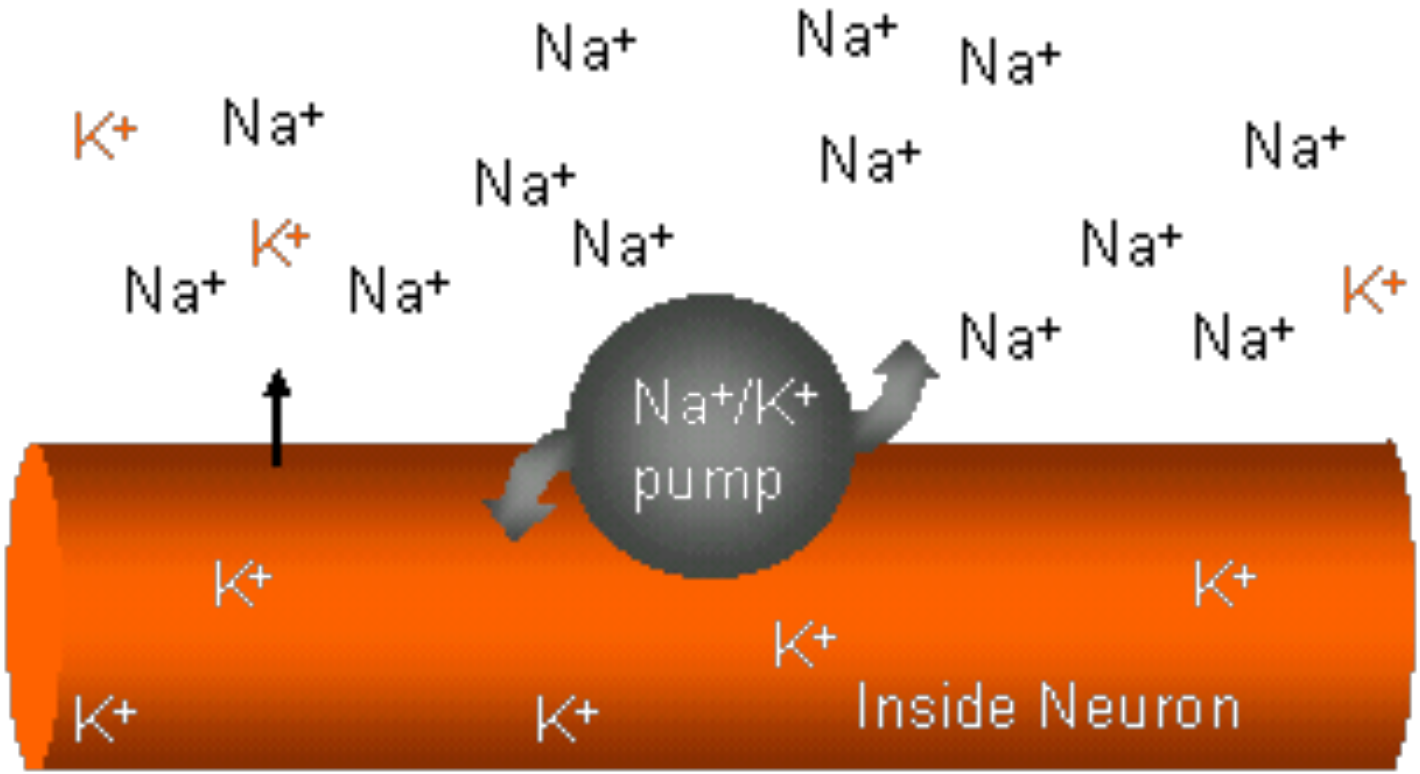
ELECTROPHYSIOLOGY

Neurons communicate with each other - here's how:

When the neuron is "at rest", it maintains a small electric charge

Atoms generally have equal numbers of protons and electrons that "cancel" each other out…. when the number is unequal, it becomes an electrically "charged" ion

Movement of charged ions creates an electrical "current"

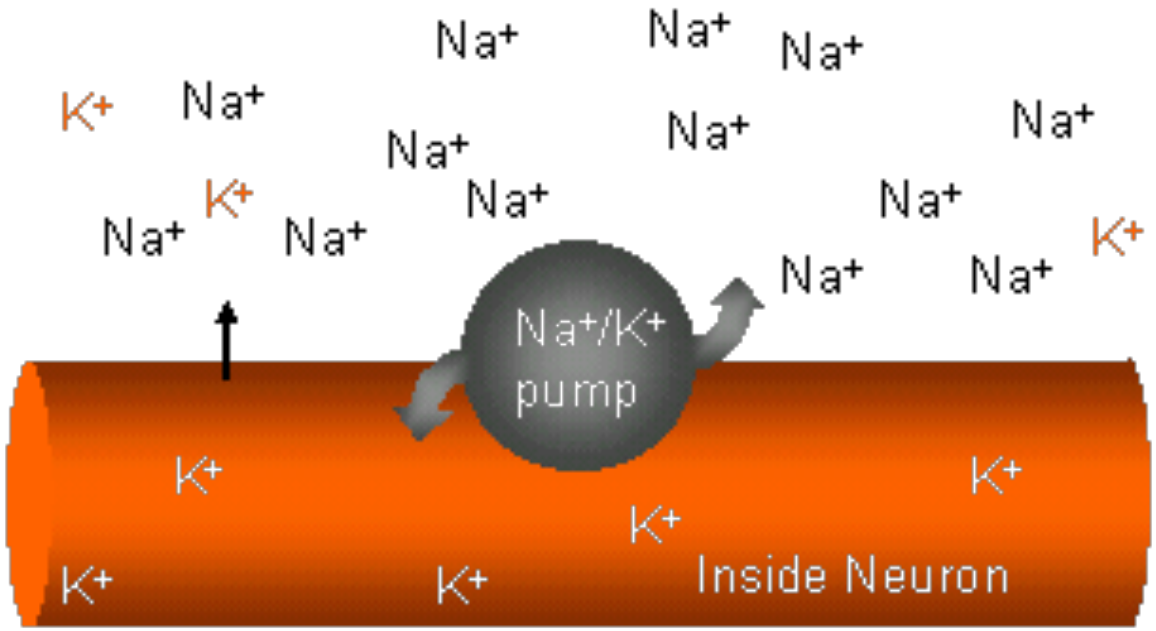


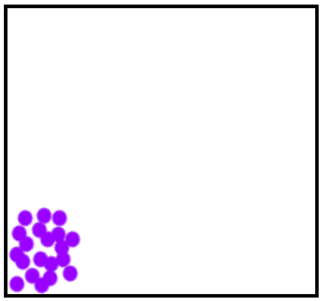
ELECTROPHYSIOLOGY

- Important ions for maintaining neuronal charge:
  - large organic proteins / organelles (anions / A-) INSIDE
  - potassium (K+) MORE INSIDE
  - chloride (Cl-) MORE OUTSIDE
  - sodium (Na+) MORE OUTSIDE

Forces acting on ions across the membrane (through "ion channels")

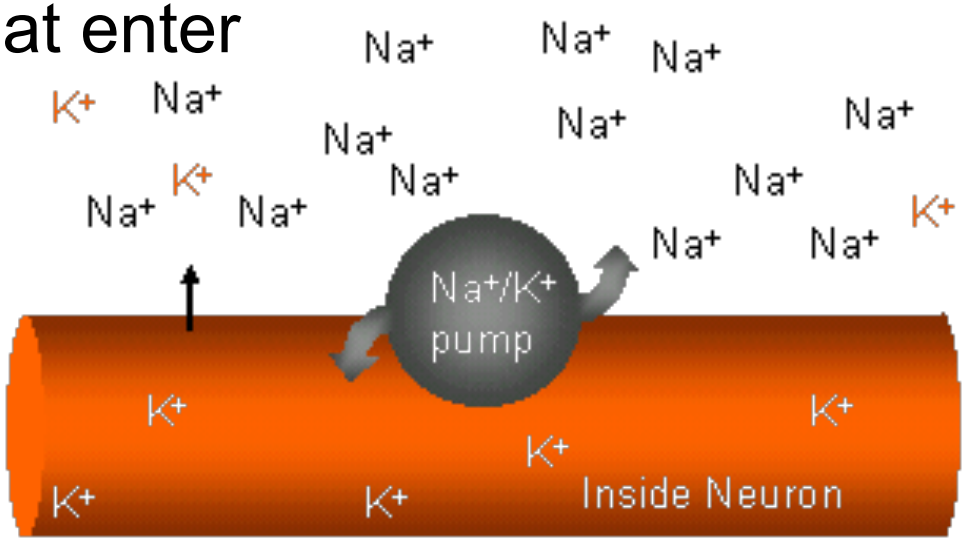
- chemical / concentration / diffusion gradient
  - concentrations of a molecule tend to equalize
- electrical gradient (charge)
  - opposite charges attract / like charges repel





ELECTROPHYSIOLOGY

- K+
  - more inside > forced out *(passive)*
  - outside +, so pushed back in *(passive)*
- Cl-
  - more outside > forced in *(passive)*
  - inside -, so pushed back out *(passive)*
- Na+
  - more outside > forced in
  - inside -, so pulled in
    - requires energy (ATP) to ACTIVELY PUMP it back out
      - *sodium-potassium pump* pushes 3 Na+ out for every 2 K+ that enter

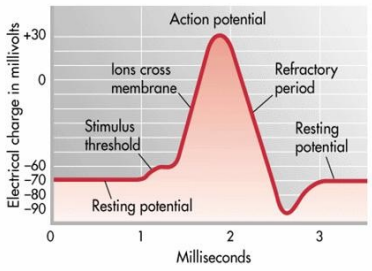


ELECTROPHYSIOLOGY

- the difference in charge between the inner / outer membrane at rest attains equilibrium (*Nernst Potential*)
  - mainly the result of K+ (a positive ion) leaving the neuron
    - creates a continuous “negative” current of ~ -70 mV
  - “polarized” like a battery (inside -, outside +)

- applying a positive charge to the inside of the cell membrane makes it less negative (more positive)
  - depolarizes the neuron - more likely to “fire” an action potential

- applying a negative charge to the inside of the cell membrane makes it more negative (less positive)
  - hyperpolarizes the neuron - less likely to “fire” an action potential



ELECTROPHYSIOLOGY

- the brain uses ~ 20% the body's energy (~10w), and ~20-40% of that goes toward operating the pump

- certain functions require more energy than others:
  - e.g., auditory processing (fast / precise) requires more energy than the olfactory system (slow)

- specific tasks may require certain areas of the brain, which slightly increases those areas' energy demands
  - basis of fMRI etc

- unlike muscles, which can store excess carbohydrates, the brain doesn't have an energy reserve
  - brain needs constant supply of oxygen / energy
  - evolution sacrificed backup power for increased efficiency, but made brain more susceptible to injury
  - pump failure (e.g., during heart attack / stroke) > buildup of Na+ > massive depolarization > rapid firing of APs > excitotoxicity

ELECTROPHYSIOLOGY

- How NTs depolarize / hyperpolarize neurons:
  - NTs from the axon terminals of presynaptic neurons (or drugs) bind with receptors on postsynaptic dendrites or soma
    - opens ion channels in membrane, allowing ions to move into or out of the cell
      - creates an electrical current (*postsynaptic potential*) that travels down the dendrite toward the postsynaptic neuron's soma > axon hillock

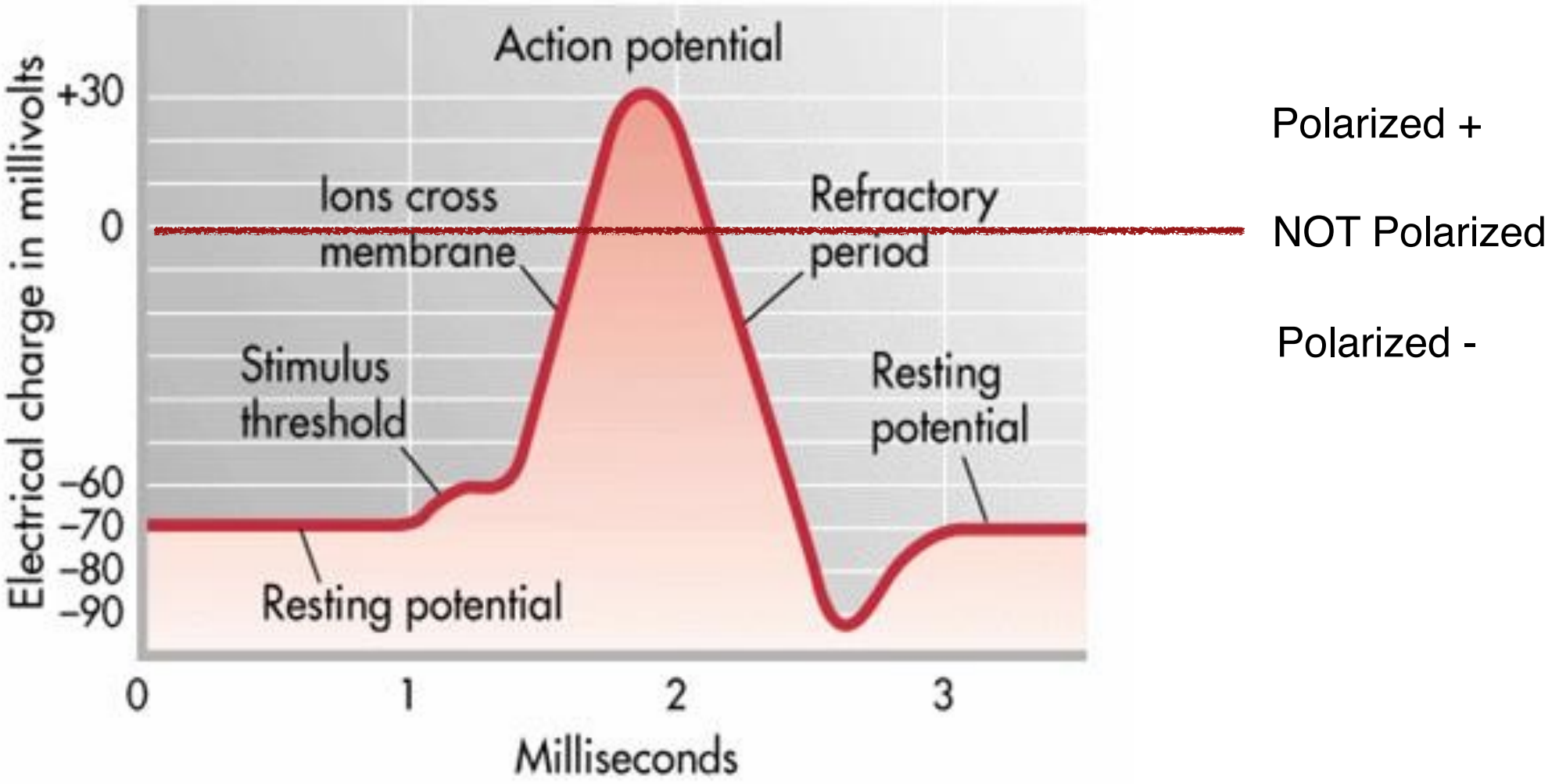
- postsynaptic potential can be excitatory or inhibitory
  - excitatory (EPSP) - depolarizing current
  - inhibitory (IPSP) - hyperpolarizing current

  - **determined by ion channels opened, not the transmitter**

- EPSPs and IPSPs are fast, graded and passive (get smaller with time / distance)

ELECTROPHYSIOLOGY

- a large enough depolarization (up to “threshold” level) will lead to generation of an*action potential* (electrical signal / nerve impulse / spike)
  - traveling reversal of membrane potential
  - local section of axon becomes positive compared to outside



ELECTROPHYSIOLOGY

1. *Threshold* of depolarization is reached (more EPSP than IPSP reach the *axon hillock*), opening *voltage-gated Na*+ channels

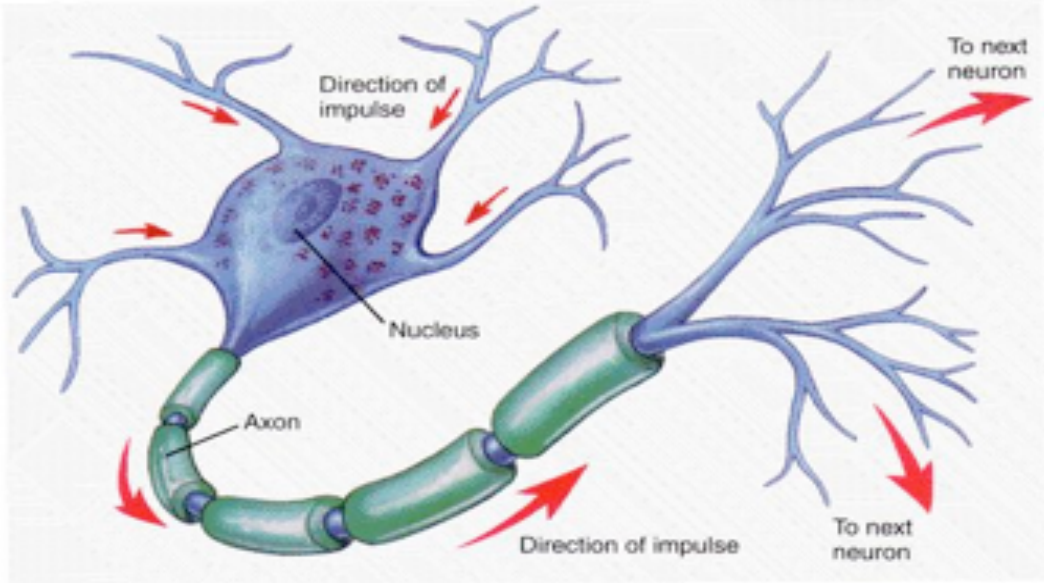
2. Na+ ions rush IN, bringing inside of membrane up to ~+40 mV (adds about 110 mV - polarity is reversed)

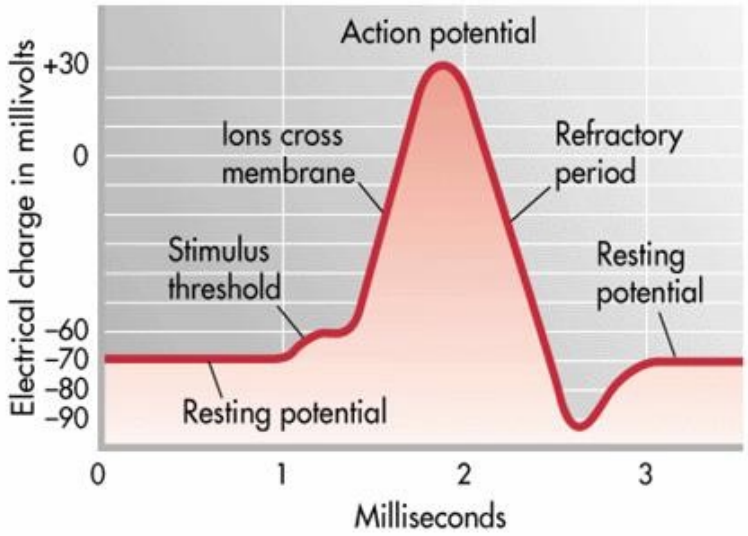
3. *Voltage-gated K*+ channels open, allowing K+ to rush OUT

4. After ~ 1 ms, Na+ channels close, but K+ is still leaving

5. K+ channels close and K+ ions diffuse away from outer membrane (*refractory period)*

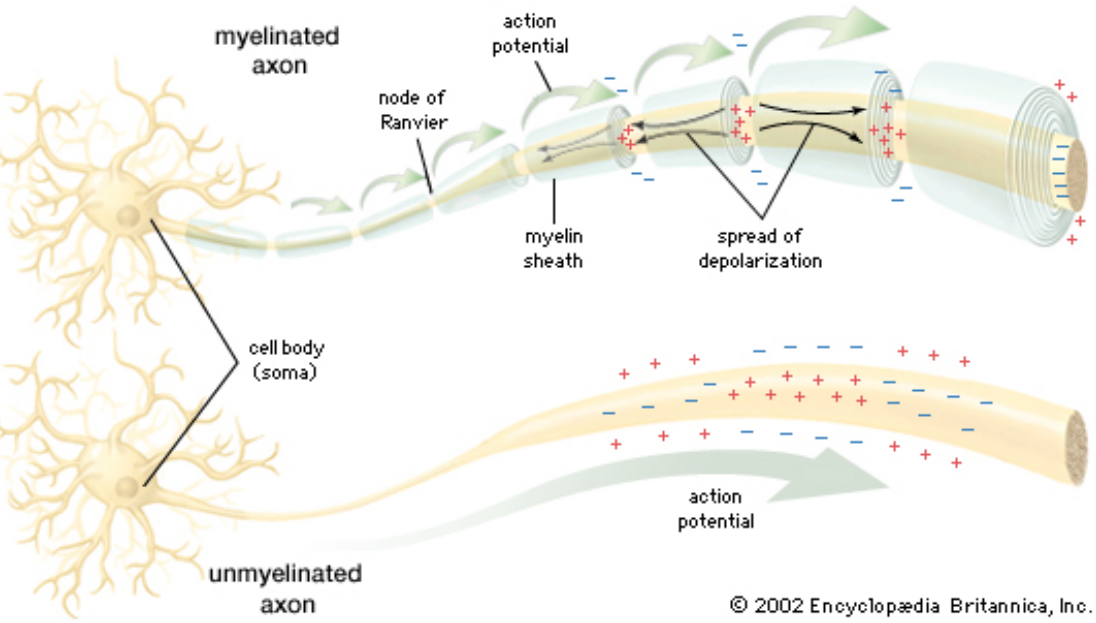
6. Back to resting potential of ~-70 mV

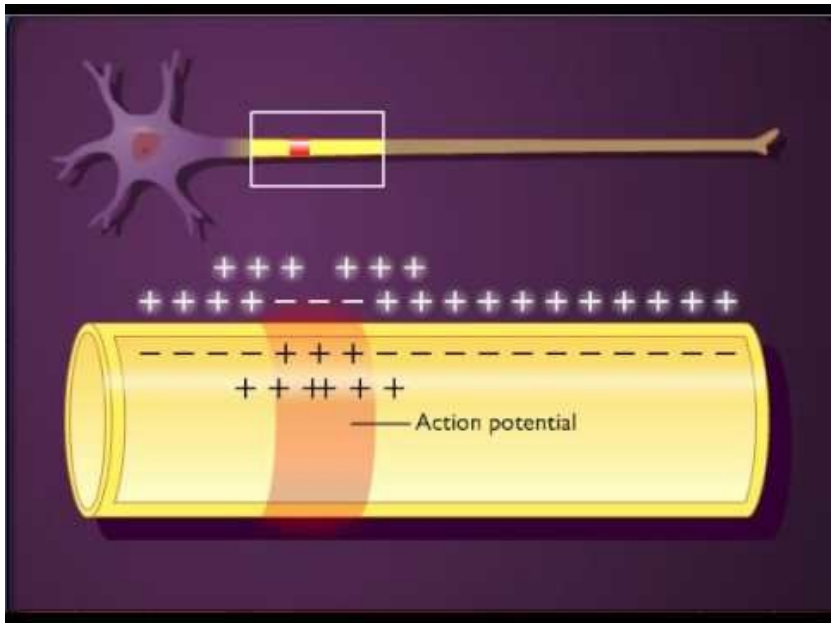




ELECTROPHYSIOLOGY

- action potential is not “graded” (ALL OR NONE)
  - is not “passive” (does not decay over time or distance)
    - self-supporting and regenerative
- this reversal in membrane potential travels down the length of the axon like burning of a wick



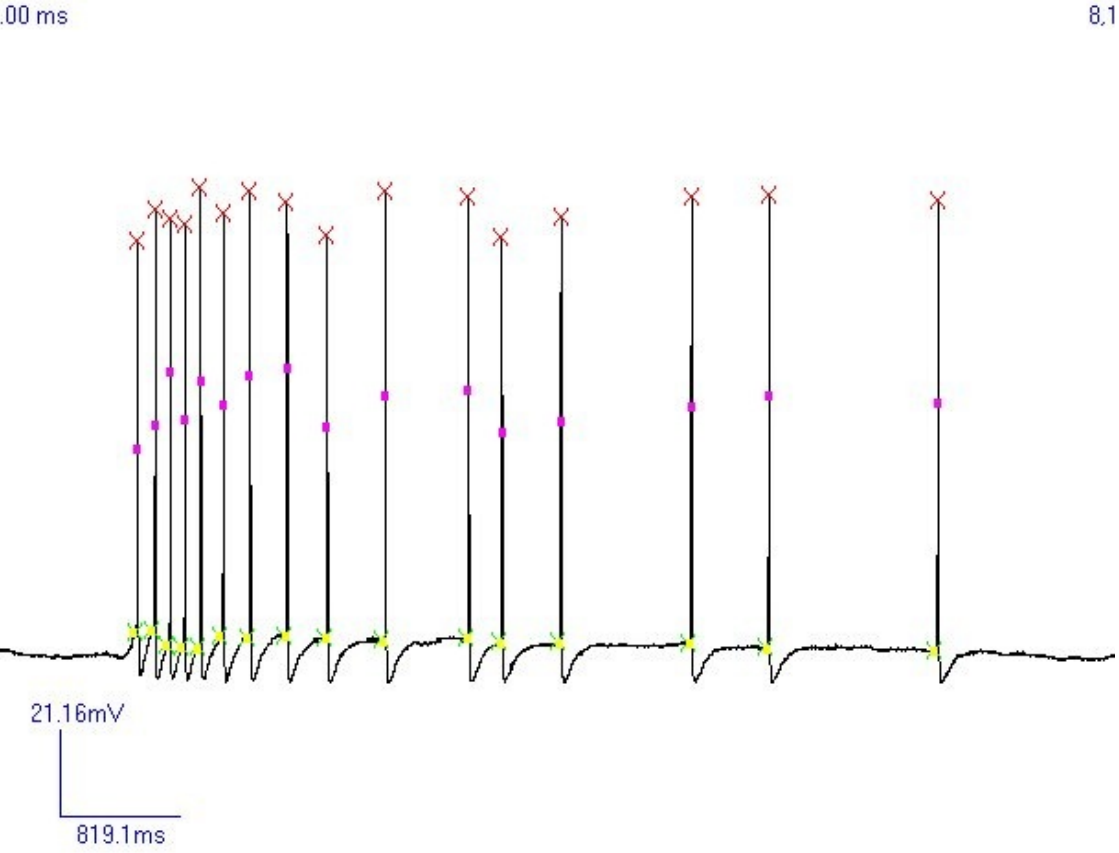


ELECTROPHYSIOLOGY

- Neuronal membrane potentials typically "drift", so neurons usually have a baseline rate of firing

- frequency of firing (spike rate) transmits *information*
- more spikes > more NT > larger PSP……

- dendrite = analog component (graded)
- axon = "digital" component (all-or-none)



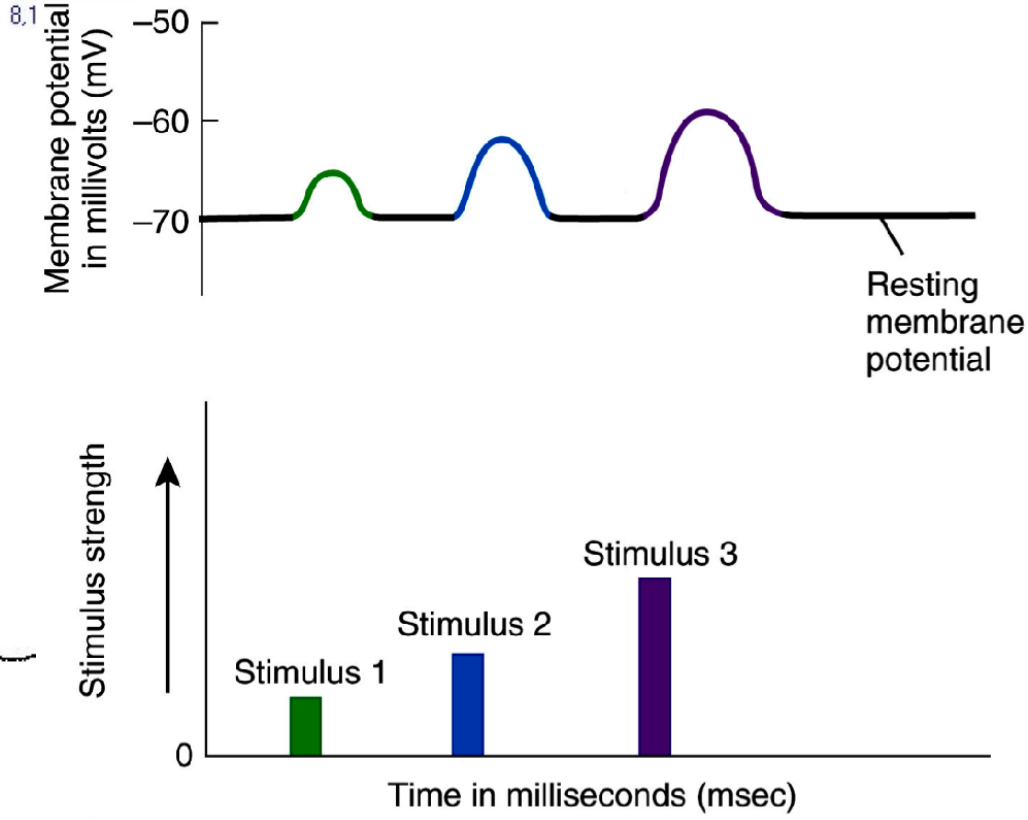
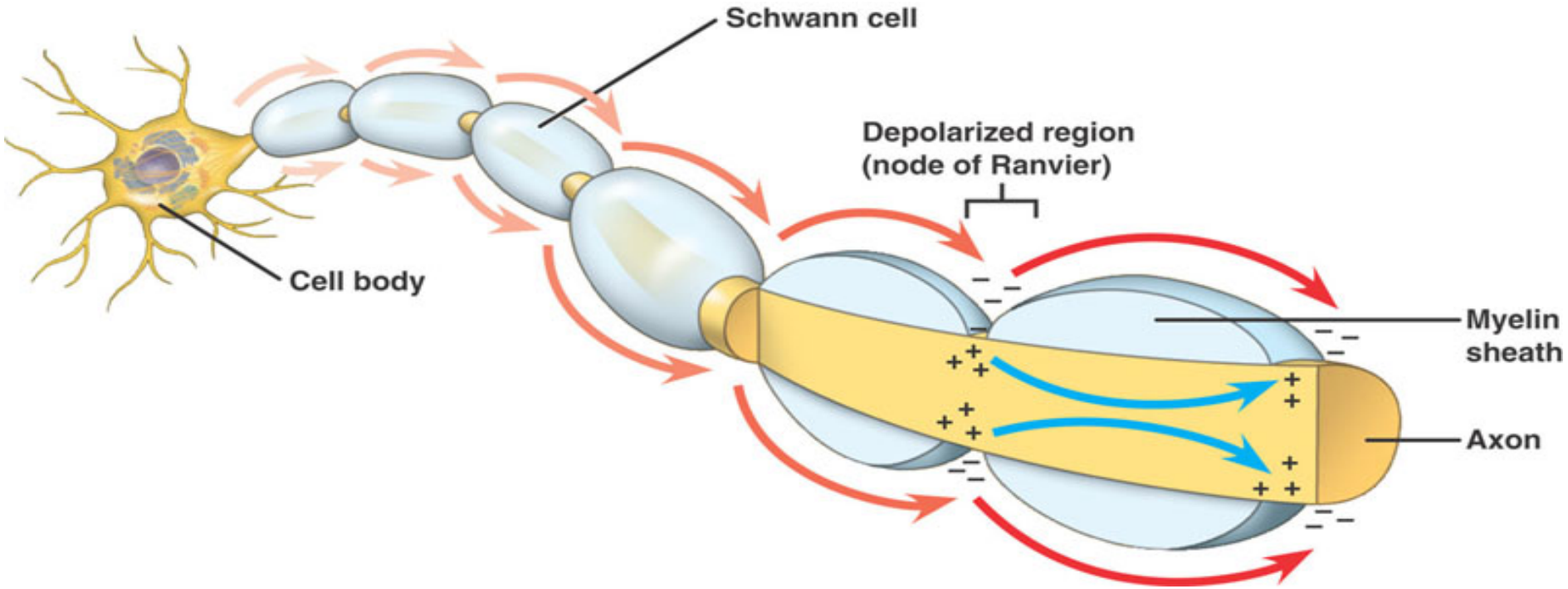


Figure 12.17 Tortora - PAP 12/e

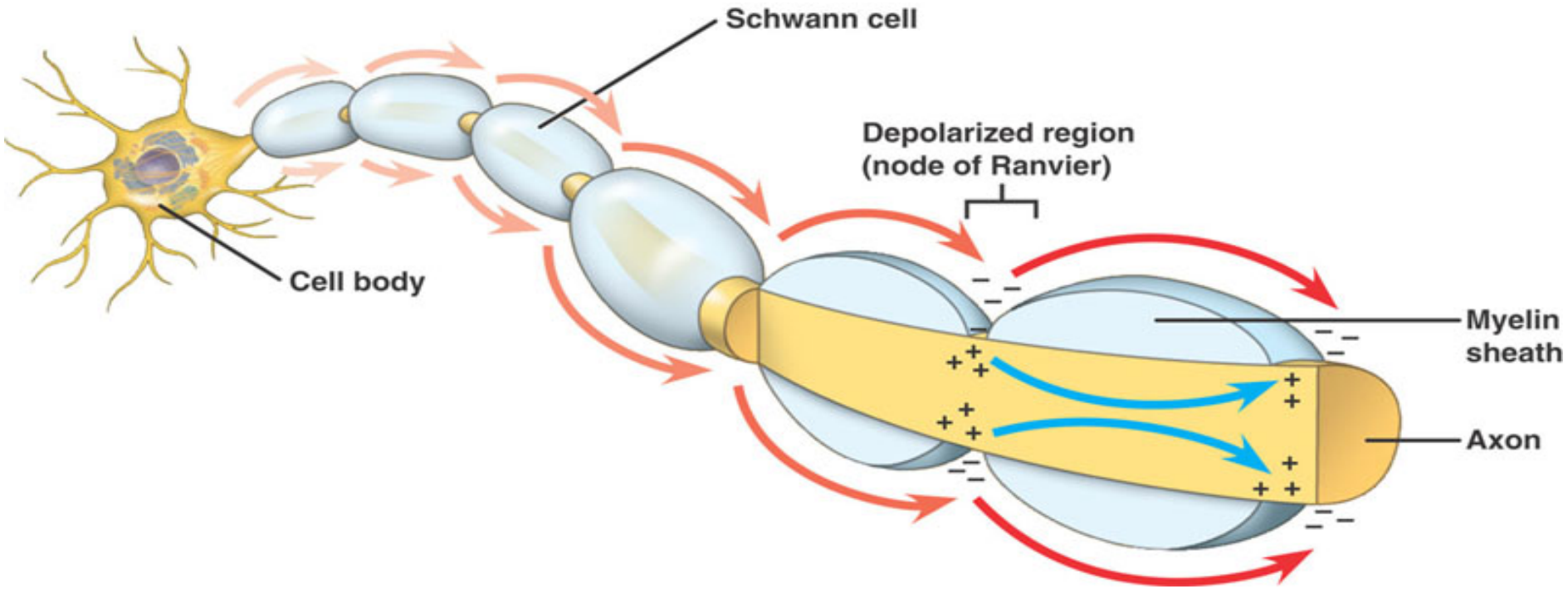
ELECTROPHYSIOLOGY

- axons are poor conductors of electricity compared to wires
  - opening/closing ion channels takes time:
- 2 ways to speed up conduction:
  - increase diameter > reduced “resistance”
  - insulate membrane > reduced current “leakage”
- thin, unmyelinated axons ~1-4.5 mph
- thick myelinated axons ~180-265 mph



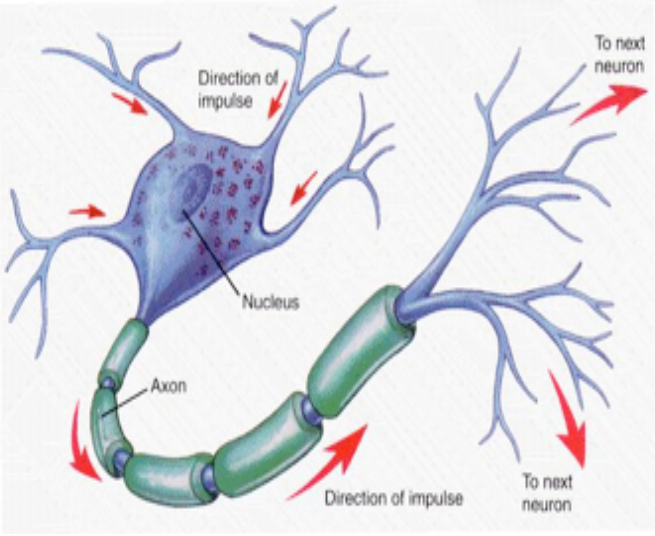
ELECTROPHYSIOLOGY

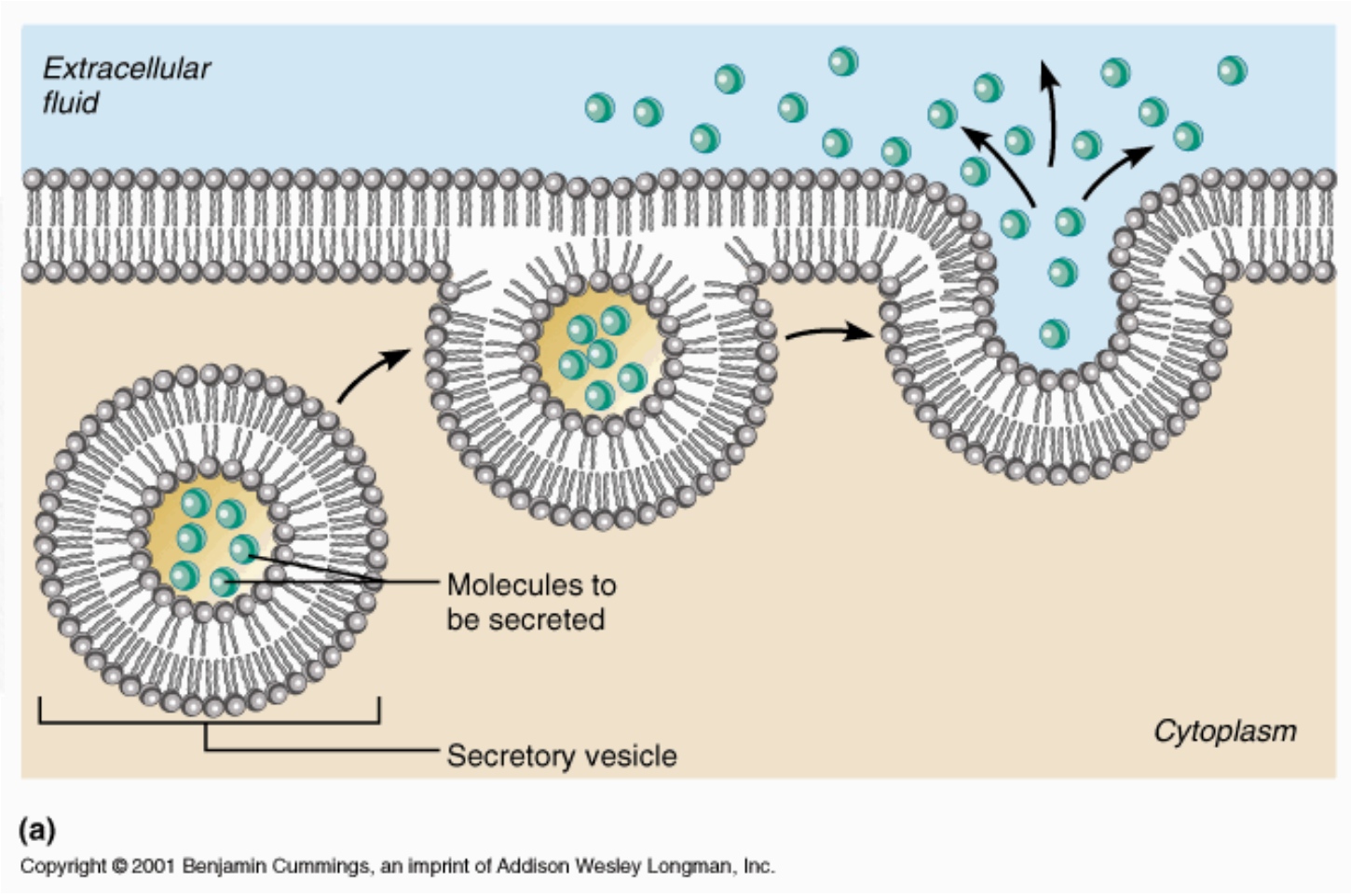
- along LONG projection axons, *myelin* acts as an insulator (preventing electrical leakage) and the signal *jumps* from node to node
  - *saltatory* conduction
    - faster
      - opening / closing of ion channels only happens at Nodes
    - less energy (fewer Na-K pumps are required)



SYNAPTIC TRANSMISSION

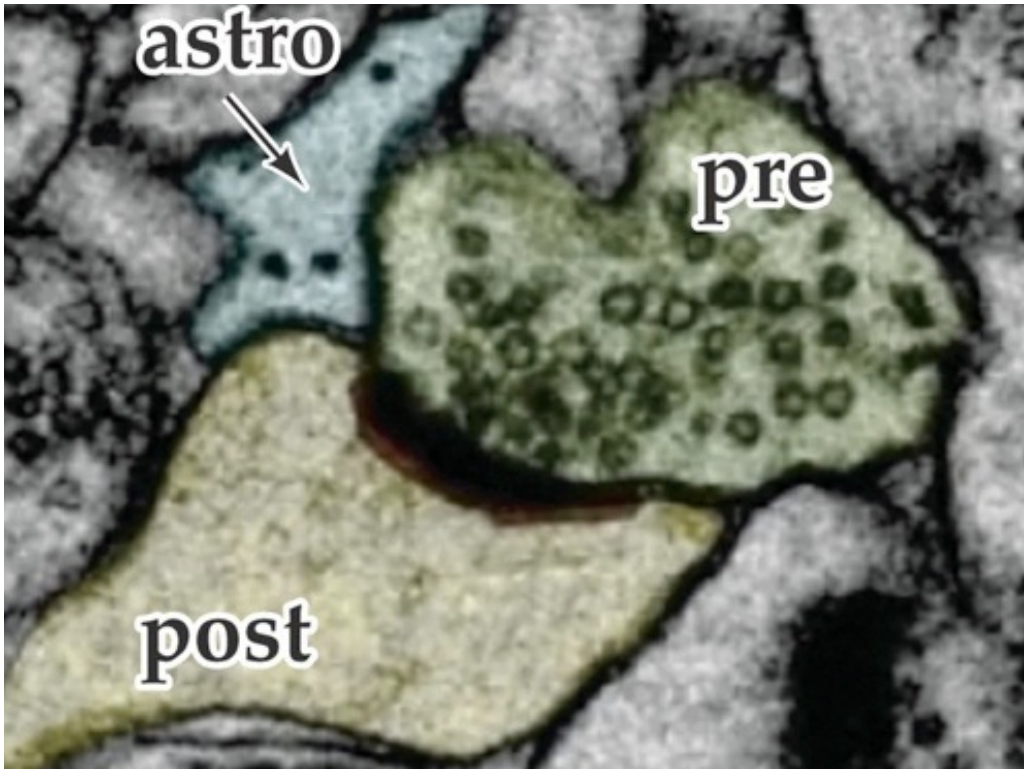
- Action potential reaches axon terminal, opening voltage-gated Ca++ channels, inducing release of NT vesicles from axon terminal (*presynaptic*) onto next neuron (*postsynaptic*) via *exocytosis*



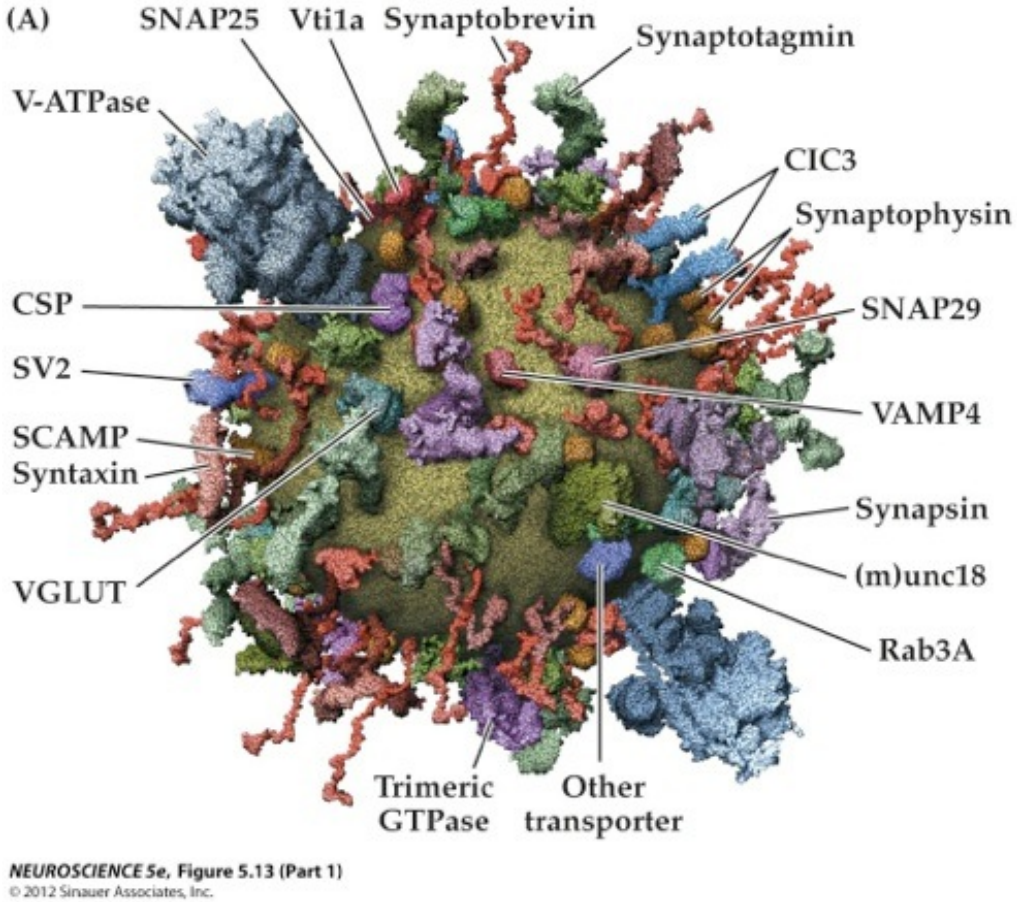


SYNAPTIC TRANSMISSION

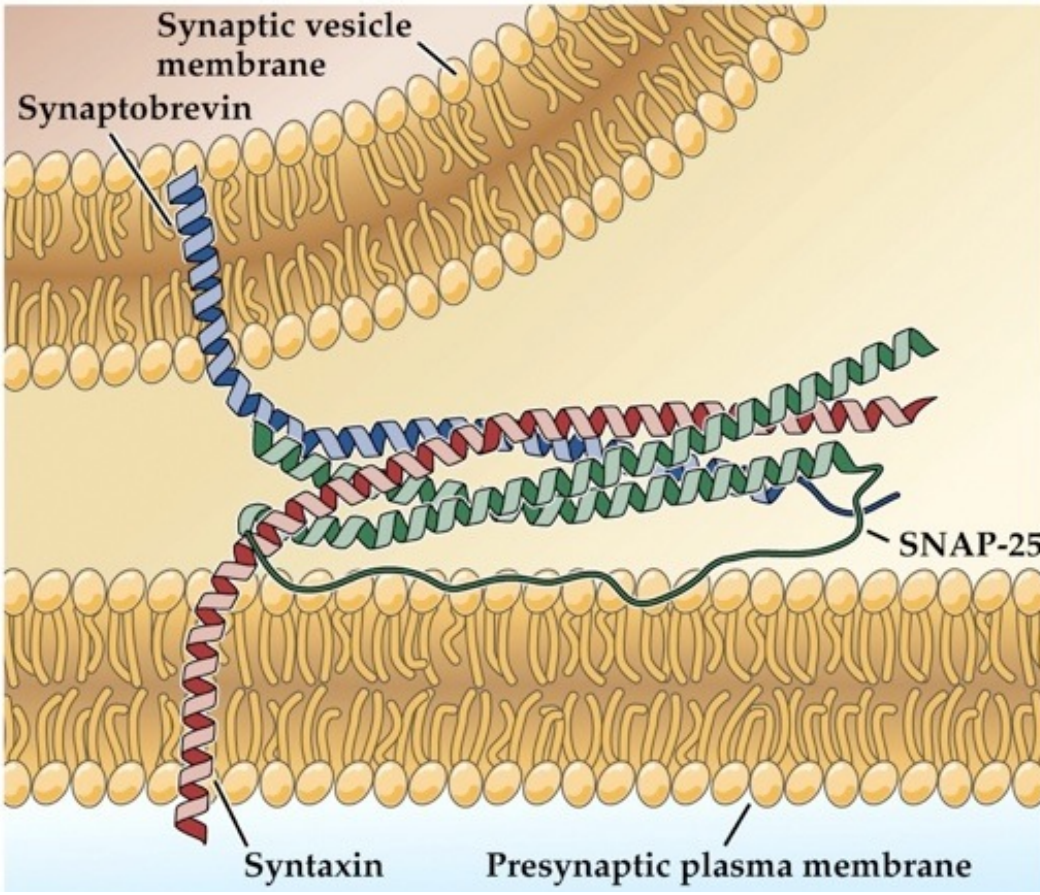
- 2 “pools” of neurotransmitter vesicles in the axon terminal:
  - freely floating
  - reserve pool
    - bound to inside of axon terminal membrane by “SNARE” proteins on the vesicle and presynaptic membranes



SYNAPTIC TRANSMISSION



NEUROSCIENCE 5e, Figure 5.13 (Part 1)

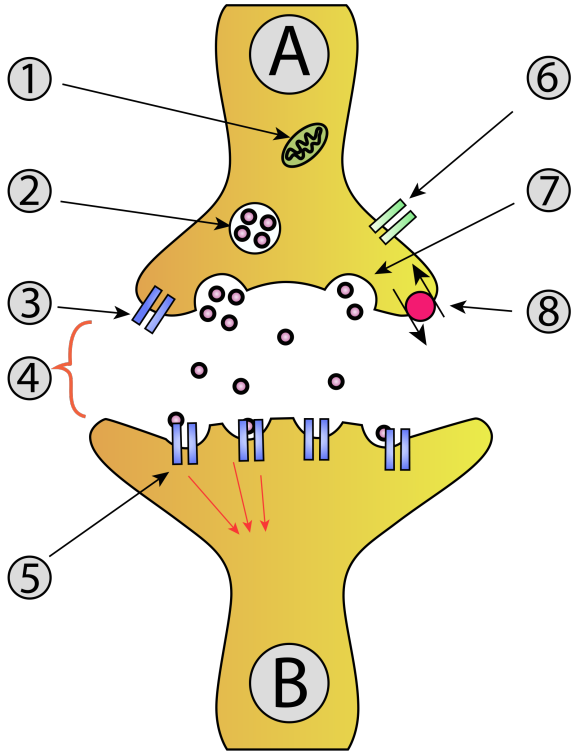


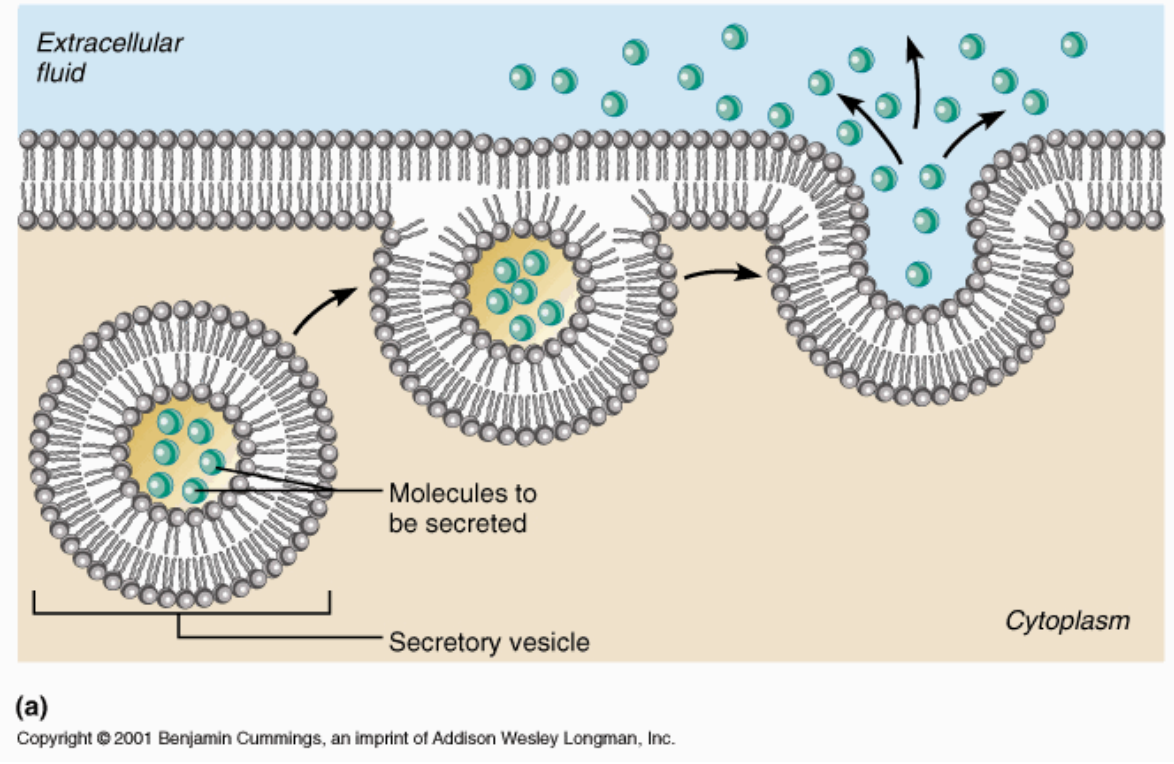
Sort of like velcro

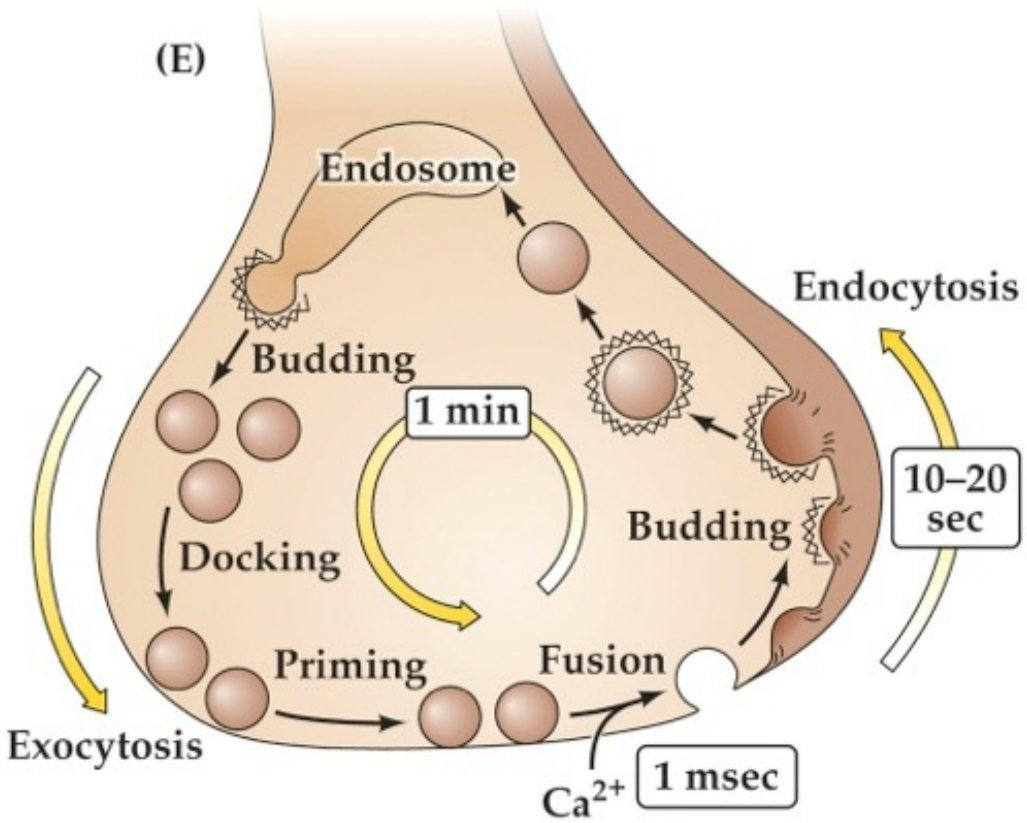
SYNAPTIC TRANSMISSION

- AP causes entry of Ca++ through voltage-gated Ca++ channels
  - Ca++ binds to one of the SNARE molecules (*synaptotagmin*), causing it to bind more tightly with the neuronal membrane and "meld together" (*exocytosis*), releasing NTs into cleft

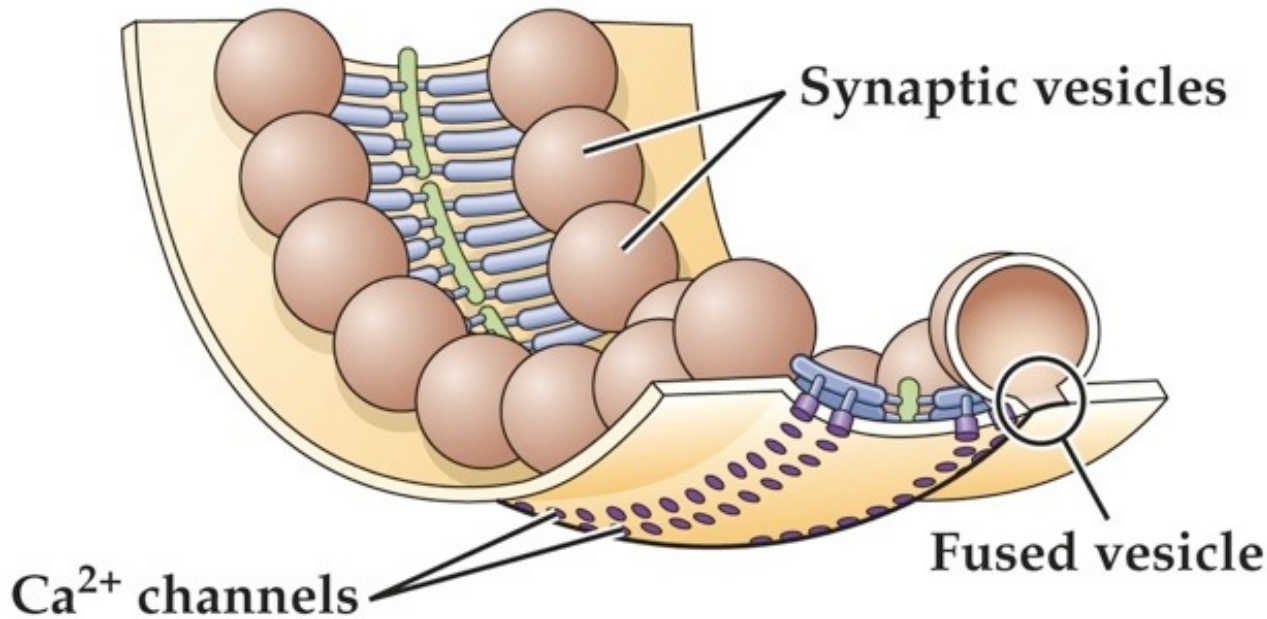
- *endocytosis* is the reverse - when a piece of neuronal membrane is "pinched off" to create new vesicles inside axon terminal



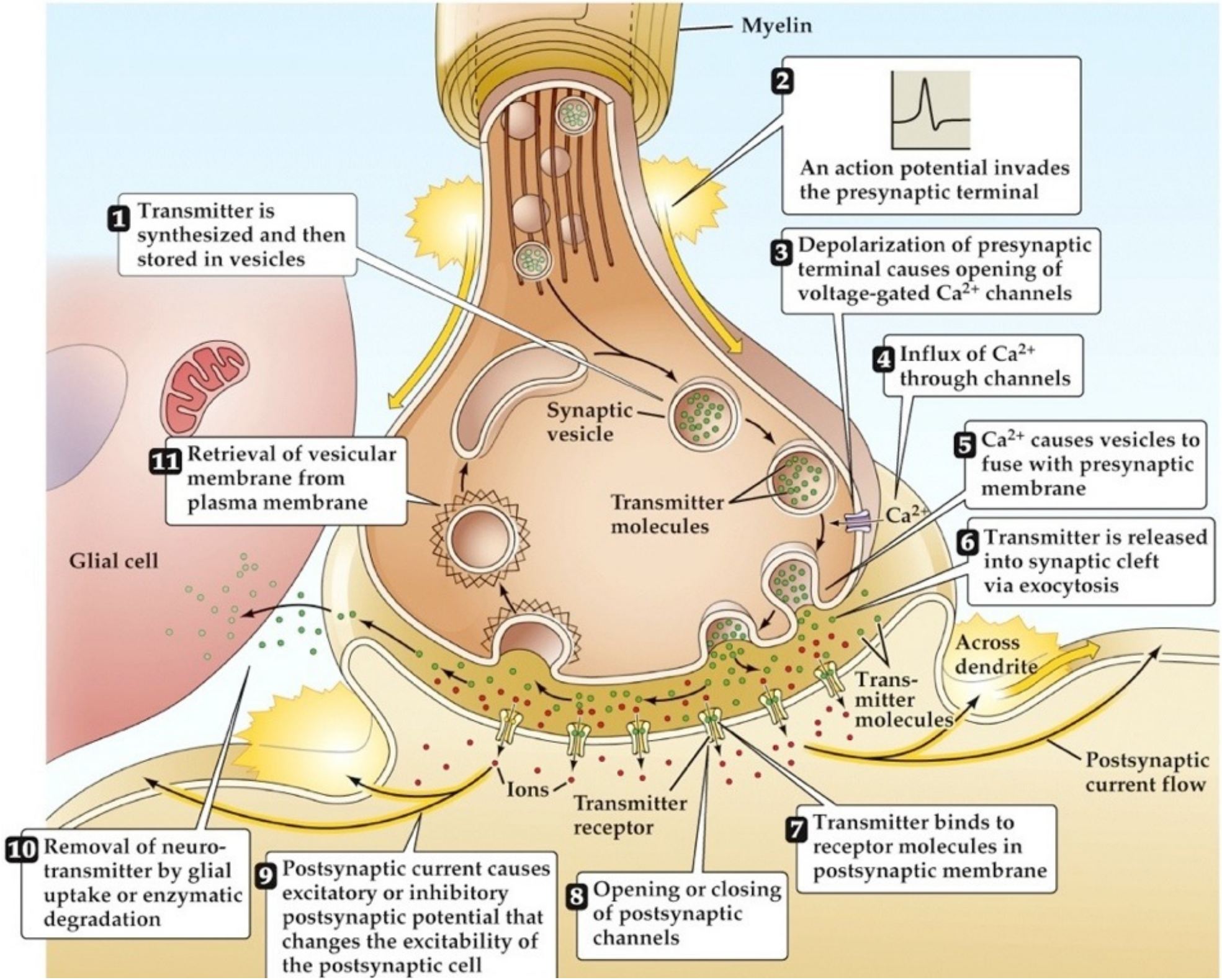




NEUROSCIENCE 5e, Figure 5.9 (Part 2)



NEUROSCIENCE 5e, Figure 5.8 (Part 3)

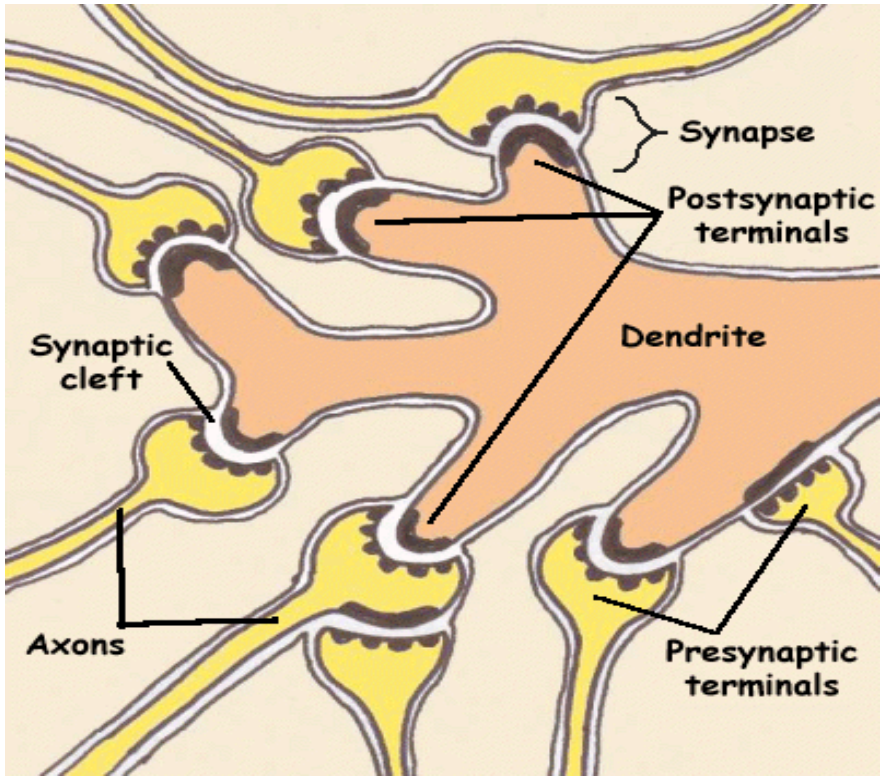

Myelin
2
An action potential invades the presynaptic terminal
1 Transmitter is synthesized and then stored in vesicles
3 Depolarization of presynaptic terminal causes opening of voltage-gated Ca^{2+} channels
4 Influx of Ca^{2+} through channels
Synaptic vesicle
5 Ca^{2+} causes vesicles to fuse with presynaptic membrane
11 Retrieval of vesicular membrane from plasma membrane
Transmitter molecules
Ca^{2+}
6 Transmitter is released into synaptic cleft via exocytosis
Glial cell
Across dendrite
Trans-mitter molecules
Postsynaptic current flow
Ions
Transmitter receptor
7 Transmitter binds to receptor molecules in postsynaptic membrane
10 Removal of neuro-transmitter by glial uptake or enzymatic degradation
9 Postsynaptic current causes excitatory or inhibitory postsynaptic potential that changes the excitability of the postsynaptic cell
8 Opening or closing of postsynaptic channels

SYNAPTIC TRANSMISSION

- Synaptic Relationships
  - axo-dendritic - usually excitatory
  - axo-somatic - usually inhibitory
    - axo-axonic - usually inhibitory

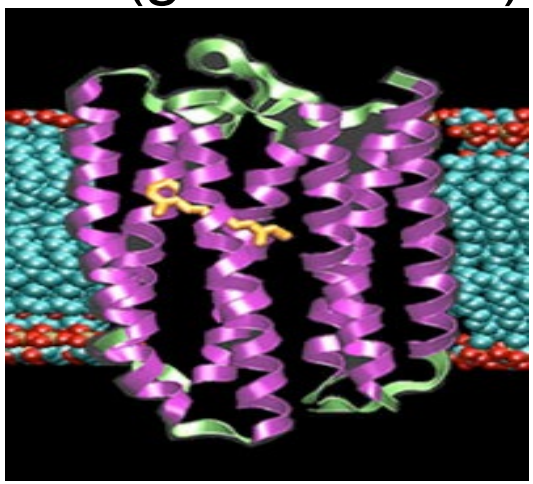
- ~90% of a neuron's surface is dendrite (thus, usually excitatory)

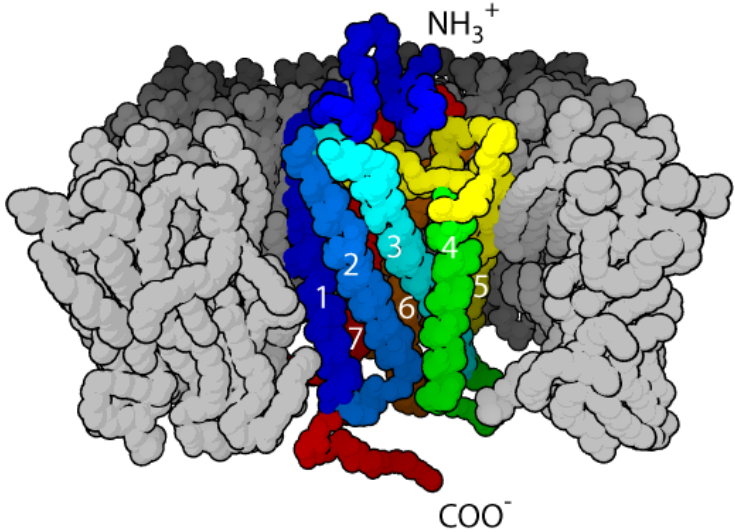
- NT binds with *receptors* embedded in postsynaptic membrane



SYNAPTIC TRANSMISSION

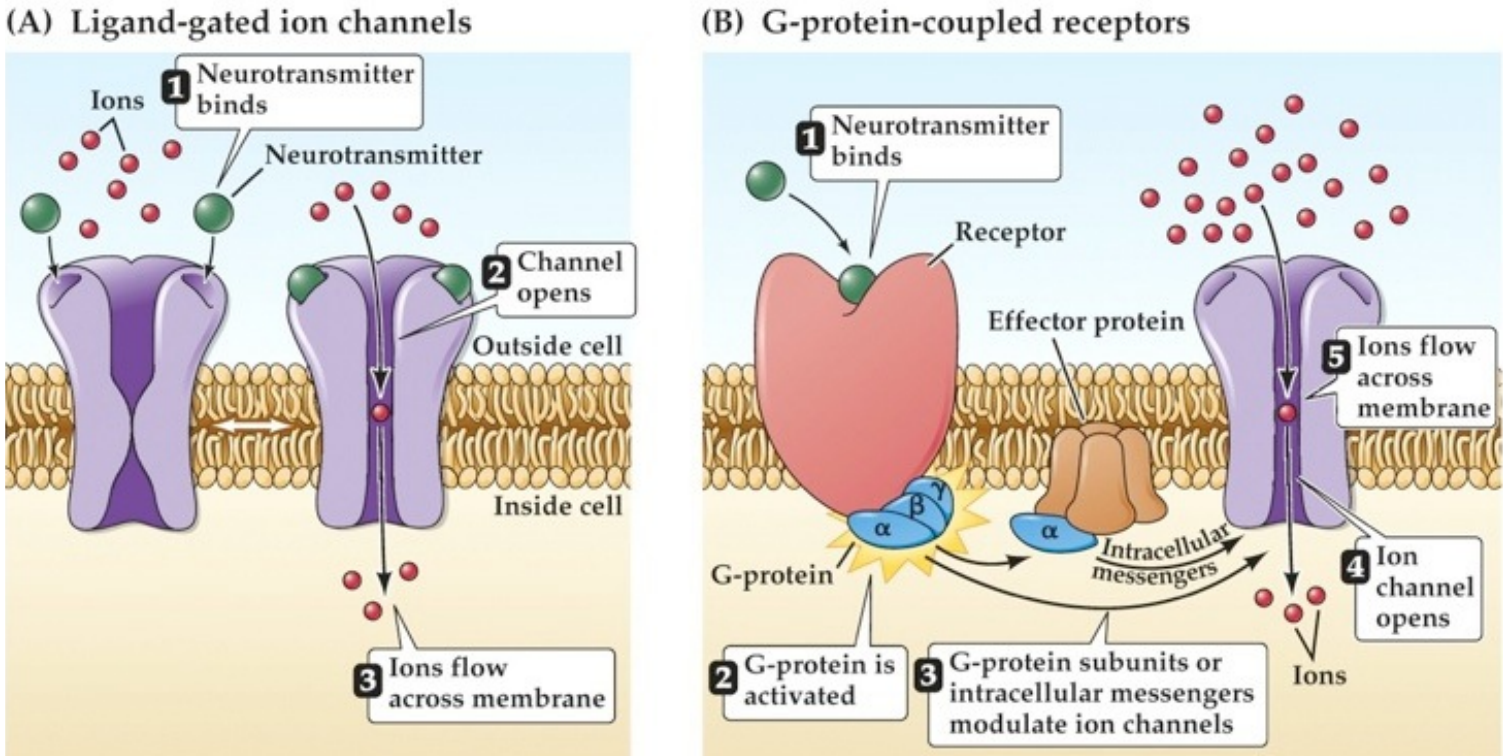
- A receptor is a large “membrane-spanning” protein with sites for binding NTs (and/or drugs)
  - composed of several “subunits” - loops of amino acids embedded in membrane
    - subunits can be arranged in several configurations
- NTs (*ligands / 1st messengers*) / drugs fit in space between loops
  - “activates” receptor, usually by changing its shape
  - generally, the more receptors activated, the larger the effect (graded PSP)





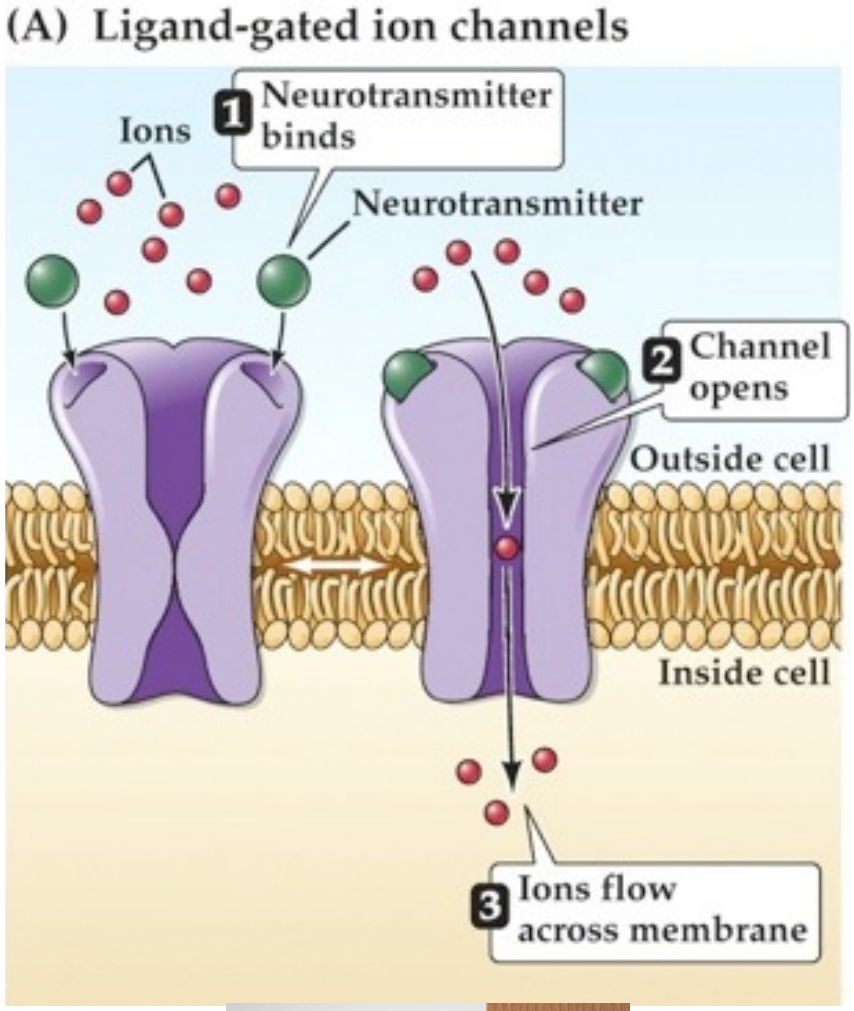
SYNAPTIC TRANSMISSION

- 2 type of receptors that induce PSPs
  - ionotropic
  - metabotropic



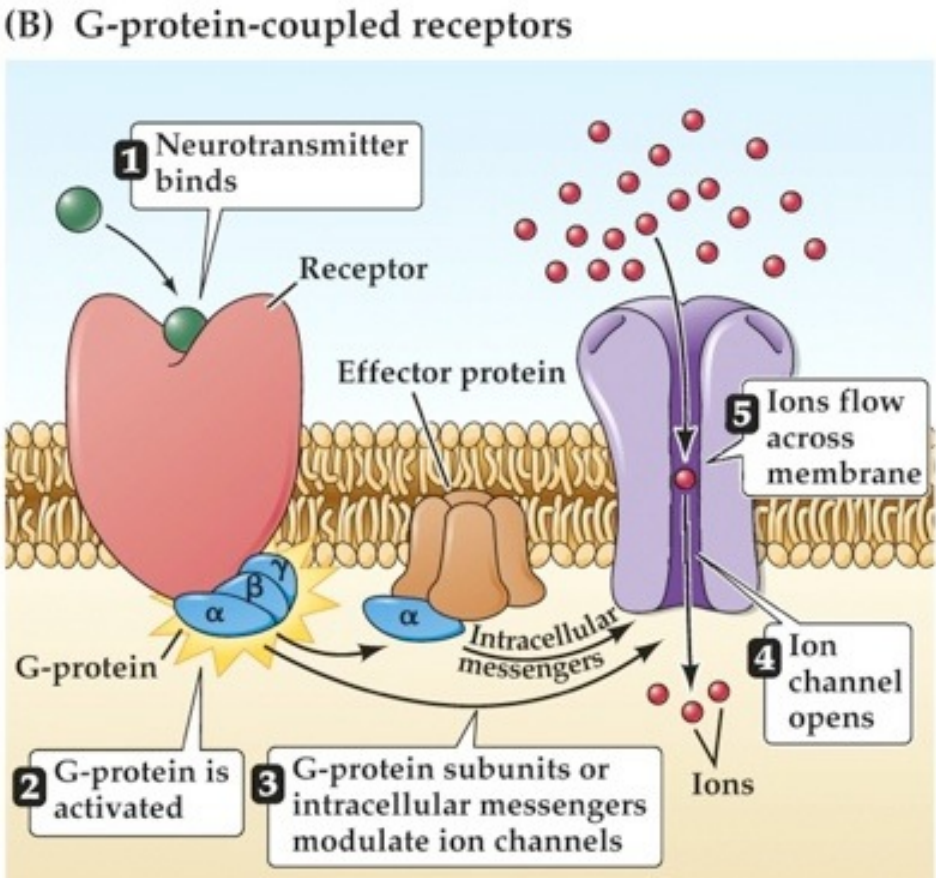
SYNAPTIC TRANSMISSION

- Ionotropic “gated ion channel” receptors:
  - form pores / channels in neuronal membrane
    - open when NT in the synapse binds on the outside, or
      - voltage change
      - temperature
      - mechanical stretch
      - light (optogenetics)
    - fast (~1 ms)
    - allows passive flow of charged ions through membrane
    - current changes neuronal polarity
      - e.g., Na+ in = EPSP / K+ out or Cl- in = IPSP



SYNAPTIC TRANSMISSION

- Metabotropic receptors:
    - NT binding causes activation of intracellular enzymes (e.g., *adenylate cyclase*)
        - requires energy
    - Use a “2nd messenger” / middleman to open gated ion channels from inside the cell
        - Glycoproteins (g-proteins)
        - tyrosine kinases
        - guanylyl cyclase
        - slower and longer lasting than ionotropic
            - several seconds / minutes



SYNAPTIC TRANSMISSION

After NT binds to receptor (or fails to), it needs to be removed from the synapse:

- transport / carrier / “reuptake" receptors
    - on pre-synaptic axon terminals OR local glial cells
        - binds NT and brings back into neuron for re-use
            - against concentration gradient (requires energy - similar to Na-K pump)
- OR enzymatic degradation