Chemical and Electrical Synapses

Two Kinds of Synapses

1. Chemical
2. Electrical

- Both types of synapses relay information, but do so by very different mechanisms.
- Much more is known about chemical than about electrical synapses.

  - Information gleaned from NMJ in frog leg (sciatic n. – gastrocnemius m.).
  - However, this is n-m, rather than n-n.
  - n-m relay is much faster than n-n.

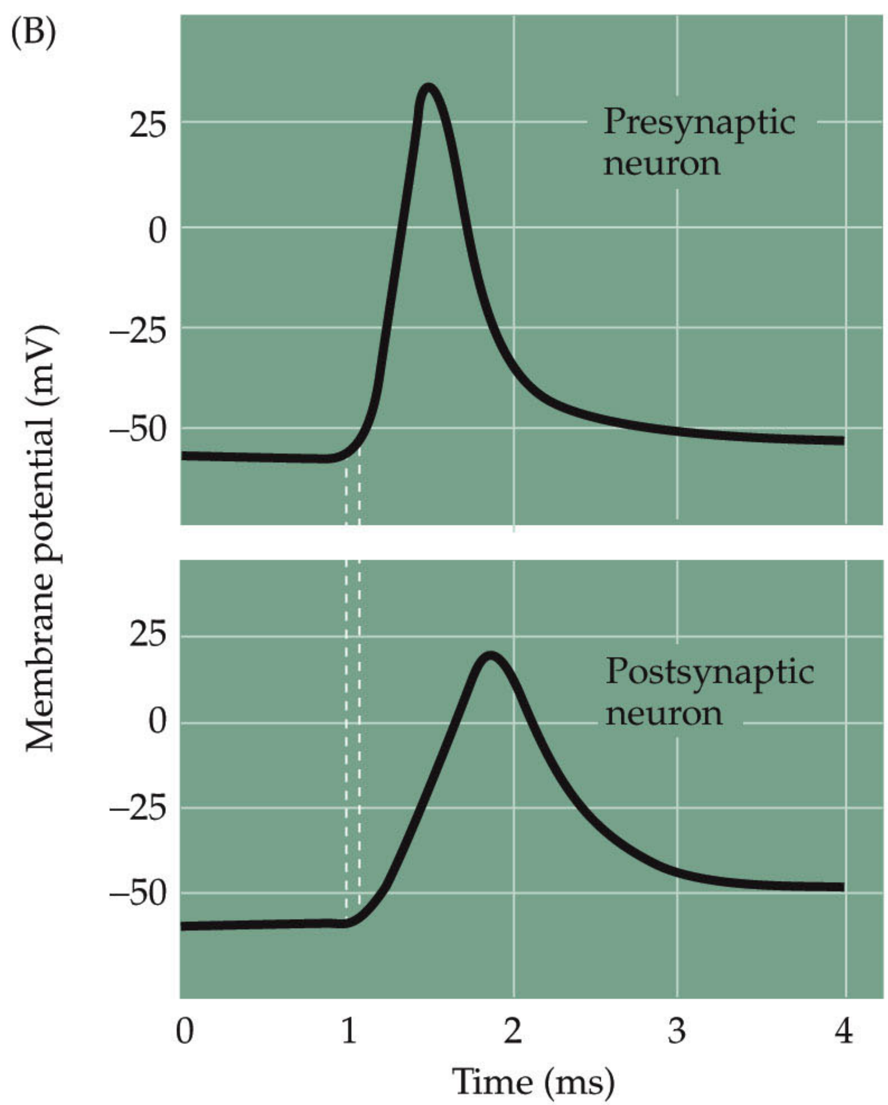
Electrical Synapses

- Symmetrical morphology.
- Bidirectional transfer of information, but can be unidirectional.
- *Pre*- and *post*synaptic cell membranes are in close apposition to each other (~ 3.5 *vs*. ~ 20 nm in other cells), separated only by regions of cytoplasmic continuity, called *gap junctions*.

  - Ions can flow through these gap junctions, providing low-resistance pathway for ion flow between cells without leakage to the extracellular space: signal transmission = electrotonic transmission.

  - Instantaneous, fast transfer from 1 cell to the next (< 0.3 msec), unlike the delay seen with chemical synapses.

Electrical synapses are built for speed



NEUROSCIENCE, Fourth Edition, Figure 5.2 (Part 2)

Electrical Synapses (cont')
Putative Functions

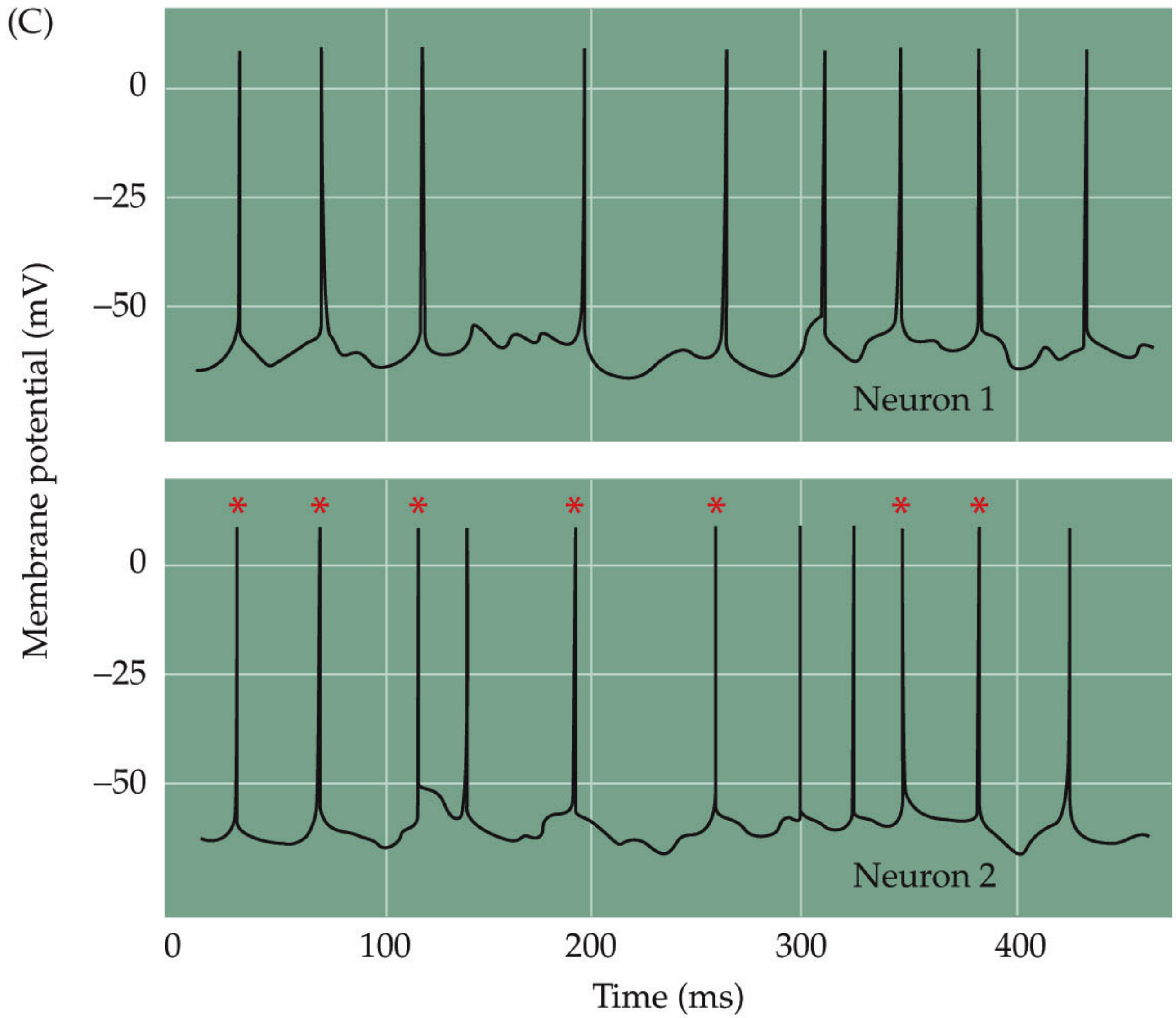
- Synchronization of the electrical activity of large populations of neurons;

  - *e.g.*, the large populations of neurosecretory neurons that synthesize and release biologically active peptide neurotransmitters and hormones are extensively connected by electrical synapses.

  - *e.g.*, Synchronization may be required for neuronal development, including the development of chemical synapses.

  - *e.g.*, Synchronization may be important in functions that require instantaneous responses, such as reflexes and pacemakers.

Electrical coupling is a way to synchronize neurons with one another



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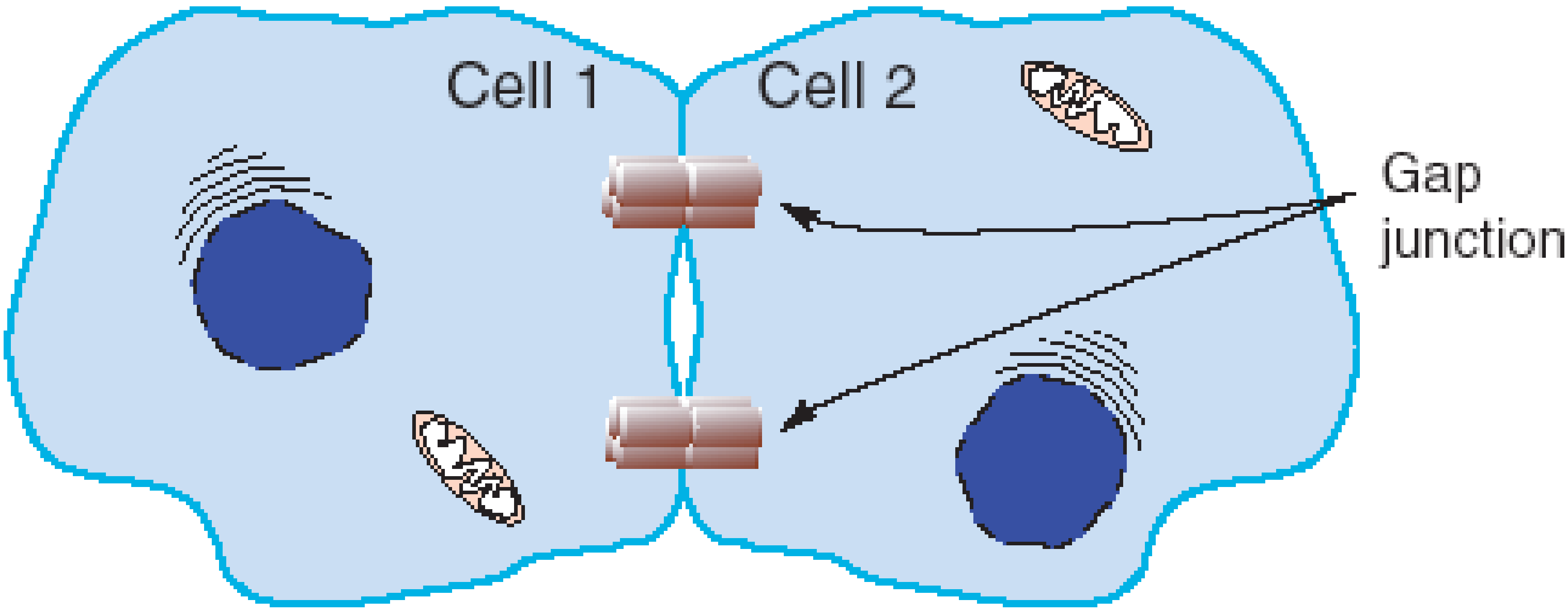
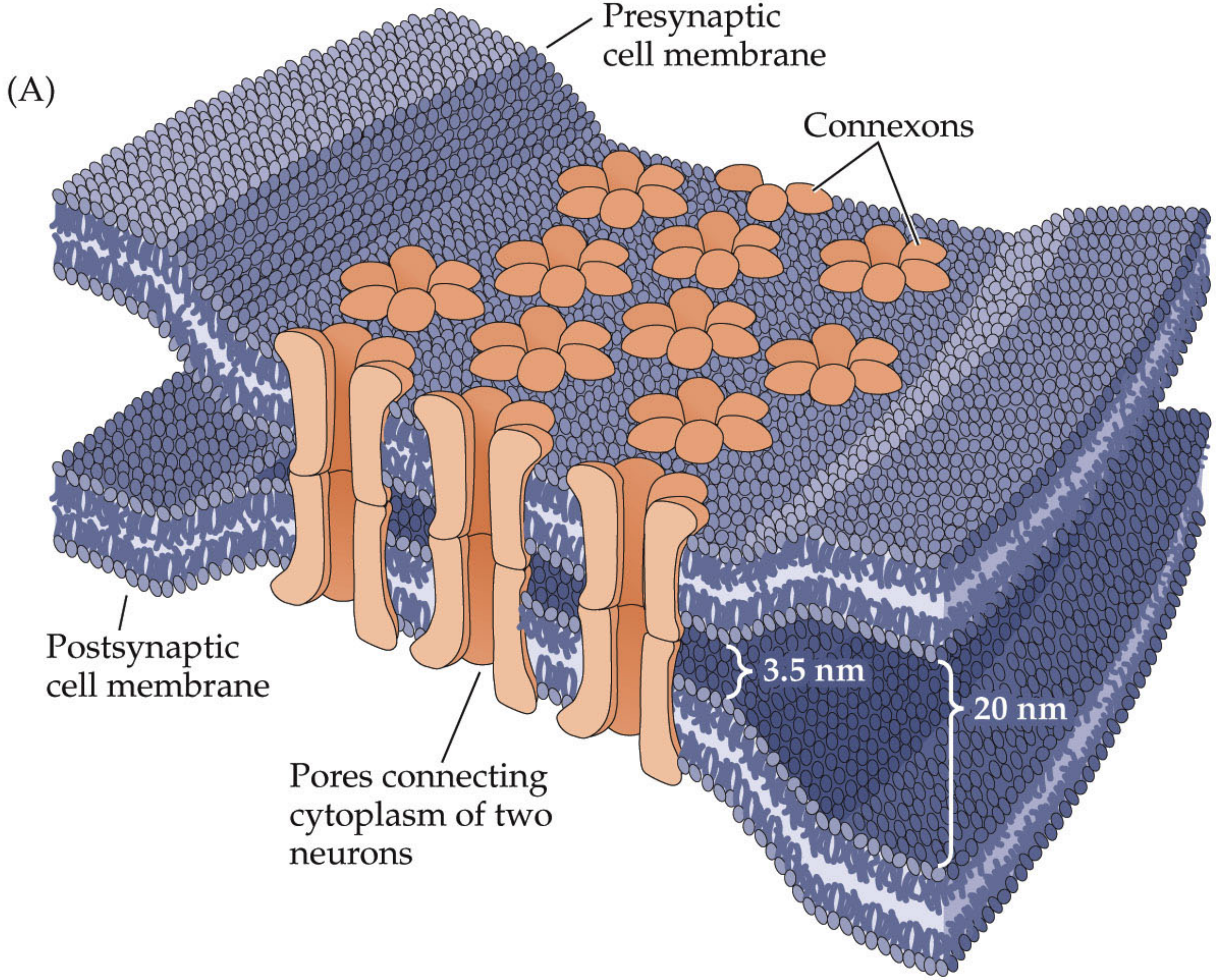
Electrical synapses



Gap junctions are formed exclusively from hexameric pores, called connexons (Cx36), which connect cells with each other for robust electrical coupling.

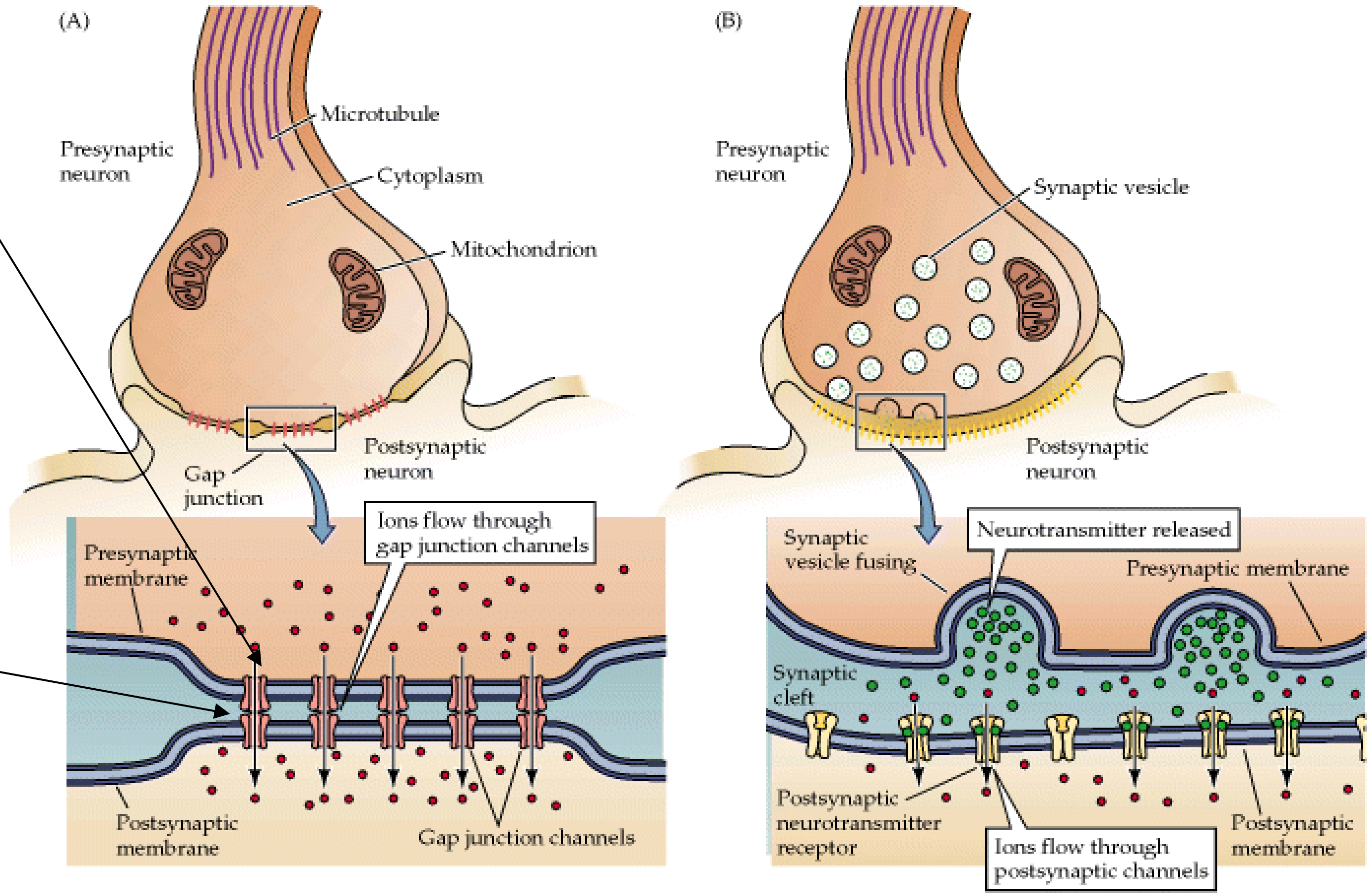


***NEUROSCIENCE*, *Fourth Edition*, Figure 5.2 (Part 1)**

Electrical Synapses: Anatomy

A. Have **bridged = gap junctions** between presynaptic and post-synaptic cells

B. Space between the pre- and post-synaptic cells is **~3.5 nm vs. 20 nm** for “normal” cells

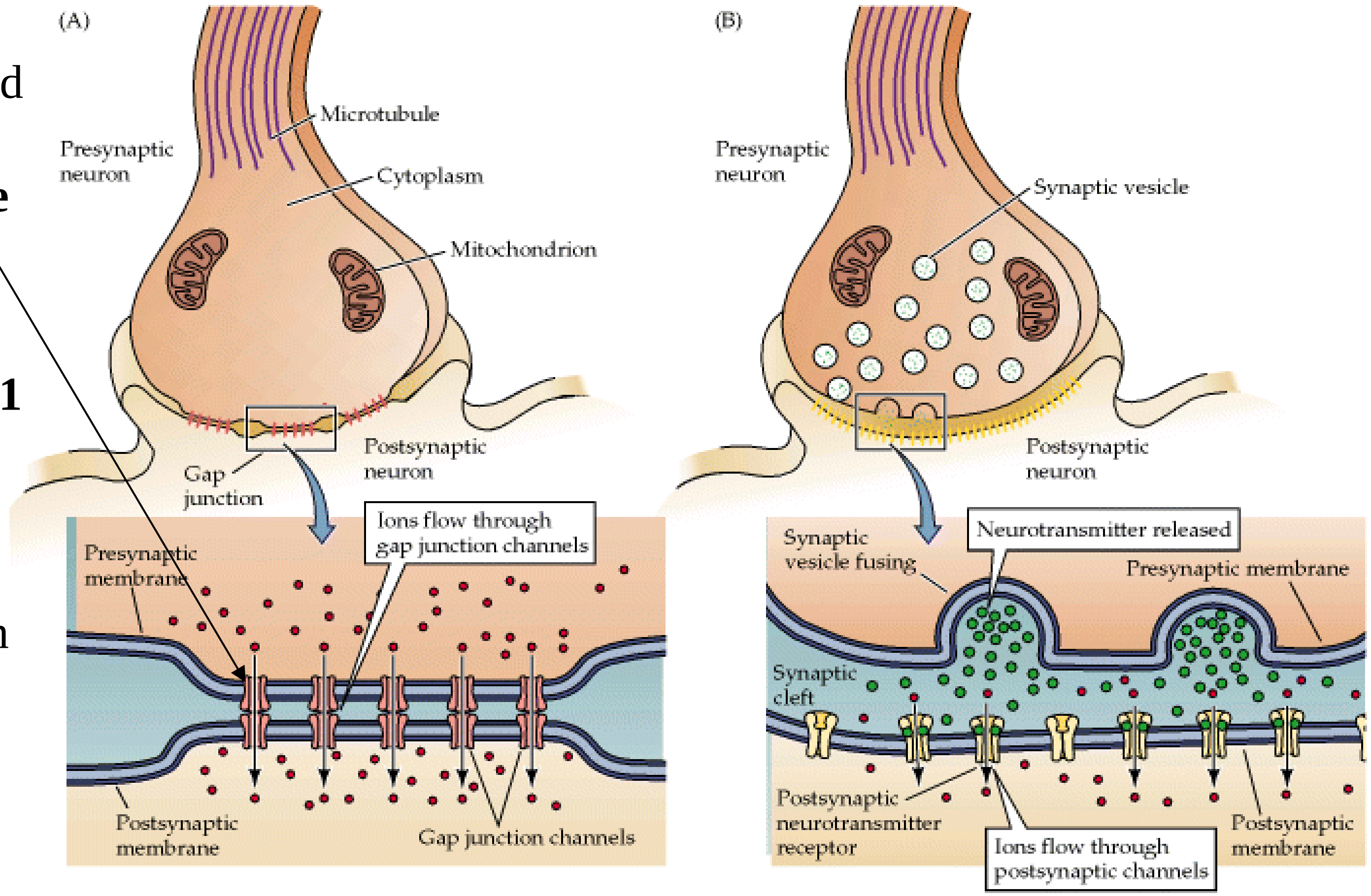


Electrical Synapses: Anatomy (cont'd)

C. **Extracellular space** is bridged by **hemi-channels** that span the pre-synaptic and post-synaptic membranes and **meet in the middle of the extracellular space**

1. **1 channel = 1 presynaptic hemi-channel (connexon) + 1 post-synaptic hemi-channel (connexon)**

(6 protein subunits of **connexin** make up each connexon)



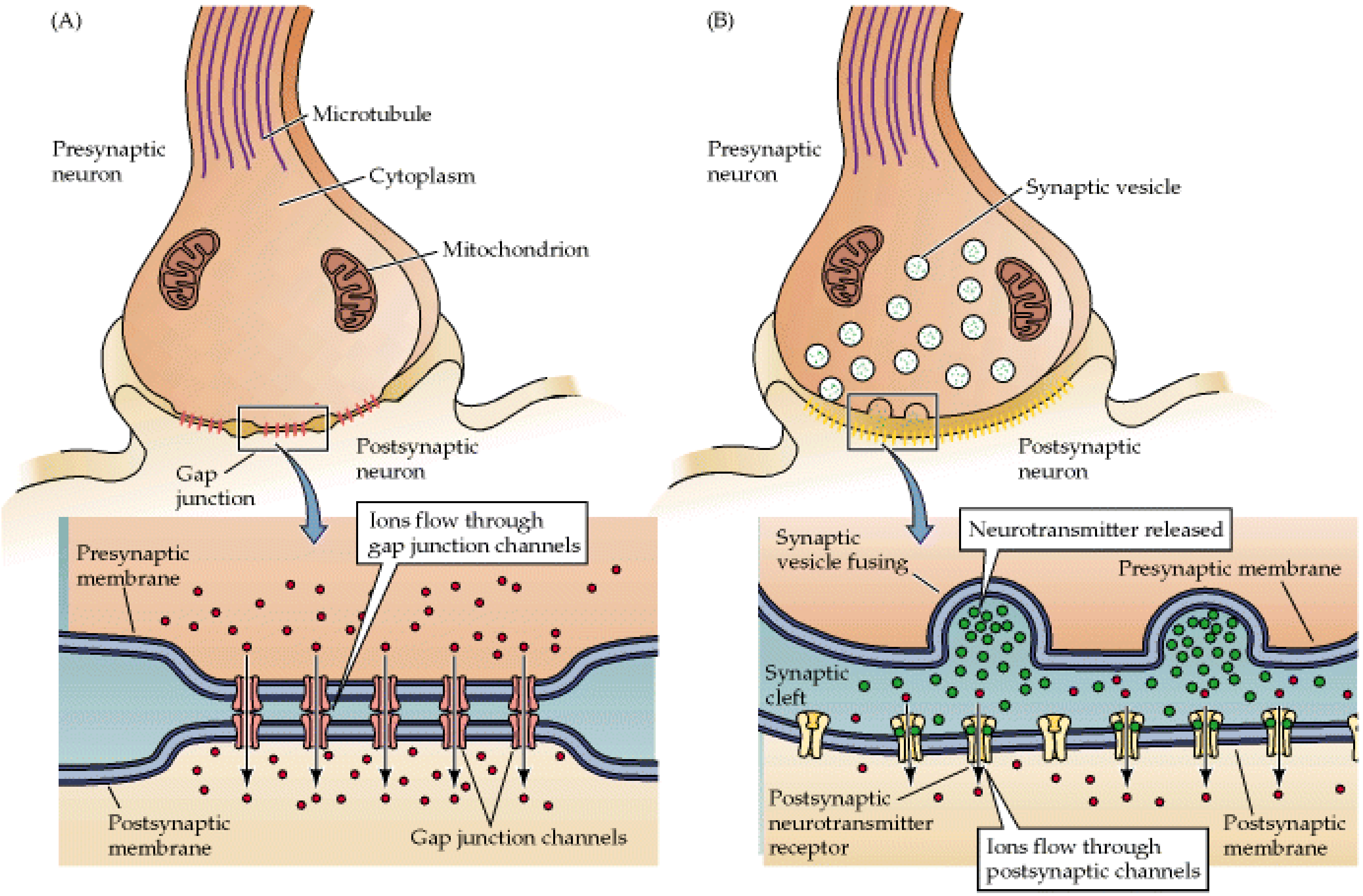
Electrical Synapses: Anatomy (cont'd)

D. Channels allow **metabolic and electrical continuity** between cells-

1. diameter is ~1.5 nm

2. Na^+, K^+,

cAMP, sucrose, small peptides, etc. can cross



Chemical Synapses

- Asymmetric morphology with distinct features found in the *pre*- and *post*synaptic parts.
- Enlarged extracellular space with no cytoplasmic continuity = Synaptic cleft is ~ 200-300 A wide.
- CHO moities intersperse the synapse.
- Most presynaptic endings are axon terminals.
- Most postsynaptic elements in the CNS are dendrites.

Chemical Synapses (cont'd)

- Convergence.
- Divergence.
- Presynaptic ending:

  - swelling of the axon terminal.

  - mitochondria.

  - a variety of vesicular structures, clustered at/near the very edge of the axon terminal.

Chemical Synapses (cont'd)

- Postsynaptic element

  - comprised largely of an electron-dense structure, called the *postsynaptic density (PSD)*.

    Function of PSD?

    - Anchor receptors for neurotransmitters in the postsynaptic membrane.

    - Involved in the conversion of a chemical signal into an electrical one = *transduction*.

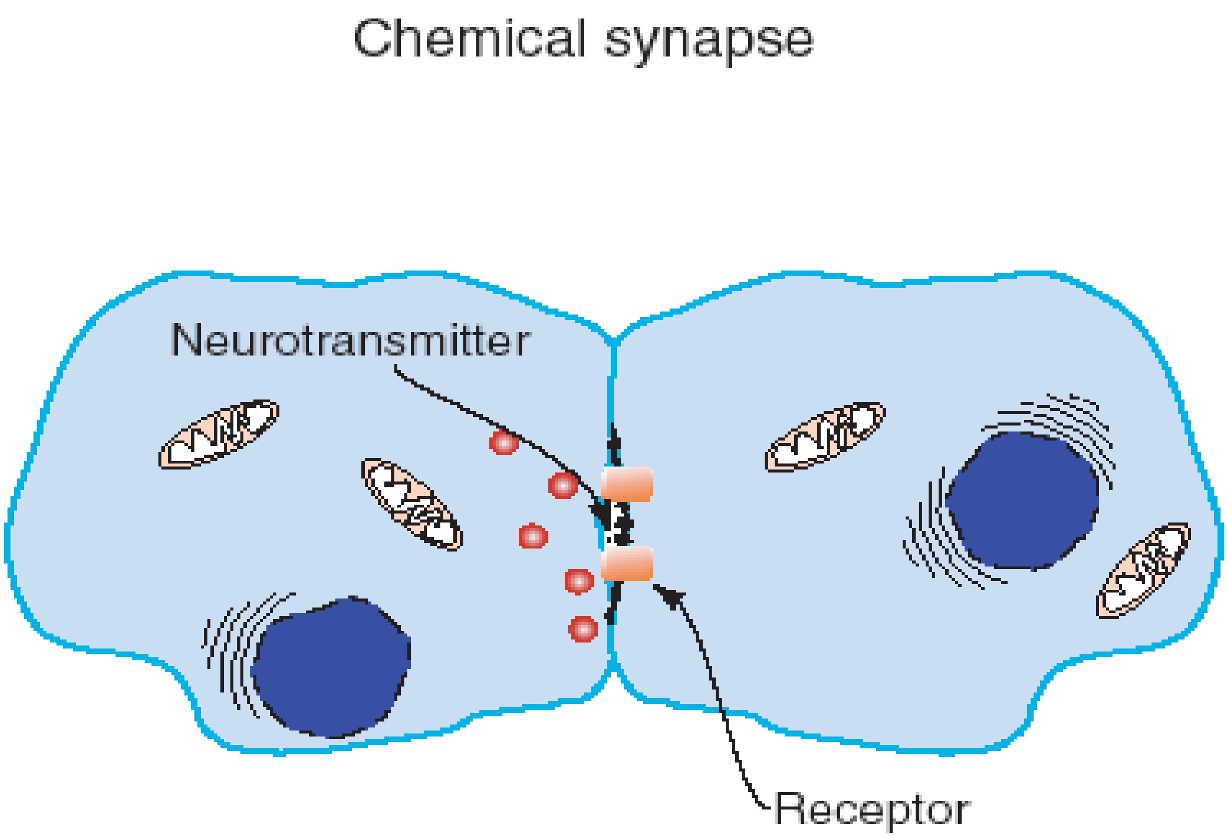
Chemical Synapses (cont'd)

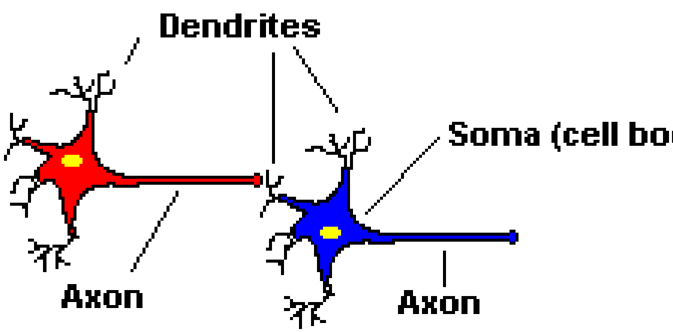
- Associated with the morphological asymmetry is that chemical synapses are, for the most part, *unidirectional*.
- There is a delay of ~0.3 – 5 msec between the arrival of information at the presynaptic terminal and its transfer to the postsynaptic cell.

  This delay may reflect the several steps required for signal transmission = the release and action of a chemical neurotransmitter, which is usually Ca^{2+}-dependent.

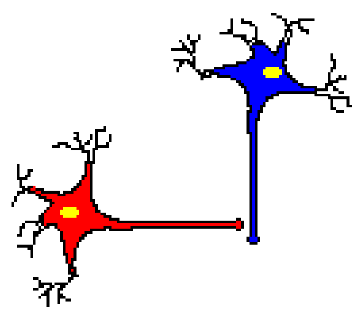
  The response of the postsynaptic neuron may be sustained (long-lasting), much longer than the presynaptic signal the evoked it.

  This may reflect long-lasting changes in the target (receiving) cell.
- The most common type of synapse in the vertebrate nervous system.

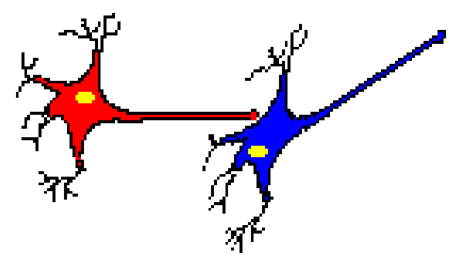




Axon-dendrite



Axo-axonic



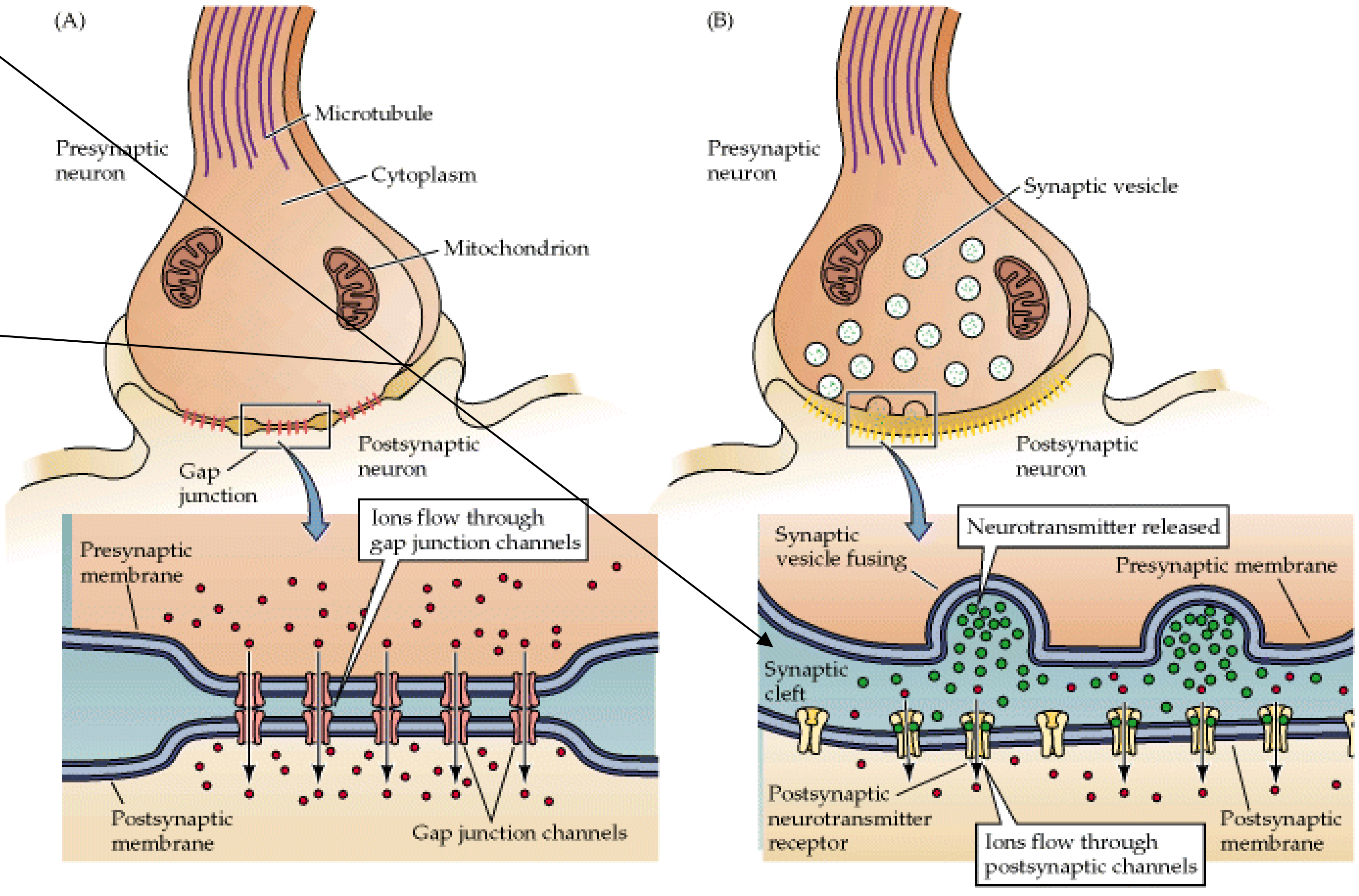
Axon-soma

Chemical Synapses: Anatomy

e.g. **Neuromuscular junction** = highly specialized synapse

A. Pre- and post-synaptic cells **lack cytoplasmic continuity**

B. The **extracellular space** between the cells = **synaptic cleft** is **enlarged** (20-50 nm versus 20 nm for usual extracelluar space)



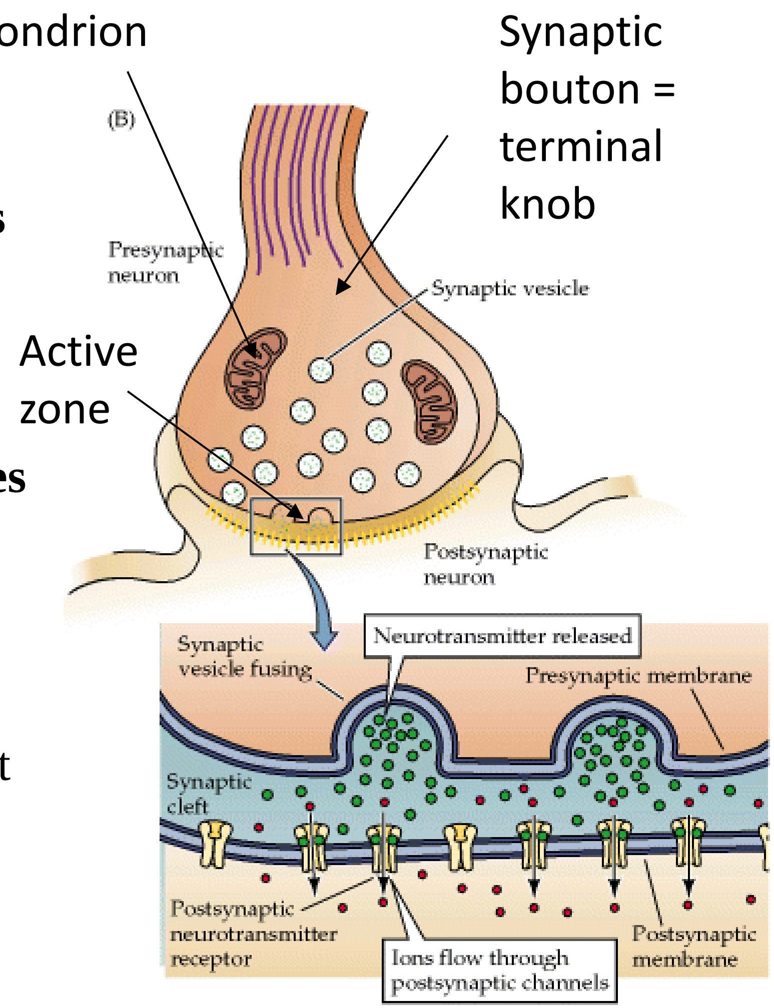
Chemical Synapses: Anatomy (cont’d)

e.g. **Neuromuscular junction** = highly specialized synapse

C. **Axon** of **pre-synaptic cell** is **highly branched** and **terminates** in **terminal knobs = synaptic boutons**

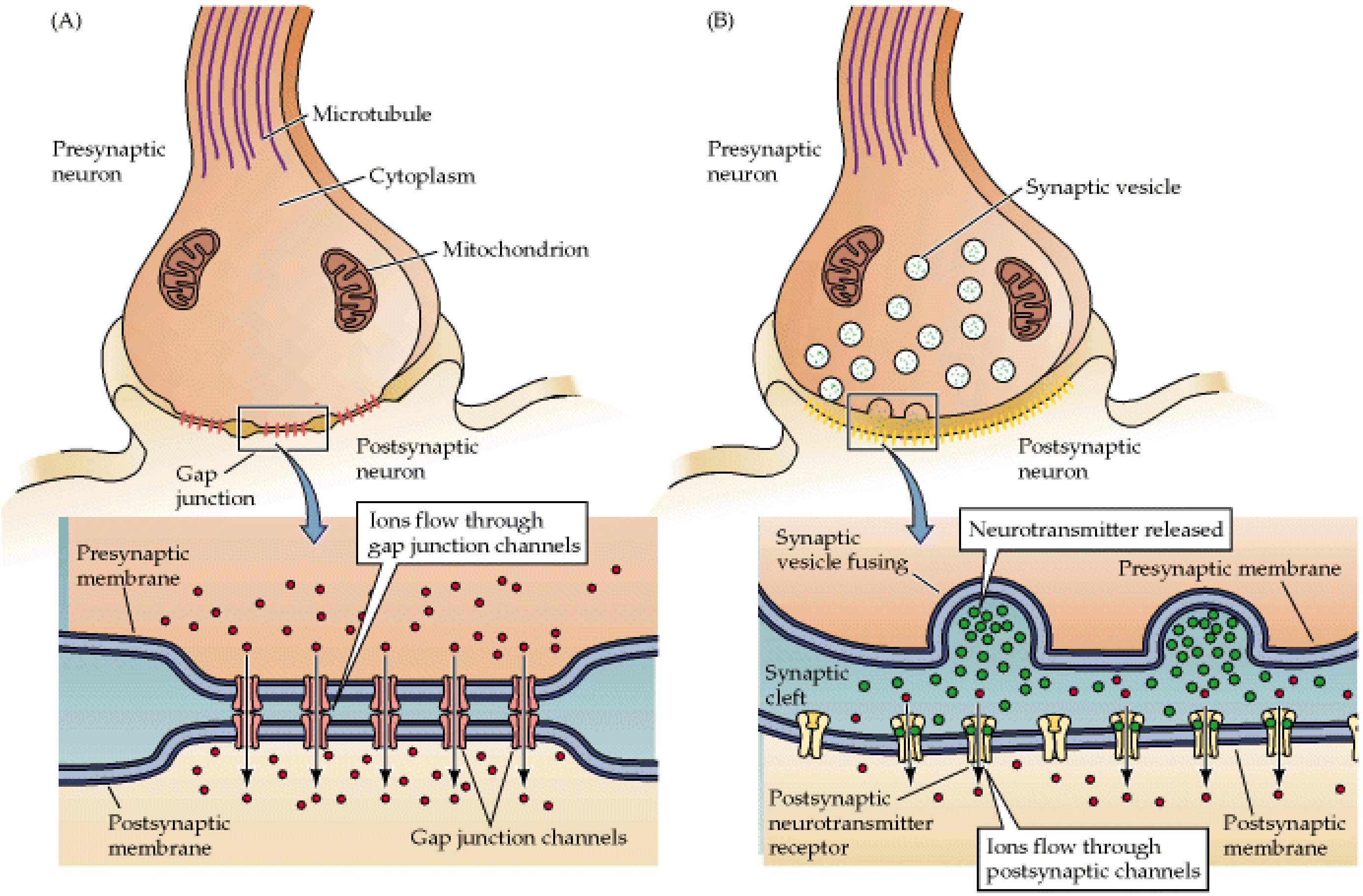
D. Both **pre-** and **postsynaptic cells** have **membrane specializations** –

1. **presynaptic boutons** with –
   - **a. Synaptic vesicles = neurotransmitter vesicles**
   - b. Lots of **mitochondria**
   - **c. Active zones** for **docking/release** of contents of **vesicles**
2. **post-synaptic membrane** with **membrane spanning neurotransmitter receptor protein** that serves as **both receptor** and **ion channel**

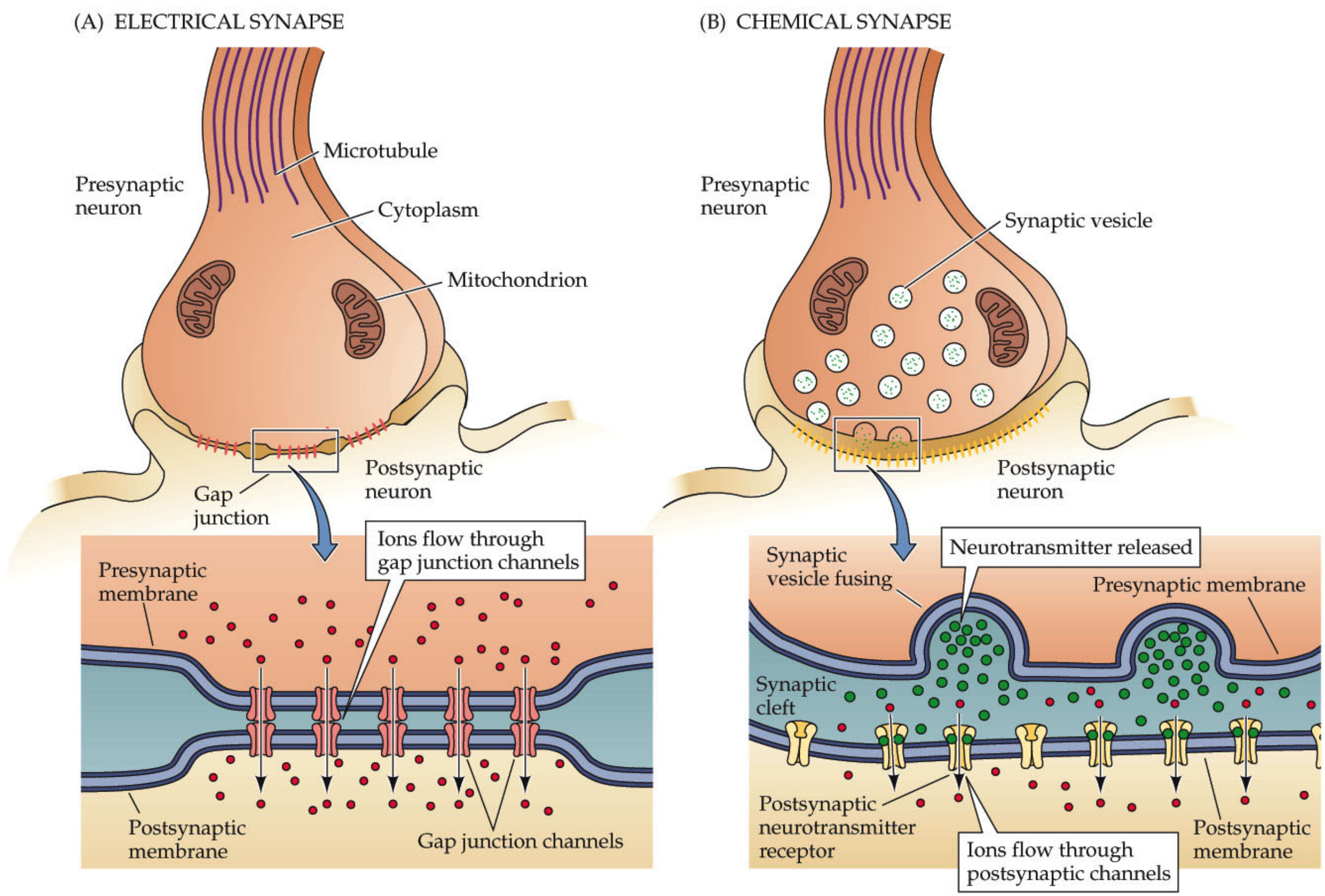


Chemical Synapses: Anatomy (cont'd)

E. In the **CNS**, **ion channels** can be **distinct** from the **neurotransmitter receptor molecule** and can be either **directly gated** or **gated via activation** of a **second messenger system**

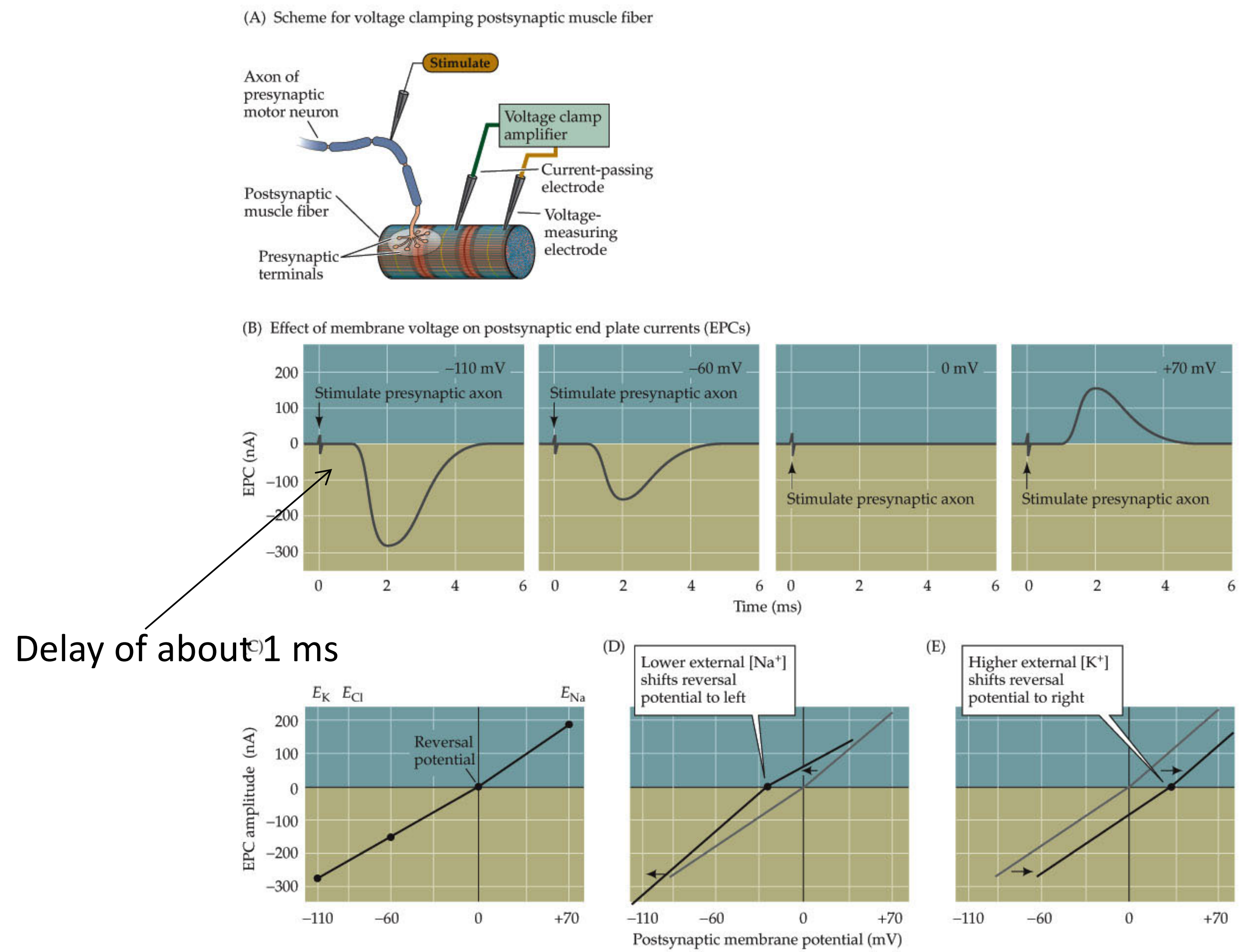


Summary Comparison of the 2 Principal kinds of Synapses: Electrical and Chemical



***NEUROSCIENCE*, *Fourth Edition*, Figure 5.1**

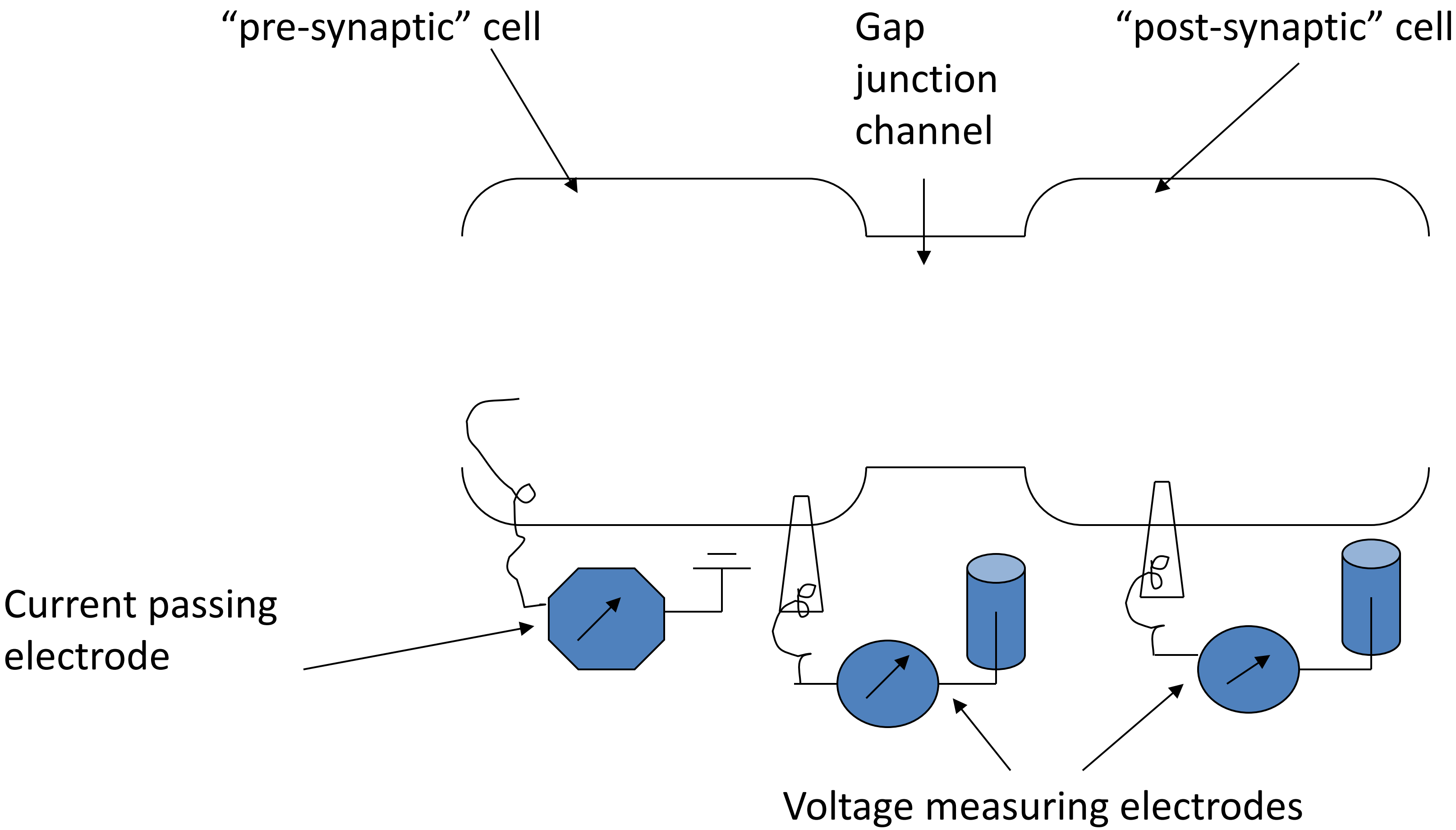
Contrast with chemical synapse:



NEUROSCIENCE, Fourth Edition, Figure 5.17

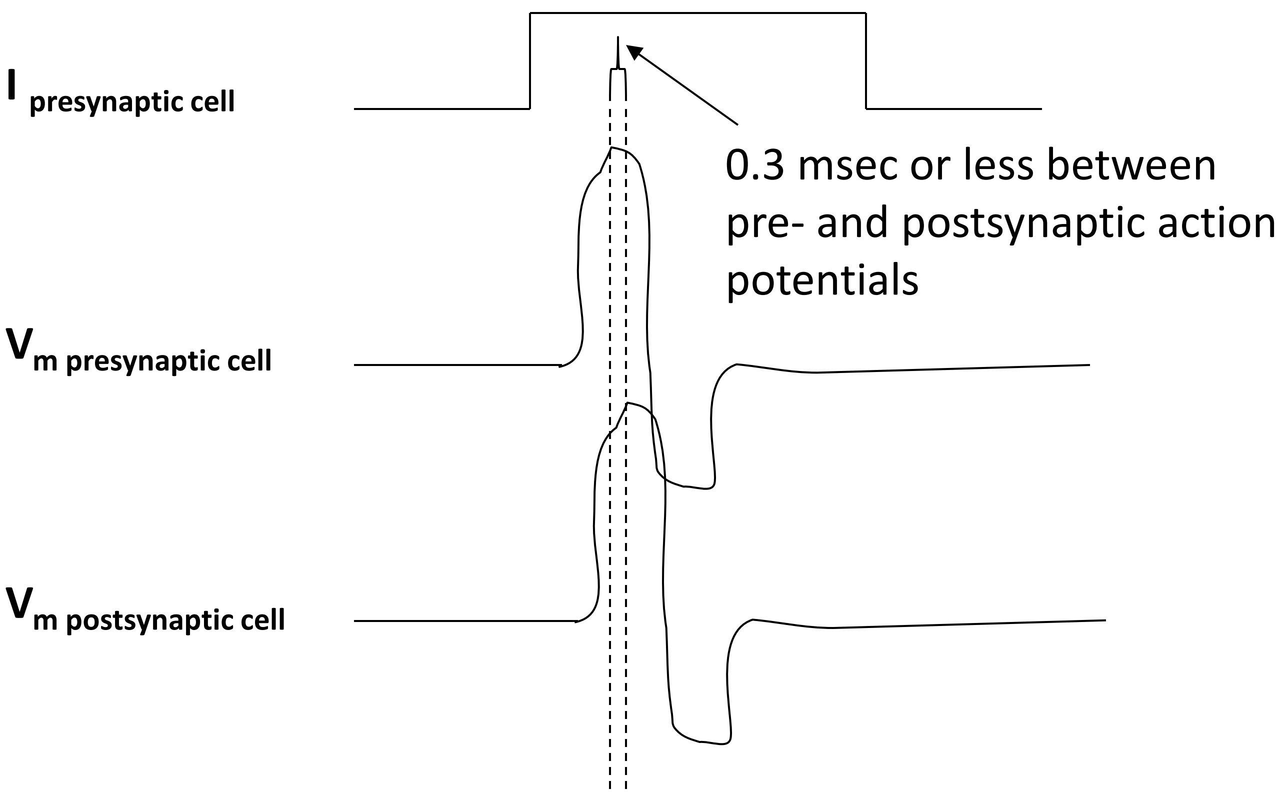
Physiology of Electrical Synapses:

A. Experimental set-up:



Physiology of Electrical Synapses: (cont'd)

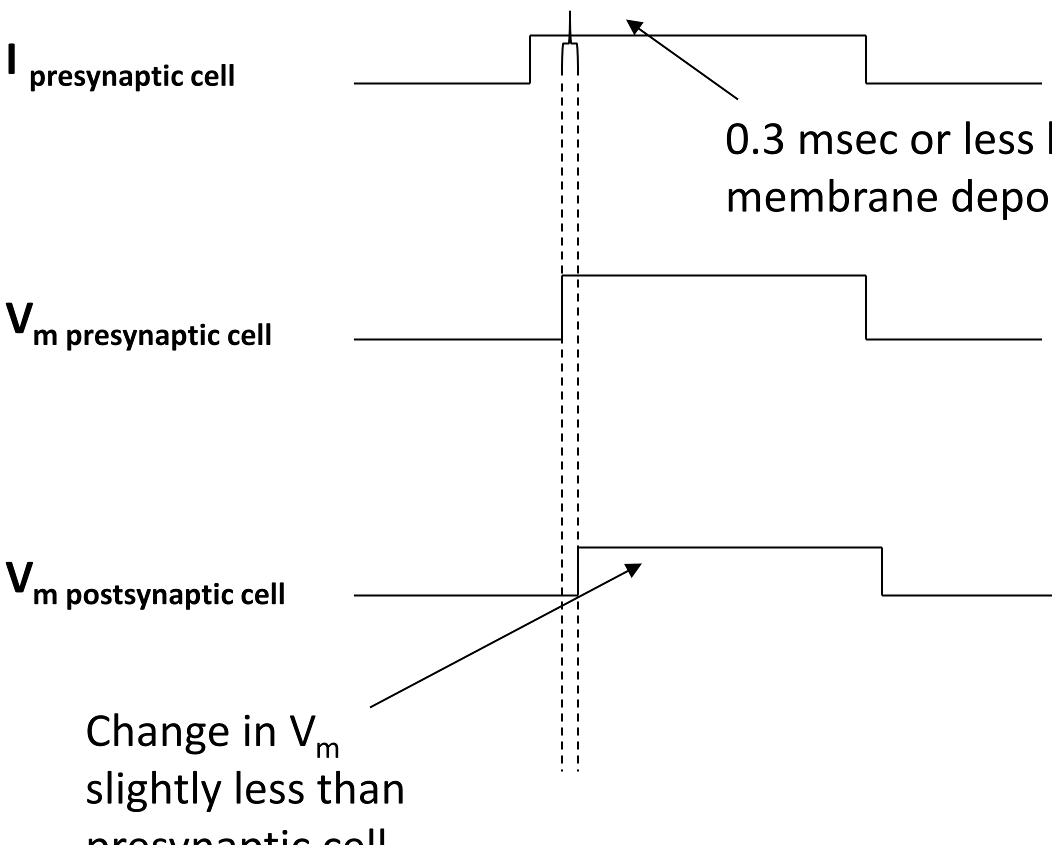
B. Experiment #1: inject **threshold** current in presynaptic cell



Thus, **very short synaptic delay**

Physiology of Electrical Synapses: (cont’d)

C. Experiment #2: inject **subthreshold** current in presynaptic cell



Thus,

1) **very short synaptic delay** and **little decrement** of original signal,

and,

2) does **not** require a **threshold depolarization** for **signal transmission**

Physiology of Electrical Synapses: (cont'd)

D. Experiment #3: inject **subthreshold** current in postsynaptic cell

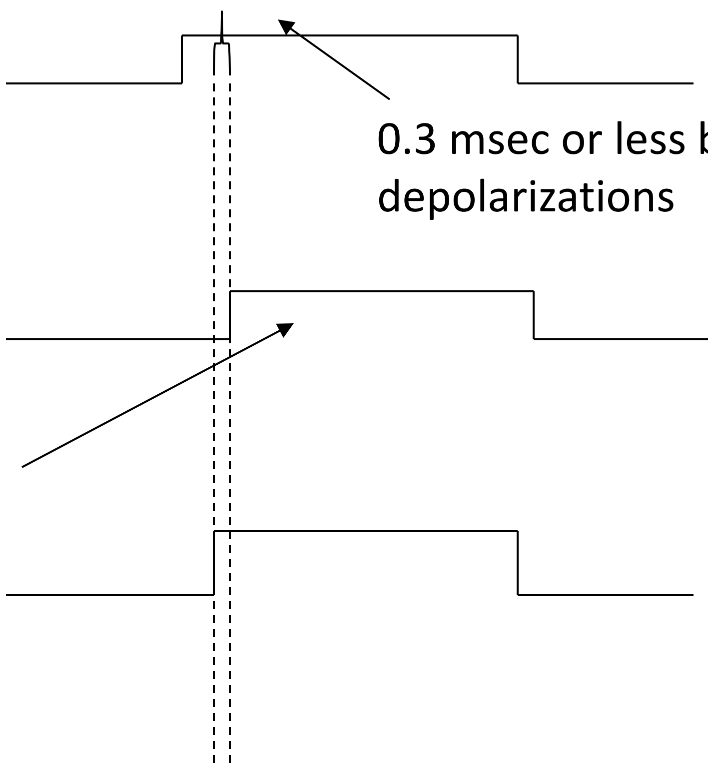
I **presynaptic cell**

0.3 msec or less between membrane depolarizations

V_m **presynaptic cell**

Change in V_m slightly less than postsynaptic cell

V_m **postsynaptic cell**

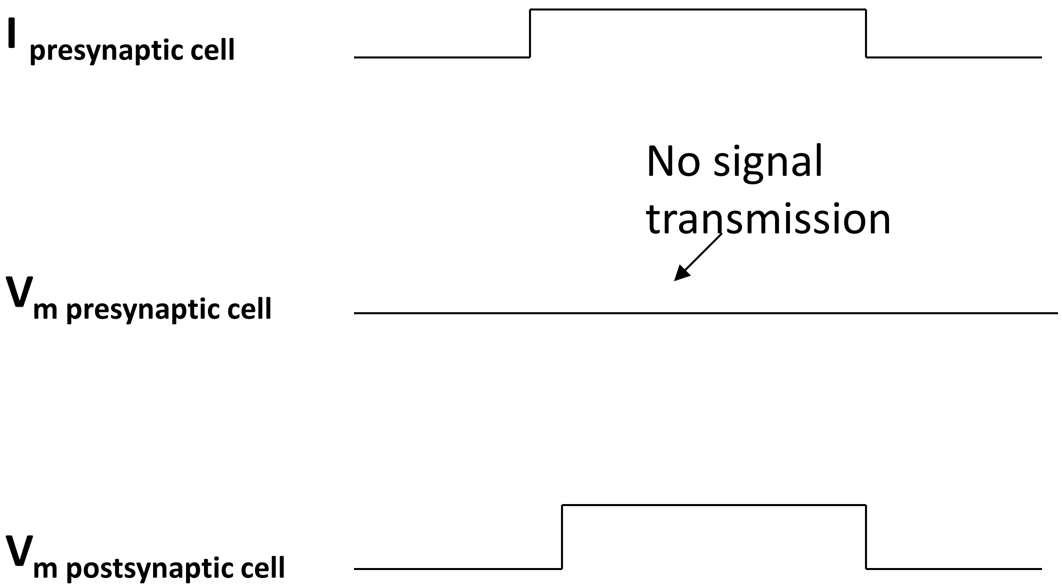


1. Thus, **bidirectional synaptic transmission** exists.

2. Together with **short synaptic delay** and **small decrement** in signal the results suggest that **signal transmission** is via **electrotonic current transmission**.

Physiology of Electrical Synapses: (cont'd)

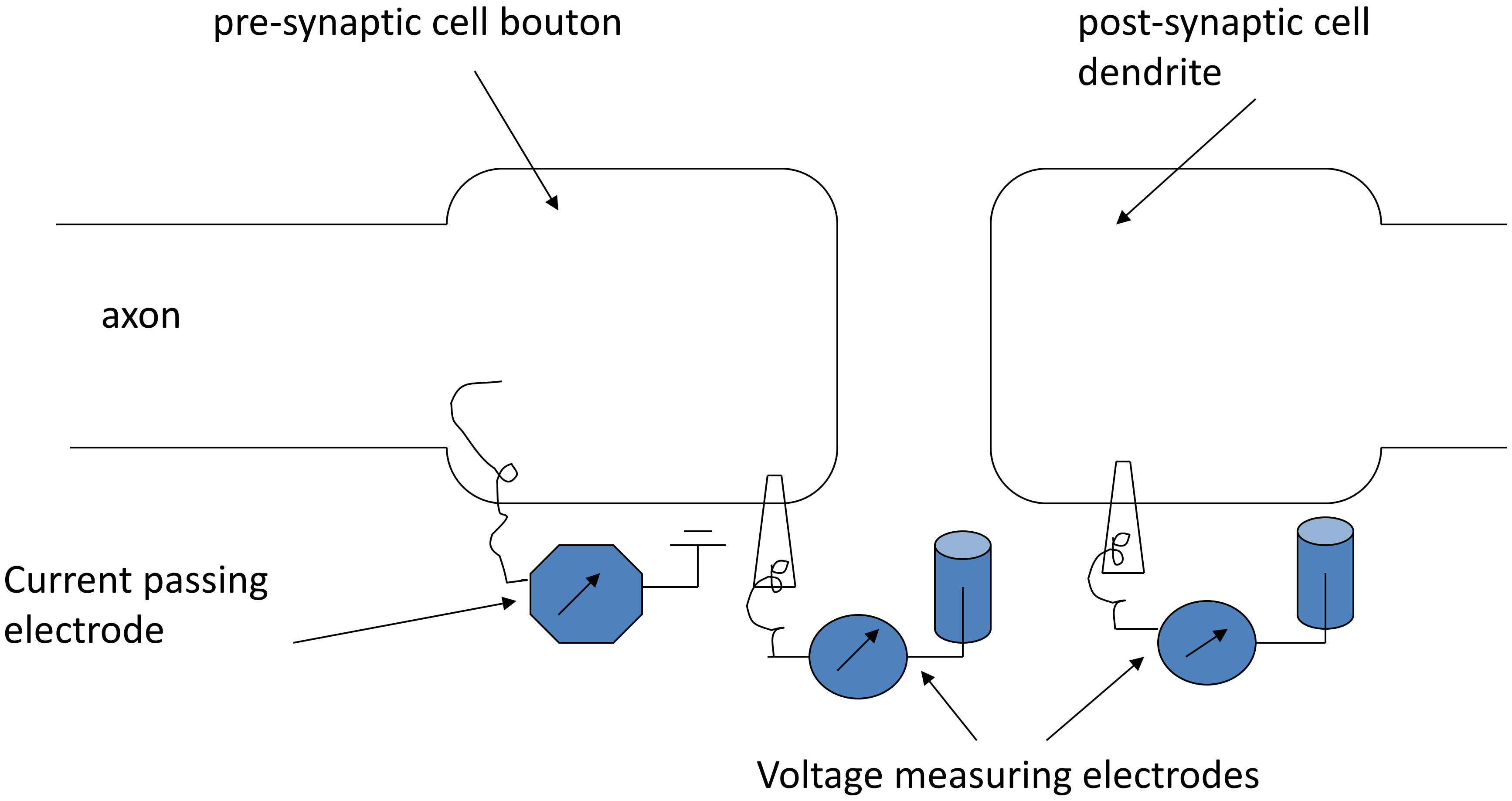
E. Experiment #4: inject **subthreshold** current in postsynaptic cell



Thus, **unidirectional synaptic transmission** also exists. **Rectifying electrical synapses** that conduct current in a single direction. May be due to **heterotypic channels** formed from **different forms** of the **connexin protein**.

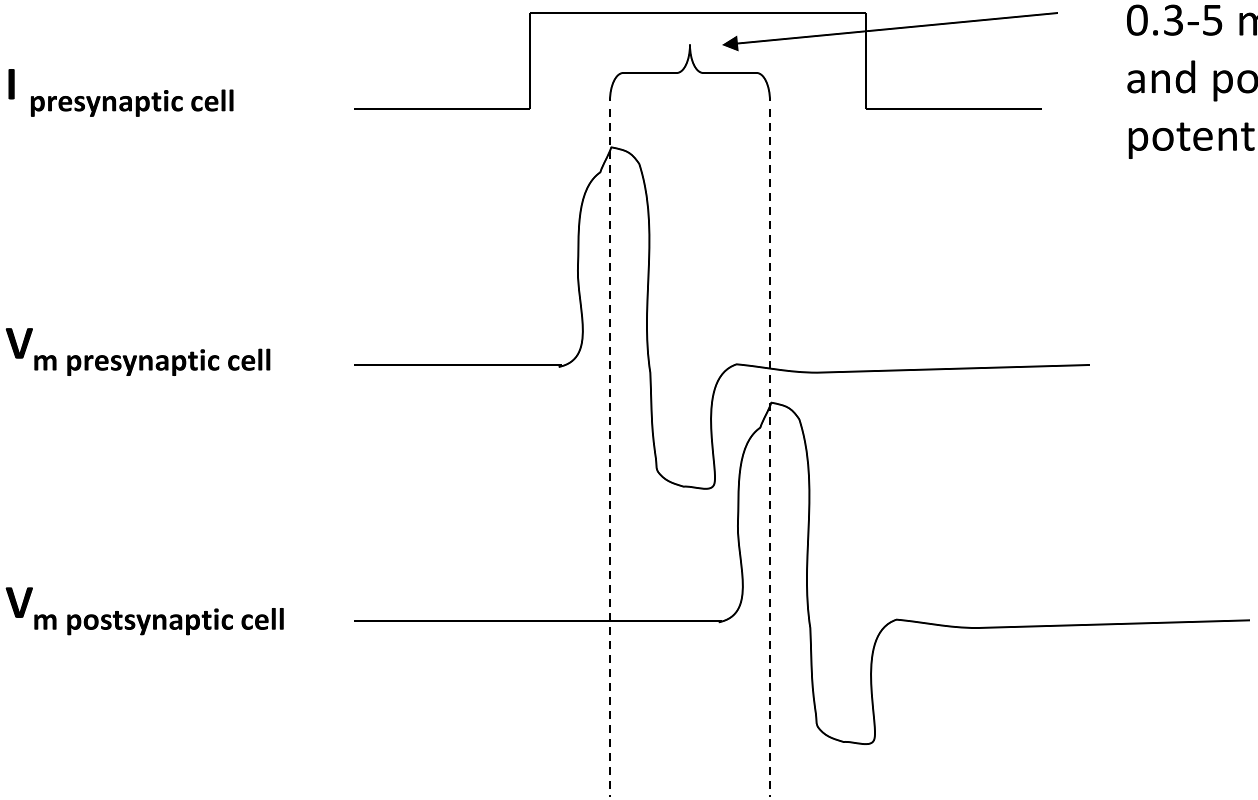
Physiology of Chemical Synapses:

A. Experimental set-up:



Physiology of Chemical Synapses: (cont’d)

B. Experiment #1: inject **threshold** current in presynaptic cell

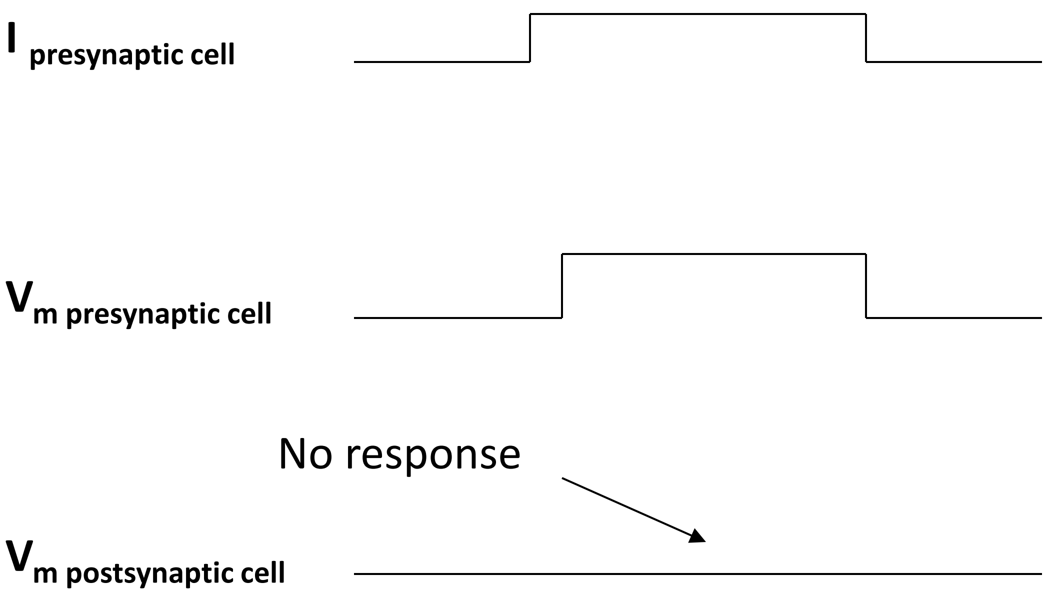


0.3-5 msec delay between pre- and postsynaptic action potentials

Thus, **synaptic delay** is significantly **longer** than for an electrical synapse.

Physiology of Chemical Synapses: (cont'd)

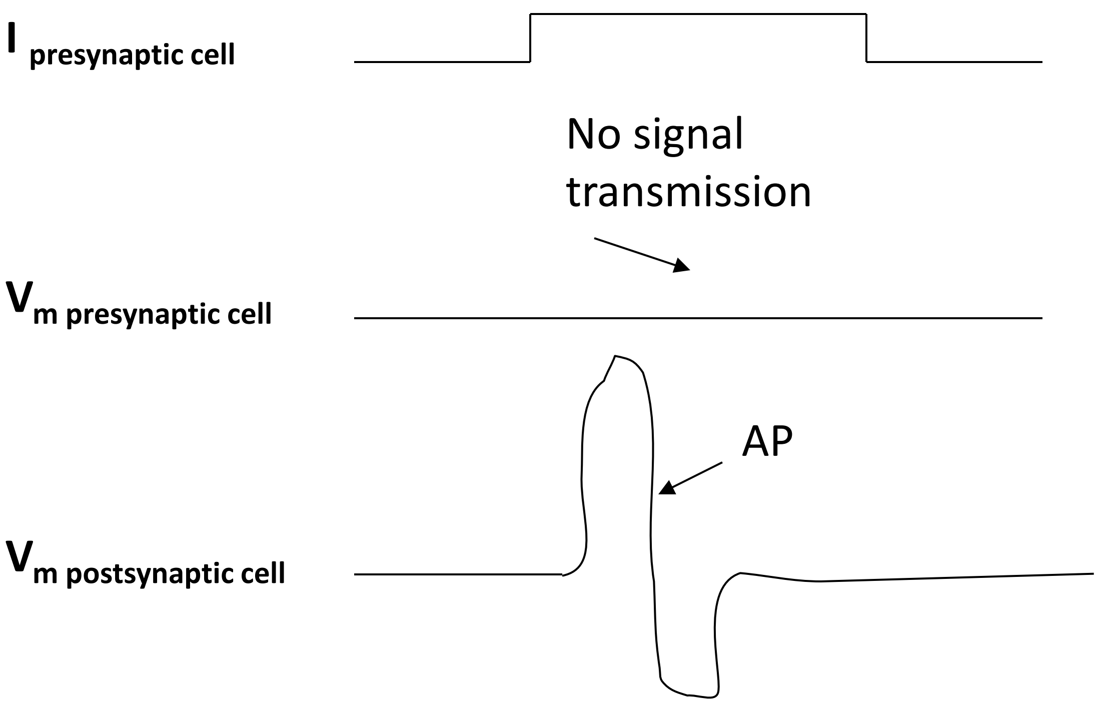
C. Experiment #2: inject **subthreshold** current in presynaptic cell



Thus, requires a t**hreshold change in V_m** in the **presynaptic cell** for **signal transmission**.

Physiology of Chemical Synapses: (cont’d)

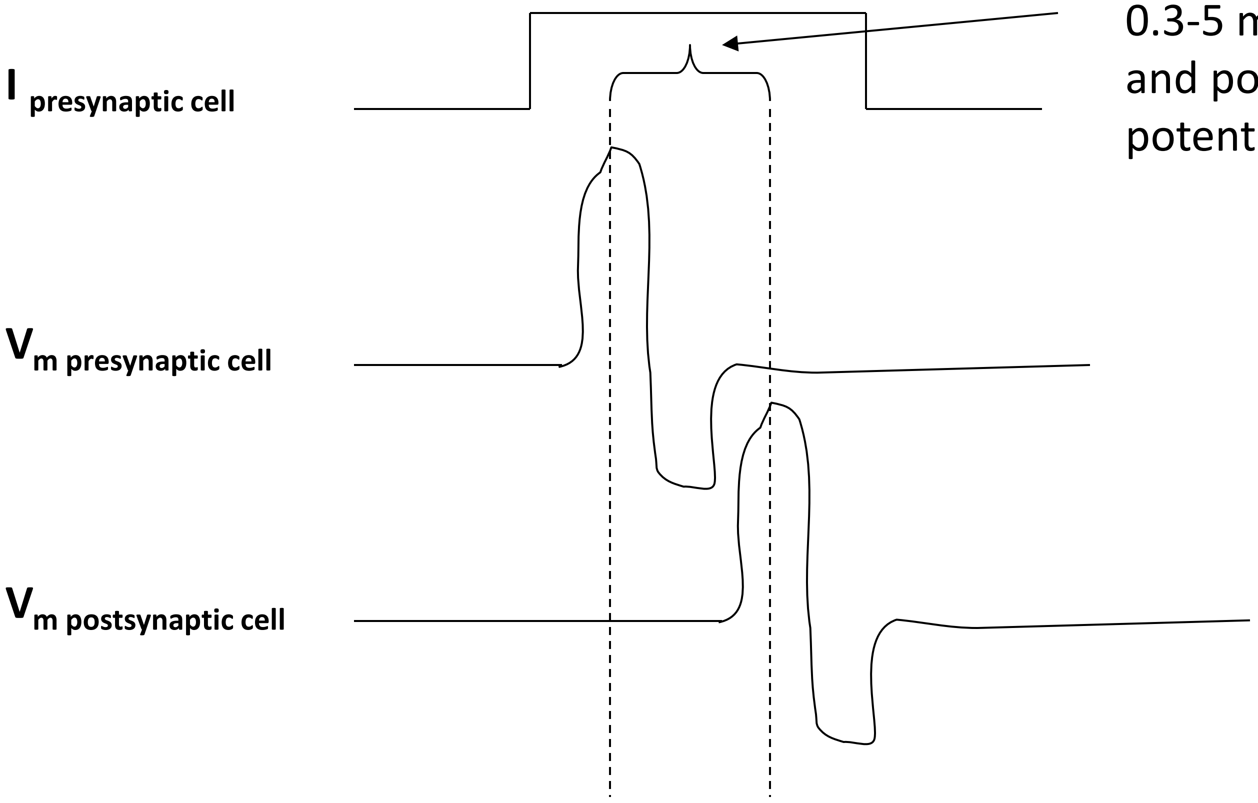
D. Experiment #3: inject **threshold** current in postsynaptic cell



Thus, signal transmission is **unidirectional.** Together with other experimental results, this result suggests that **signal transmission** is **not via electrotonic current transmission** and that it **requires** a **presynaptic AP**.

Physiology of Chemical Synapses: (cont'd) What Current is Required for Signal Transmission

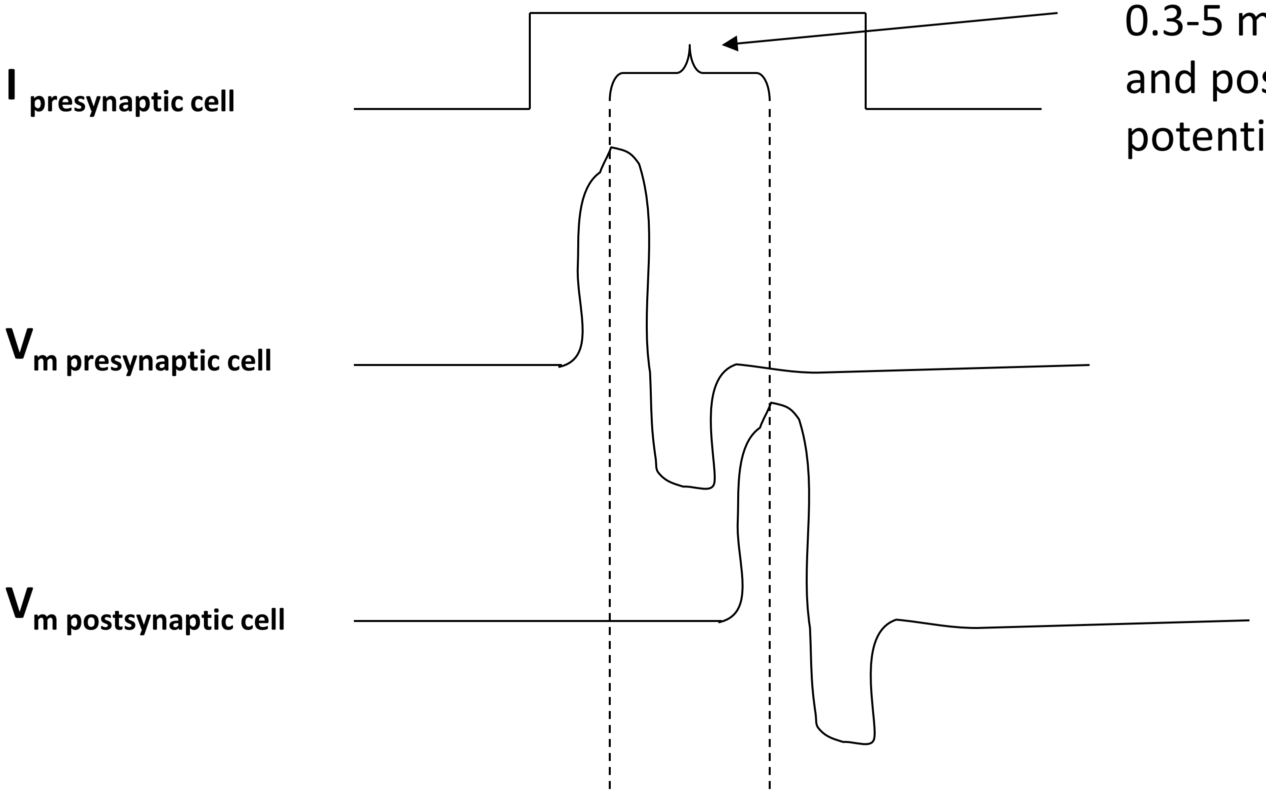
E. Experiment #4: inject **threshold** current in **presynaptic cell** bathed in **tetrodotoxin to block Na^+ current**



Thus, the **Na^+ current** is **not required** for **chemical synaptic transmission**.

Physiology of Chemical Synapses: (cont'd) What Current is Required for Signal Transmission

F. Experiment #5: inject **threshold** current in **presynaptic cell** bathed in **tetraethylammonium ion to block K^+ current**

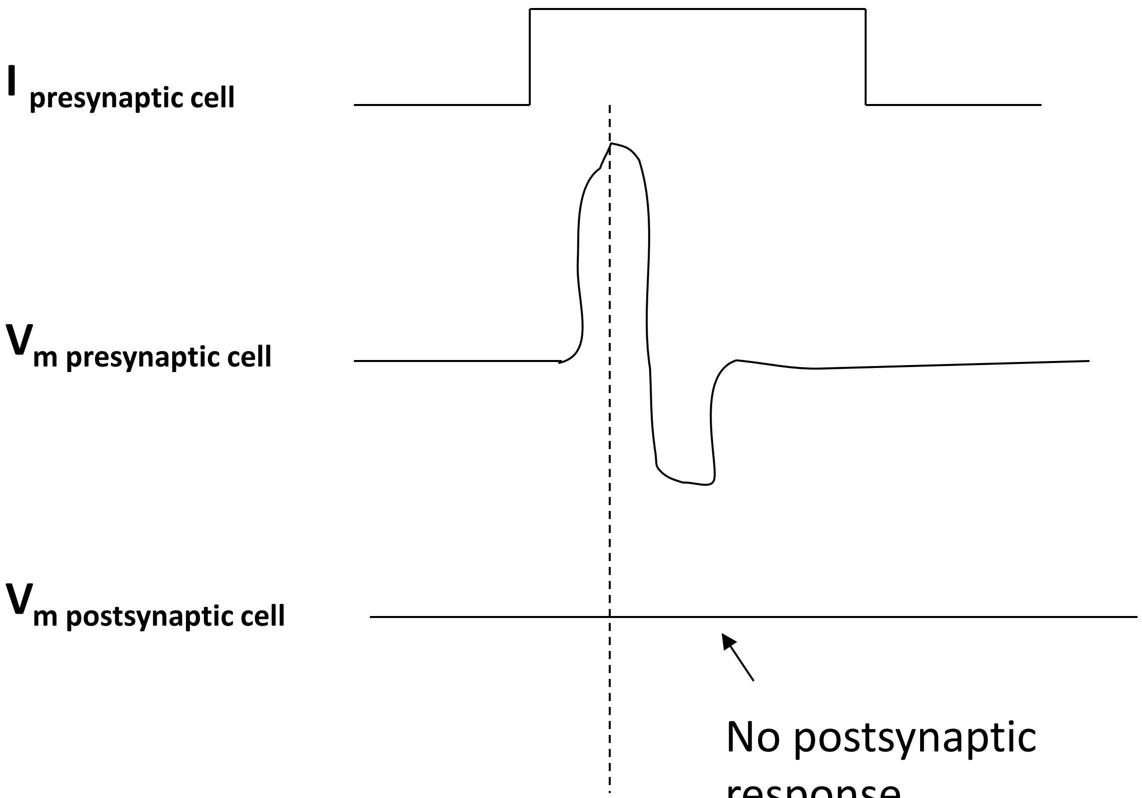


0.3-5 msec delay between pre- and postsynaptic action potentials

Thus, the **K^+ current** is **not required** for **chemical synaptic transmission**.

Physiology of Chemical Synapses: (cont'd) What Current is Required for Signal Transmission

G. Experiment #6: inject **threshold** current in **presynaptic cell** bathed in **Ca^{2+}-free medium**

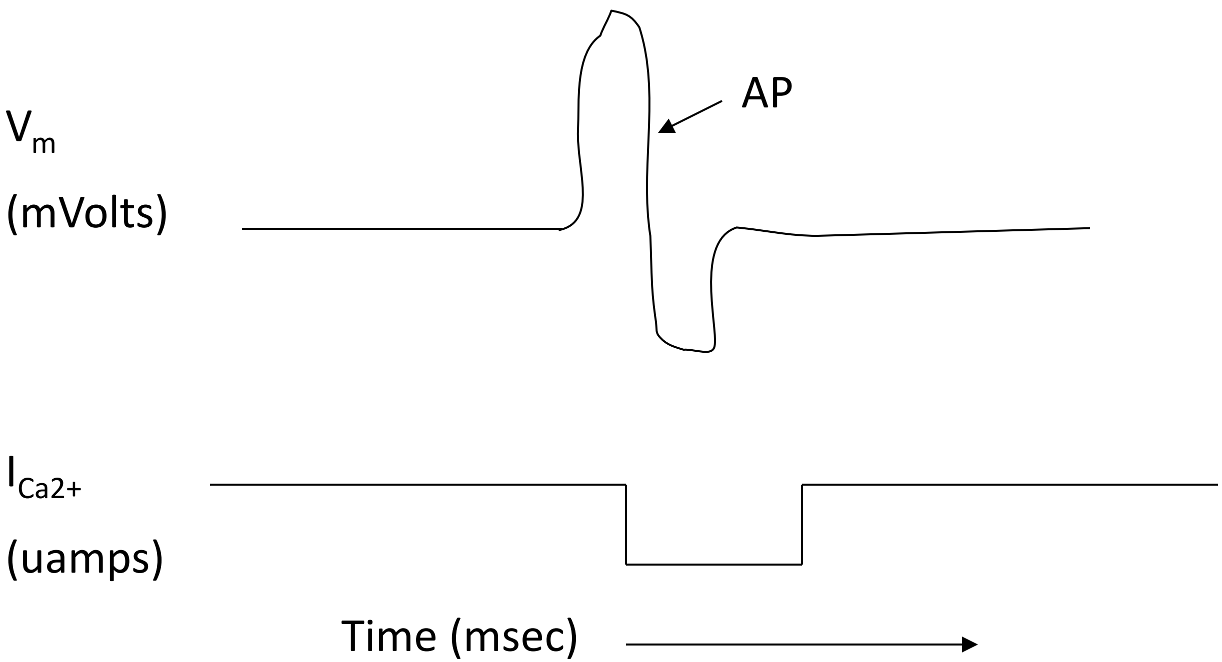


Thus, the **Ca^{+} current is required** for **chemical synaptic transmission**.

The Calcium Dependent Model of Neurotransmitter Release:

A. Where does synaptic delay come from?

1. Slow opening of voltage-gated Ca^{2+} channels -



Majority of synaptic delay

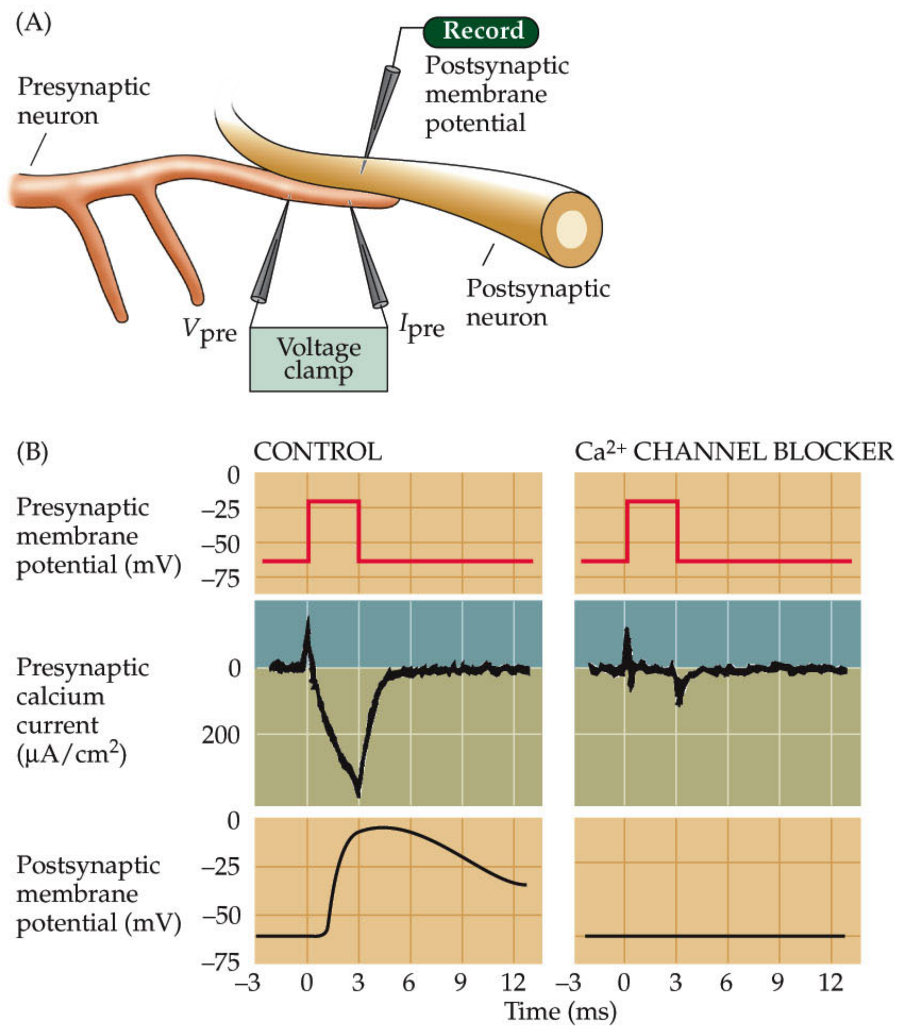
The Calcium Dependent Model of Neurotransmitter Release: (cont'd)

Where does synaptic delay come from? (continued)

2. Time for exocytosis of synaptic vesicles
3. Diffusion of neurotransmitter across the synapse
4. Molecular events at the postsynaptic membrane that lead to AP production following neurotransmitter binding

Calcium influx is necessary for neurotransmitter release

Voltage-gated calcium channels



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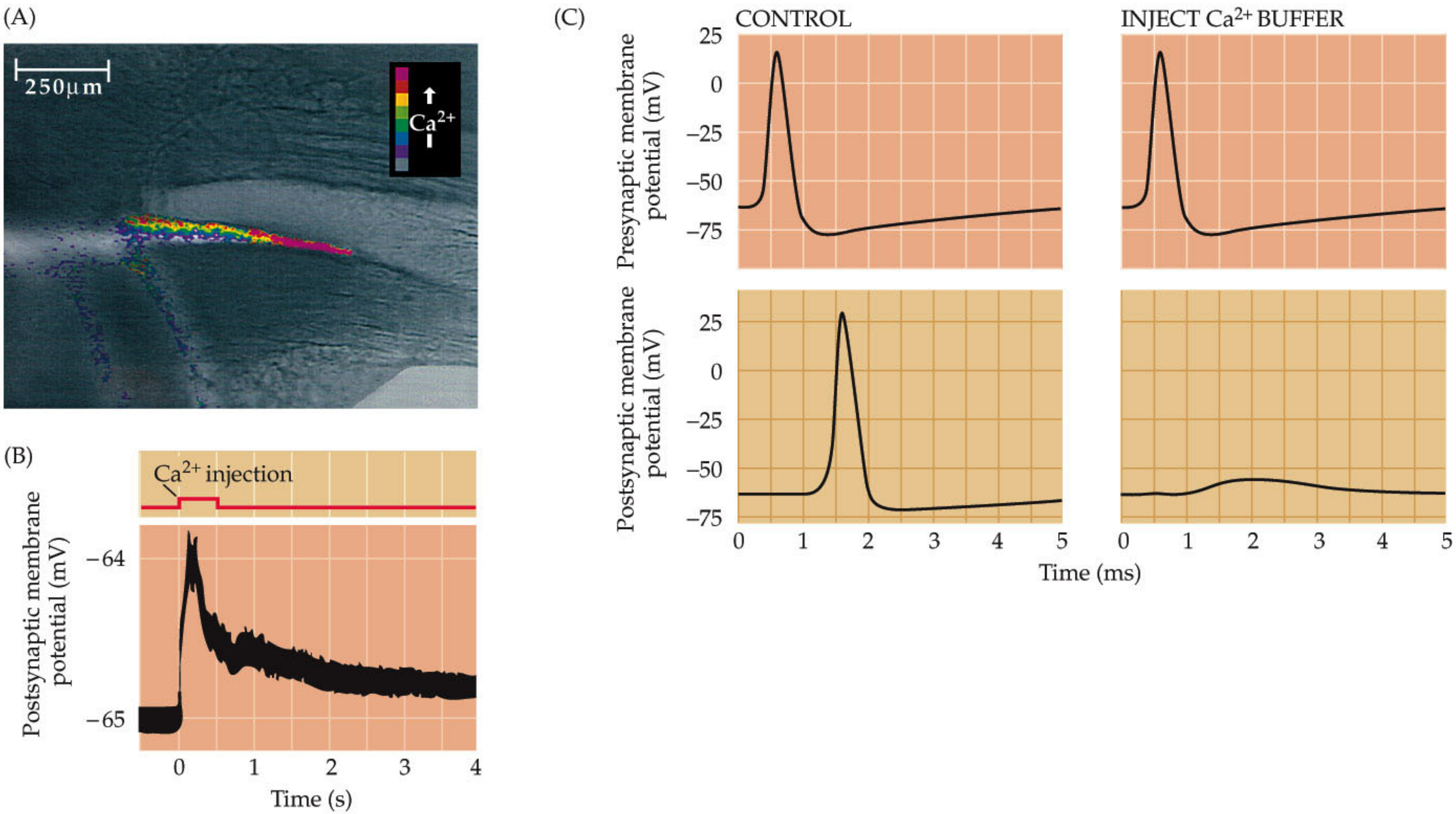
Calcium influx is sufficient for neurotransmitter release



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