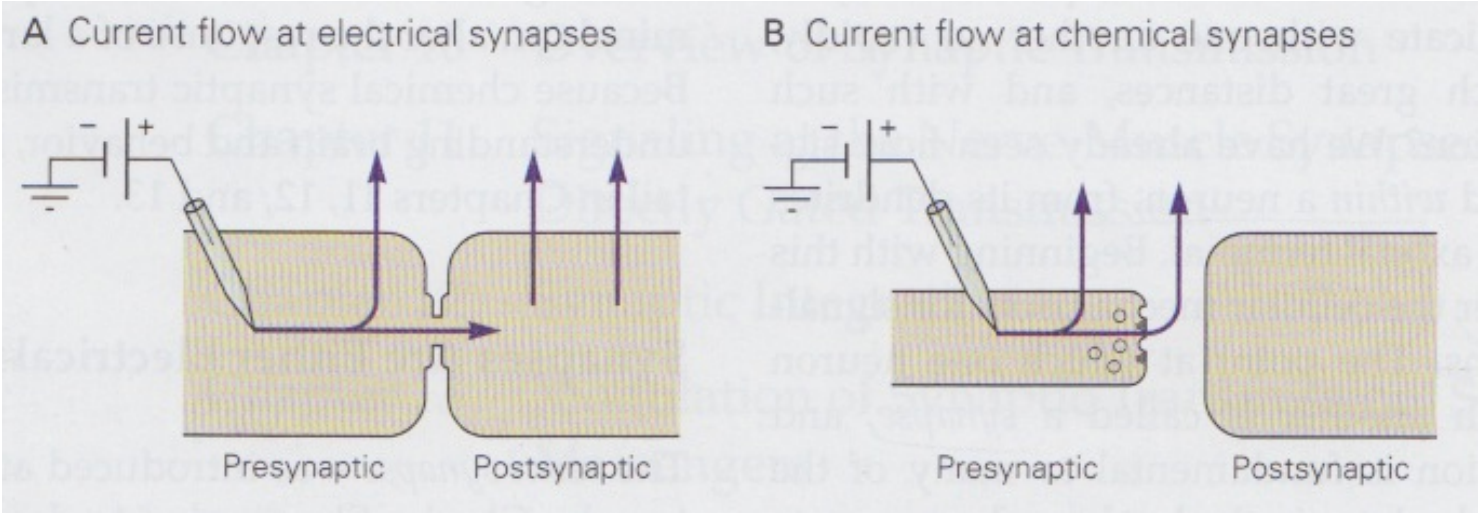
• Chemical synapses – the presynaptic current *must* reach threshold for an action potential before the cell can release neurotransmitter and affect the postsynaptic cell.

Electrical vs. Chemical Synapses



- Electrical synapses – largely excitatory
- Chemical synapses – can be excitatory or inhibitory

Electrical vs. Chemical Synapses



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

Electrical vs. Chemical Synapses

- Most synapses are chemical.

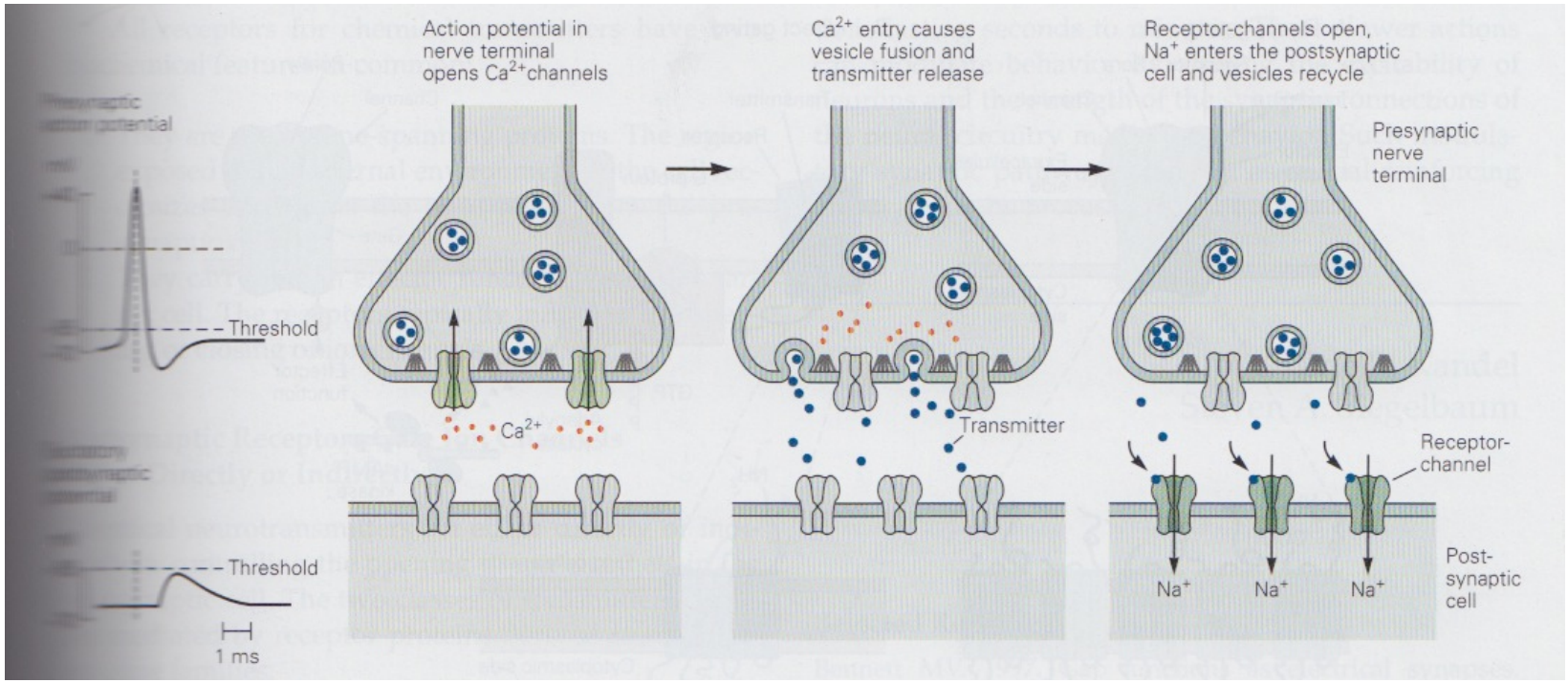
- Chemical synapses are capable of more variable signaling than electrical synapses (vis-à-vis excitatory / inhibitory effects, synaptic plasticity, signal amplification).

- 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.

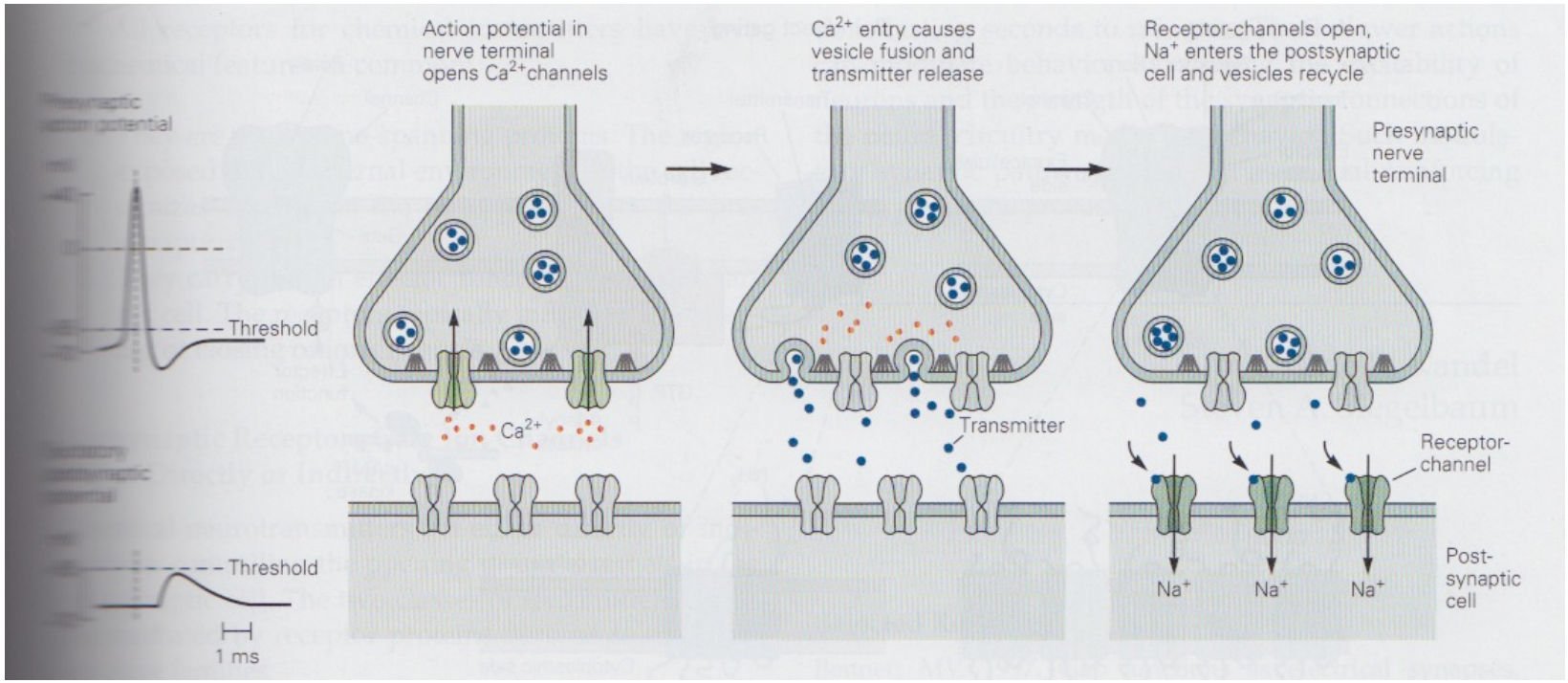
Synaptic Transmission at Chemical Synapses



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.

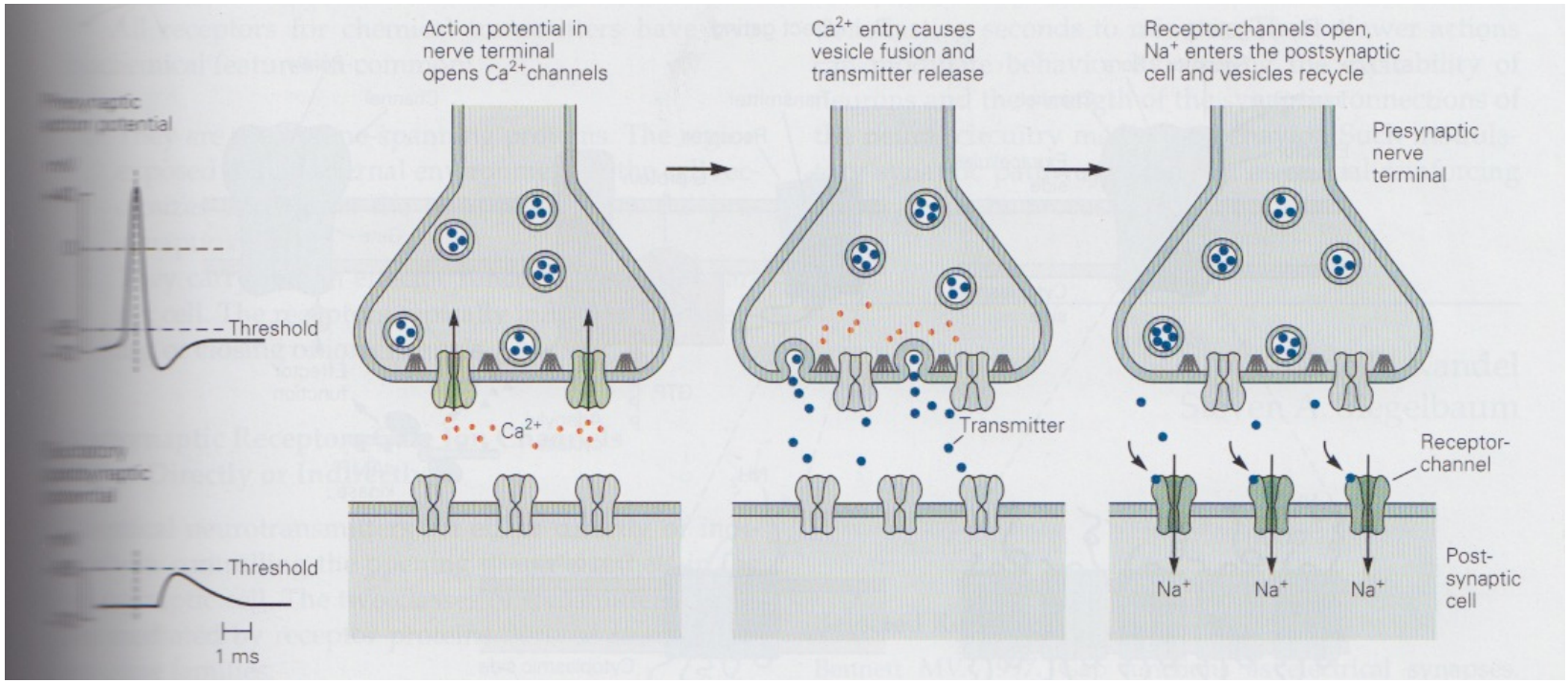
Synaptic Transmission at Chemical Synapses



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.

Synaptic Transmission at Chemical Synapses



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 release 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

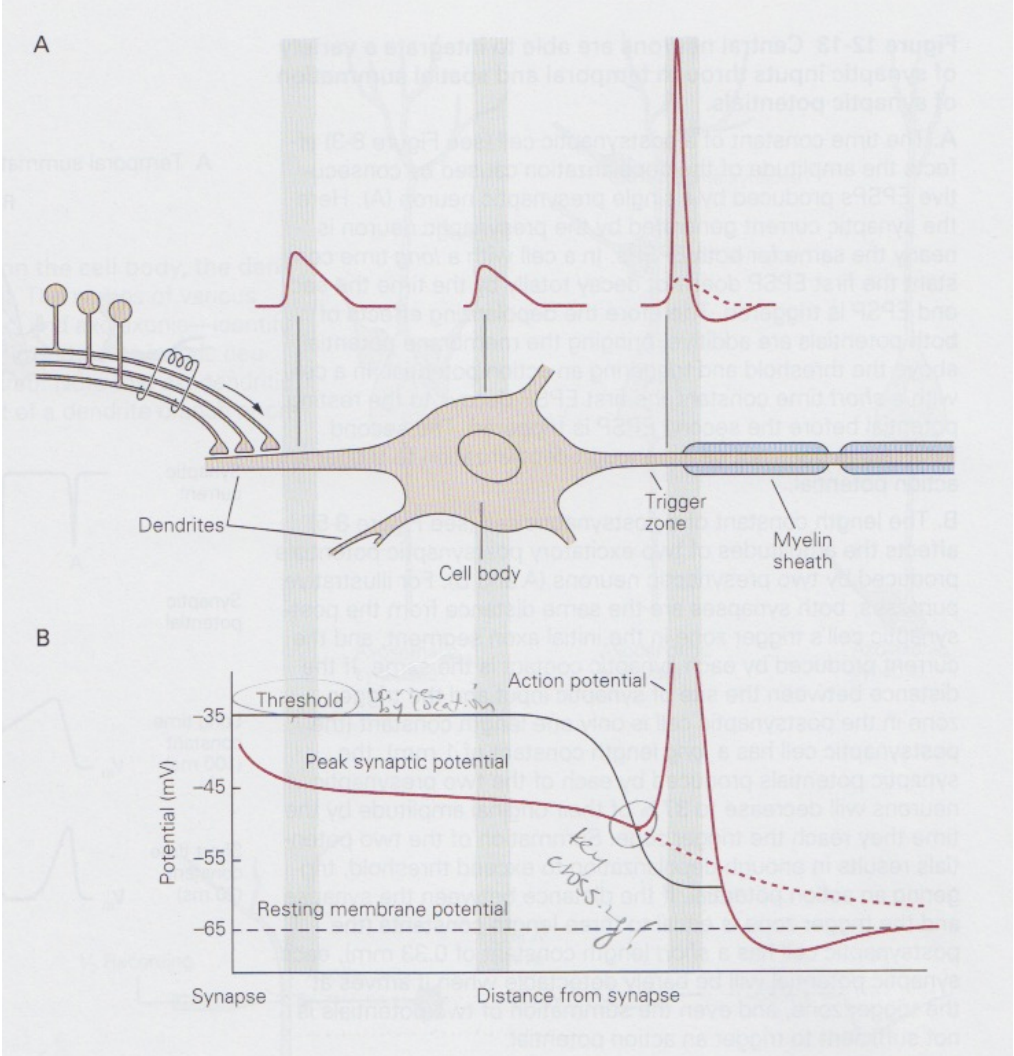
- Everything that we've talked about so far involves just one synapse.
- But, a typical neuron receives > 10^3 synaptic connections.
- These synaptic connections may be excitatory or inhibitory.
- Some connections are strong, some are weak.
- How does a neuron integrate its inputs to "decide" whether 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.

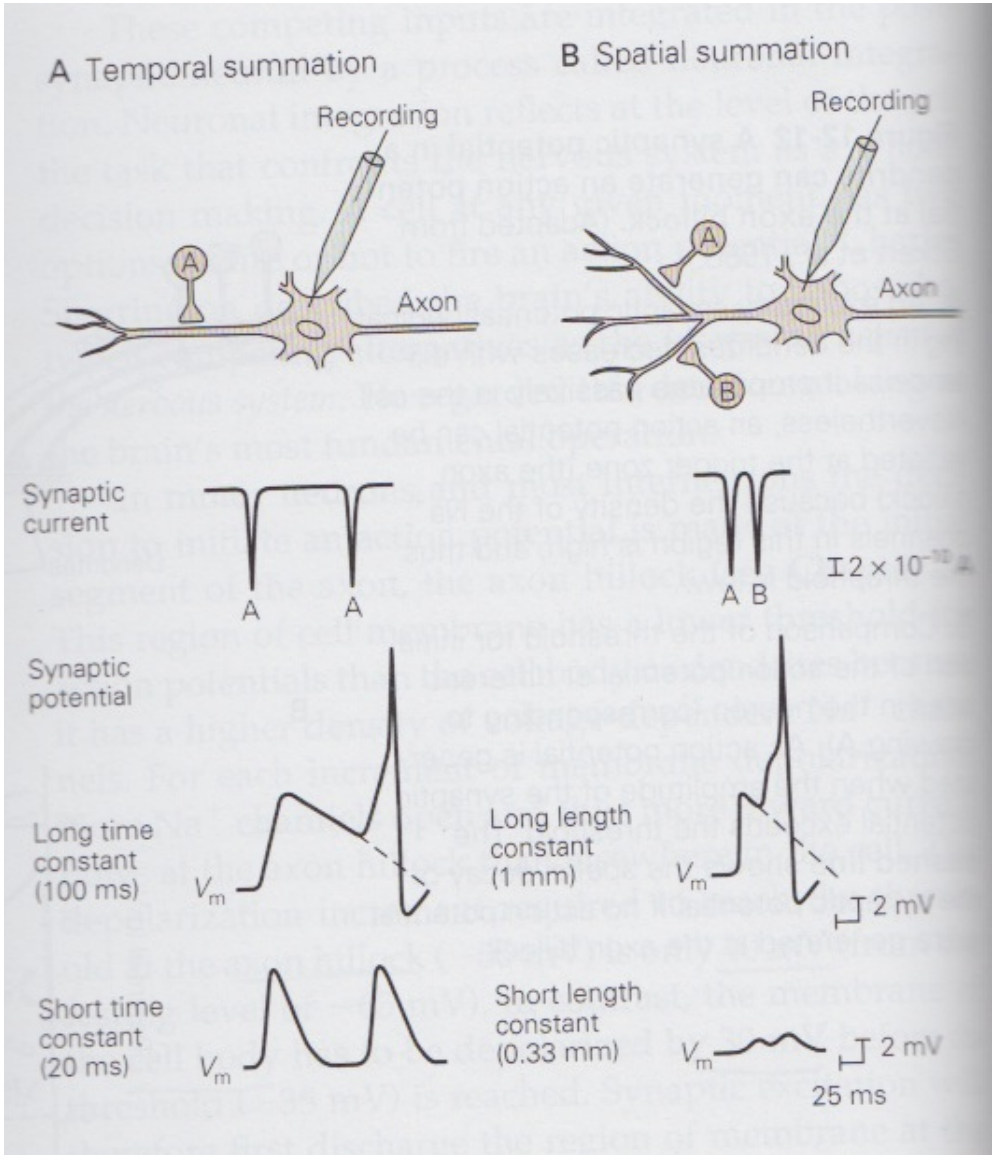
Action potential typically generated at axon hillock

- 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.

