

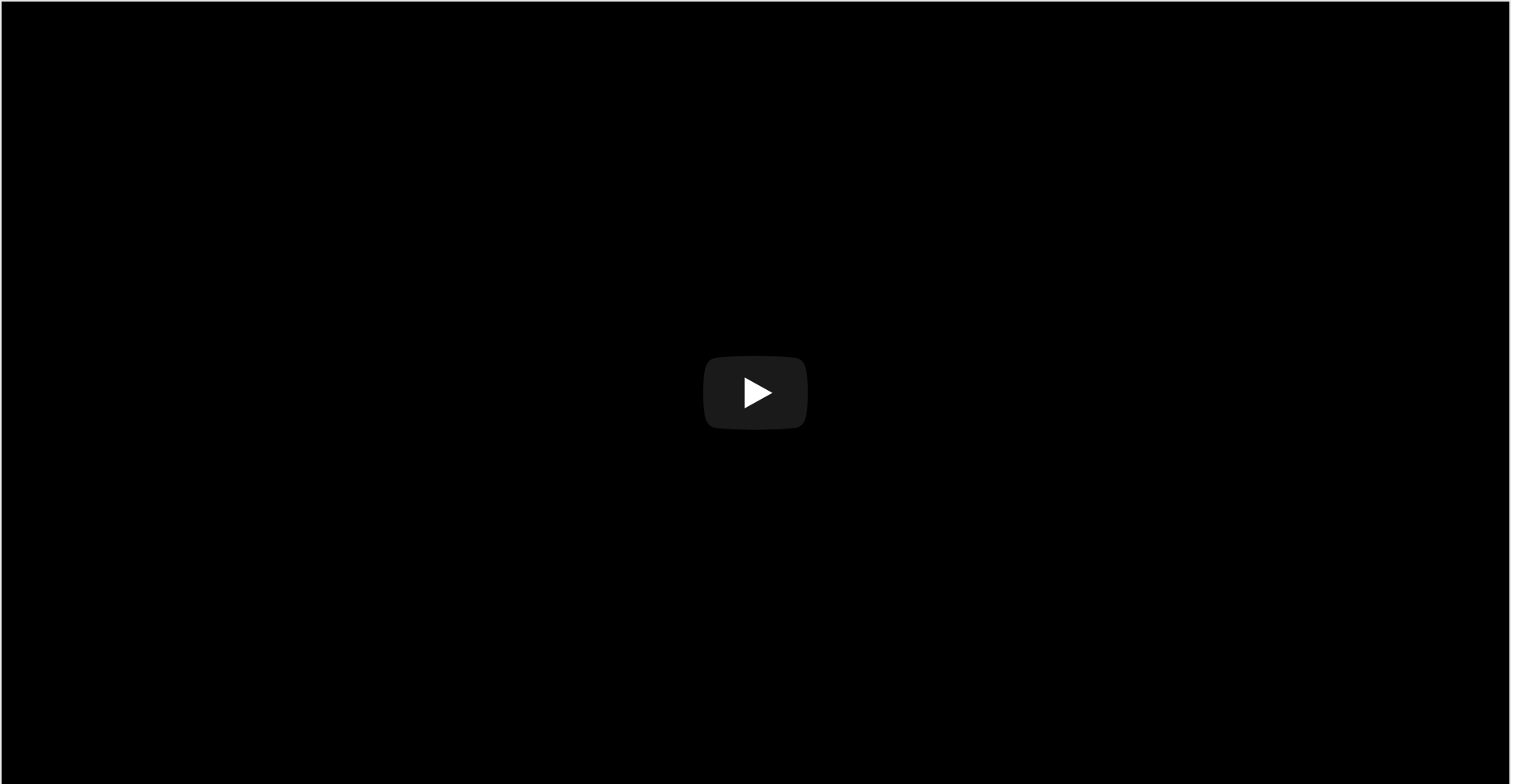
PSYCH 260

Neurochemistry I

Rick O. Gilmore

2021-09-30 16:58:49

Prelude (4:44)



<https://www.youtube.com/watch?v=f8FAJXPBdOg>

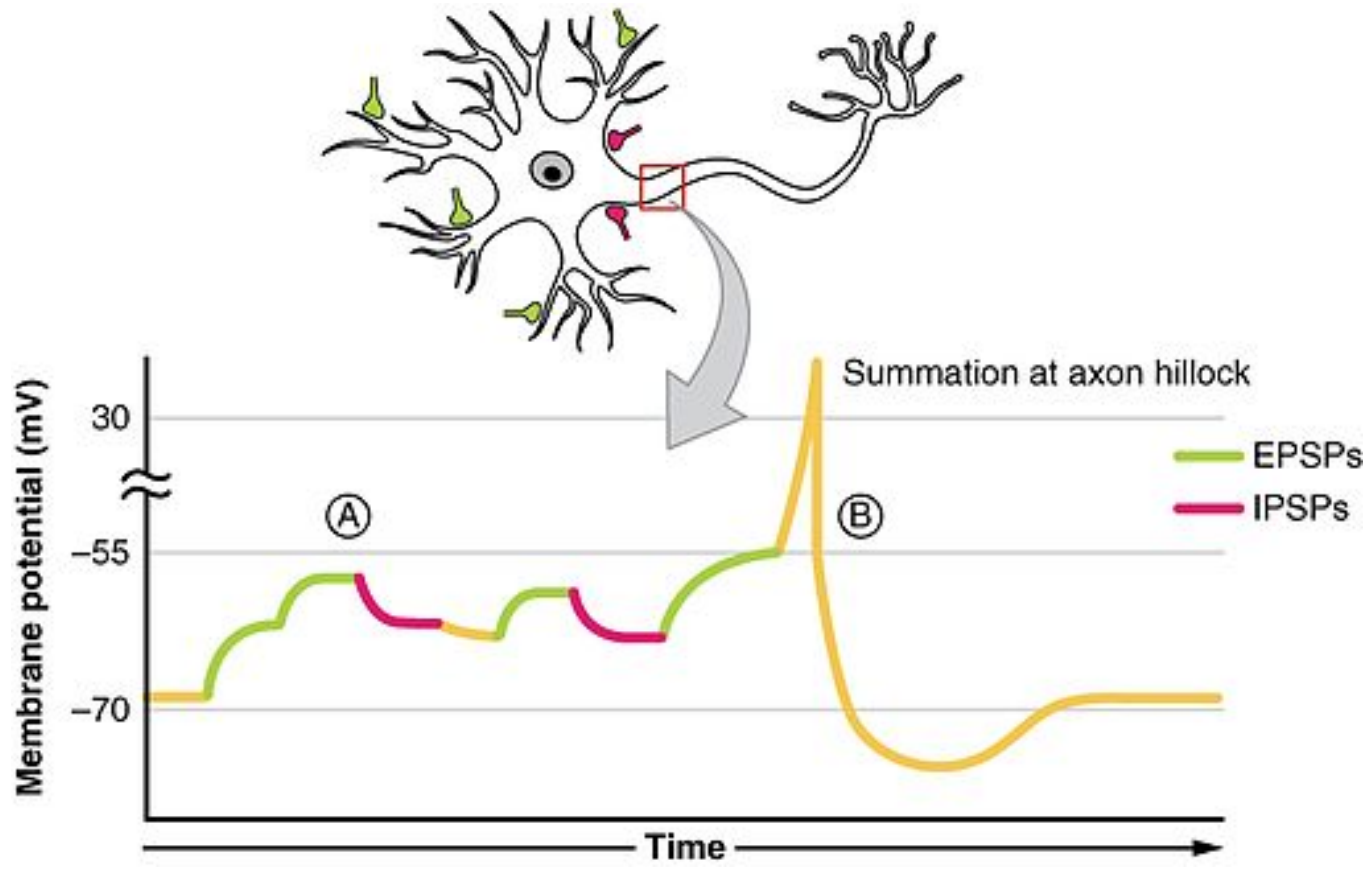
Today's Topics

- How neurons talk to one another
- Synaptic communication

In the beginning

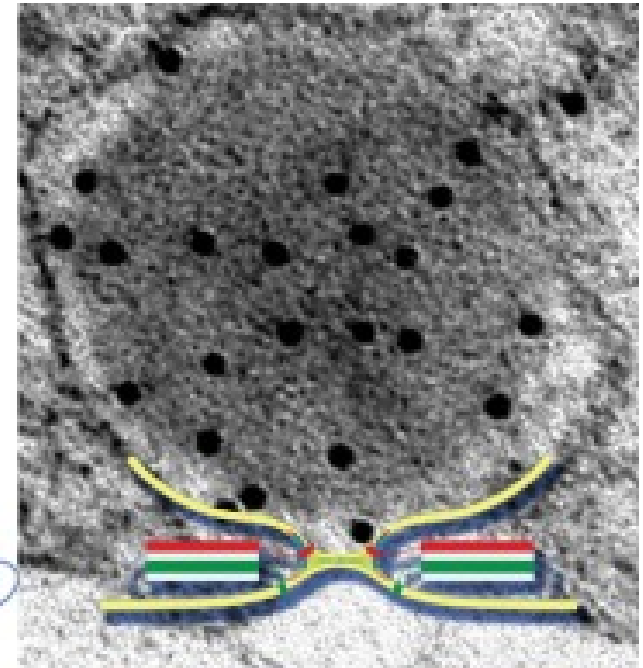
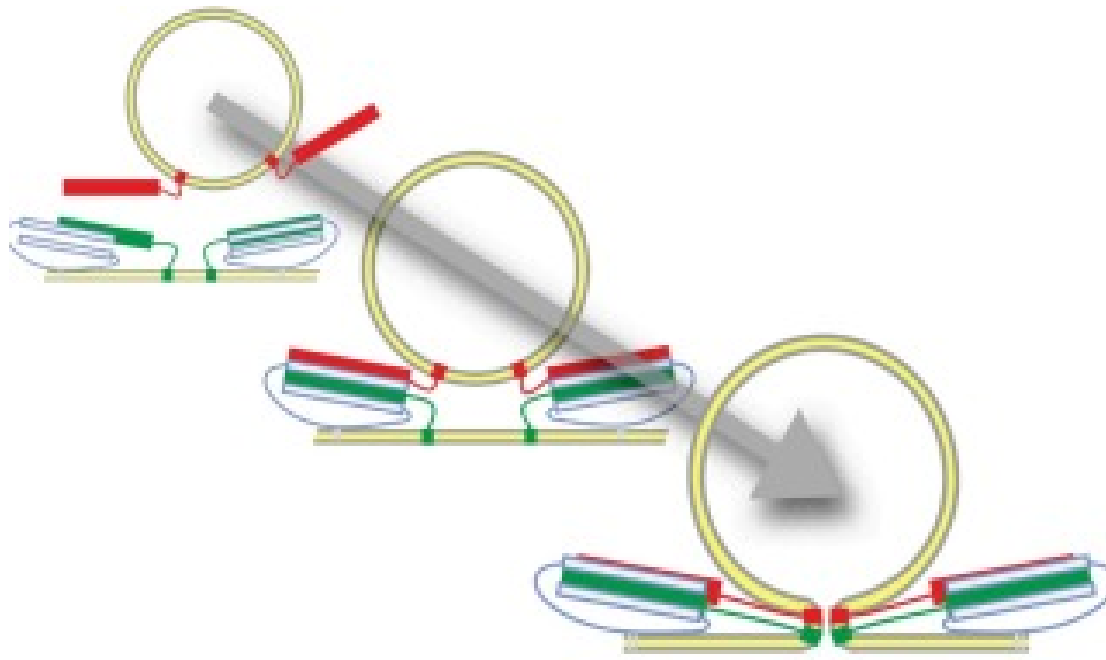
- Soma receives input from dendrites
- Axon hillock sums/integrates
- If $\text{sum} > \text{threshold}$, AP “fires”

Illustration of summation

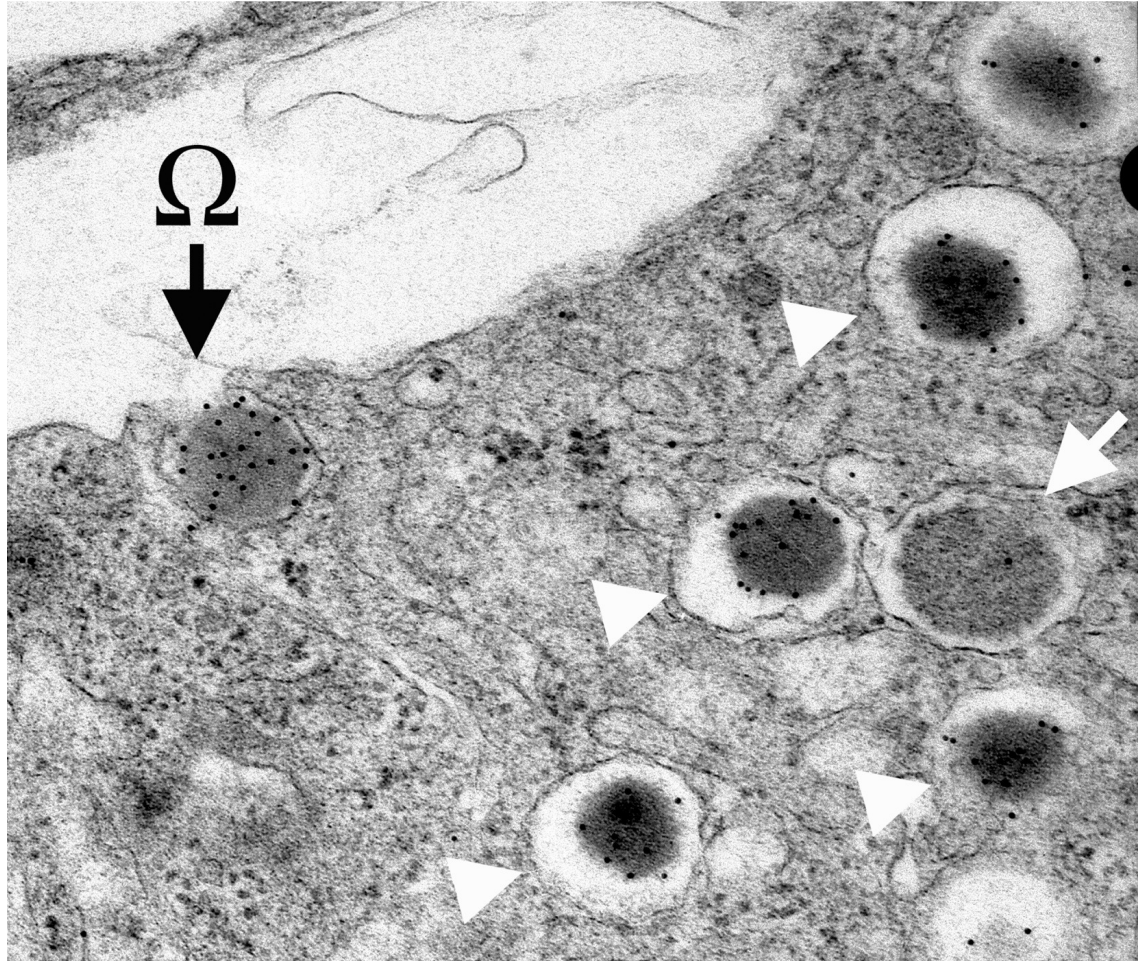


Steps in synaptic transmission

- Rapid change in voltage triggers neurotransmitter (NT) release
- *Voltage-gated calcium Ca^{++} channels* open
- Ca^{++} causes *synaptic vesicles* to bind with presynaptic membrane, merge,
- NTs released via *exocytosis*



(Hastoy, Clark, Rorsman, & Lang, 2017)



(Hastoy, Clark, Rorsman, & Lang, 2017)



200 nm

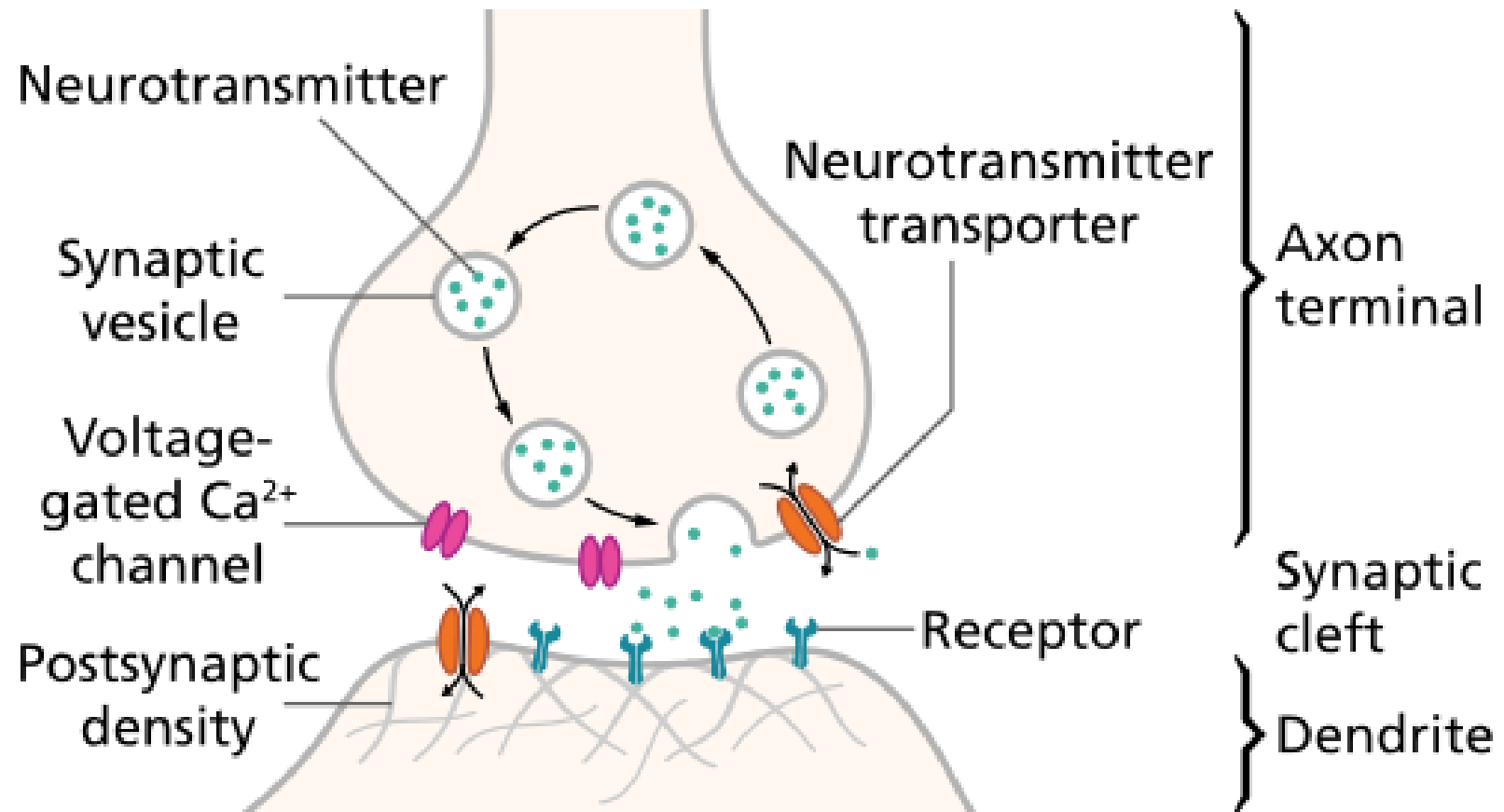
Embryonic brain 80416

3/10/0 REMF

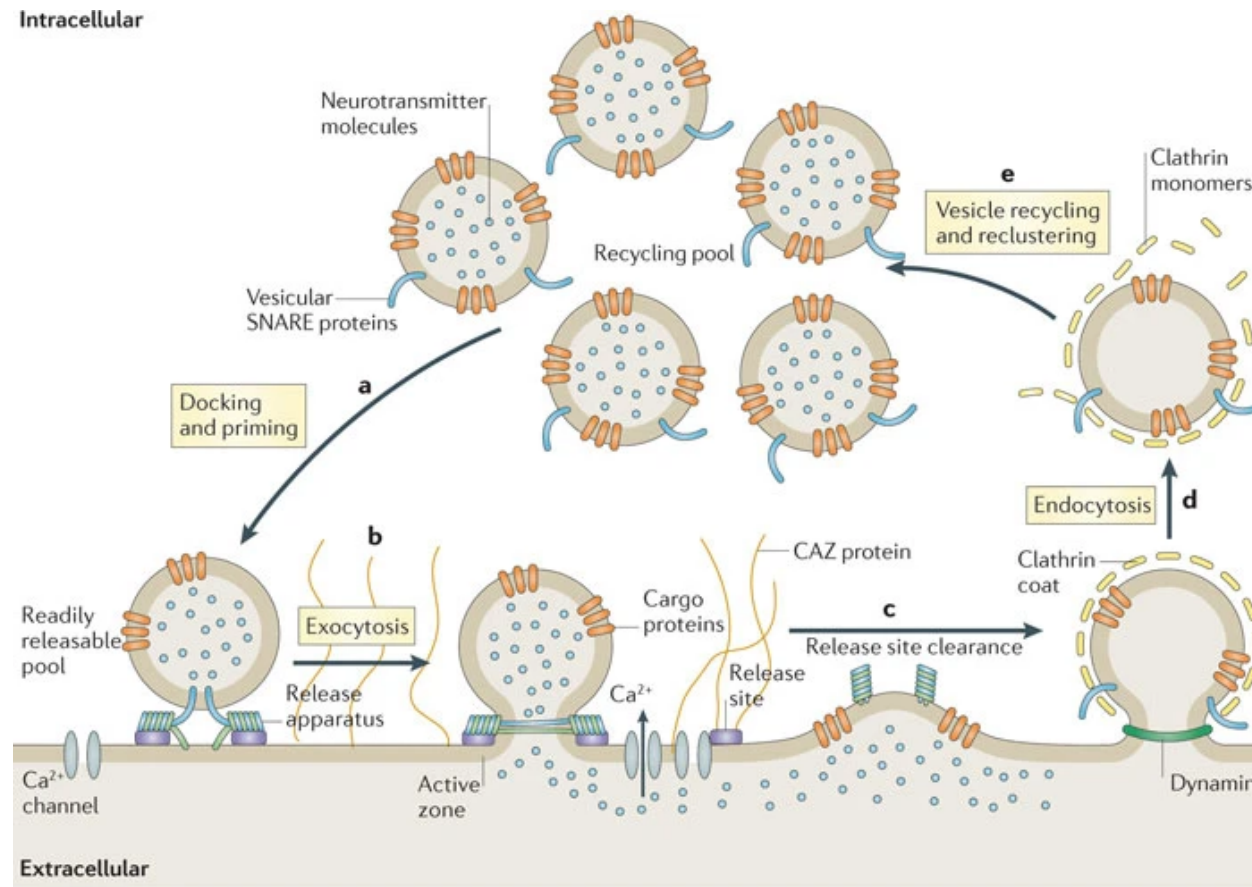
Steps in synaptic transmission

- NTs diffuse across *synaptic cleft*
- NTs bind with *receptors* on *postsynaptic membrane*
- Receptors respond
- NTs unbind, are inactivated

Synaptic transmission



Exocytosis



Nature Reviews | Neuroscience

(Haucke, Neher, & Sigrist, 2011)

Why do NTs move from presynaptic terminal toward postsynaptic cell?

- Electrostatic force pulls them
- Force of diffusion

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- Electrostatic force pulls them
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Relative sizes

- Neural membrane ~8 nm
- Synaptic vesicles ~40-60 or ~90-120 nm
- Synaptic cleft ~20-50 nm
- Cleft small relative to vesicles

Postsynaptic receptor types

- *Ionotropic* (receptor + ion channel)
 - Ligand-gated
 - Open/close ion channel
 - Ions flow in/out depending on membrane voltage and ion type
 - Fast-responding (< 2 ms), but short-duration effects (< 100 ms)

Postsynaptic receptor types

- *Metabotropic* (receptor only, no attached ion channels)
 - Trigger G-proteins attached to receptor
 - G-proteins activate 2nd messengers
 - 2nd messengers open/close adjacent channels, change metabolism
 - Slower, but longer-lasting effects

Receptor types

Ionotropic receptor

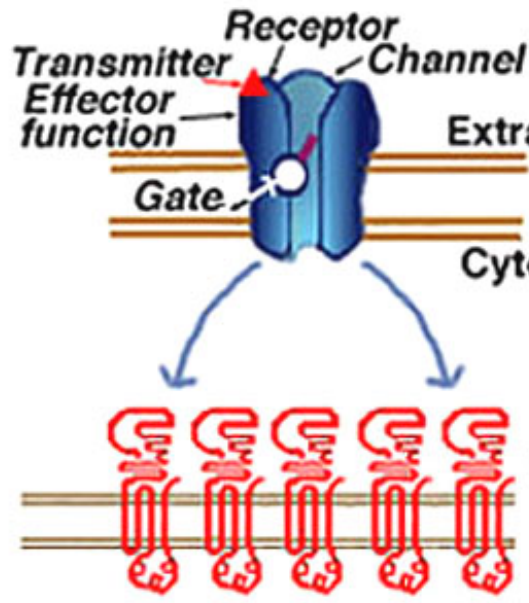


Fig. 5a. Ionotropic receptors and their associated ion channels form one complex (top). Each iGluR is formed from the co-assembly of multiple (4-5) subunits (From Kandel et al., 1991).

Metabotropic receptor

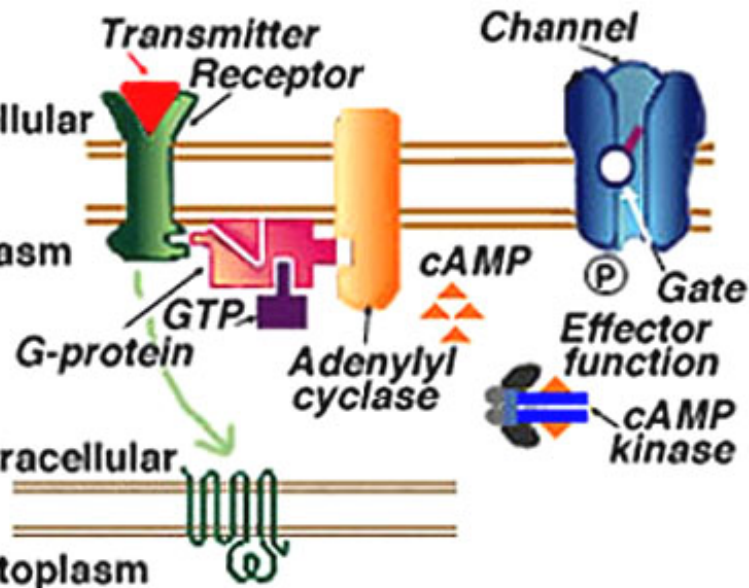


Fig. 5b. Metabotropic receptors are coupled to their associated ion channels by a second messenger cascade (top). Each mGluR is composed of one polypeptide, which is coupled to a G-protein (from Kandel et al., 1991).

Receptors generate *postsynaptic potentials* (PSPs)

- Small voltage changes
- Amplitude scales with # of receptors activated
- Number of receptors activated \sim # of vesicles released

Postsynaptic potential types

- *Excitatory PSPs (EPSPs)*
 - Depolarize neuron (make more +)
 - Move membrane potential closer to threshold
- *Inhibitory (IPSPs)*
 - Hyperpolarize neuron (make more -)
 - Move membrane potential away from threshold

Mechanisms of NT inactivation

- *Buffering*
 - e.g., glutamate into astrocytes (Anderson & Swanson, 2000)
- *Reuptake* via transporters
 - molecules in membrane that move NTs inside
 - e.g., serotonin via serotonin transporter (SERT)
- *Enzymatic degradation*
 - e.g., Acetylcholinesterase (AChE) degrades acetylcholine (ACh)

Questions to ponder

- Why must NTs be inactivated?

Questions to ponder

- Why must NTs be inactivated?
 - Keeps messages discrete, localized in time and space

What sort of PSP would *opening* a Na⁺ channel produce?

- Excitatory PSP, Na⁺ flows in
- Excitatory PSP, Na⁺ flows out
- Inhibitory PSP, Na⁺ flows in
- Inhibitory PSP, Na⁺ flows out

What sort of PSP would *opening* a Na⁺ channel produce?

- Excitatory PSP, Na⁺ flows in
- Excitatory PSP, Na⁺ flows out
- Inhibitory PSP, Na⁺ flows in
- Inhibitory PSP, Na⁺ flows out

What sort of PSP would *opening* a Cl⁻ channel produce?

Remember $[Cl\text{-out}] \gg [Cl\text{-in}]$; Assume resting potential ~ -60 mV

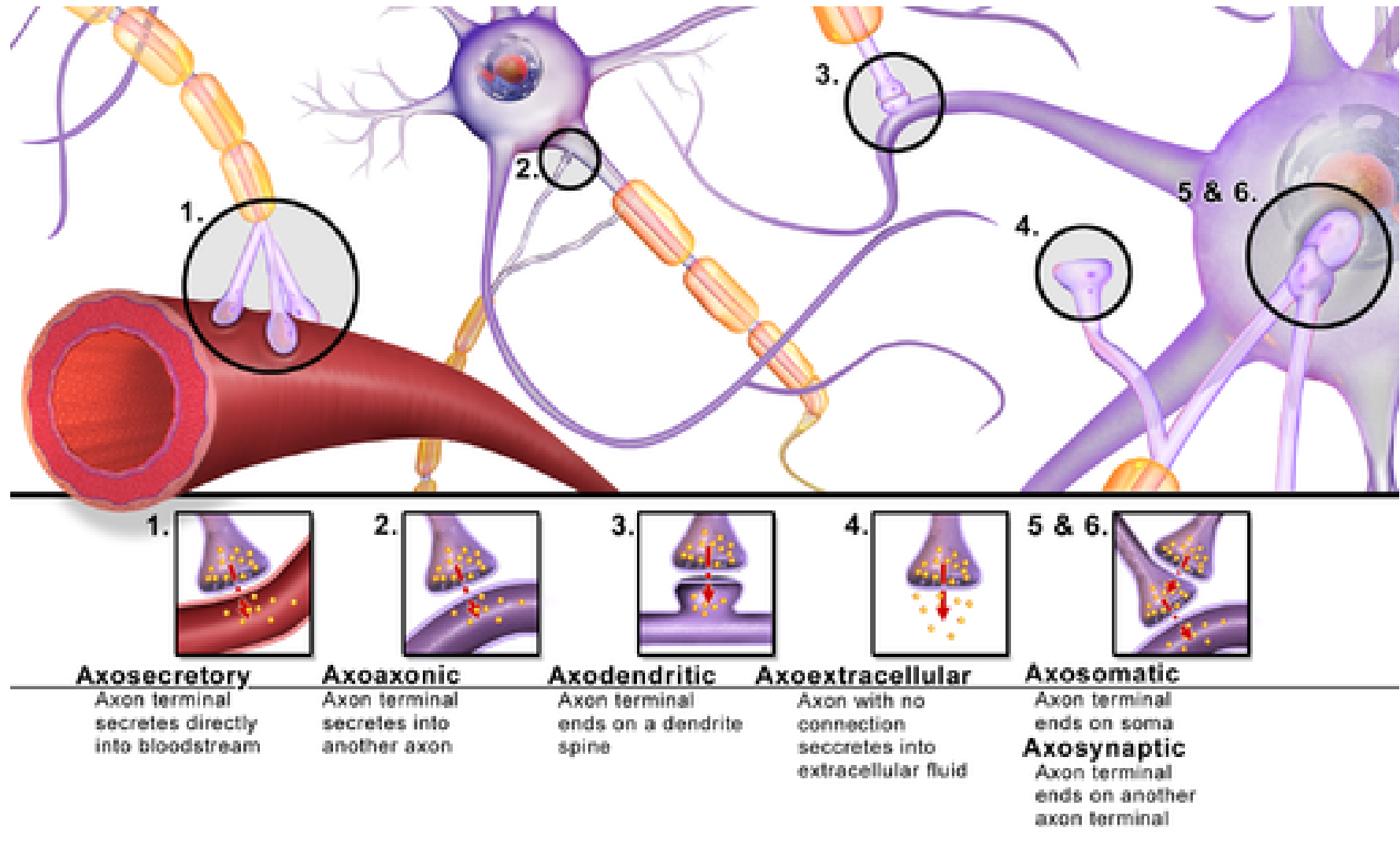
- Excitatory PSP, Cl⁻ flows in
- Excitatory PSP, Cl⁻ flows out
- Inhibitory PSP, Cl⁻ flows in
- Inhibitory PSP, Cl⁻ flows out

What sort of PSP would *opening* a Cl⁻ channel produce?

Remember $[Cl\text{-out}] \gg [Cl\text{-in}]$; Assume resting potential ~ -60 mV

- Excitatory PSP, Cl⁻ flows in
- Excitatory PSP, Cl⁻ flows out
- **Inhibitory PSP, Cl⁻ flows in**
- Inhibitory PSP, Cl⁻ flows out

Types of synapses



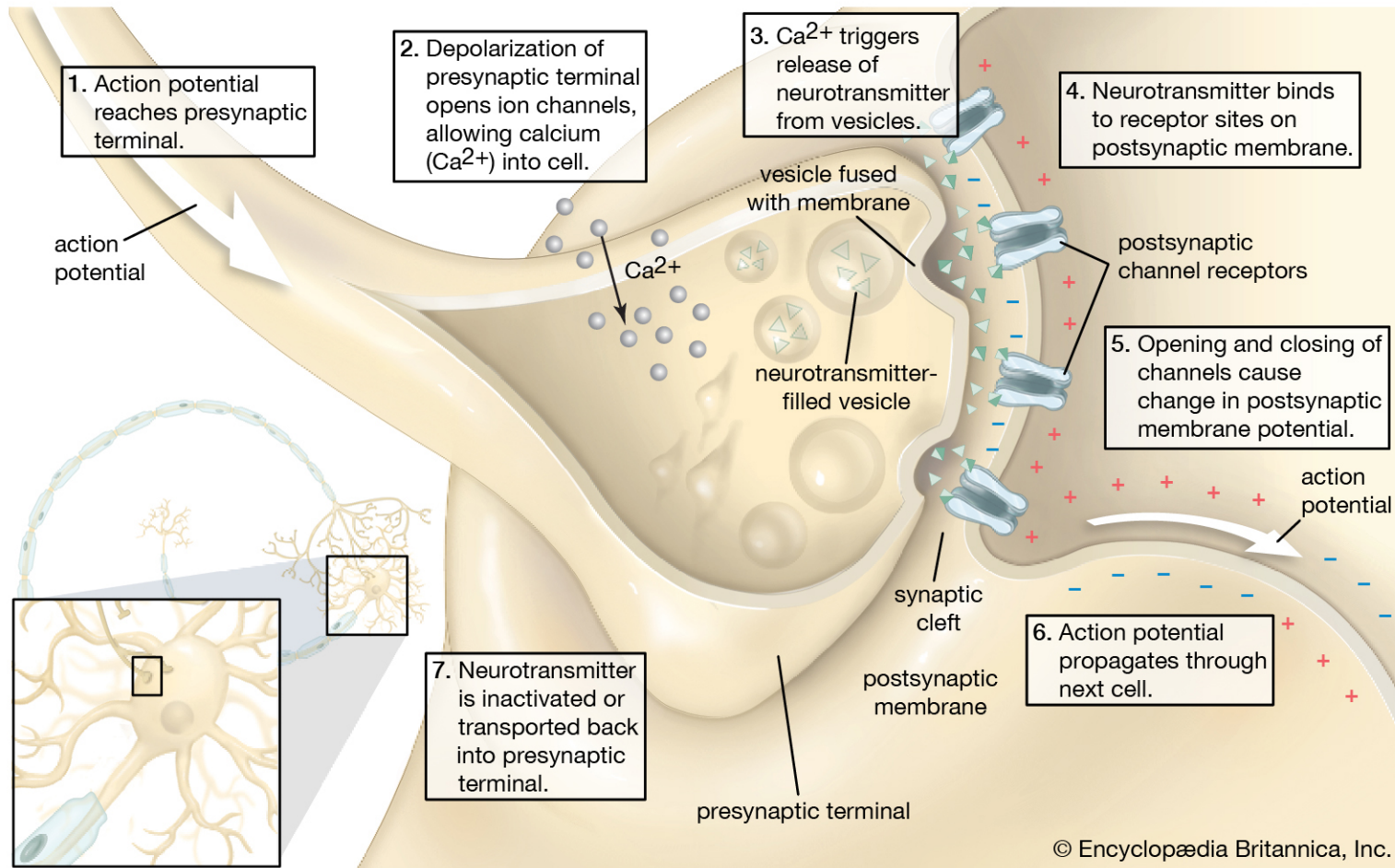
Types of synapses

- Axodendritic (axon to dendrite)
- Axosomatic (axon to soma)
- Axoaxonic (axon to axon)
- Axosecretory (axon to bloodstream)

Synapses on

- dendrites
 - usually excitatory
- cell bodies
 - usually inhibitory
- axons
 - usually modulatory (change $p(\text{fire})$)

Summary of chemical communication



<https://www.britannica.com/science/neurotransmitter>

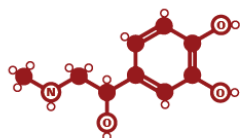
Neurotransmitters

THE STRUCTURES OF NEUROTRANSMITTERS

STRUCTURE KEY: ● Carbon atom ○ Hydrogen atom ○ Oxygen atom N Nitrogen atom R Rest of molecule

ADRENALINE

Fight or flight neurotransmitter



Produced in stressful or exciting situations. Increases heart rate & blood flow, leading to a physical boost & heightened awareness.

NORADRENALINE

Concentration neurotransmitter



Affects attention & responding actions in the brain, & involved in fight or flight response. Contracts blood vessels, increasing blood flow.

DOPAMINE

Pleasure neurotransmitter



Feelings of pleasure, and also addiction, movement, and motivation. People repeat behaviours that lead to dopamine release.

SEROTONIN

Mood neurotransmitter



Contributes to well-being & happiness; helps sleep cycle & digestive system regulation. Affected by exercise & light exposure.

GABA

Calming neurotransmitter



Calms firing nerves in CNS. High levels improve focus; low levels cause anxiety. Also contributes to motor control & vision.

ACETYLCHOLINE

Learning neurotransmitter



Involved in thought, learning, & memory. Activates muscle action in the body. Also associated with attention and awakening.

GLUTAMATE

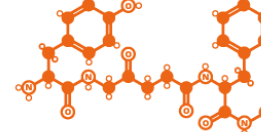
Memory neurotransmitter



Most common brain neurotransmitter. Involved in learning & memory, regulates development & creation of nerve contacts.

ENDORPHINS

Euphoria neurotransmitters



Released during exercise, excitement, & sex, producing well-being & euphoria, reducing pain. Biologically active section shown.



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<https://www.compoundchem.com/2015/07/30/neurotransmitters>

What are they?

- Chemicals produced by neurons
- Released by neurons
- Bound by neurons and other cells
- Send messages (have physiological effect on target cells)
- Inactivated after release

Neurotransmitters

Family	Neurotransmitter
Amino acids	Glutamate (Glu)
	Gamma aminobutyric acid (GABA)
	Glycine
	Aspartate

Glutamate

- Primary excitatory NT in CNS (~ 1/2 all synapses)
- Role in learning (via NMDA receptor)
- Transporters on neurons and glia (astrocytes and oligodendrocytes)
- Linked to umami (savory) taste sensation, think monosodium glutamate (MSG)
- Dysregulation in schizophrenia ([McCutcheon, Krystal, & Howes, 2020](#)), mood disorders ([Małgorzata, Paweł, Iwona, Brzostek, & Andrzej, 2020](#))

Glutamate

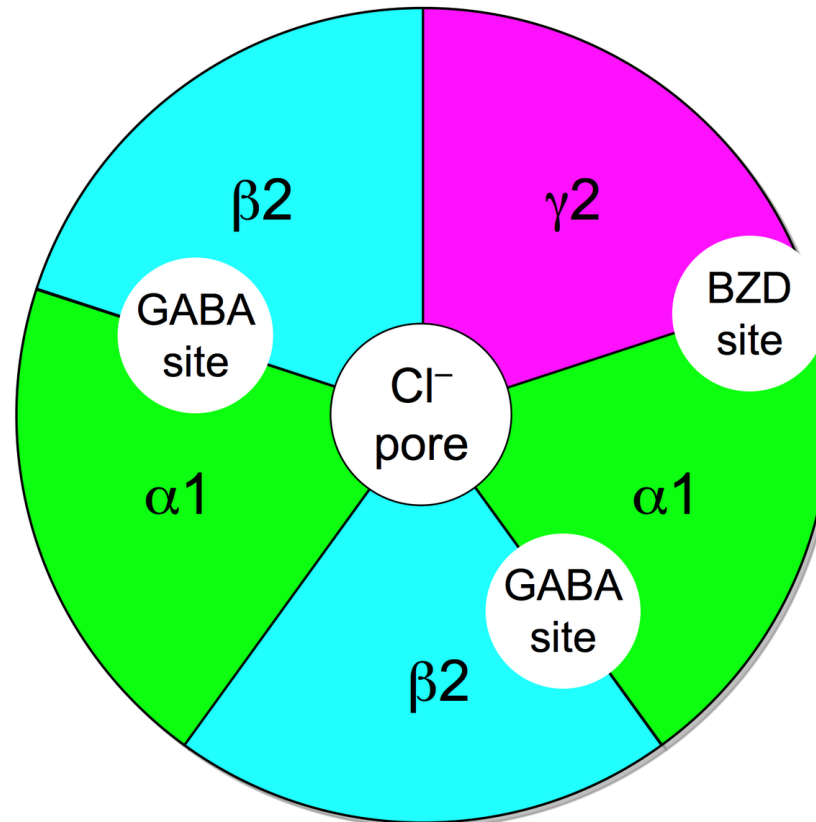
Type	Receptor	Esp Permeable to
Ionotropic	AMPA	Na ⁺ , K ⁺
	Kainate	
	NMDA	Ca ⁺⁺
Metabotropic	mGlu	

γ -aminobutyric Acid (GABA)

- Primary inhibitory NT in CNS
- Excitatory in developing CNS, $[Cl^-]_{in} \gg [Cl^-]_{out}$
- Binding sites for benzodiazepines (e.g., Valium), barbiturates, ethanol, etc.
- Synthesized from glutamate
- Inactivated by transporters

Type	Receptor	Esp Permeable to
Ionotropic	GABA-A	Cl-
Metabotropic	GABA-B	K+

GABA



"GABAA-receptor-protein-example" by [Chemgirl131](#) at [English Wikipedia](#) - Transferred from [en.wikipedia](#) to Commons by [Sreejithk2000](#) using [CommonsHelper](#).. Licensed under Public Domain via [Commons](#).

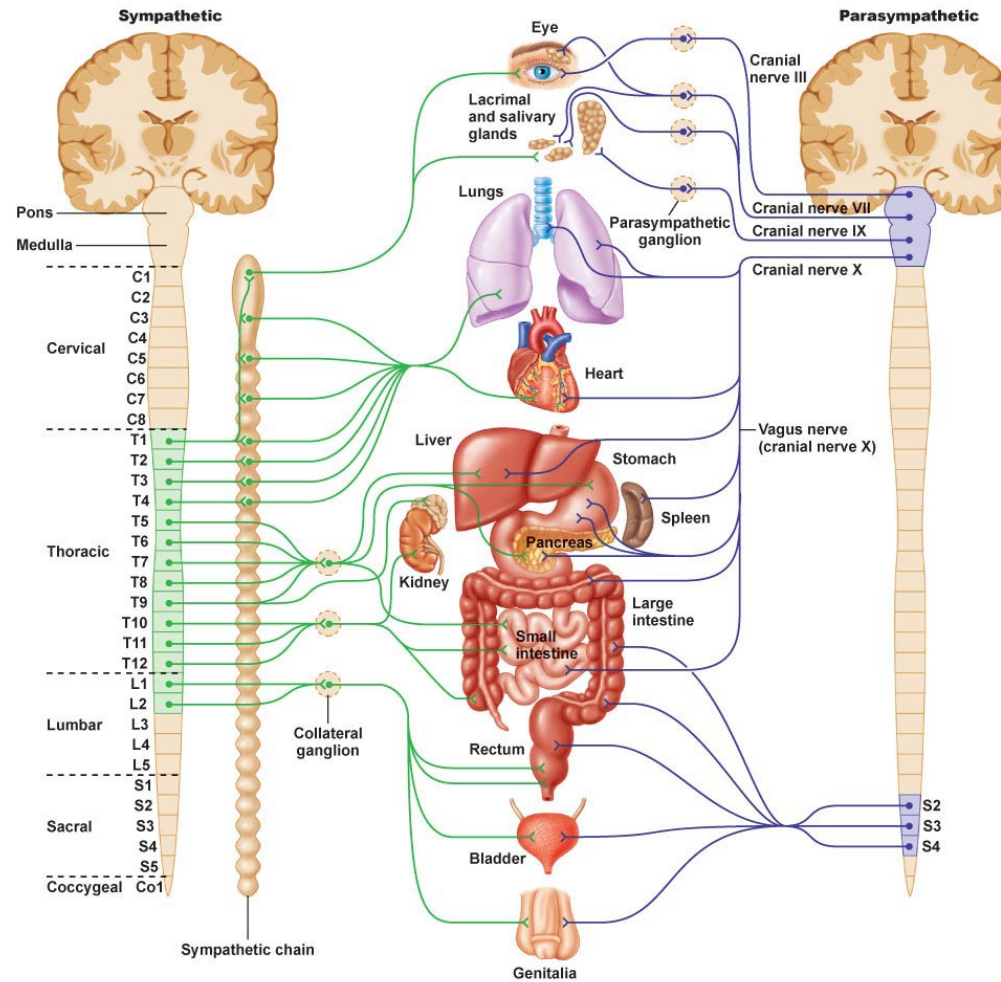
Other amino acid NTs

- *Glycine*
 - Spinal cord interneurons
 - Also inhibitory
- *Aspartate*
 - Like Glu, stimulates NMDA receptor

Acetylcholine (ACh)

- Primary NT of CNS output
- Somatic nervous system (neuromuscular junction)
- Autonomic nervous system
 - Sympathetic branch: preganglionic neuron
 - Parasympathetic branch: pre/postganglionic
- Inactivation by acetylcholinesterase (AChE)

ACh anatomy



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<http://myzone.hrvfitltd.netdna-cdn.com/wp-content/uploads/2014/09/Image-1.jpg>

Acetylcholine

Type	Receptor	Esp Permeable to	Blocked by
Ionotropic	Nicotinic (nAChR)	Na ⁺ , K ⁺	e.g., Curare
Metabotropic	Muscarinic (mAChR)	K ⁺	e.g., Atropine

Curare



<http://www.general-anaesthesia.com/images/indian-curare.jpg>

Atropine

- aka, nightshade or belladonna



<https://aapos.org/glossary/dilating-eye-drops>

How to stop your prey

Substance	Effect
Japanese pufferfish toxin	Blocks voltage-gated Na ⁺ channels
Black widow spider venom	Accelerates presynaptic ACh release
Botulinum toxin (BoTox)	Prevents ACh vesicles from binding presynaptically
Sarin nerve gas	Impedes ACh breakdown by AChE
Pesticides	Impede AChE
Tetanus toxin	Blocks release of GABA, glycine

Next time...

- More on NTs!

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