Introduction to Neuroinformatics

Synapses II

31.10.219

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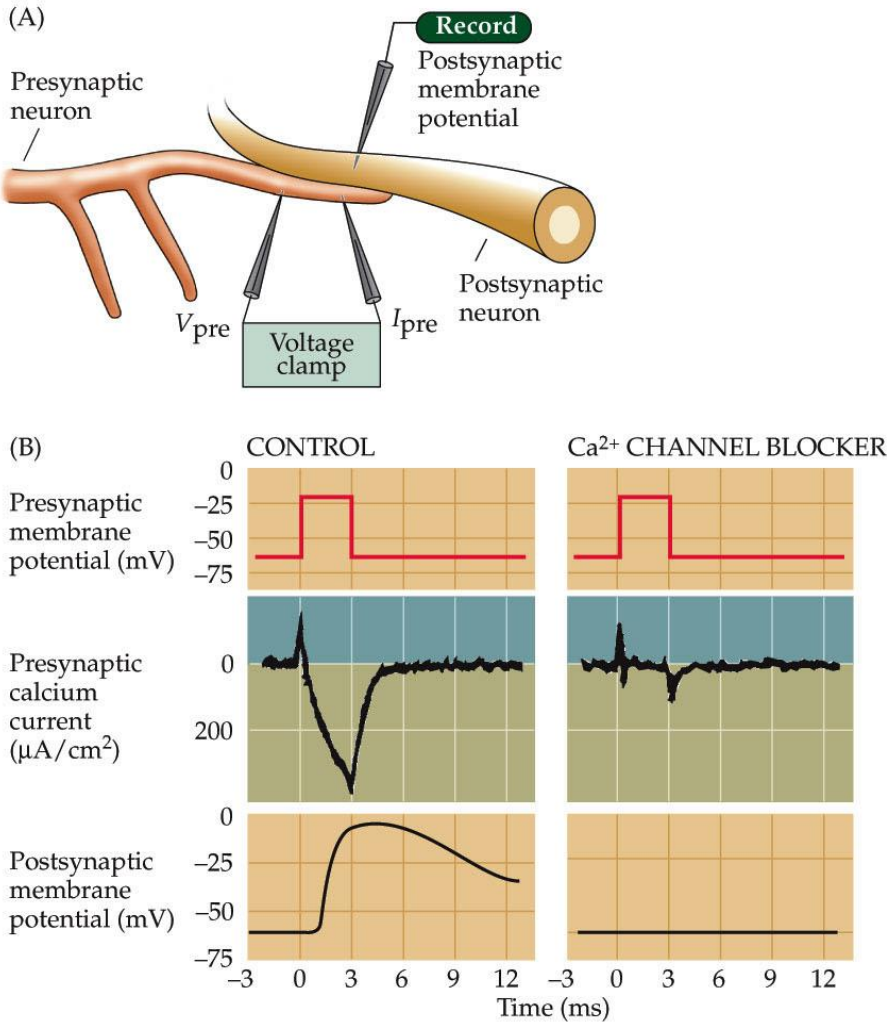
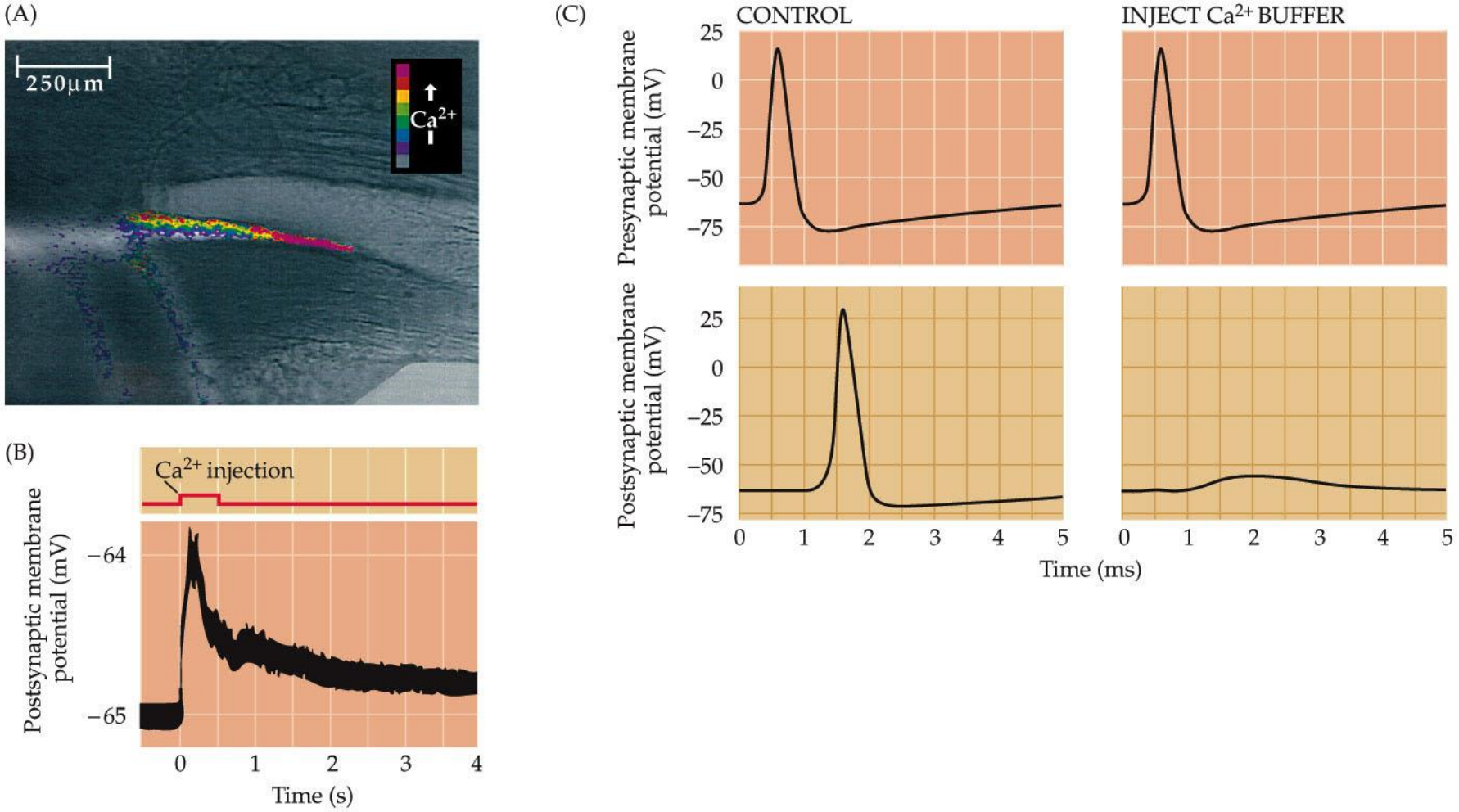
Calcium influx is necessary for neurotransmitter release

Voltage-gated calcium channels



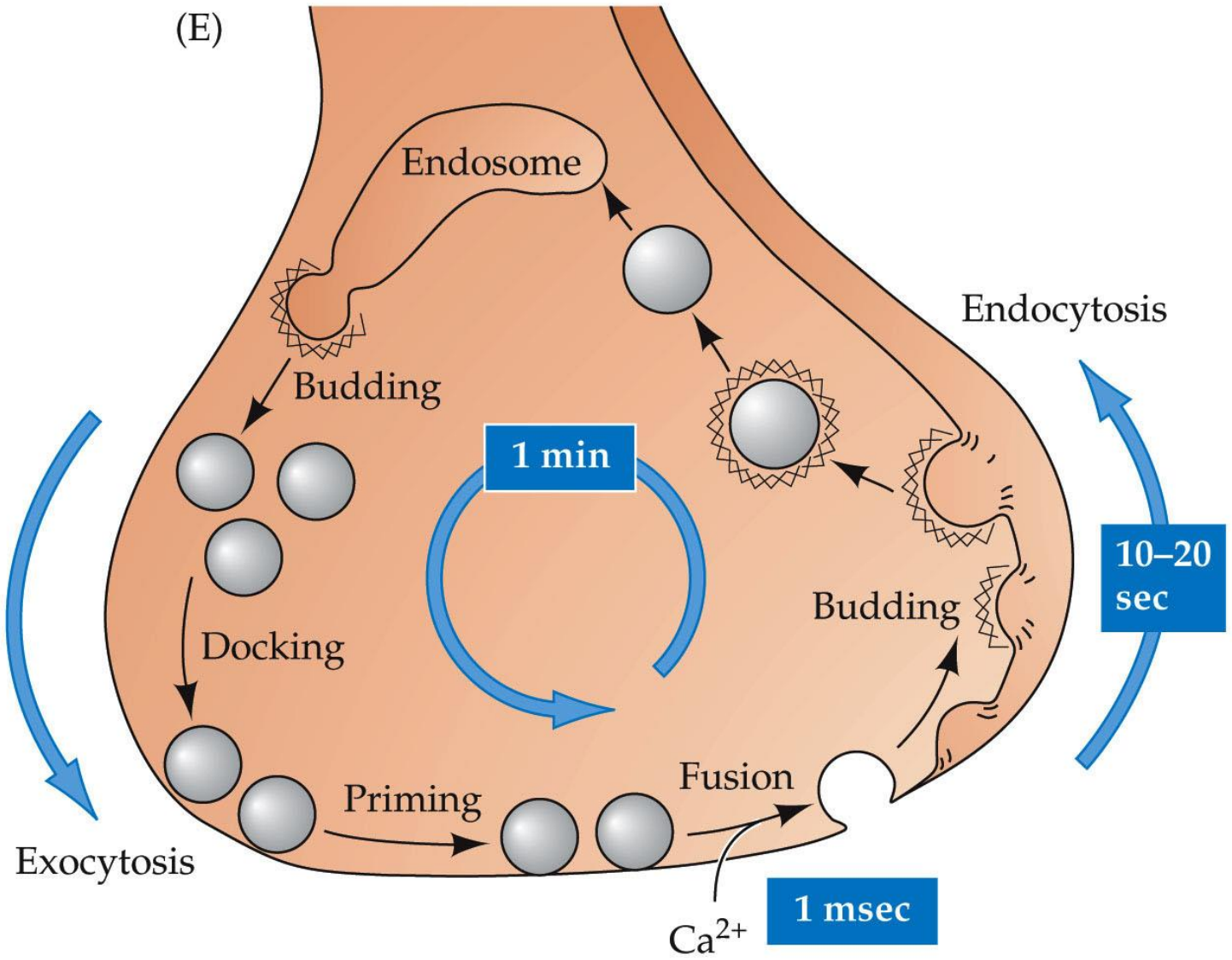
NEUROSCIENCE, Fourth Edition, Figure 5.10

Calcium influx is sufficient for neurotransmitter release



NEUROSCIENCE, Fourth Edition, Figure 5.11

The synaptic vesicle cycle



NEUROSCIENCE, Fourth Edition, Figure 5.9 (Part 2)

Synaptic vesicle release consists of three principal steps:

1. Docking

   Docked vesicles lie close to plasma membrane (within 30 nm)

1. Priming

   Primed vesicles can be induced to fuse with the plasma membrane by sustained depolarization, high K^+, elevated Ca^{++}, hypertonic sucrose treatment

2. Fusion

   Vesicles fuse with the plasma membrane to release transmitter. Physiologically this occurs near calcium channels, but can be induced experimentally over larger area (see 'priming'). The 'active zone' is the site of physiological release, and can sometimes be recognized as an electron-dense structure.

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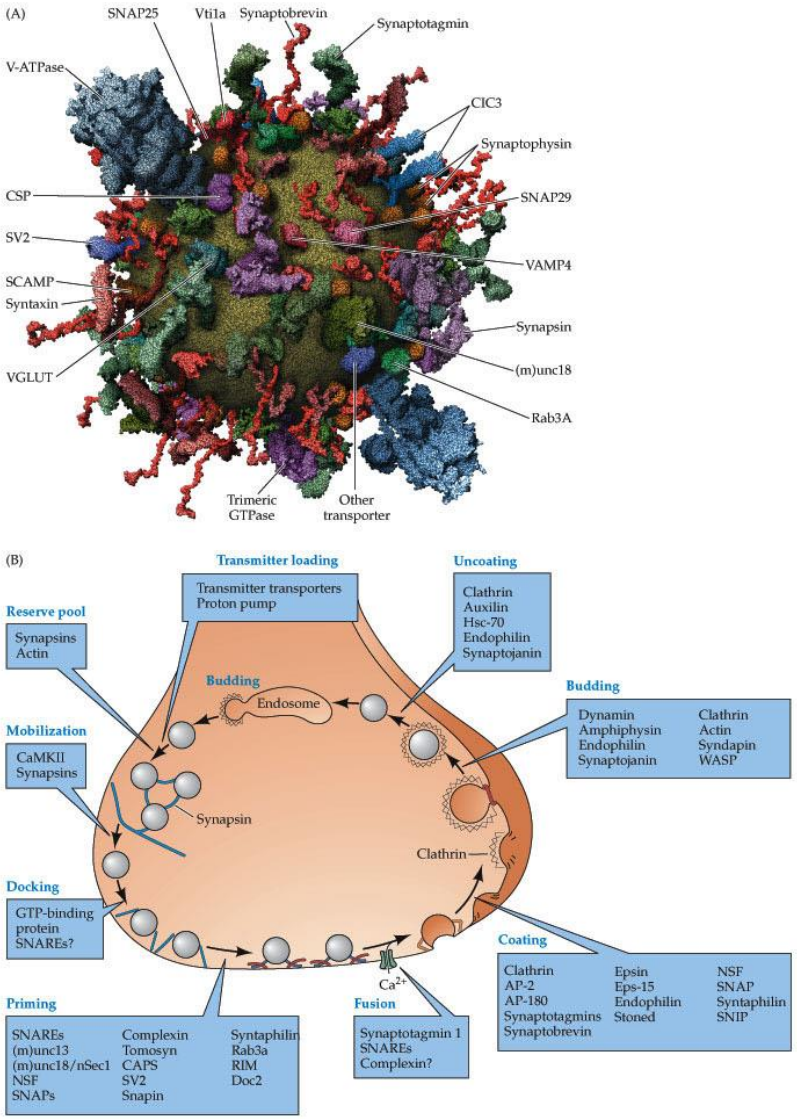
Vesicle release requires many proteins on vesicle and plasma membrane

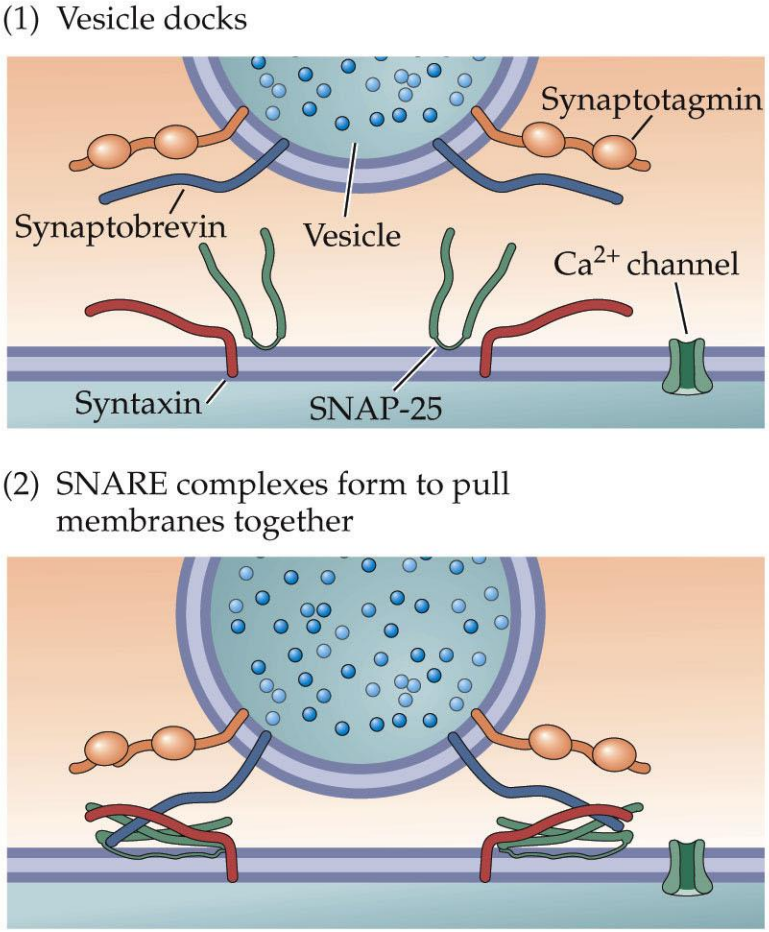


NEUROSCIENCE, Fourth Edition, Figure 5.13

Priming

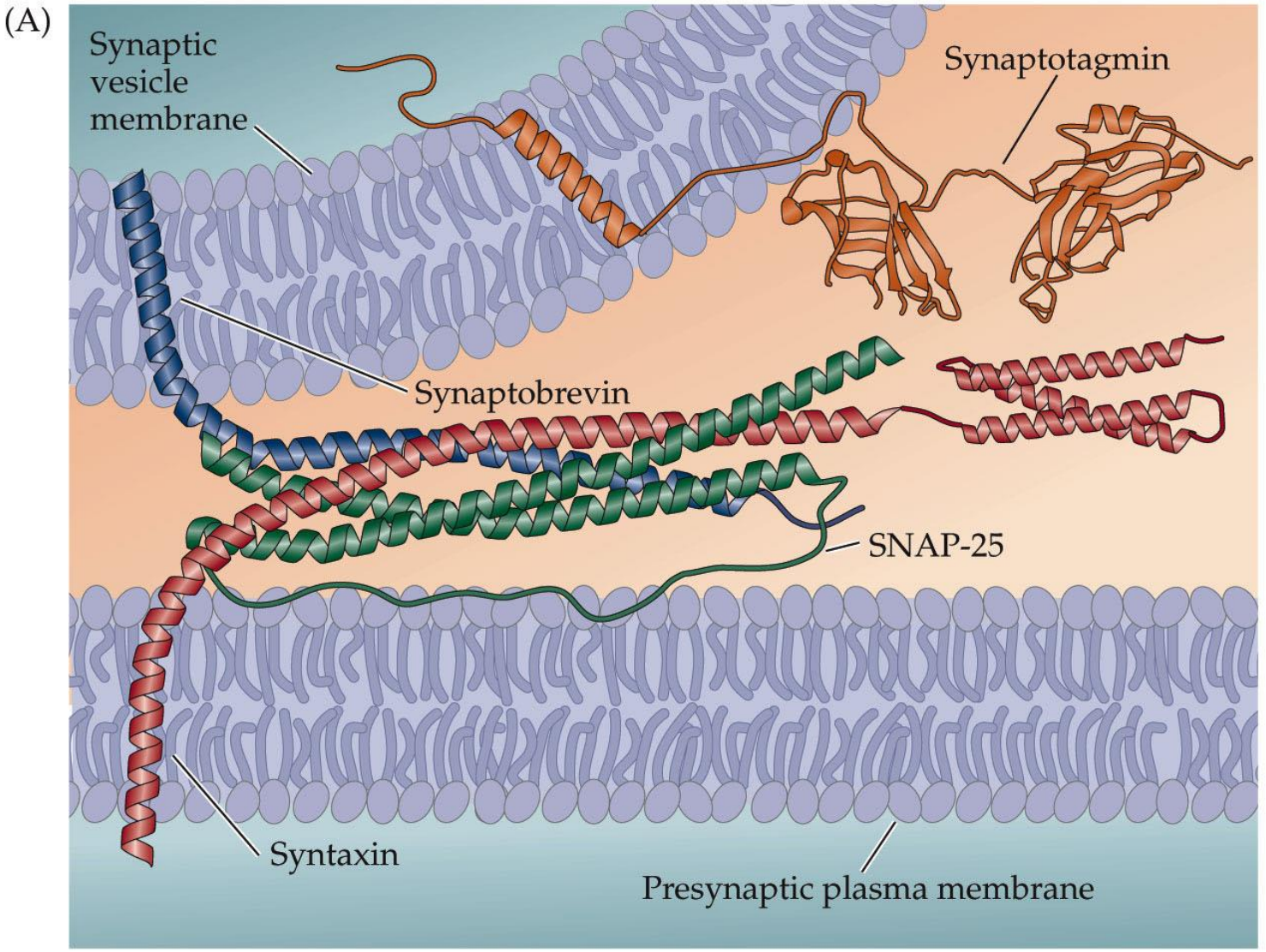
Vesicles in the reserve pool undergo priming to enter the readily-releasable pool

At a molecular level, priming corresponds to the assembly of the SNARE complex



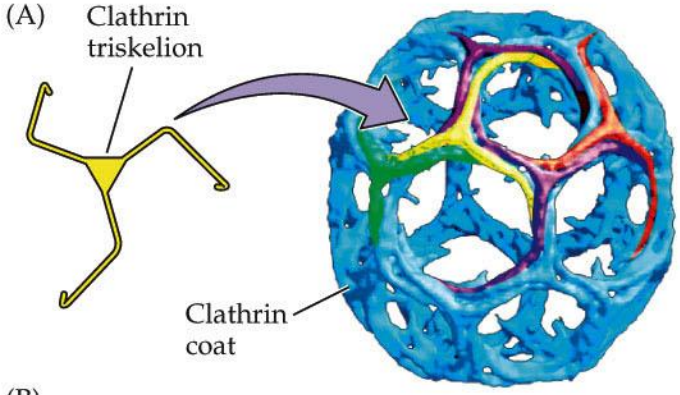
***NEUROSCIENCE, Fourth Edition,* Figure 5.14 (Part 2)**

The SNARE complex

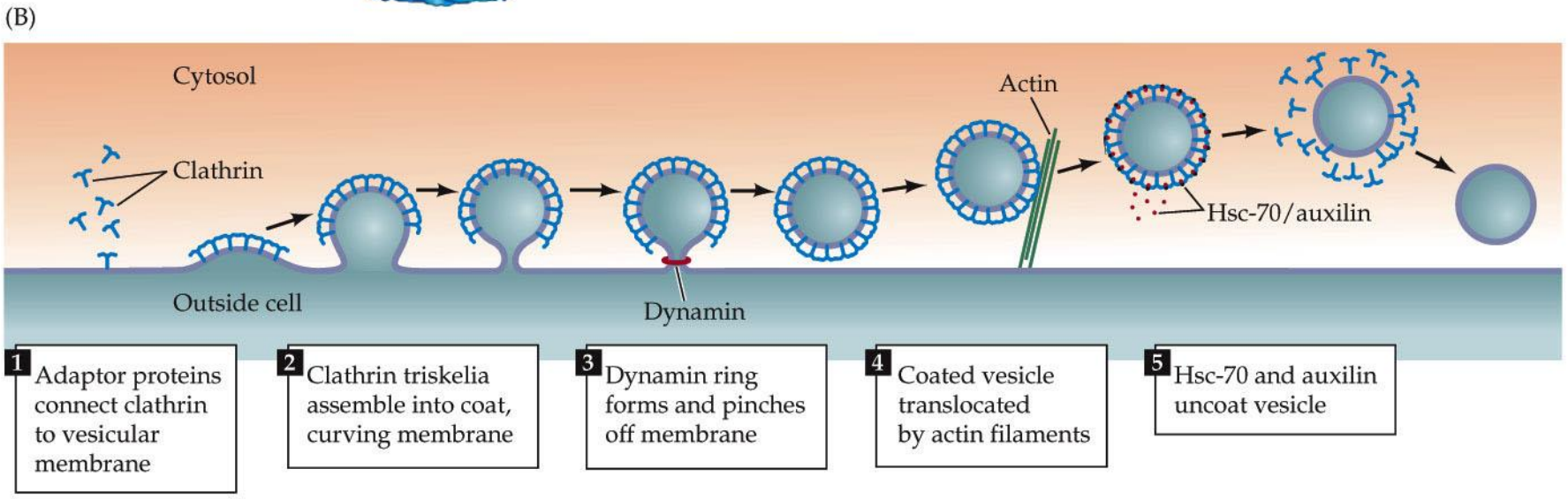


***NEUROSCIENCE, Fourth Edition,* Figure 5.14 (Part 1)**

Endocytosis retrieves synaptic vesicle membrane and protein from the plasma membrane following fusion



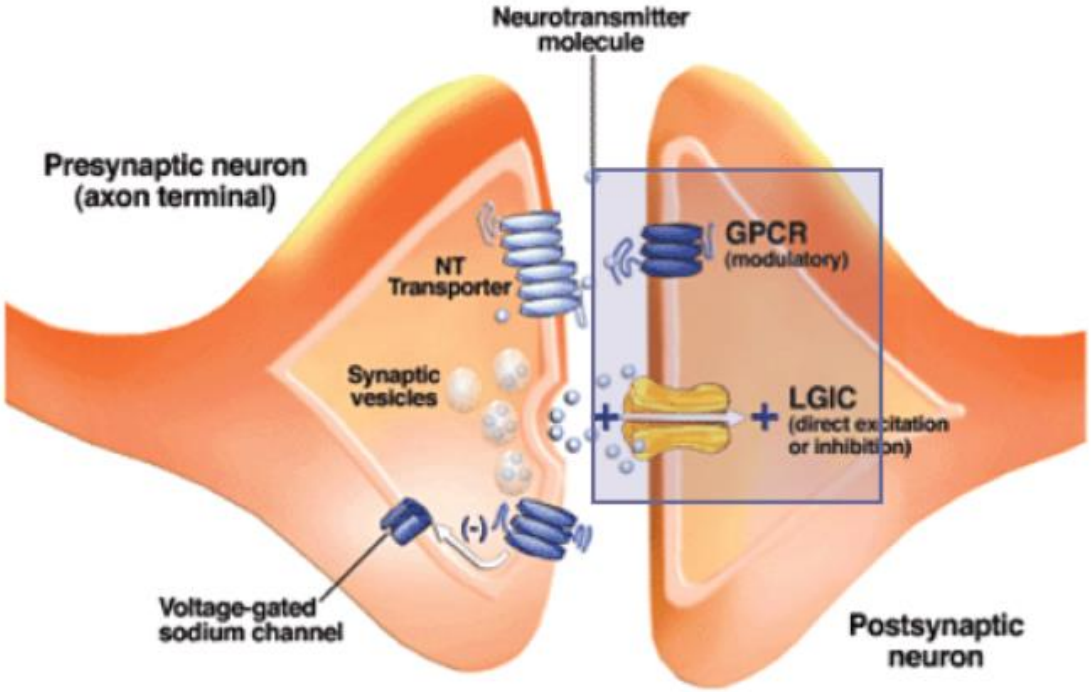
The ATP-ase NSF disassembles the SNARE complex



NEUROSCIENCE, Fourth Edition, Figure 5.15

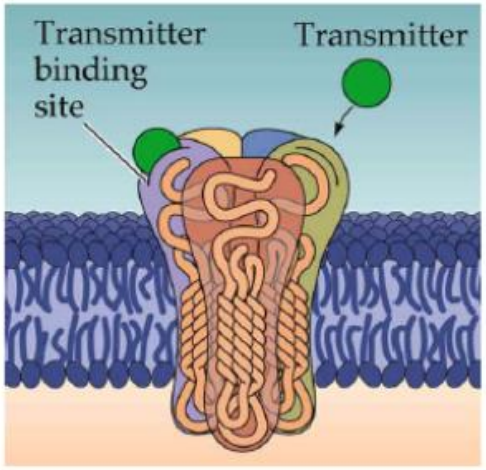
Post-synaptic Receptors

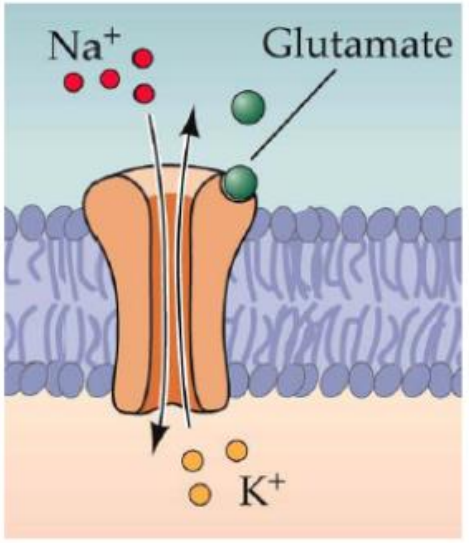
- **Neurotransmitters cross synaptic-cleft and can bind to two types of receptors:**
  - Ionotropic (Ligand-gated ion channels; LGIC)
  - Metabotropic (G-protein coupled receptors; GPCR)



Post-synaptic Receptors

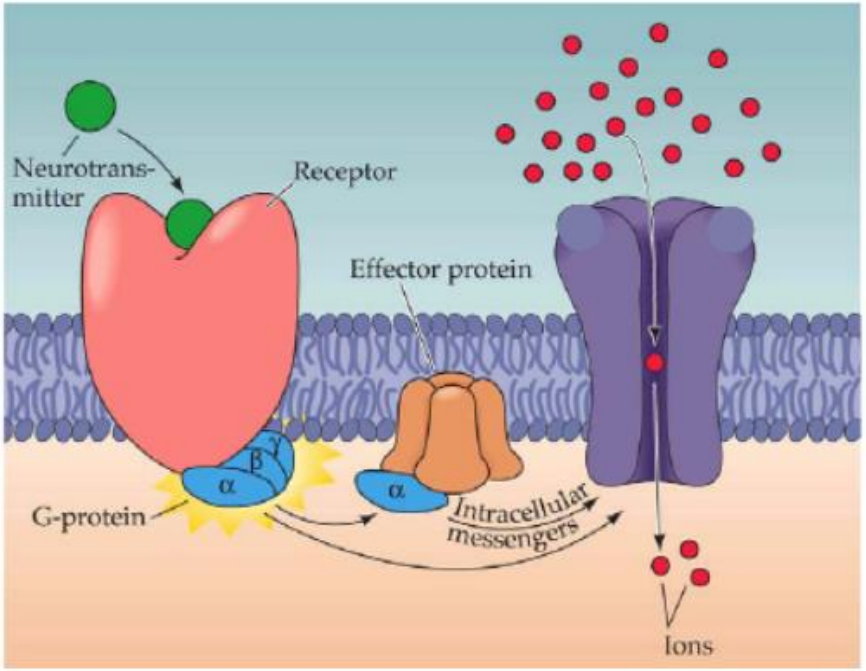
- **Ionotropic**
  - Contains a ligand-binding site
  - A normally-closed ion channel that opens after binding with the neurotransmitter
  - Contribute to fast changes in the membrane potential



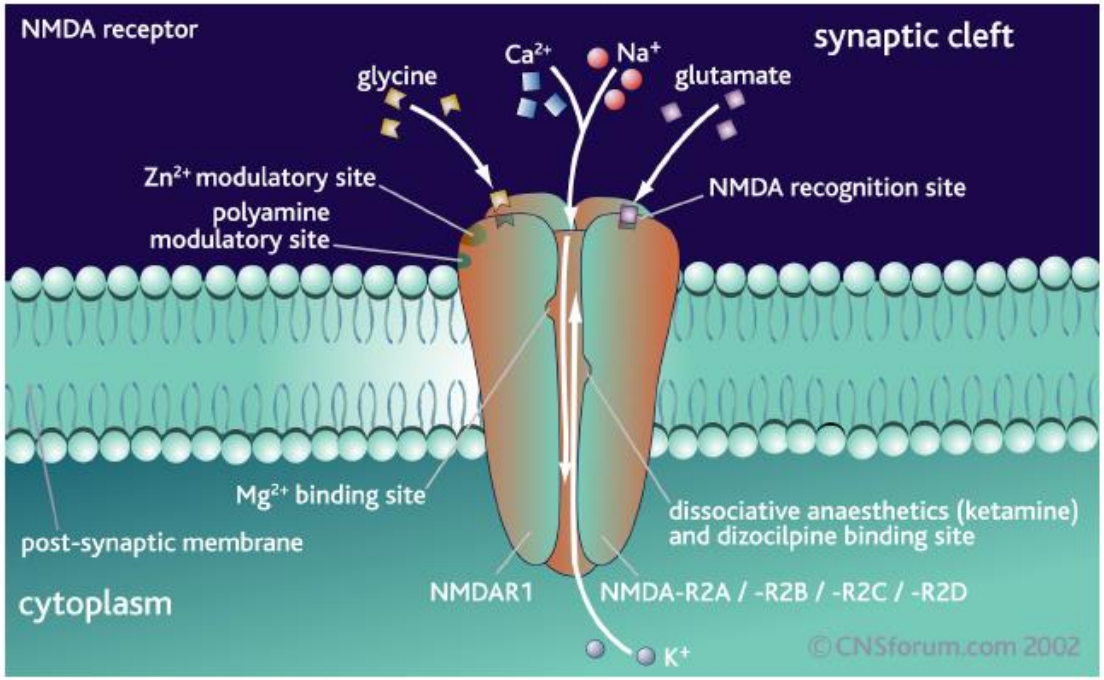


Post-synaptic Receptors

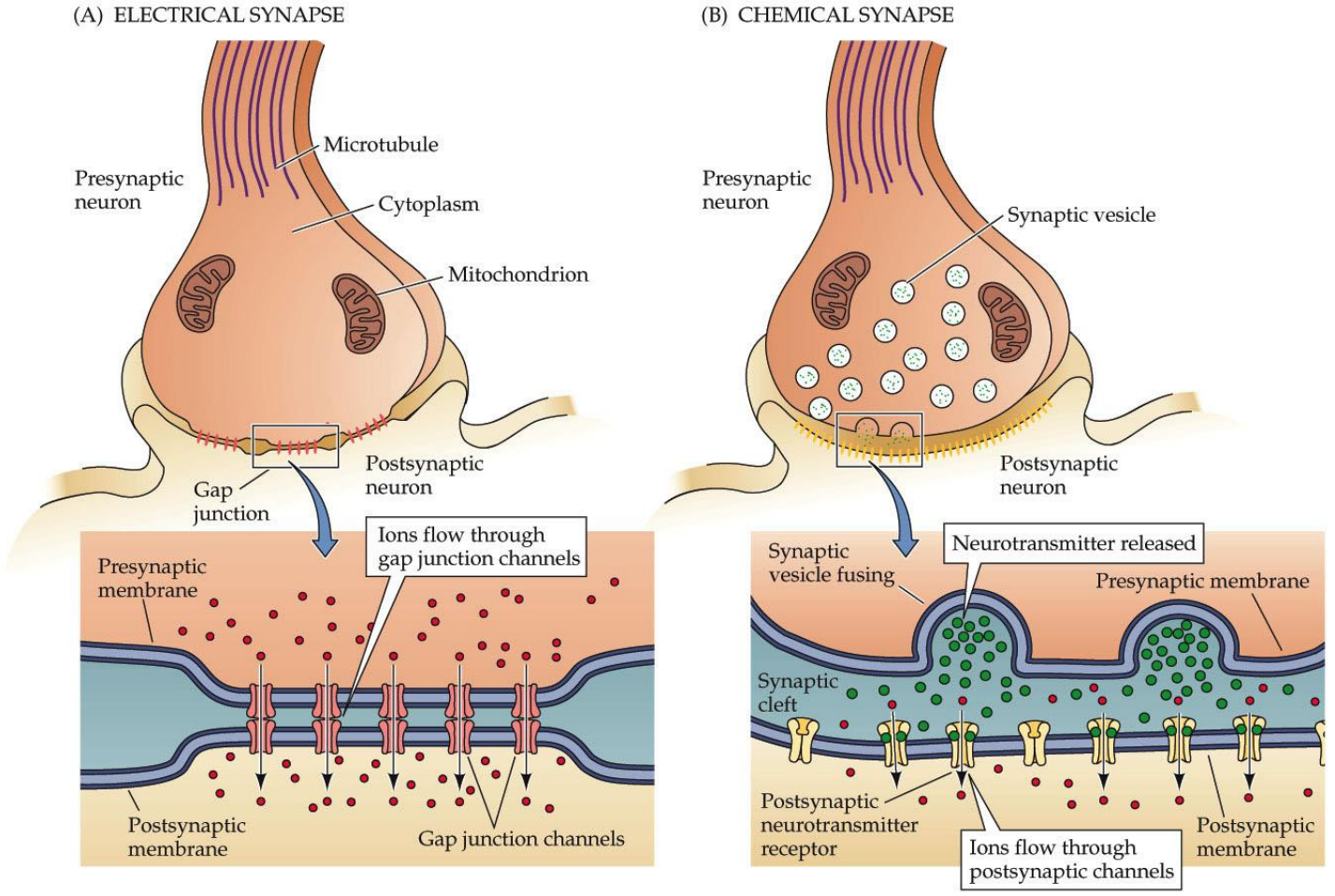
- **Metabotropic**
  - G-protein coupled receptor
  - Secondary messenger involved
  - Slow postsynaptic processes (plays a role in synaptic plasticity)



NMDA Receptor

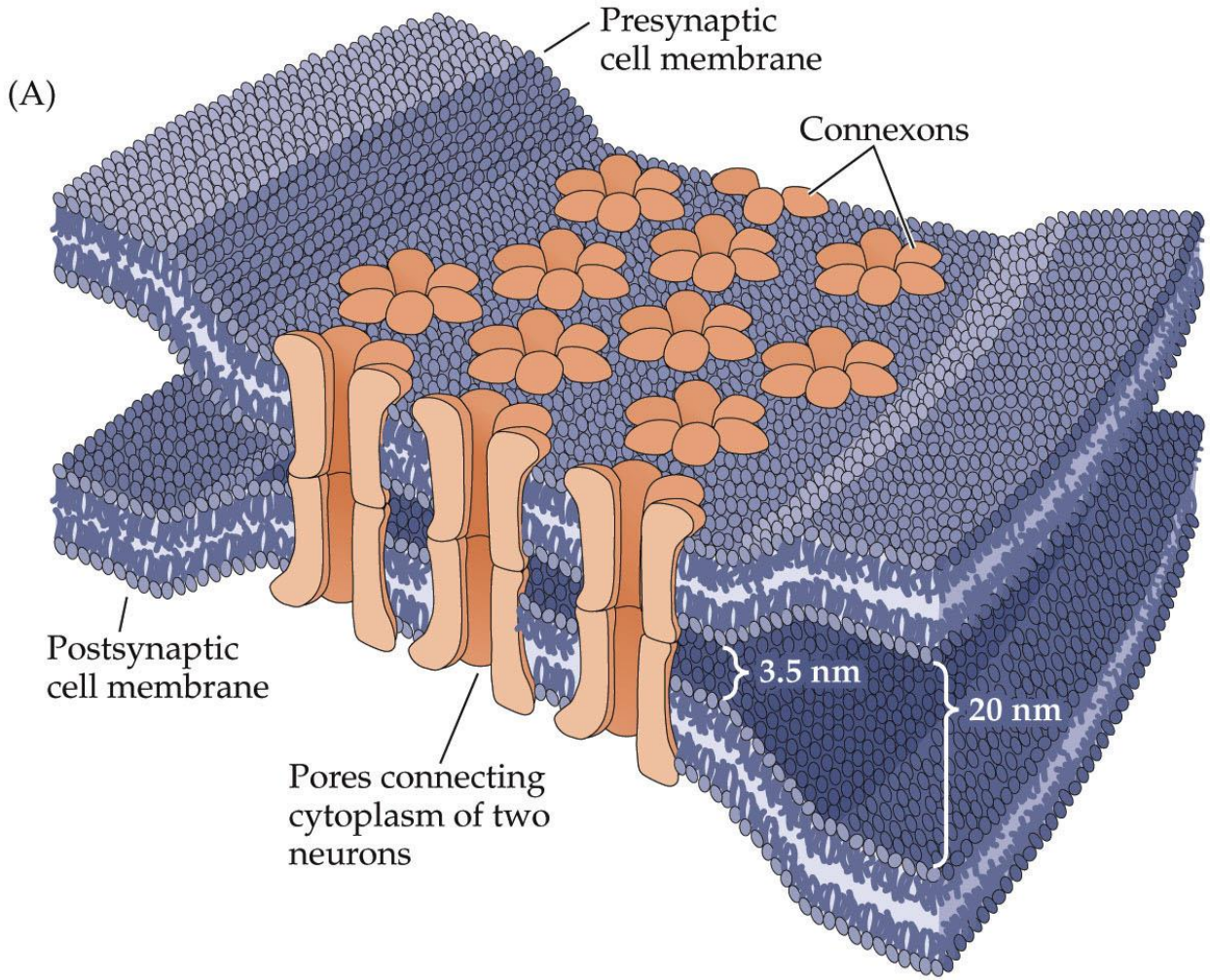


Two principal kinds of synapses: electrical and chemical



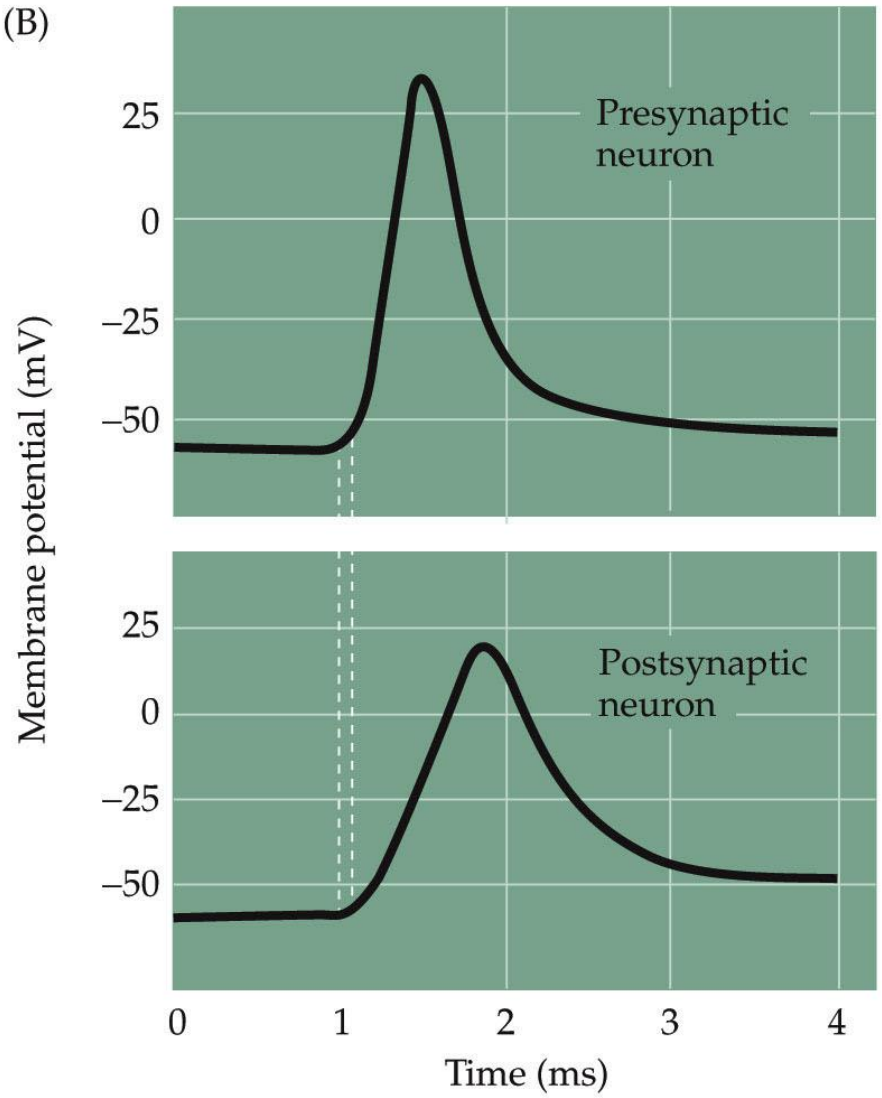
NEUROSCIENCE, Fourth Edition, Figure 5.1

Gap junctions are formed where hexameric pores called connexons connect with one between cells



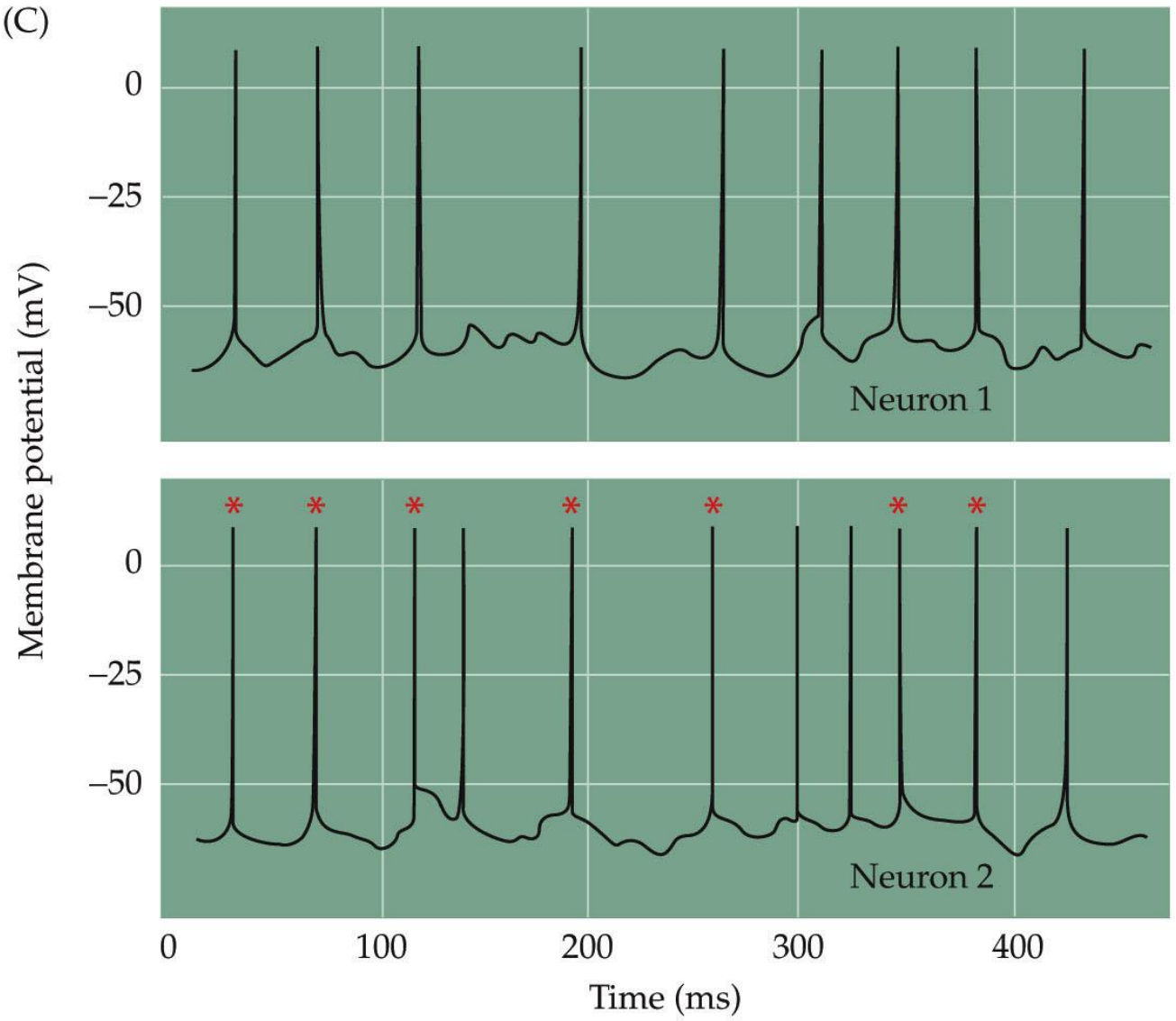
NEUROSCIENCE, Fourth Edition, **Figure 5.2 (Part 1)**

Electrical synapses are built for speed



***NEUROSCIENCE, Fourth Edition,* Figure 5.2 (Part 2)**

Electrical coupling is a way to synchronize neurons with one another



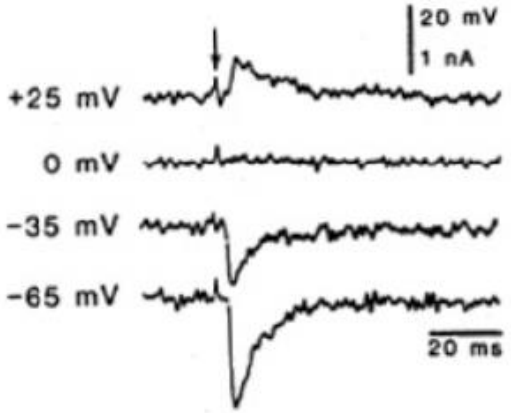
***NEUROSCIENCE, Fourth Edition,* Figure 5.2 (Part 3)**

Electrical vs. Chemical Synapse

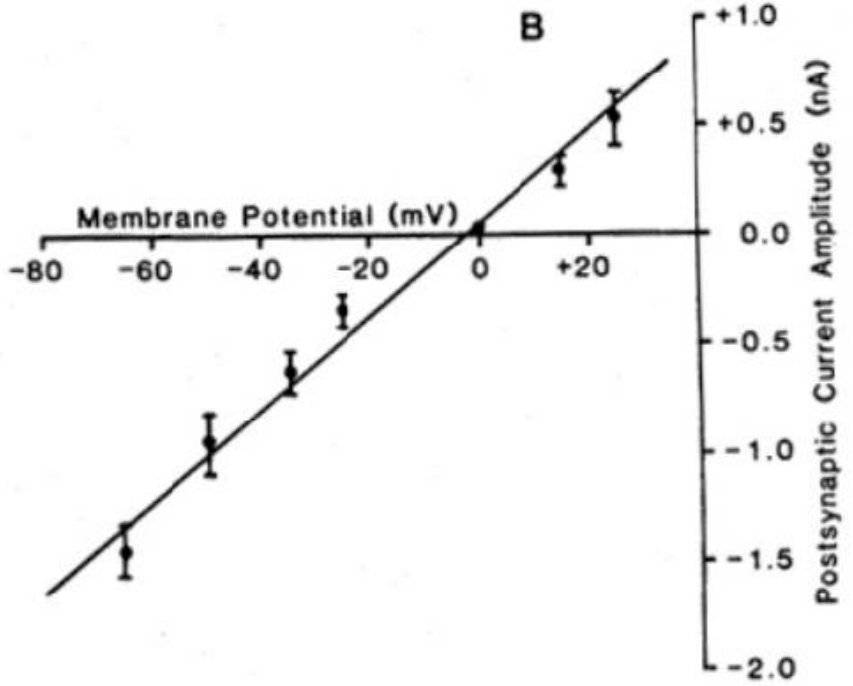
Electrical Synapse	Chemical Synapse
simple primitive system	highly developed structure
often symmetrical, bidirectional	polarized, structurally and functionally
gap junction (connexins)	pre: active zone post: postsynaptic density
very fast, no synaptic delay	slower, synaptic delay (~ 0.5 ms)
Ca2+-independent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

Modeling Synapses

Voltage clamp data



I-V curve

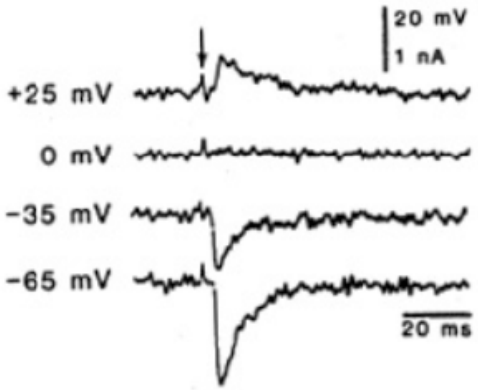


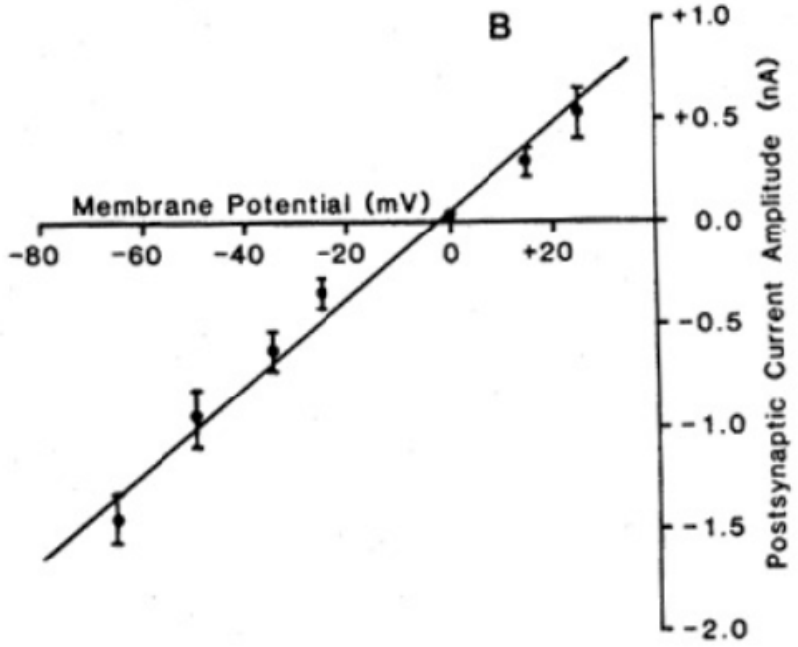
What do these plots tell you?

Modeling Synapses

I-V curve

Voltage clamp data (Excitatory Synapse)





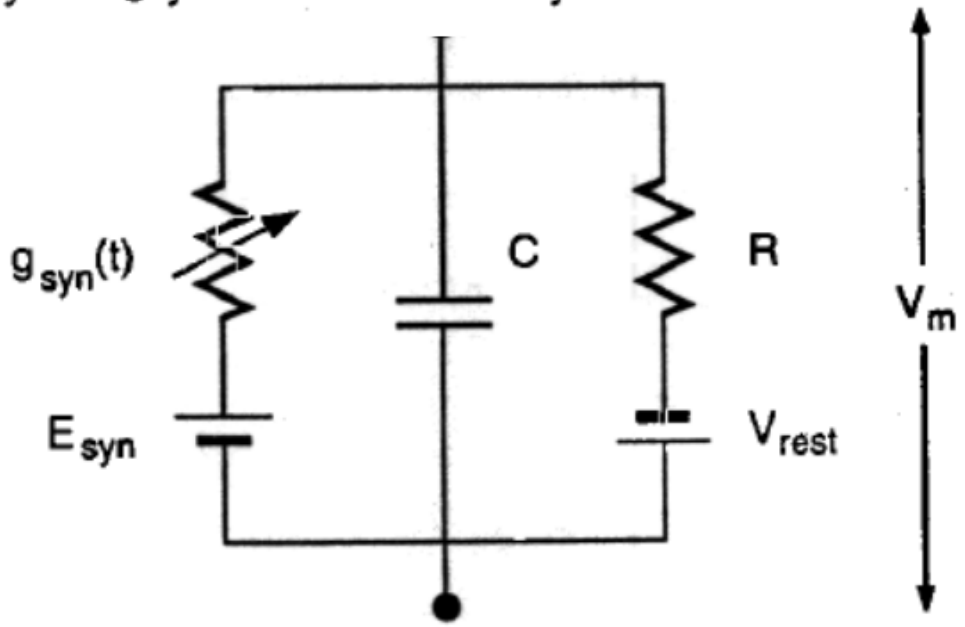
What do these plots tell you?

Synaptic input well capture by Ohm's law

Equivalent circuit of a fast chemical synapse

Koch, Biophysics of Computation, Chapter 1

$$I_{syn} = g_{syn}(t)(V_m(t) - E_{syn})$$

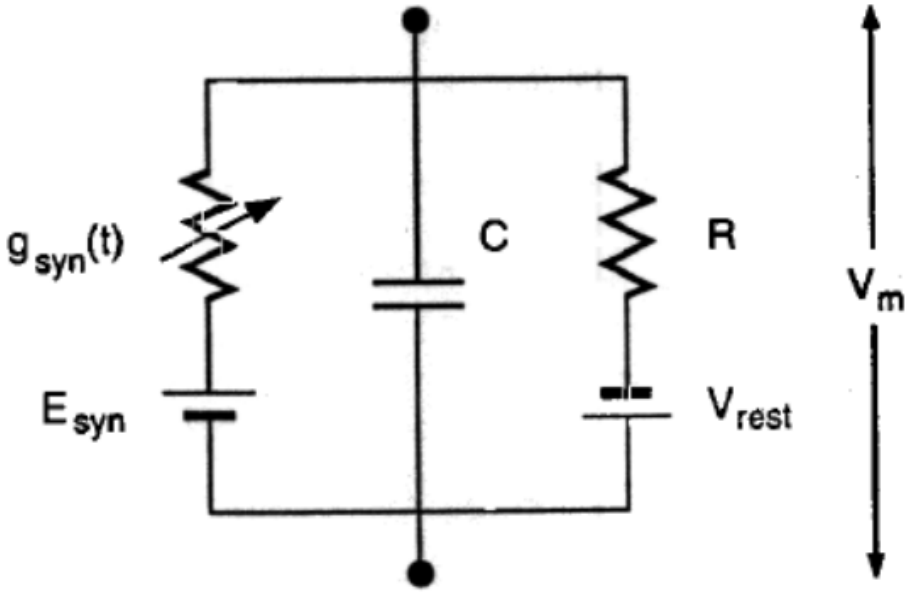


Modified membrane patch equation with a synapse:

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

Equivalent circuit of a fast chemical synapse

Koch, Biophysics of Computation, Chapter 1



Rewriting, we get:

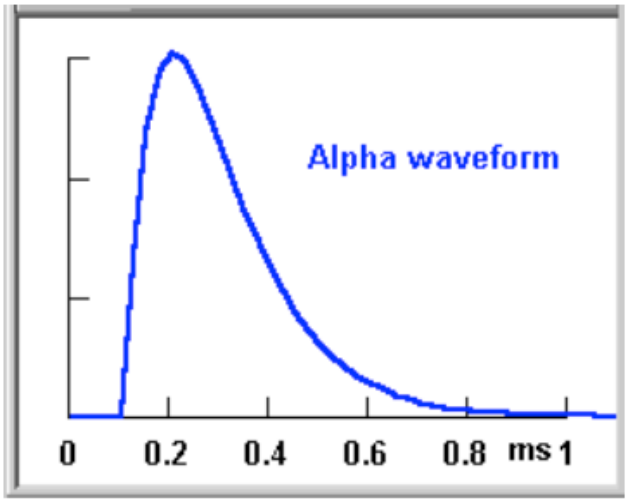
$$\tau \frac{dV_m}{dt} = -(1 + Rg_{syn}(t))V_m + Rg_{syn}(t)E_{syn} + V_{rest}$$

$$[\tau = RC]$$

Alpha Function

- **Synaptic input is usually approximated by an 'alpha function' of the form**

$$g_{syn}(t) = g_{peak} \cdot t \cdot \exp\left(-t / t_{peak}\right)$$



Multiple Synaptic Input

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

- Since current add:

$$C\frac{dV_m}{dt} = \sum_{i=0}^{n} g_{syn,i}(t)(E_{syn,i} - V_m) + \frac{V_{\text{rest}} - V_m}{R}$$

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 $V_m << E_{syn}$, we can approximate synaptic input as a const 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

$$R g_{syn} << 1$$

$$V_\infty = R g_{syn} E_{syn}$$

Scales linearly with synaptic input

Case 2: Large synaptic input

$$R g_{syn} >> 1$$

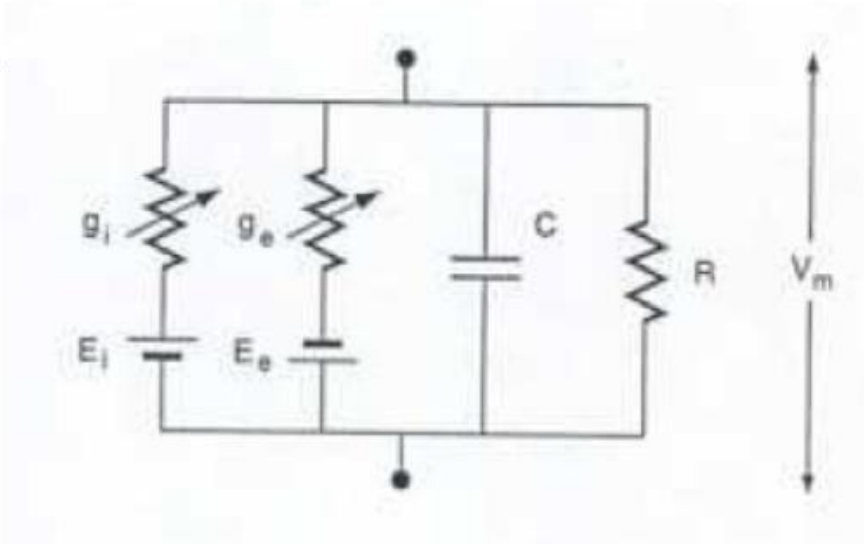
$$V_\infty = E_{syn}$$

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:

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

$$G_{in} = g_e + g_i + \frac{1}{R}$$

$$\tau' = \frac{C}{G_{in}}$$

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 appe
in the denominat

This is reason why shunting inhibition is often referred to as
'divisive inhibition'

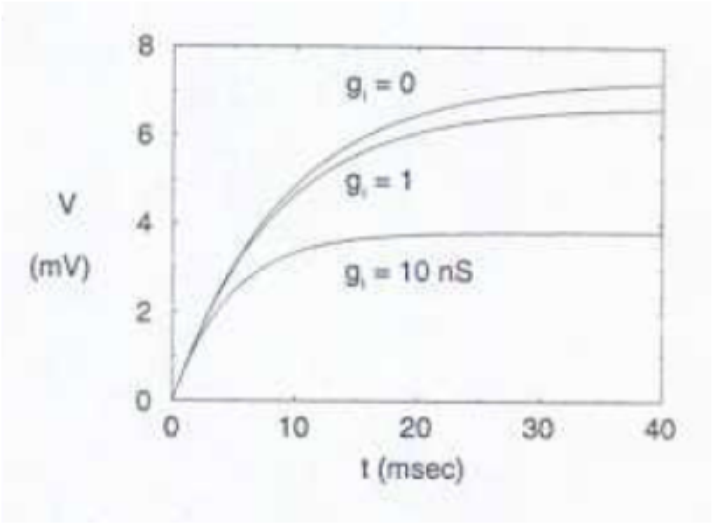
Shunting Inhibition

Solving ODE:

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

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

$$V\infty = \frac{g_e E_e}{g_e + \frac{1}{R} + g_i}$$



Plasticity

- **Hebb's law:**
  - Neurons that fire together wire together

Spike-time Dependent Plasticity

- LTP