COGS 17 section A02

structure & function of cells in the nervous system

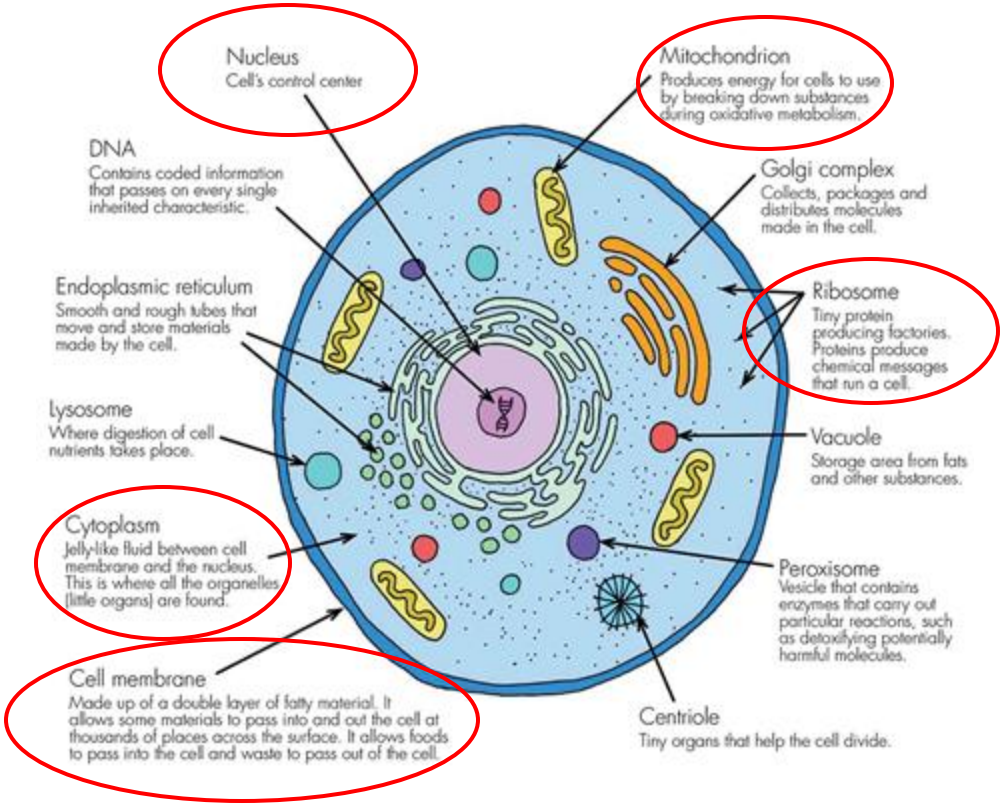
week 2 guiding questions

section resources repo

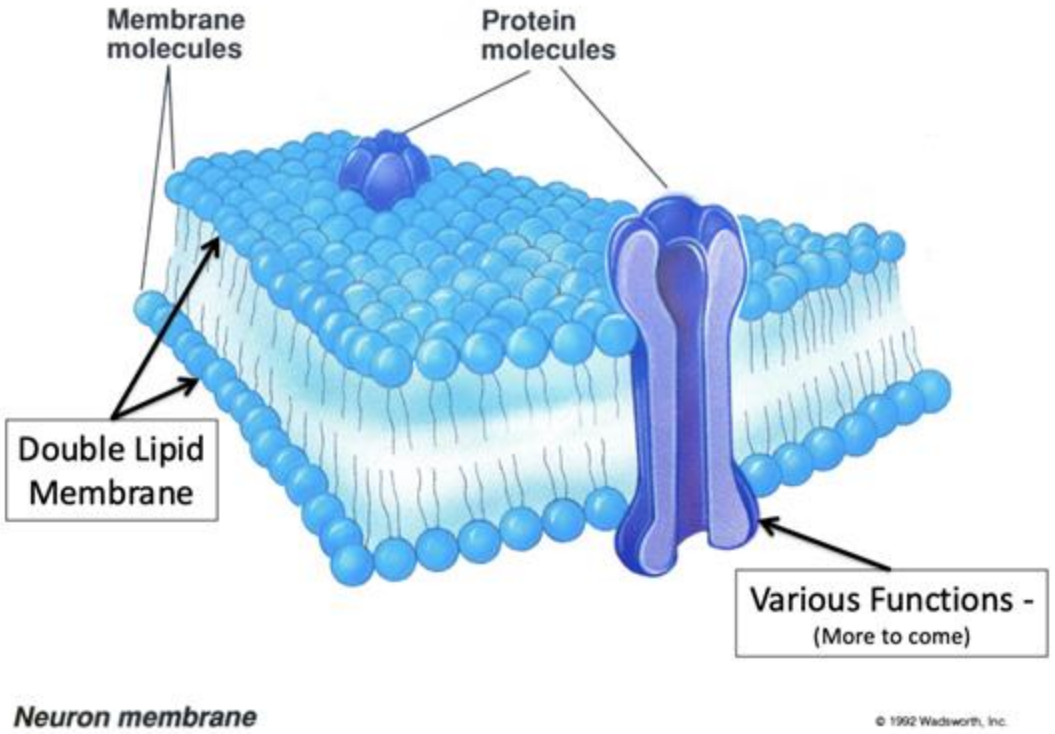
reminders

- homework 2 due wednesday @ 11:59 PM
- homework 3 due next **monday (**4/21) @ 11:59 PM
- midterm 1 next tuesday!! (range: week 1-3)
    - during class time, 125 points

basic subcellular features



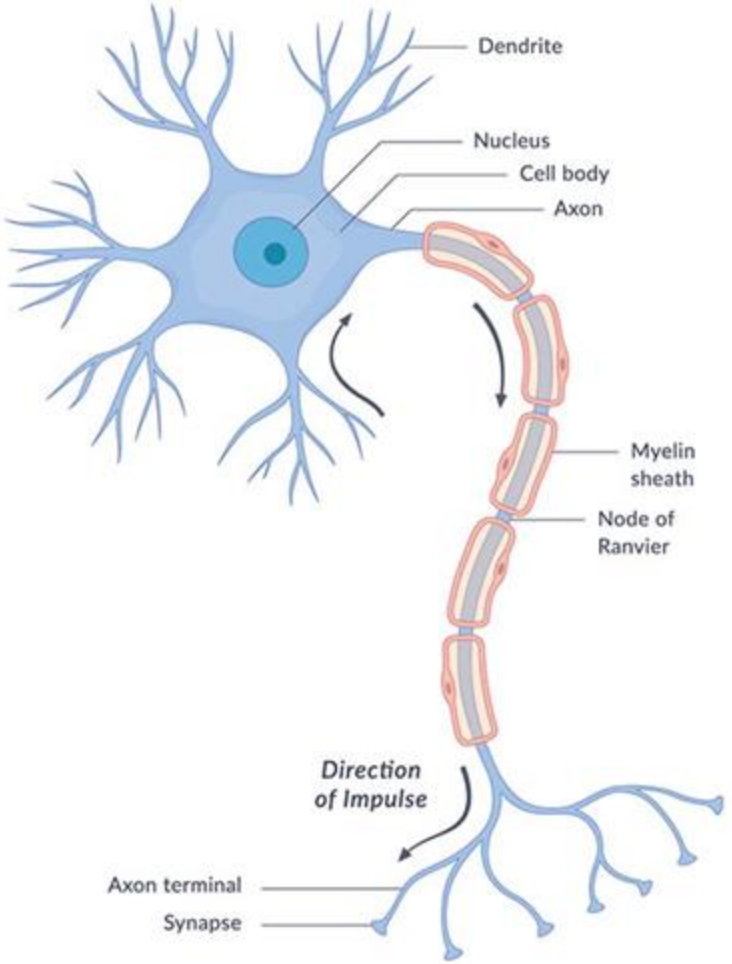
phospholipid bilayer



neurons ≠ glia !!

neurons

- = soma (cell body) + axon (wrapped in myelin sheath) + dendrites
- specialized for information transfer
- via processes
  - **dendrites:** *incoming* message receiver
    - branching from soma
    - receptor sites interact with NT
  - **axon:** *outgoing* message sender
    - ends in presynaptic terminals → NT released
- via membrane (selective permeability)
  - controls the cell's electrochemical state via ion gates/channels

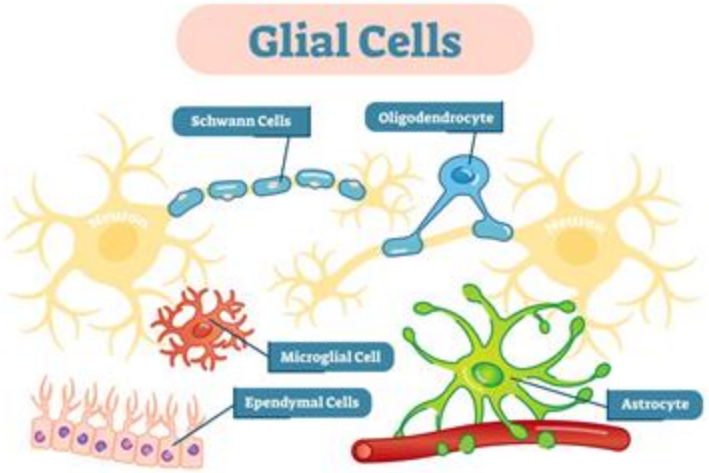


neurons ≠ glia !!

glia (“glue”) **cells**

- 10x as many in brain and 1/10 size compared to neurons
- not involved in information transfer; supports structural & chemical integrity of neurons and nervous system

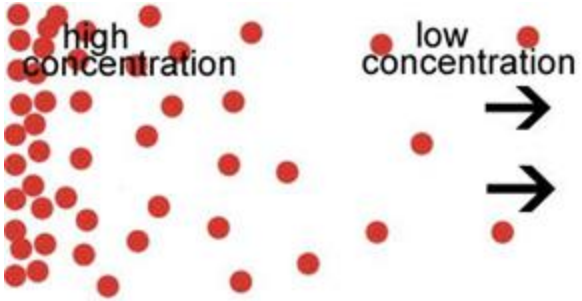
astrocytes: nutrients & cleaning, form BBB, recycle NTs
microglia: immune cells, remove toxins, repair neural damage
schwann cells: myelination in PNS
oligodendrocytes: myelination in CNS
ependymal cells: line ventricles, secrete CSF
radial glia: migration and growth of neurons during development



important concepts before we jump into nerve impulses…

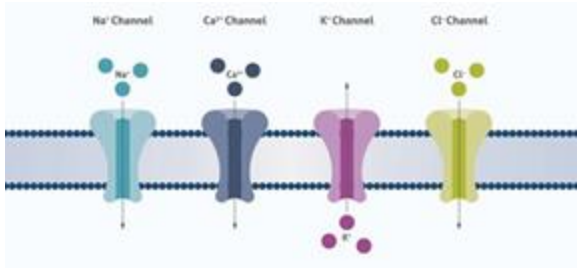
nature always seeks balance: gradients naturally move toward **equilibrium**

- **concentration gradient**
  - molecules move from high to low concentration (diffusion)
- **electrical gradient**
  - like charges (+/+, -/-) repel, opposite (+/-) charges attract (electrostatic pressure)



in the neuron

- ion (charged particles) distribution inside vs outside cell is controlled
  - recall BBB – selective permeability of membranes
- membrane potential
  - difference in *electrical charge* across membrane
  - measured in millivolts (mV)
- key ions: sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), chloride (Cl^-)



resting potential

typical neuron: -70 mV (more positive outside)

established by sodium/potassium pump

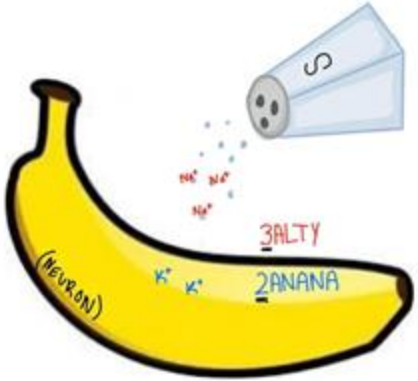
- actively transport 3 Na^+ out and 2 K^+ in
  - Na^+ concentration outside : inside = 10:1 → wants to enter cell but membrane impermeable to charged ions
  - K^+ concentration outside : inside = 1:10 → wants to exit cell but blocked by electrical gradient (outside is positive)

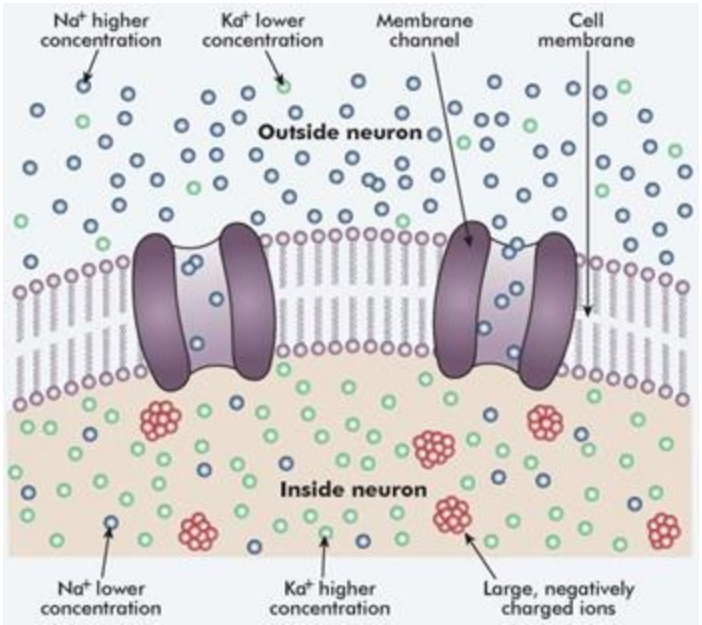
other ions and factors

- closed Ca^{2+} gates keep Ca^{2+} out of the cell
- negative proteins inside cell too large to get out
- Cl^- stays outside, attracted to positive environment

result

- neuron is **polarized** (strong electrochemical difference across membrane)





action potential

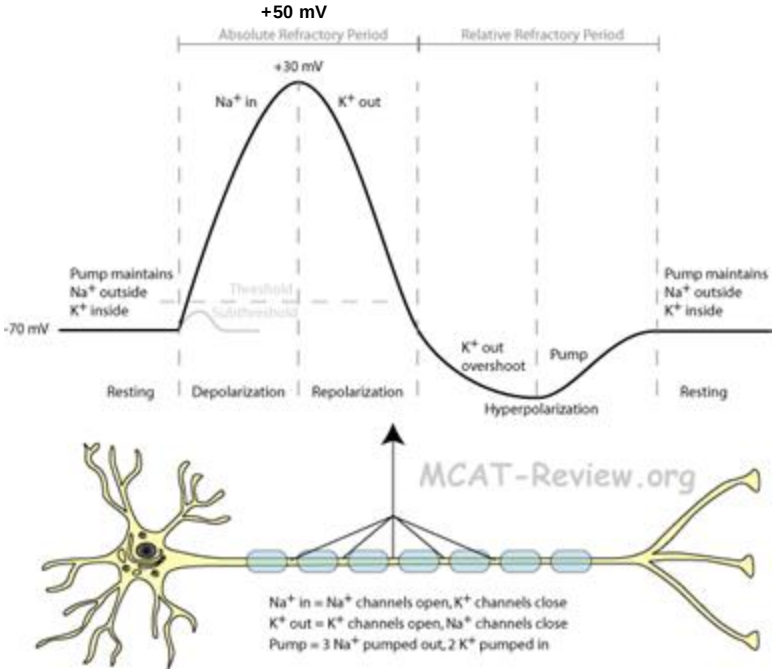
action potential = **depolarization** of neuron → cell fires

propagation process

- electricals stimulation from presynaptic neuron → NTs release → NTs bind to postsynaptic neuron → trigger action potential at **axon hillock** (where axon joins soma)

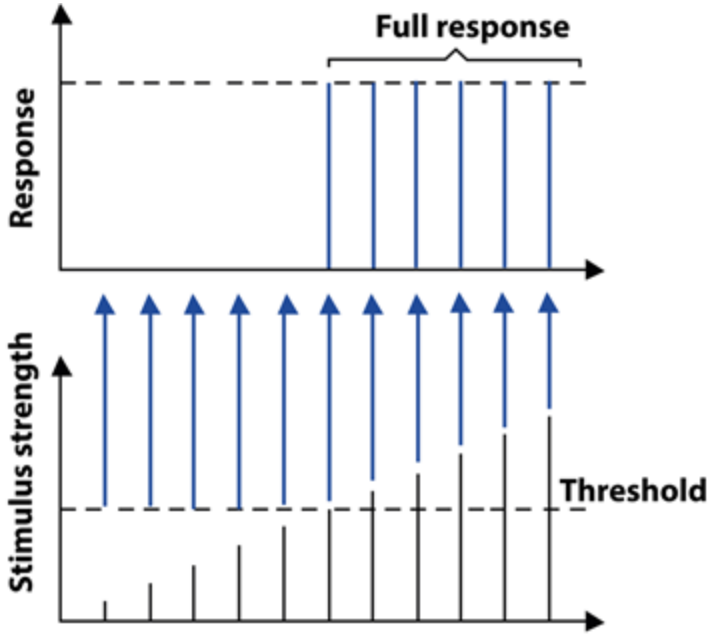
mechanism (depolarization occurs *locally* throughout the entire axon)

- Na+ channels open → *influx* of Na^+ depolarizes membrane to +50 mV
  - adjacent Na^+ gates open down axon, previous gates close
- at peak, K^+ gates open (as Na+ gates close) → *efflux* of K^+ repolarizes membrane
- when depolarization reaches axon terminal –
  - Ca^{2+} channels open at axon terminal and Ca^{2+} enters → NTs release
- restoration
  - K^+ outflow makes membrane positive outside (hyperpolarize) → K^+ gates start closing
  - repolarization: Na^+/K^+ pump actively restores resting potential to -70 mV (3 Na^+ out / 2 K^+ in)
  - Ca^{2+} pump actively removes Ca^{2+} from terminal
  - cells cannot fire during repolarization – **refractory period**



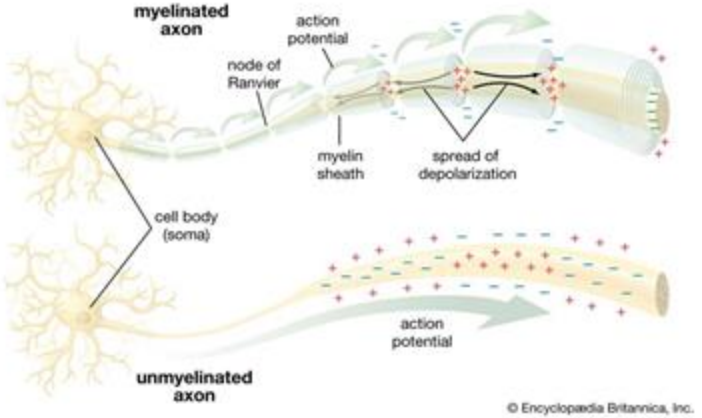
all-or-none law

- action potential is always the same size (amplitude) and speed (velocity) *regardless* of stimulus intensity
- stimulus intensity depends on
  - frequency of firing (spikes/second)
  - pattern of firing (timing between spikes)



myelination

- speeds up action potentials
- **myelin:** insulating sheath of glial cells wrapped around axons
  - **oligodendrocytes** in CNS; **schwann cells** in PNS
- **electrical conduction** travels fast along myelinated segments but weakens fast too
  - solution: **nodes of ranvier** (rechargers)
    - unmyelinated gaps of axon
    - electric signal boosted by slow ionic conduction
      - moves fast under next myelinated segment (no ions moving here)
        - "jumping" from node to node – **saltatory conduction**
- **multiple sclerosis**
  - neurodegenerative disease
  - degraded myelin → signal decay quickly and action potentials fail
    - no Na+ gates under previously sheathed axon



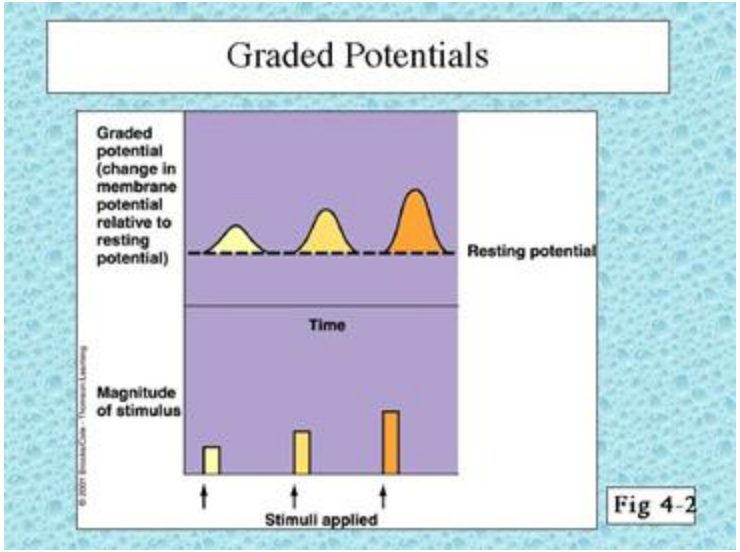
graded potentials – variable signal strength

neurons don’t always need action potential to trigger NT release!

- vary in amplitude – depends on stimulus strength
- proportional to NT release – more input = more output
- NOT ALL-OR-NONE, electrical signal scales with intensity

examples

- receptor cells (eg. retina, cochlea) can react to outside world with graded potential
  - strong stimulus → more NT released vice versa
- lateral inhibitor cells
  - suppress neighboring cells to strengthen signal of center cell
  - cell more excited → stronger neighboring inhibition
- local neurons
  - rapid electrical conduction can cause NT release
  - small size with no axon/dendrites & nearby cell communication → signal doesn’t degrade over short distance



the synapse = presynaptic cell + synaptic cleft + postsynaptic cell

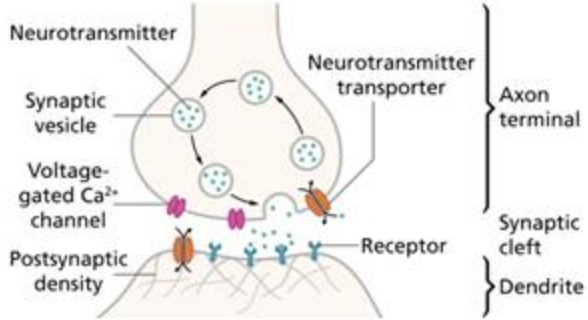
presynaptic cell releases NT into **synaptic cleft** via **exocytosis**

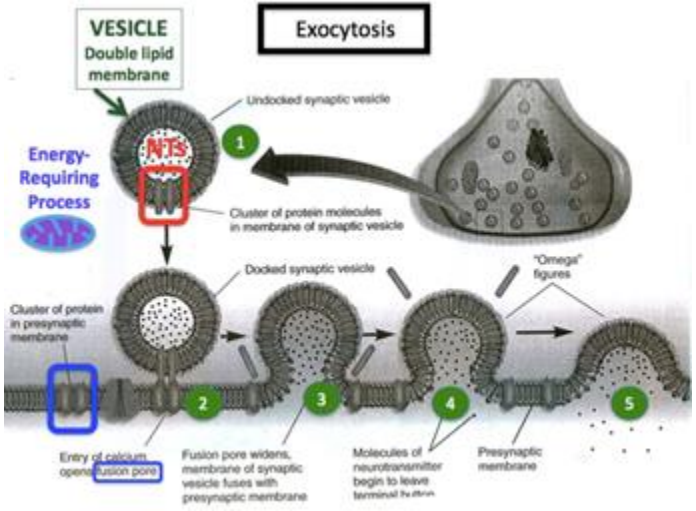
- NTs are packaged in vesicles
- depolarization→ Ca^{2+} channels open and Ca^{2+} enters → vesicle fuses w/ presynaptic cellular membrane → vesicle releases NT into cleft

following exocytosis, NTs *passively* diffuse across cleft and bind to specific receptors on postsynaptic cell

after binding:

- NT detaches from receptors and float around
- NTs deactivated (to prevent continuous stimulation)
  - by enzymes / glial cells / presynaptic cell reuptake





polarity of postsynaptic cells

EPSP (excitatory postsynaptic potential)

- increases cell's likelihood of releasing NTs → more likely to fire
- cell becomes *hypo*(less)polarized, usually by Na^+ entering cell

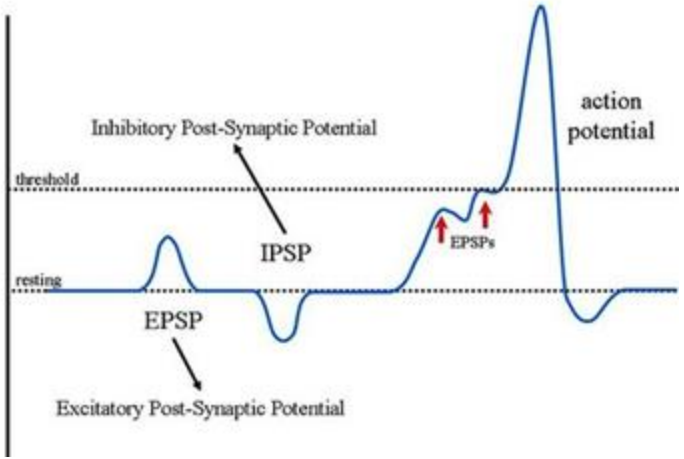
IPSP (inhibitory postsynaptic potential)

- decreases cell's likelihood of releasing NTs → less likely to fire
- cell becomes *hyper*(more)polarized, usually by K^+ exiting or Cl^- entering

summation

- neuron's response = total effect of all EPSPs + IPSPs
  - threshold reached → action potential
- temporal summation: one or more cells repeatedly stimulate another in rapid succession
- spatial summation: multiple cells converge on single location of cell at the same time

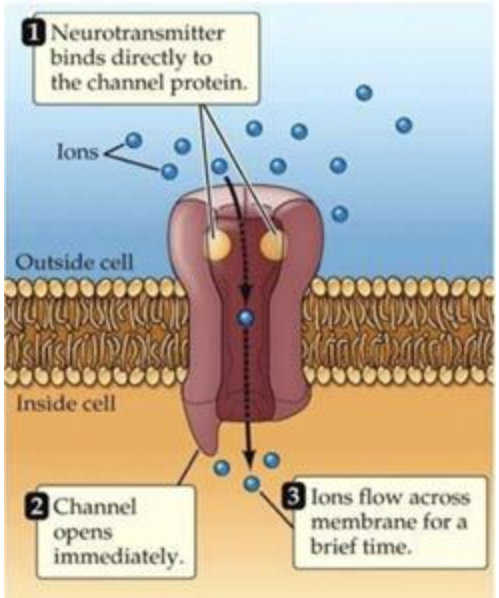
* note: some neurons can fire spontaneously without NT input (typically in graded potentials) – **spontaneous activity**



synaptic mechanisms

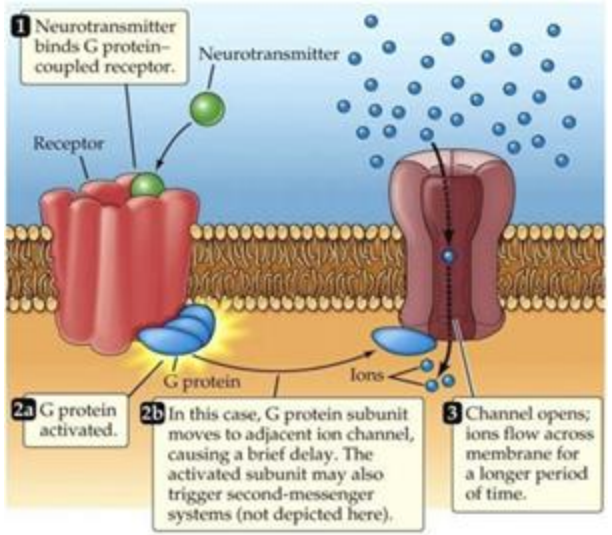
ionotropic receptors

- directly affects ion gates
- rapid and short-lived responses
- best for sending info about rapidly changing inputs



metabotropic receptors

- cause metabolic changes in postsynaptic cell
- NT triggers G-protein activation and second messenger to open ion channel
- slower but longer-lasting effects



neurotransmitters & their functions

Neurotransmitter	Functions
Acetycholine (Ach)	- All neuro-muscular junctions - Cortical arousal
GABA	- Suppress cortical activity - Regulate anxiety
Glutamate	- Most common NT - Learning - Perception - Schizophrenia
Serotonin (5HT)	- Often acts as a neuromodulator - Mood, sleep, perception
Dopamine	- Reinforcement - Attention - Motor control
Norepinephrine	- Arousal - Attention
Epinephrine (adrenalin)	- Arousal - Attention
Substance P	- Pain (damage, itch, extreme temperatures, etc)
Endorphins	- Counter effects of Substance P
Hormones	- Testosterone, estrogen, cortisol, oxytocin, endorphins, etc

agonists vs antagonists

agonist: *increases* effect of an NT
antagonist: *decreases* effect of an NT

examples

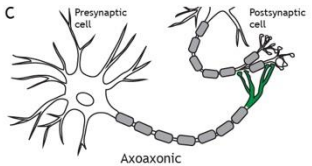
- acetylcholinesterase breaks down ACh in the cleft
  - AChE blocker = ACh agonist (blocks breakdown, prolongs effect)
  - choline reuptake blocker = ACh antagonist (reduces ACh synthesis)
- serotonin (5-HT) reuptake
  - Prozac (antidepressant): blocks reuptake – 5-HT agonist
  - MAO: converts 5-HT to its inactive form – 5-HT antagonist
- can also act in presynaptic cell to affect NT release
  - antagonists (eg. Reserpine) prevent NT packaging in vesicles
  - agonists (eg. black widow spider venom) cause massive NT release

other factors affecting function

1. DNA sequence activation can initiate protein production for structural/chemical changes in cell
2. receptor site plasticity
    a. repeated activity → more dendritic spines & more receptors
    b. some drugs block receptors by mimicking NTs
3. NT transport and production efficiency
    a. some NTs take hours/days to replenish
        i. transported to terminal by kinesin proteins along microtubules
    b. some NTs (eg. Ach) are produced directly in terminal and recycled efficiently
4. some precursors for NTs are dependent on diet

exception: *pre*synaptic receptor sites

- **autoreceptors**
    - some axons have receptors for their own NT
        - activation triggers *negative* feedback (inhibitory)
- **axoaxonic synapses**
    - one axon terminal regulates another terminal's NT release
    - presynaptic terminal may have receptor sites for inhibitory/excitatory NT from another cell



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