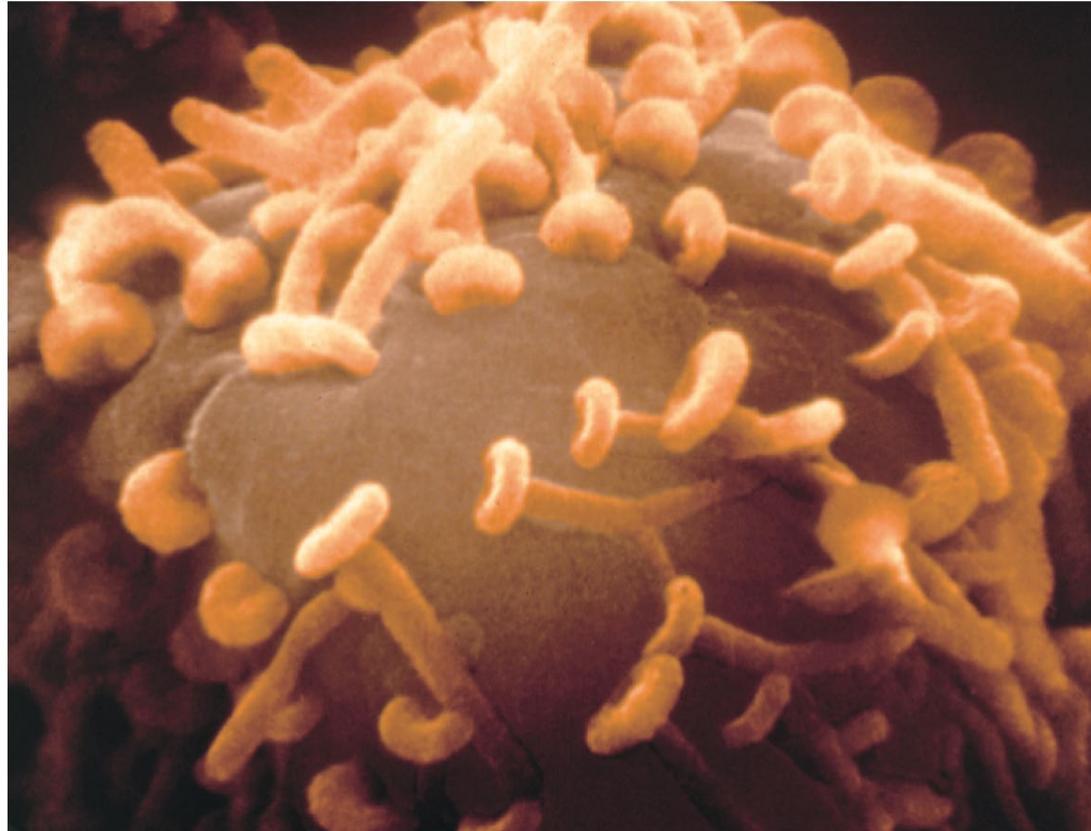


## Chapter 12.3

# Synapses and Neurotransmitters



# The Discovery of the Synaptic Cleft

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Early physiologists thought neurons were “continuous thread like fibers” that transmitted an electrical signal between the brain and the target tissue. (i.e. the reticular theory)

–Camillo Golgi – Italian physician developed a “silver staining technique” to visualize nervous tissue (1873) for the first time.

–Ramón y Cajal used the “Golgi method” to show gaps (i.e. synapse) between neurons (early 1890's) which led to the “**neuron doctrine**”

–Cajal's work challenged the notion of the day about a “pure” electrical nervous system and his work led to the “**neuron doctrine**” and discredited the reticular theory

–Cajal showed that the brain's function was dependent on the “chemical synapse” which is now recognized as a type of **electro-chemical junction** // 50 nanometers wide (1 x 10<sup>-9</sup> meters)

–In the 1970s Dr. Eric Kandel demonstrated how the **synapse change during learning**. He also showed differences in how synapses changed between short term and long-term learning. (see Dr. Kandel's videos)

# The Discovery of Neurotransmitters

---

Otto Loewi, in 1921, demonstrated how neurons communicate with each other or how neurons communicate their target tissue by releasing chemicals – establishing the **chemical synapse**

flooded two exposed frog hearts with saline

stimulated vagus nerve of the first frog and the heart slowed

removed saline fluid from frog #1, added it to frog #2, and found the fluid from frog #1 slowed heart of frog #2

named it Vagusstoffe (“vagus substance”) // later re-named **acetylcholine**. **This was the discovery of the first neurotransmitter.**

**takes 0.50 milliseconds for a neurotransmitter to cross this distance**

# The Synapse

*A nerve's action potential can go no further than to the synaptic knob / distal end of the axon*

*The action potential triggers the release of a neurotransmitter from synaptic knob // neurotransmitter stored in vesicles inside terminal end (synaptic knob)*

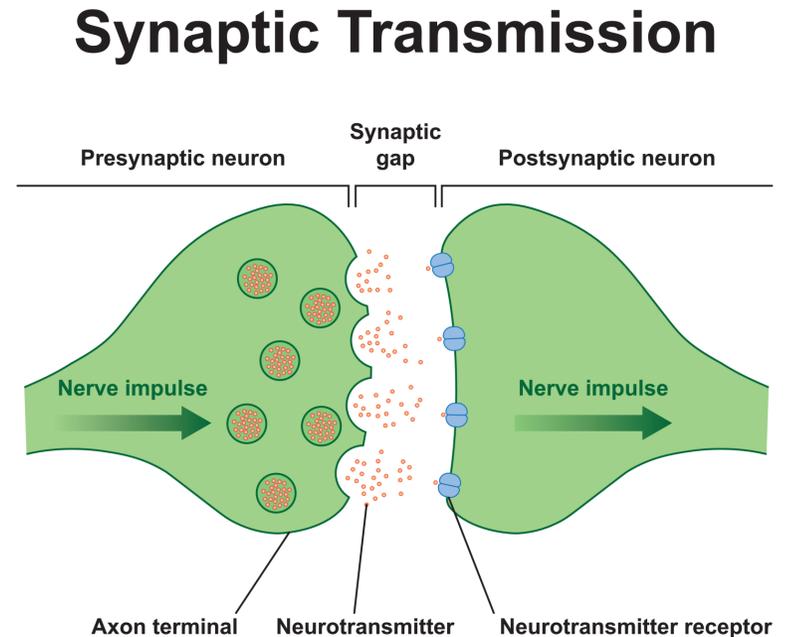
A chemical synapse consist of three components

- Pre-synaptic membrane
- Synaptic cleft
- Post-synaptic membrane

*One type of neurotransmitter may stimulate a new local potential on the post-synaptic membrane, making it more likely to create a new local potential on the post synaptic membrane.*

*Another type of neurotransmitter may inhibit forming a local potential, making it less likely to stimulate a new local potential on the post synaptic membrane.*

*What is now possible? Significance?*



# The Synapse

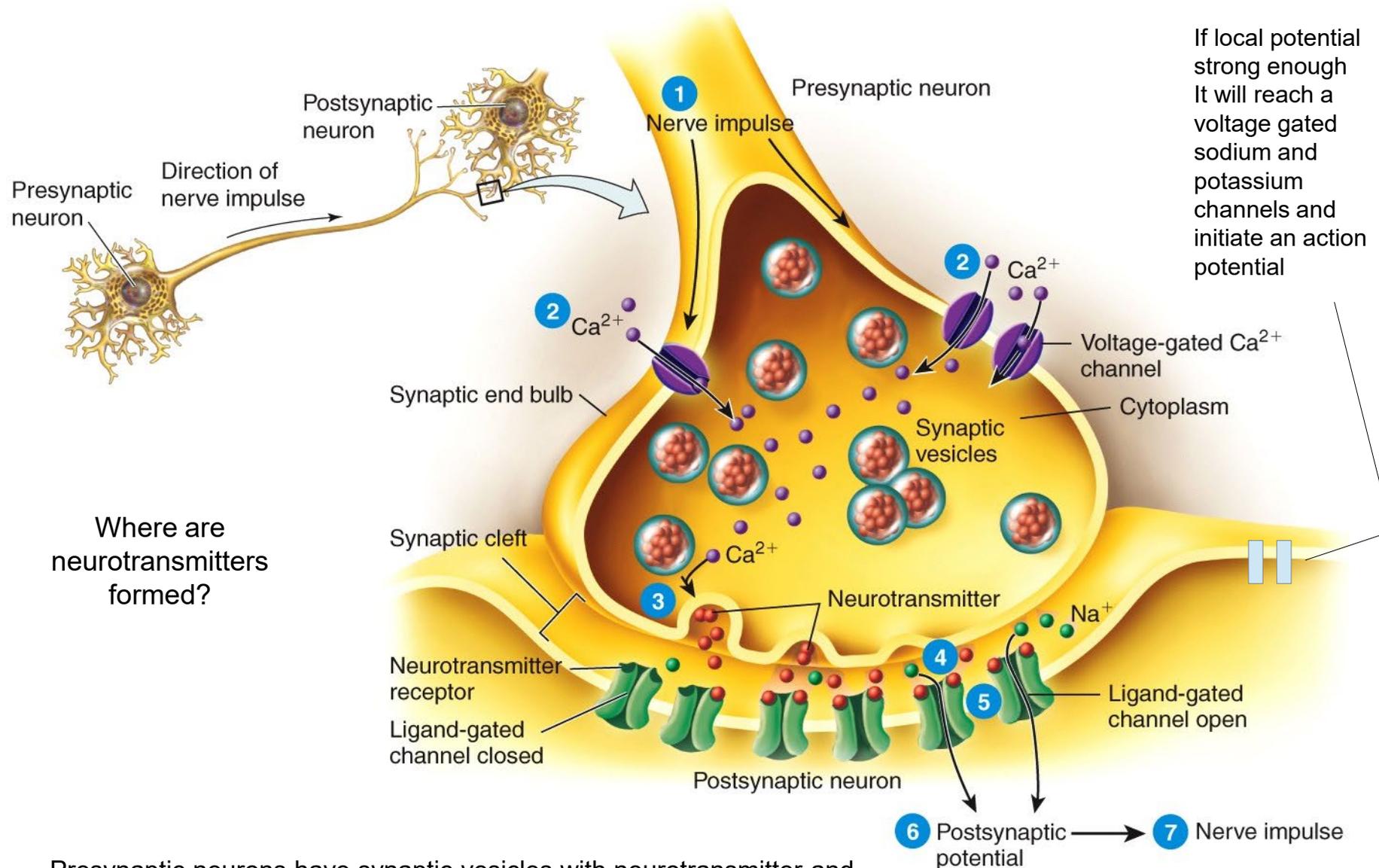
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When a synapse is between two neurons we use the following syntax.

1st neuron in the signal pathway is called the **presynaptic neuron** / it releases neurotransmitter

2nd neuron is the **postsynaptic neuron** / it has receptors for the neurotransmitter

# Structure of a Chemical Synapse



Where are neurotransmitters formed?

Presynaptic neurons have synaptic vesicles with neurotransmitter and postsynaptic neurons have **receptors** with ligand-regulated ion channels

# Synapses

---



A neuron may have an enormous number of synapses on their dendrites and/or soma

Spinal cord motor neuron soma have about **10,000 unique synaptic knobs** from other neurons // some excitatory others inhibitory

- 8,000 ending on its dendrites
- 2,000 ending on its soma

Cerebellum's soma may have as many as **100,000 synapses!!!!**

- *Note: all these incoming signals must be “integrated” (measure the excitatory VS inhibitory signals) to determine if a new action potential will be created at the axon hillock of the post synaptic neuron. In the cerebellum, 100,000 incoming signals onto a single neuron will only result in one of two possible outcomes: no action potential or an action potential on the post synaptic neuron.*

# Structure of a Chemical Synapse

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Synaptic knob stores **synaptic vesicles** containing neurotransmitters

many docked on interior face of the plasma membrane / ready to release neurotransmitter on demand into synaptic cleft

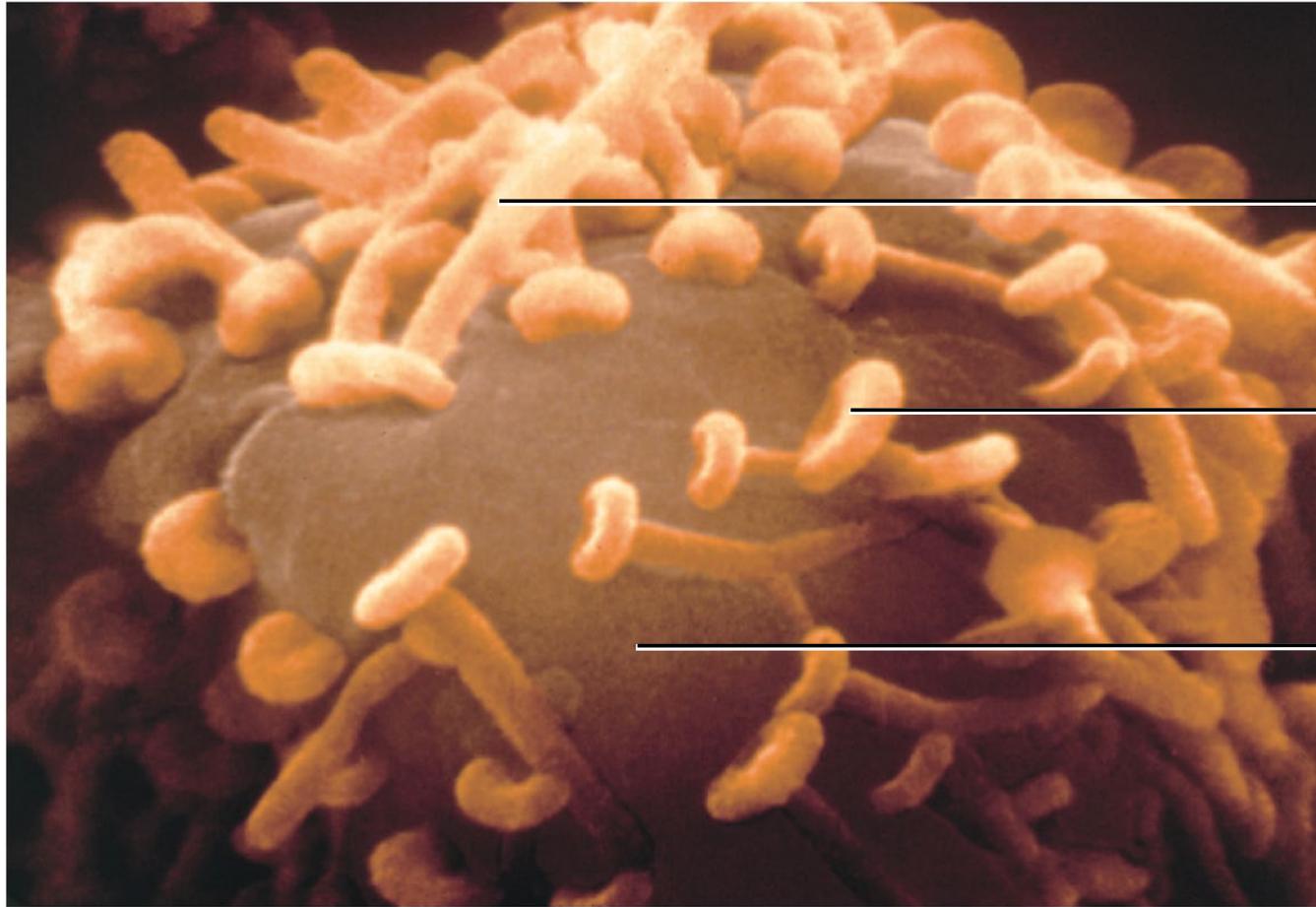
a reserve pool of synaptic vesicles are located further away from inner face of synaptic knob's membrane

**postsynaptic neuron** membrane contains **receptors** (docking stations made up of proteins) embedded into membrane / transmembrane protein

**receptors** represent ligand-regulated ion gates

Note: other gates may be regulated by voltage or mechanical stimuli

# The Synaptic Knob



**Axon of  
presynaptic  
neuron**

**Synaptic  
knob**

**Soma of  
postsynaptic  
neuron**

# Where May A Synapse Occur?

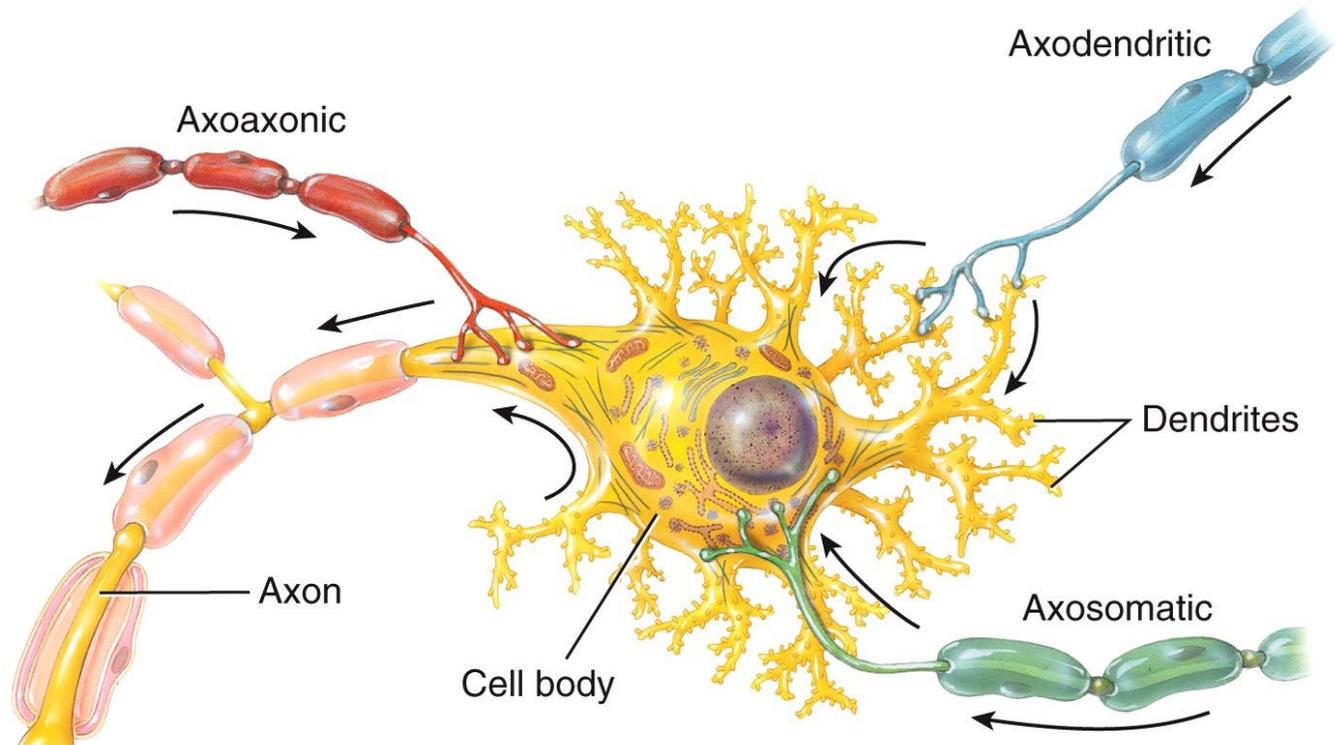
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The presynaptic neuron may synapse with

- Dendrite
- Soma
- Axon of postsynaptic neuron

Form different types of synapses

- **Axodendritic synapses**
- **Axosomatic synapses**
- **Axoaxonic synapses**



# What is a “purely electrical synapse”?

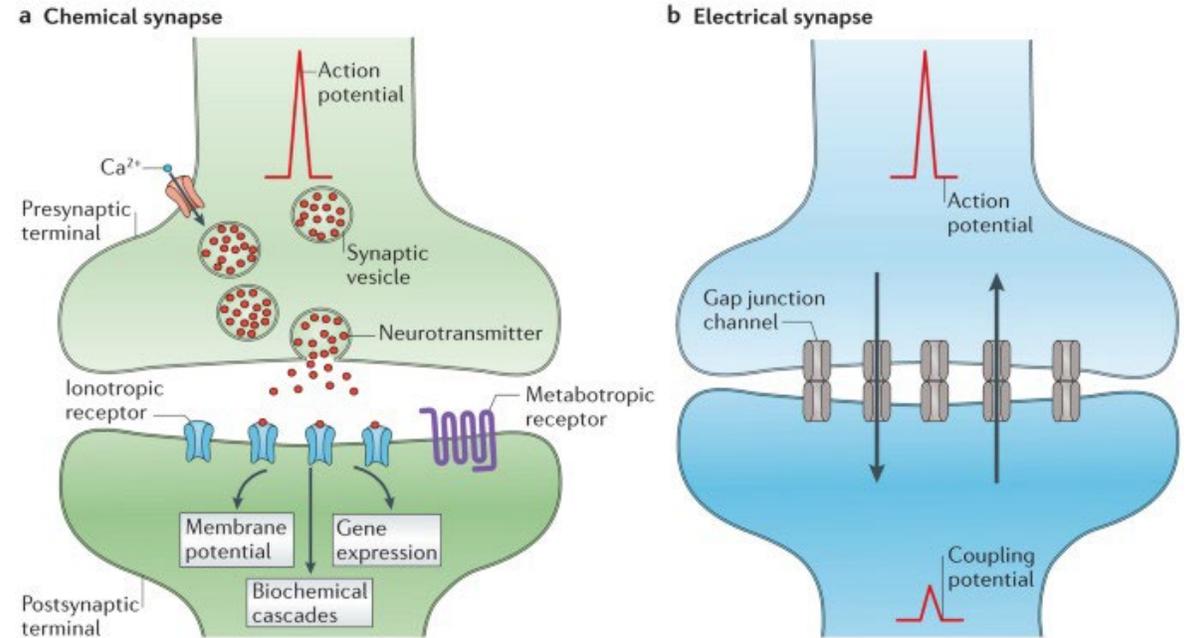
It is a gap junction! Gap junctions allow action potentials to move rapidly between adjacent cells!  
// no neurotransmitter

Occur between some neurons, neuroglia, cardiac cells and single-unit smooth muscle, embryonic cells

Gap junctions join adjacent cells /// ions or electrical current diffuse through the gap junctions from one cell to the next

**Advantage** = quick transmission // no delay for release and binding of neurotransmitter

**Disadvantage** = they can not integrate information and can not be used in making decisions



# Two Types of Neurotransmitter Receptors: Ionotropic VS Metabotropic

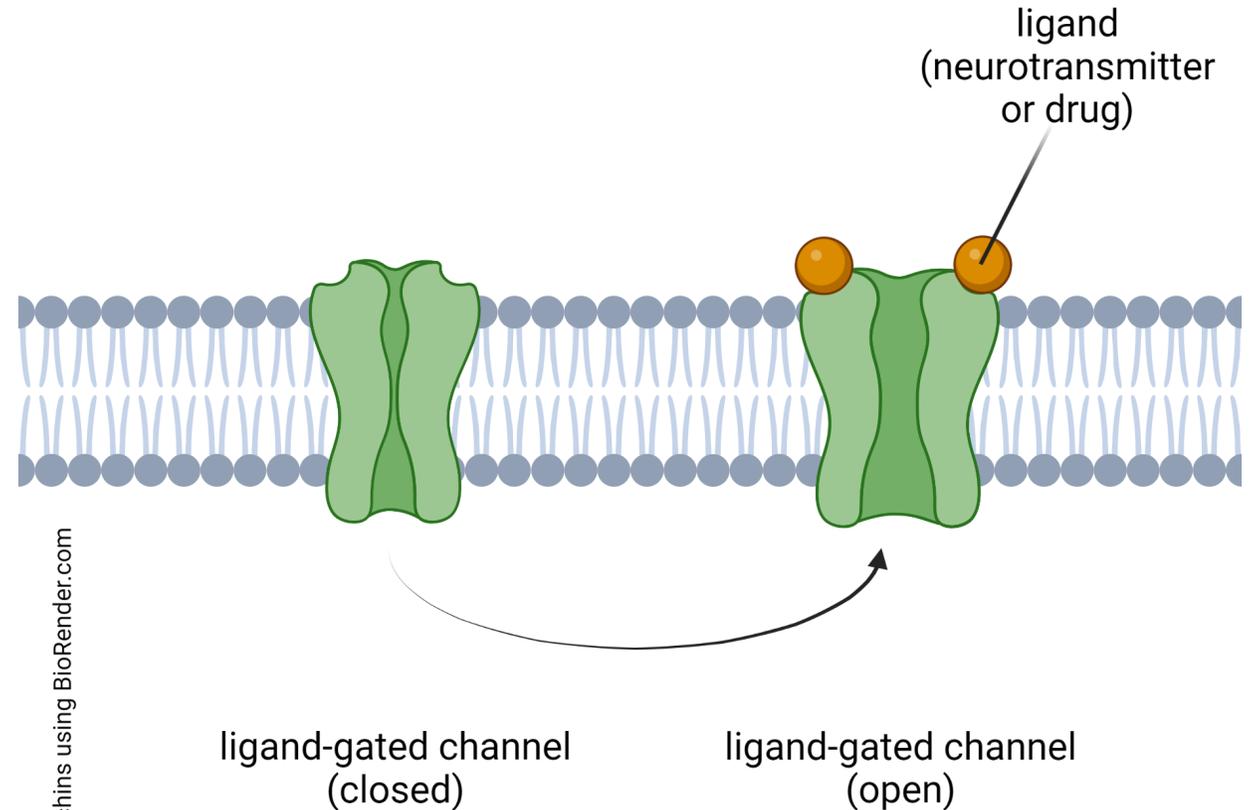
## Ionotropic receptors

Ligand binds to integral protein channels which allows either cation or anion to cross plasma membrane

Ligand receptor and ion channel are part of same protein

If cations enter cell then it **depolarizes**

If anions enter cell then it **hyperpolarizes**



# Two Types of Neurotransmitter Receptors: Ionotropic VS Metabotropic

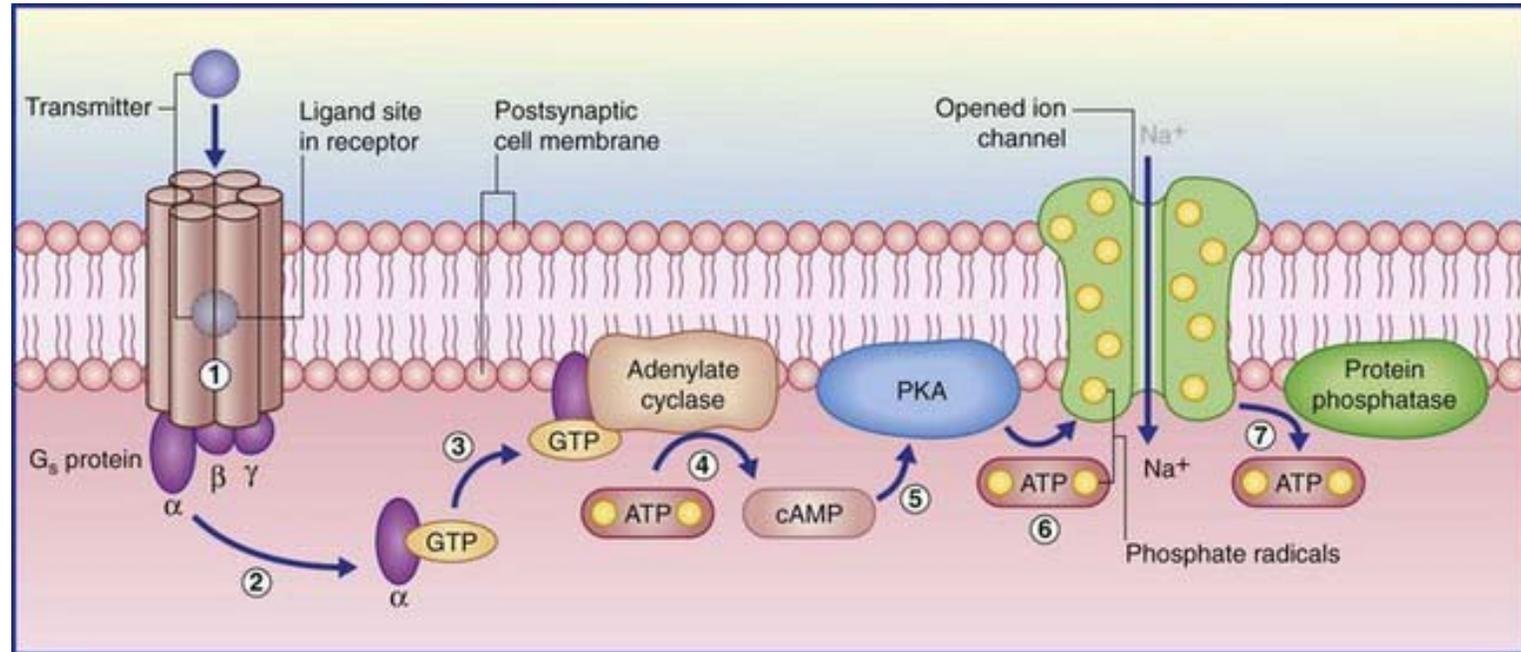
## Metabotropic receptors

ligand receptor and ion channel have different types of integral proteins

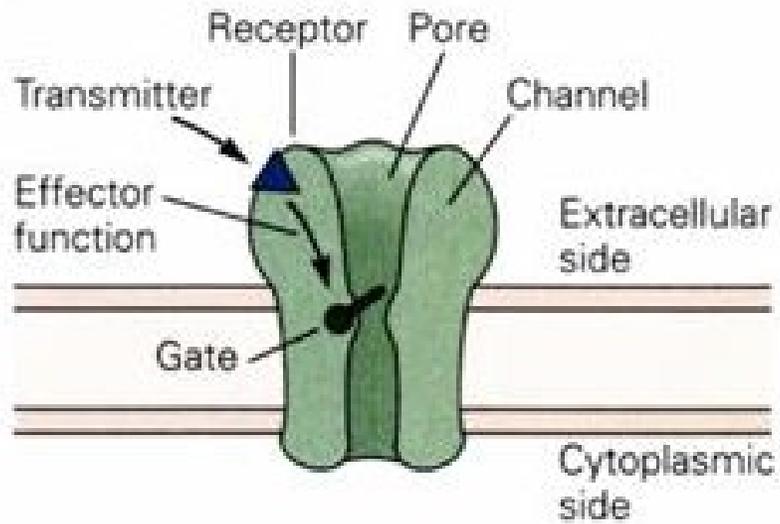
metabotropic receptors are “ligand receptors” on external face of membrane that releases “G protein” on their internal face of membrane

G protein travels to a second integral protein and this integral protein then functions as the ion channel

this is Second messenger system

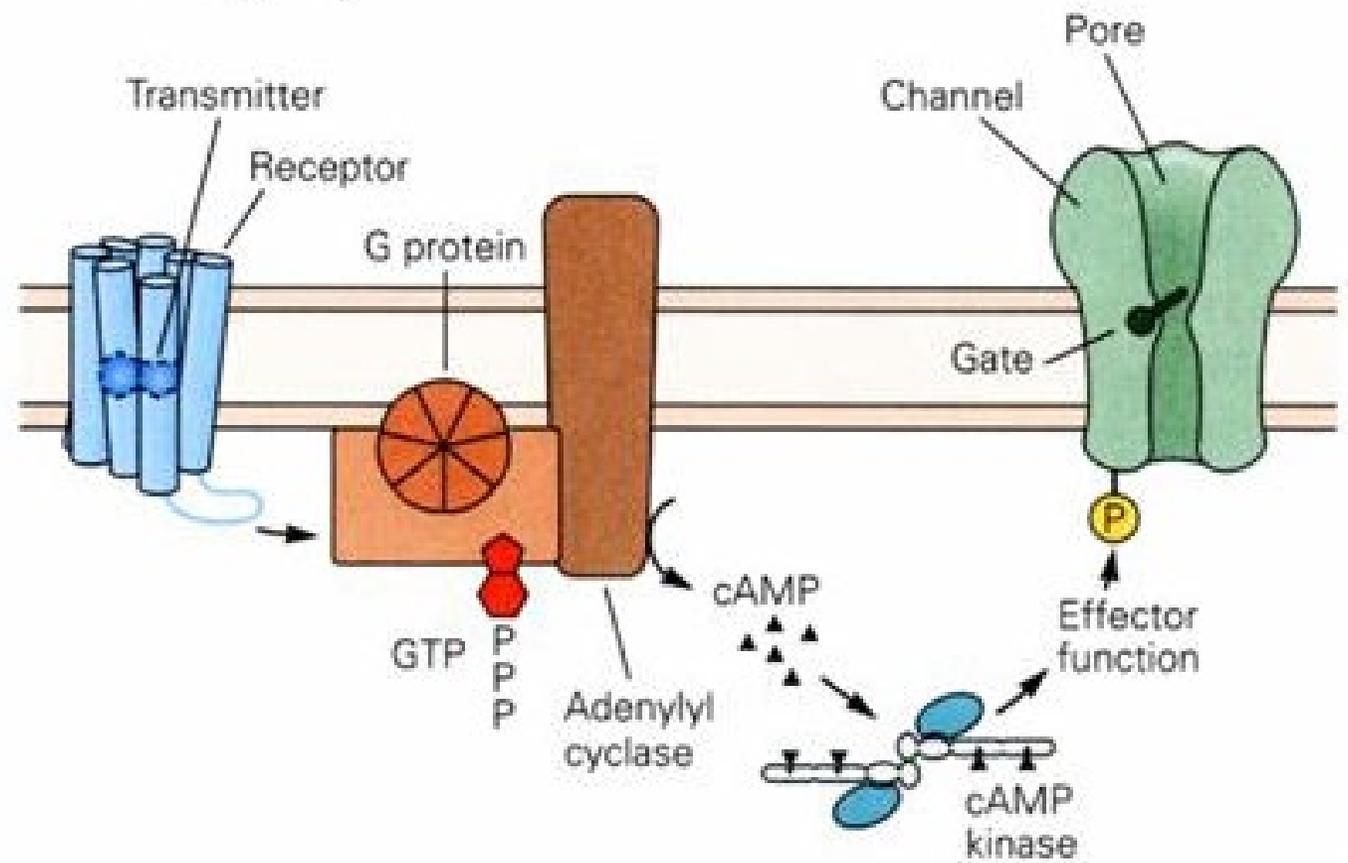


### A Direct gating



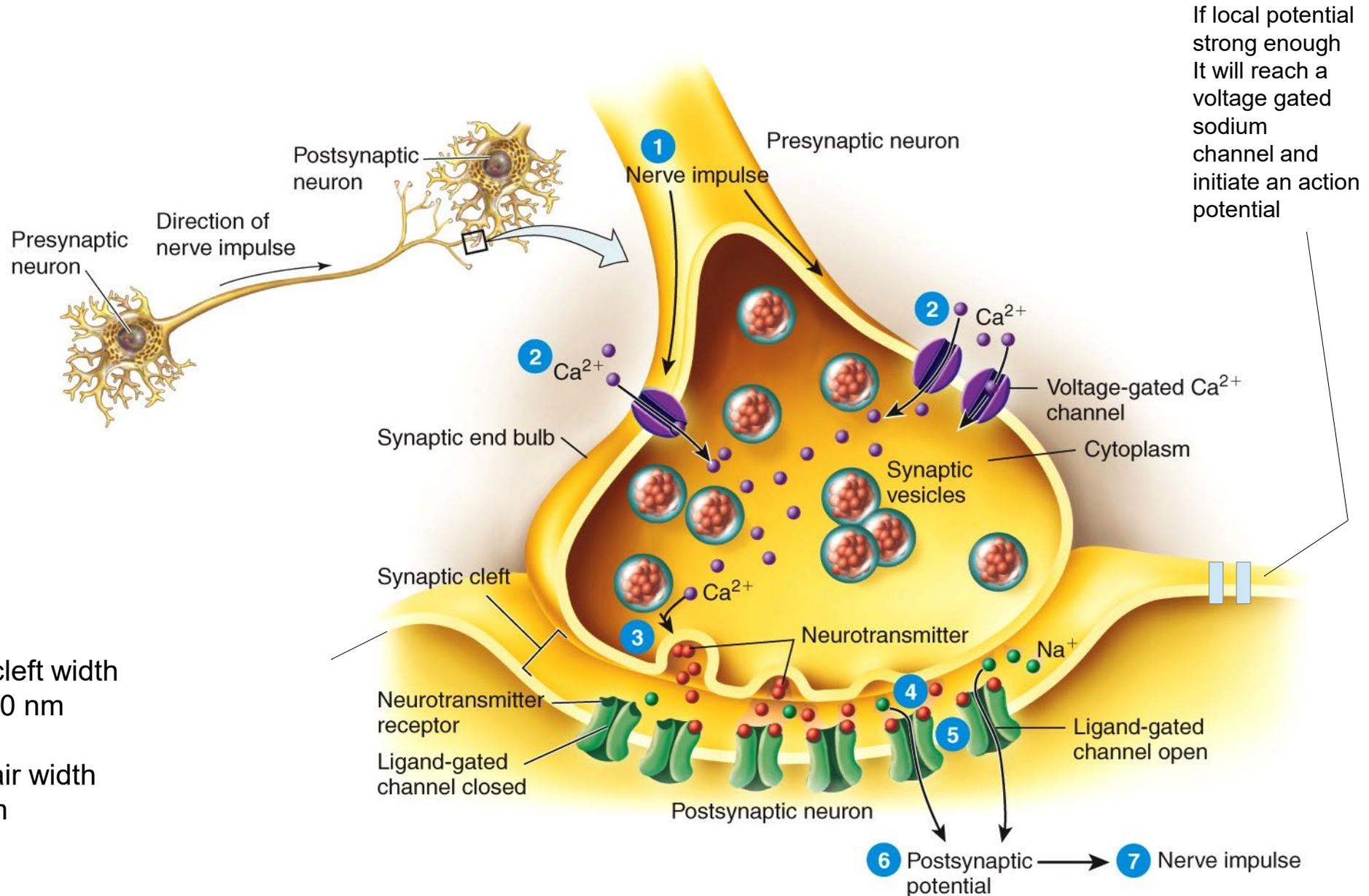
Ionotropic receptors

### B Indirect gating



Metabotropic receptors

# Structure of a Chemical Synapse



Synaptic cleft width  
average 40 nm

Human hair width  
80,000 nm

# Synaptic Transmission

**Synaptic delay** – time from the arrival of a signal at the axon terminal of a presynaptic cell to the beginning of an action potential in the postsynaptic cell

Diffusion of neurotransmitter across synaptic cleft // **0.5 msec**

What is the difference between a mono-synaptic reflex and a poly-synaptic reflex?

Significance?

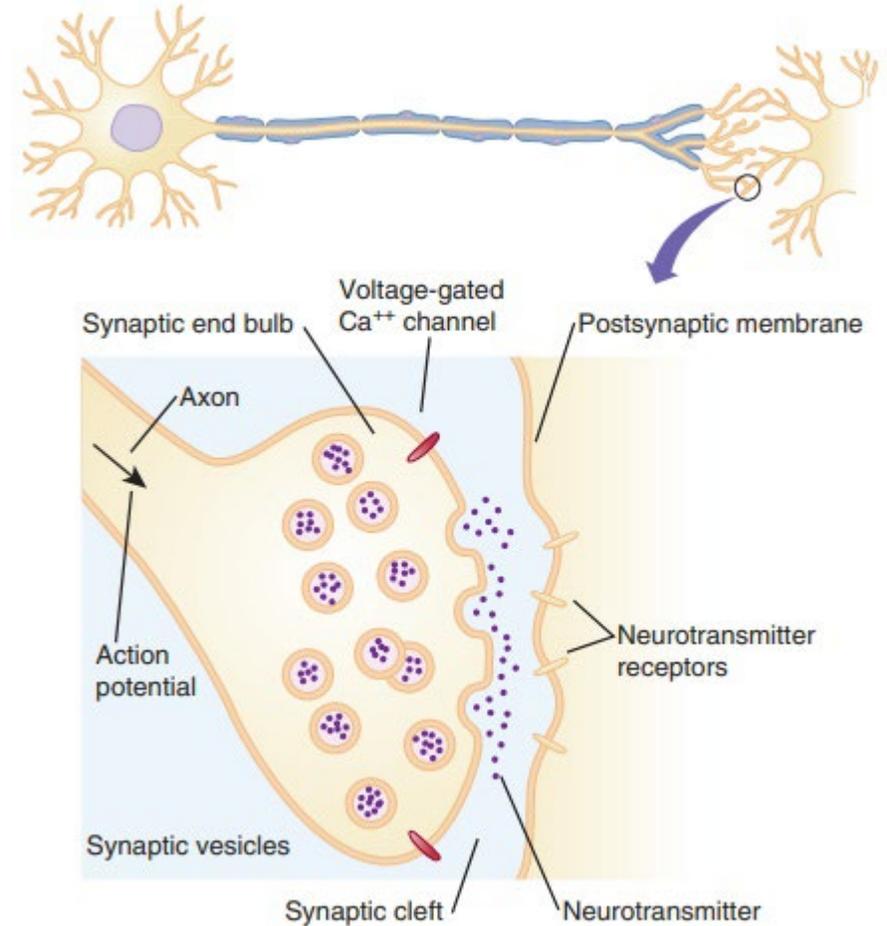


FIGURE 11-10 Chemical synapse.

# Function of Neurotransmitters at the Synapse

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Neurotransmitters are synthesized in the presynaptic neuron's soma / transported down axon by nanomotor molecules to synaptic knob

NT are released in response to an action potential (or a post-synaptic neuron's secretion)

Released neurotransmitter binds to specific receptors on the postsynaptic cell

They alter the post-synaptic membrane // moves resting membrane potential towards threshold or away from threshold

**It is the receptor and not the neurotransmitter that determines the outcome!!!**

- For example: Dopamine has two main receptors
  - DA1-Receptor stimulates neuron (increases cAMP)
  - DA2-Receptor inhibits (decrease cAMP) // stop signal transmission.

# Effects of Neurotransmitters

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The same neurotransmitter may **have different effects on different target tissues**

There are multiple receptors for some neurotransmitters /// E.g. 14 different receptor types for serotonin

It is the **receptor that determines the effect of the neurotransmitter** on the target cell /// E.g. – In different tissues, Acetylcholine may use either ionotropic or metabotropic receptors.

Ionotropic receptors are always stimulatory.

Metabotropic acetylcholine receptors can be either stimulatory or inhibitory // depends on downstream effect of the second integral protein which is activated by the G protein

*Note: **another key idea** --- the same molecule may function as a hormone, a neurotransmitter, or a neuromodulator!*

# Neurotransmitters and Related Messengers

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**Monoamines (also called Biogenic Amines)** // synthesized from amino acids by removal of the  $-\text{COOH}$  group // retaining the  $-\text{NH}_2$  (amino) group

Major monoamines are:

–the catecholamines = **epinephrine, norepinephrine, dopamine**

–the indoamines = **histamine and serotonin**

–LSD and mescaline bind to monoamine receptors

## Other Neurotransmitters

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**Neuropeptides** // substance P, endorphins, enkephalins (i.e. endogenous opioids) /// this class also include gut-brain peptides (produced by non-neural tissue but have receptors in the brain)

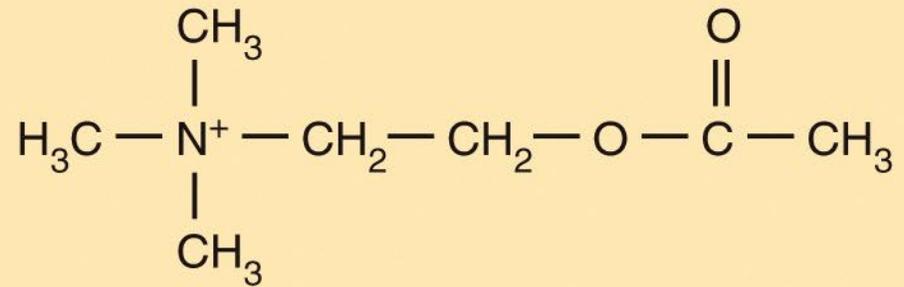
**Purines** // adenosine triphosphate (ATP) / now recognized as major neurotransmitter in CNS and PNS

**Gases & Lipids** // nitric oxide (NO) & carbon monoxide // activate guanylyl cyclase / function in brain / hydrogen sulfide // (note: NO causes smooth muscle to dilate)

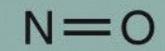
**Endocannabinoids** (or simply cannabinoids) // brain neurotransmitter / tetrahydrocannabinol (THC) interacts with the endocannabinoid receptors

## SMALL-MOLECULE NEUROTRANSMITTERS

### Acetylcholine



### Nitric oxide



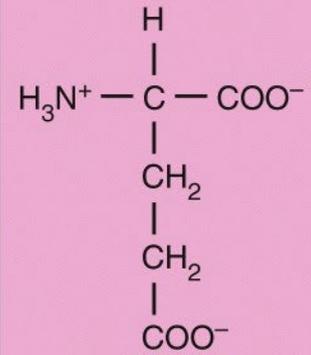
### Carbon monoxide



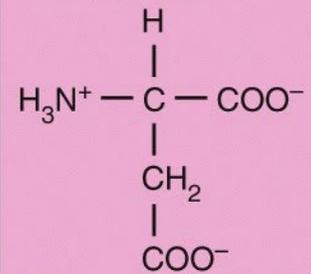
## SMALL-MOLECULE NEUROTRANSMITTERS

### Amino Acids

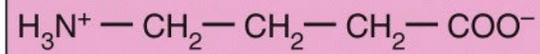
Glutamate



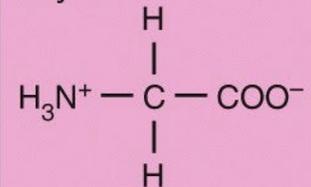
Aspartate



Gamma aminobutyric acid  
(GABA)



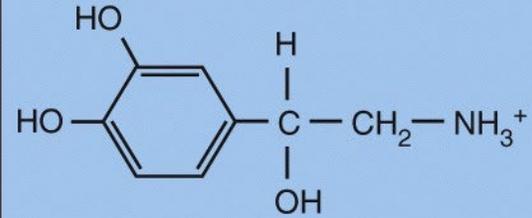
Glycine



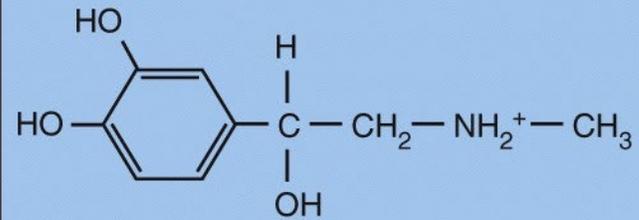
## SMALL-MOLECULE NEUROTRANSMITTERS

### Biogenic Amines

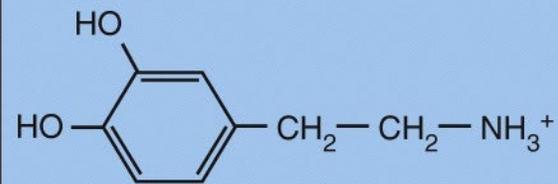
Norepinephrine



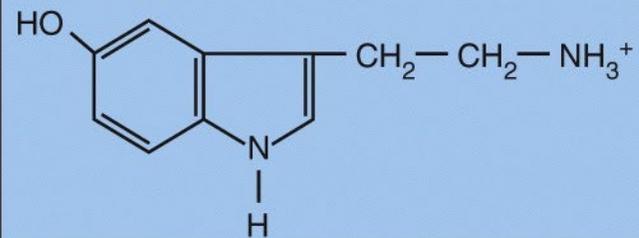
Epinephrine



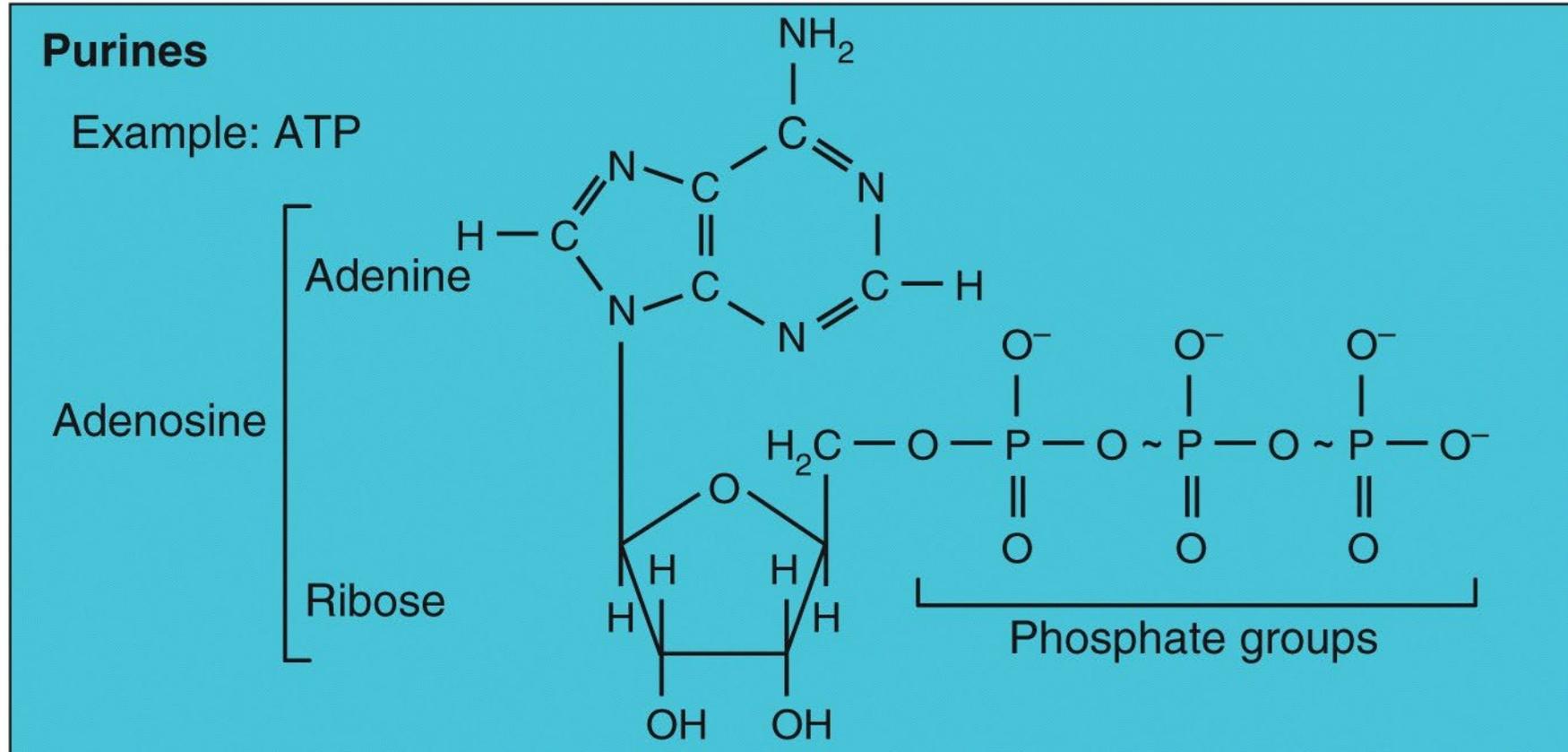
Dopamine



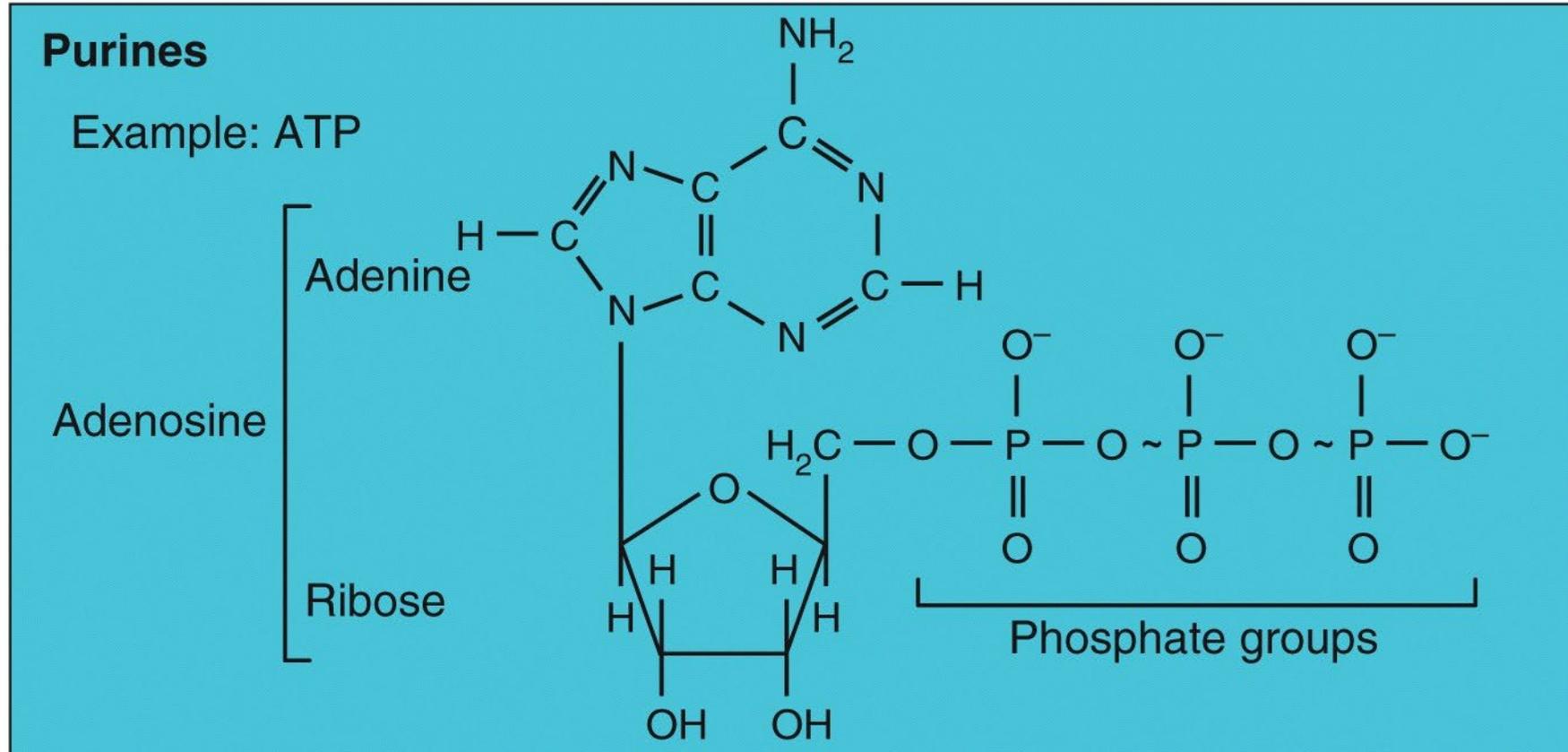
Serotonin



## SMALL-MOLECULE NEUROTRANSMITTERS

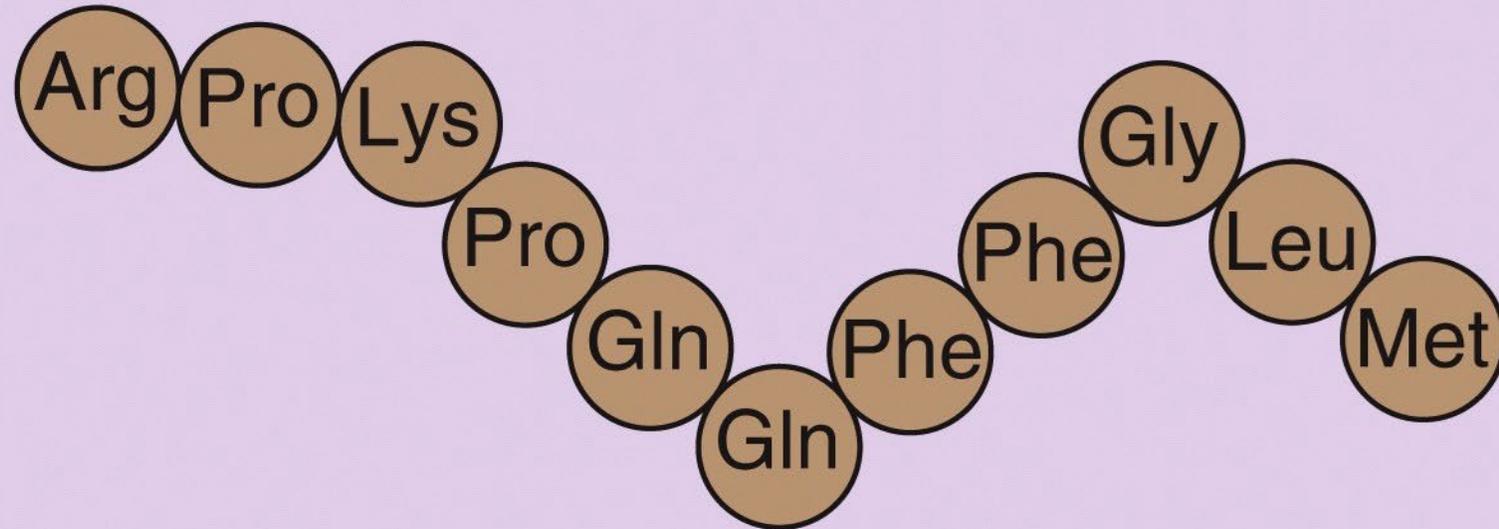


## SMALL-MOLECULE NEUROTRANSMITTERS



# NEUROPEPTIDES

Example: Substance P



# Function of Key Neurotransmitters

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## Acetylcholine

Located at neuromuscular junctions, ANS, brain and spinal cord

Largely excitatory / however some acetylcholine receptors in PNS inhibitory / uses both ionotropic and metabotropic receptors

## Monoamine

Norepinephrine – largely in ANS / in CNS area of brain stem called locus coeruleus sleep & wake cycles, attention, feeding behavior / activates sympathetic nervous system

Epinephrine – largely ANS similar effects as norepinephrine / more widely used as hormone

Dopamine – CNS / many CNS functions – coordinates movements, motivation, reward

# Key Neurotransmitters' Functions

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## Monoamines (Biogenic Amines)

Serotonin – mainly CNS brain stem with projections throughout brain / mood regulation, affects emotions, attention, cognitive functions, motor behaviors, feeding behaviors, daily rhythms

Histamine – CNS for attention and arousal // outside CNS mediator of allergic responses // note – antihistamines make you drowsy!

## Amino Acid Neurotransmitters

**Glutamate** – most important excitatory CNS – half of all CNS synapses release glutamate!

**Glycine & GABA** – two of the major inhibitory neurotransmitters

- GABA – very important in CNS

- Glycine – 1/2 synapses in spinal cord release glycine other 1/2 in CNS

# Key Neurotransmitters' Functions

---

## Neuropeptides

Substance P – released from type C sensory neurons that carry pain and temperature signals / also released in CNS, spinal cord, and gut

**Endogenous opioids** – endorphins, dynorphins, and enkephalins / eliciting pain relief (analgesia) plus euphoria / general CNS depressant / also involved in sexual attraction, aggressive or submissive behaviors

Neuropeptide Y – feeding behaviors, mediate hunger or feeling full

# Synaptic Transmission

---

Neurotransmitters are **diverse in their action**

some are **excitatory** and others are **inhibitory**

sometimes the same neurotransmitter may be excitatory or inhibitory depending on the “receptor”

effect depends on what kind of receptor the postsynaptic cell has // same neurotransmitter can cause either excitation or inhibition depending on the receptor // this is the case with metabotropic receptors

some open ligand-regulated ion gates /// **ionotropic receptors** are simply ion channels

other neurotransmitters operate through **metabotropic receptors** /// second messenger systems // provide variable downstream outcomes

# Three Different Mechanisms of Synaptic Transmission

---

Explore the function of three different types of synapses // each synapse will use a different type of neurotransmitter and post synaptic receptor

## Different modes of action

–excitatory cholinergic synapse (ionotropic)

–inhibitory GABA-ergic synapse (ionotropic)

–excitatory adrenergic synapse (metabotropic)

–Note: metabotropic = second messenger system receptor /// this maybe either inhibitory or excitatory

# Excitatory Cholinergic Synapse

---

## The excitatory junction's action

- nerve signal approaching the synapse // opens the voltage-regulated calcium gates at junction between axon and synaptic knob
- $\text{Ca}^{2+}$  enters the knob // triggers exocytosis of synaptic vesicles releasing Ach
- empty vesicles drop back into the cytoplasm to be refilled with Ach
- reserve pool of synaptic vesicles move to the active sites and release their Ach
- ACh diffuses across the synaptic cleft

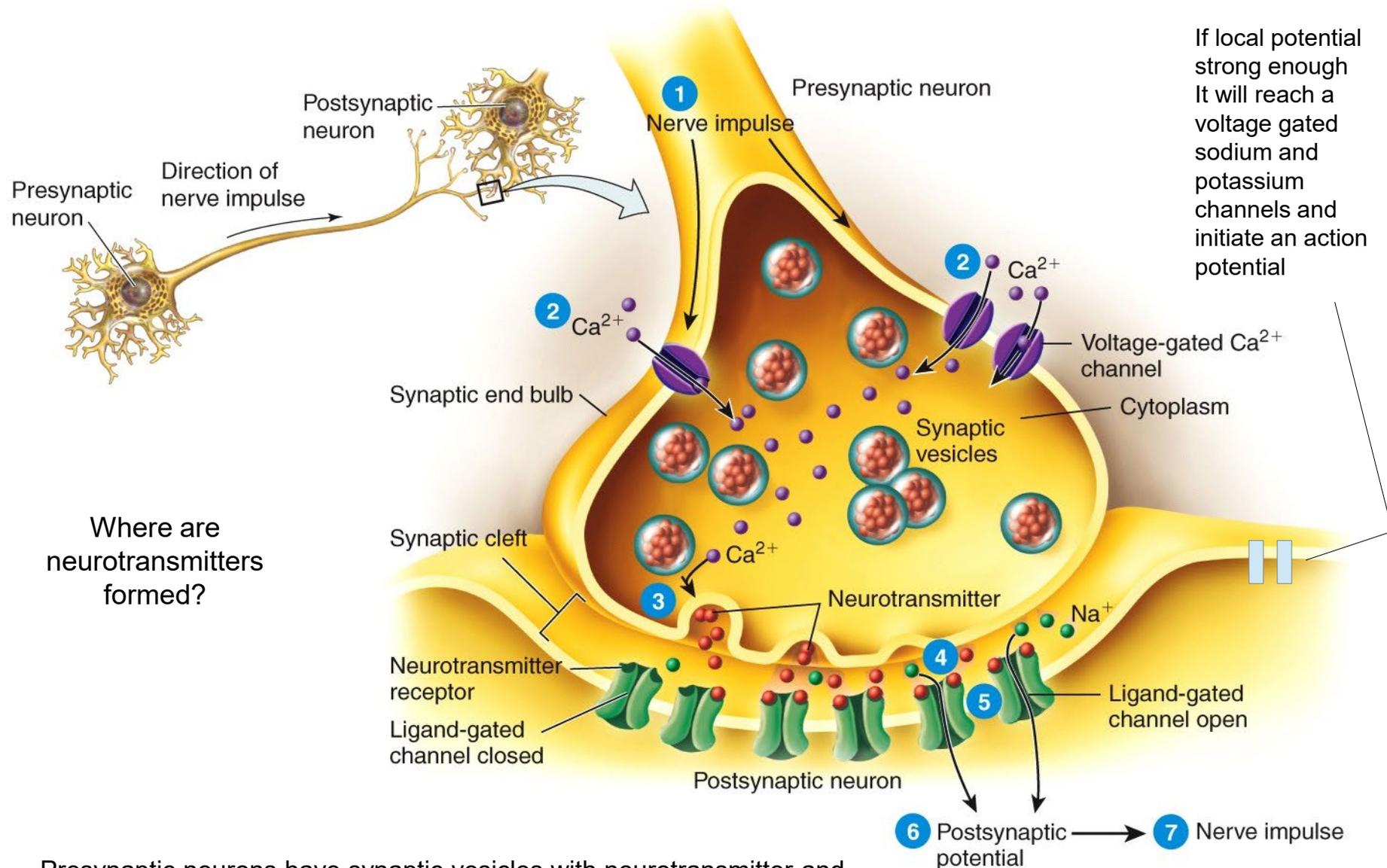
# Excitatory Cholinergic Synapse

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## Describing excitatory action (continue)

- binds to ligand-regulated gates on the postsynaptic neuron
- gates open // allowing  $\text{Na}^+$  to enter cell and  $\text{K}^+$  to leave // pass in opposite directions through same gate
- as  $\text{Na}^+$  enters the cell it spreads out along the inside of the plasma membrane and depolarizes it producing a local potential called the postsynaptic potential
- if it is strong enough and persistent enough
- it opens voltage-regulated ion gates in the trigger zone
- causing the postsynaptic neuron to fire

# Structure of a Chemical Synapse



Presynaptic neurons have synaptic vesicles with neurotransmitter and postsynaptic neurons have **receptors** with ligand-regulated ion channels

# Inhibitory GABA-ergic Synapse

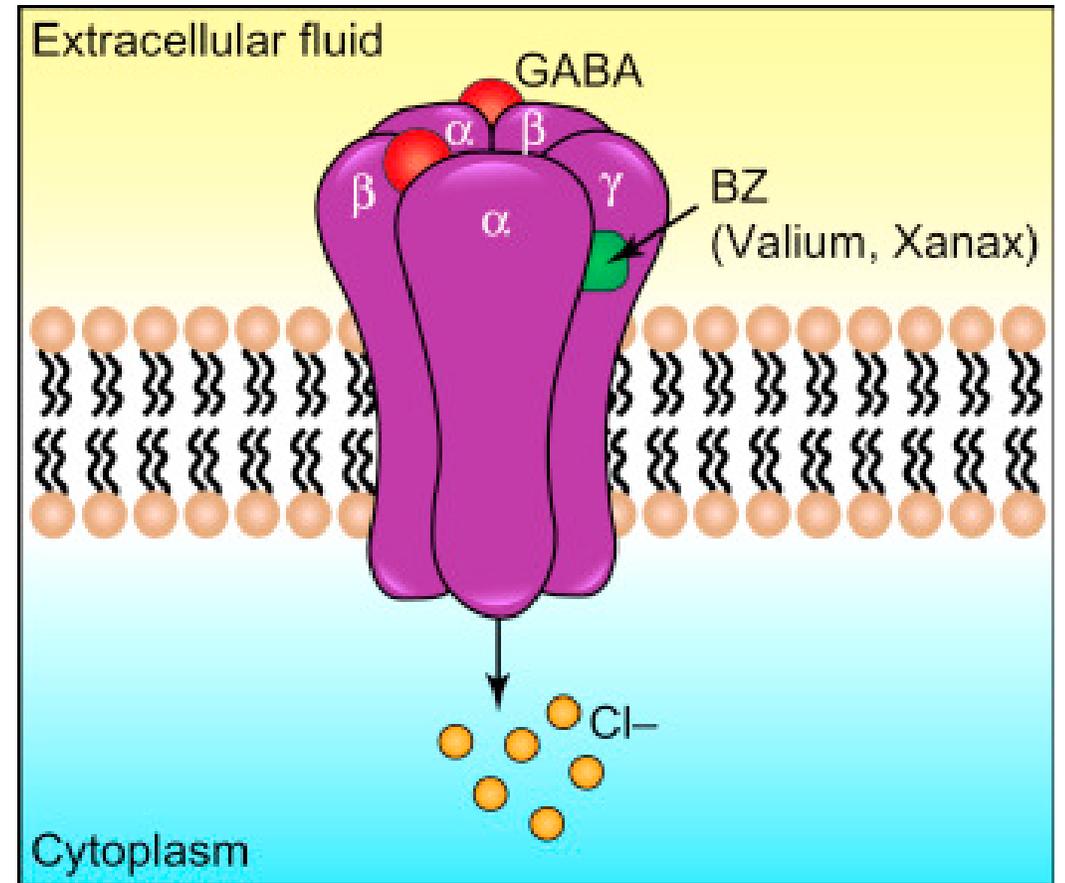
GABA-ergic synapse employs  $\gamma$ -aminobutyric acid as its neurotransmitter

nerve signal triggers release of GABA into synaptic cleft

GABA receptors are **chloride channels** /// ionotropic receptor type

$\text{Cl}^-$  enters cell and makes **the inside more negative than the resting membrane potential** /// move away from threshold!

postsynaptic neuron is inhibited // less likely to fire



# Adrenergic Excitatory Synapse

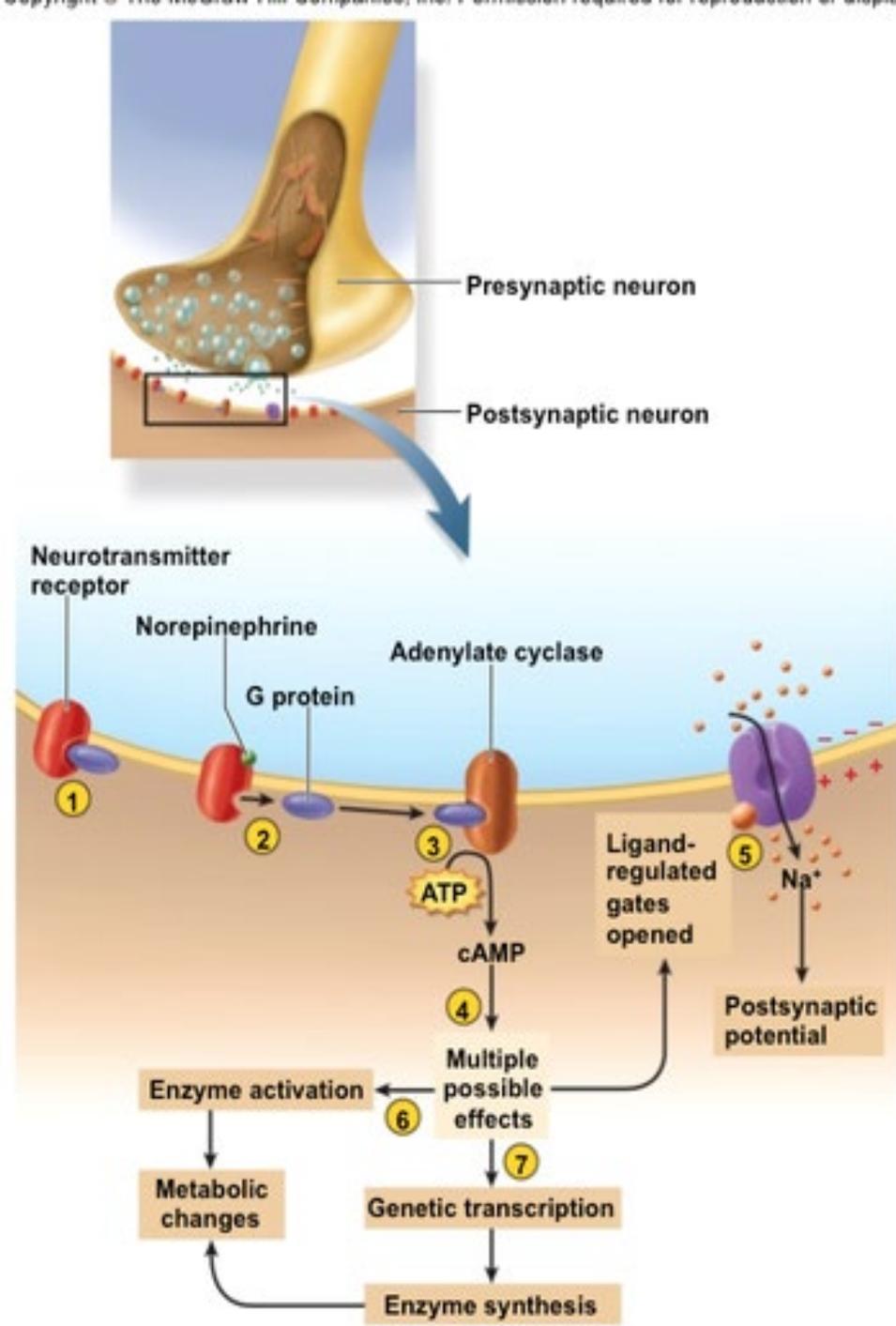


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**Adrenergic synapse** /// employs the neurotransmitter norepinephrine (NE) also called noradrenaline

- The receptor on post synaptic membrane for the adrenergic synapses is a metabotropic type receptor
- not an ion gate but a second messenger system
- a transmembrane protein associated with a G protein (i.e. metabotropic receptor)
- NE , monoamines and neuropeptides acts through **second messenger systems** (e.g. cyclic AMP (cAMP))

# Adrenergic Synapse



## The Action of Adrenergic Receptors and Their G Protein (The Second Messenger Transmission Mechanism)

---

G protein is bound to the inside surface of the transmembrane NE receptor

–binding of NE to the receptor causes the G protein to dissociate

–G protein binds to adenylate cyclase // activates this enzyme

–induces the conversion of **ATP** to **cyclic AMP**

## The Action of Adrenergic Receptors and Their G Protein (The Second Messenger Transmission Mechanism)

---

The second messenger cyclic AMP may cause many different alternative outcomes in the cell

- causes the production of an internal chemical that binds to a ligand-regulated ion gate from inside of the membrane, opening the gate and **depolarizing the cell**
- can activate preexisting **cytoplasmic enzymes** that lead to diverse metabolic changes
- can induce **genetic transcription**, so that the cell produces new cytoplasmic enzymes that can lead to diverse metabolic effects

## The Action of Adrenergic Receptors and Their G Protein (The Second Messenger Transmission Mechanism)

---

Slower to respond than cholinergic and GABA-ergic type synapses

However, second messenger systems have advantage of **enzyme amplification**

Single molecule of NE can produce vast numbers of second messengers (e.g. cAMP) in the <sub>cell</sub>

# Cessation of the Signal

---

To stop transmission there must be a mechanisms to stop the release of neurotransmitter from presynaptic neuron so postsynaptic neuron will not start a local potential

–neurotransmitter molecule binds to its receptor for only 1 msec or so // then dissociates from it

–if presynaptic cell continues to release neurotransmitter // one molecule is quickly replaced by another and the neuron stays stimulated

## Cessation of the Signal

---

When synaptic knob stops adding neurotransmitter into synaptic cleft and existing neurotransmitter is degraded then local potential stops at postsynaptic nerve fiber

Remove neurotransmitter by:

**diffusion** // neurotransmitter escapes the synapse into the nearby ECF // astrocytes in CNS absorb it and return it to neurons

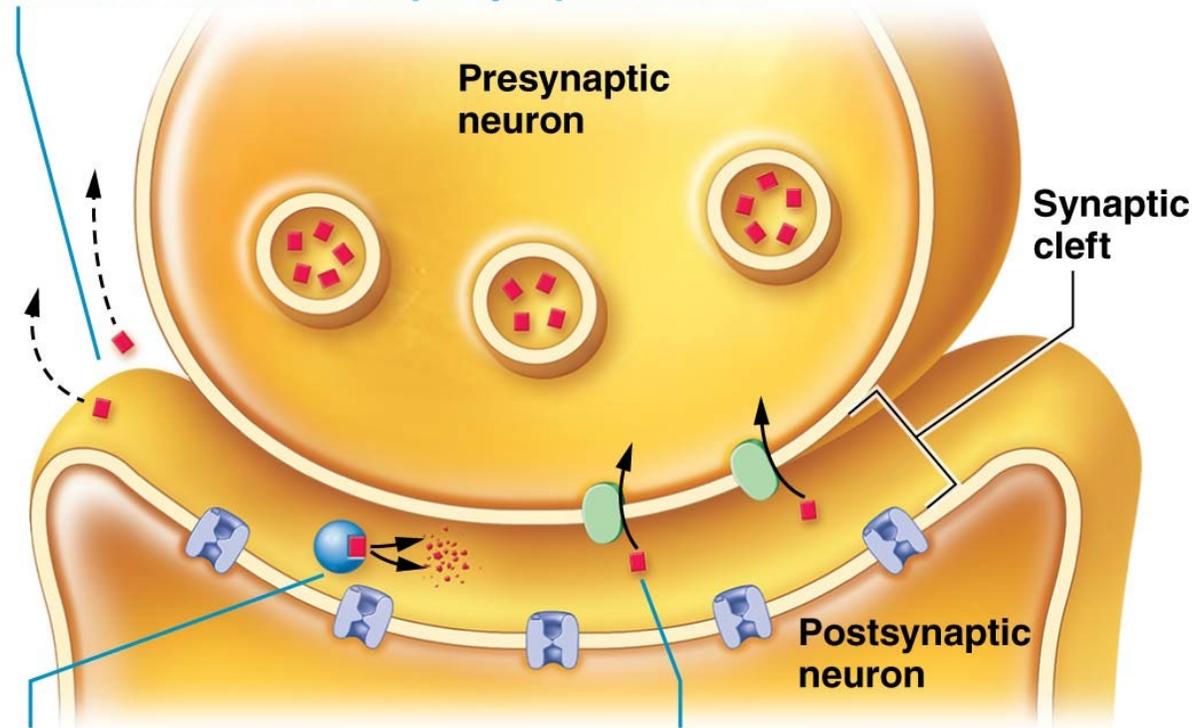
**re-uptake** // synaptic knob reabsorbs amino acids and monoamines by endocytosis //

**degradation** by enzymes // see next slide

# Methods of termination of synaptic transmission.

## Diffusion and Absorption

Neurotransmitters diffuse away from the synaptic cleft and are returned to the presynaptic neuron.



## Degradation

Neurotransmitters are degraded by enzymatic reactions in the synaptic cleft.

## Reuptake

Neurotransmitters are taken back into the presynaptic neuron.

# Cessation of the Signal

---

## Degradation of neurotransmitters by enzymes

Acetylcholinesterase (AChE) degraded by enzymes in synaptic cleft into acetate and choline // choline reabsorbed by synaptic knob

## Catecholines degradation by enzymes

monoamine oxidase (MAO) enzyme // enzyme located in synaptic knob // after release from synaptic knob neurotransmitter reabsorbed by synaptic knob and degraded by enzyme // some antidepressant drugs work by inhibiting MAO

catechol-O-methyltransferase (COMT) // enzyme located within interstitial spaces of tissue

- » Note: neither MAO & COMT are not found in blood // Why is this important?
- » Significance? Hint: adrenal gland!

# Neuromodulators

---

Hormones, neuropeptides, and other messenger molecules that **modify synaptic transmission of the neurotransmitters**

may stimulate a neuron to install more receptors in the postsynaptic membrane adjusting its sensitivity to the neurotransmitter

may alter the rate of neurotransmitter synthesis, release, reuptake, or breakdown

**enkephalins & endorphins** // important CNS neuromodulators

small peptides that inhibit spinal interneurons from transmitting pain signals to the brain

# Neuromodulators

---

**Nitric oxide (NO)** – a simple neuromodulator

–a lightweight gas release by the postsynaptic neurons in some areas of the brain concerned with learning and memory

–released by post-synaptic neuron and diffuses into the presynaptic neuron

–stimulates pre-synaptic neuron to release more neurotransmitter

–how the one neuron's tells the other neuron to '**give me more**' - this occurs during learning – positive feedback

–This is an example of a chemical communication that goes backward across the synapse

## Summation, Facilitation, and Inhibition

- one neuron can receive input from thousands of other neurons
- some incoming nerve fibers may produce EPSPs while others produce IPSPs
- neuron's response depends on whether the net input is excitatory or inhibitory
- **summation** – the process of adding up postsynaptic potentials and responding to their net effect // **occurs in the trigger zone**
- the balance between EPSPs and IPSPs enables the nervous system to make decisions

## Summation, Facilitation, and Inhibition

**temporal summation** – occurs when a single synapse generates EPSPs so quickly that each is generated before the previous one fades

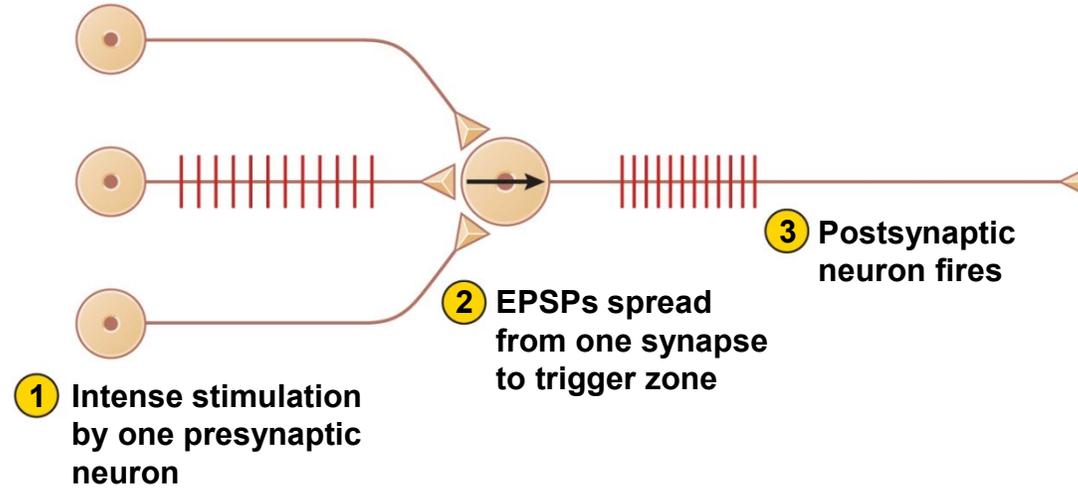
–allows EPSPs to add up over time to a threshold voltage that triggers an action potential

**spatial summation** – occurs when EPSPs from several different synapses add up to threshold at an axon hillock.

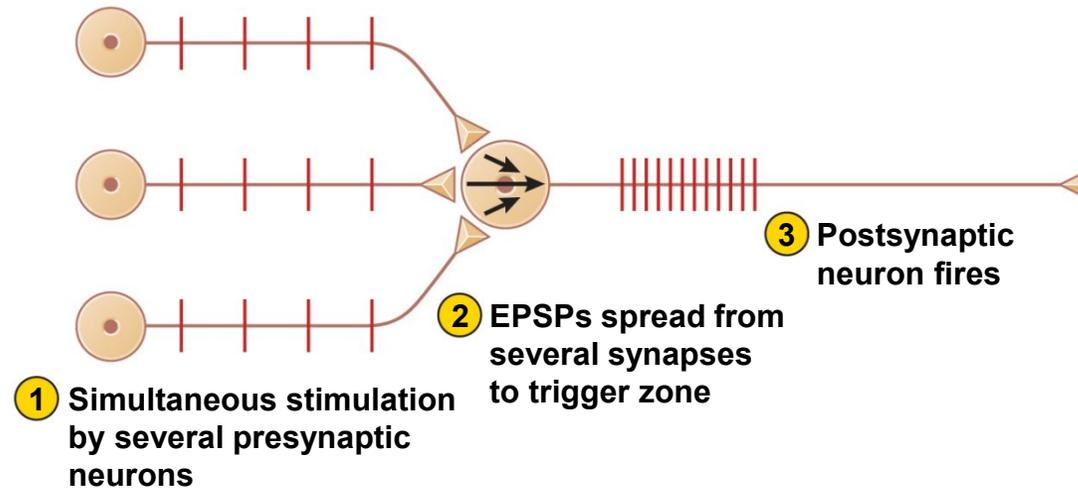
–several synapses admit enough  $\text{Na}^+$  to reach threshold

–presynaptic neurons cooperate to induce the postsynaptic neuron to fire

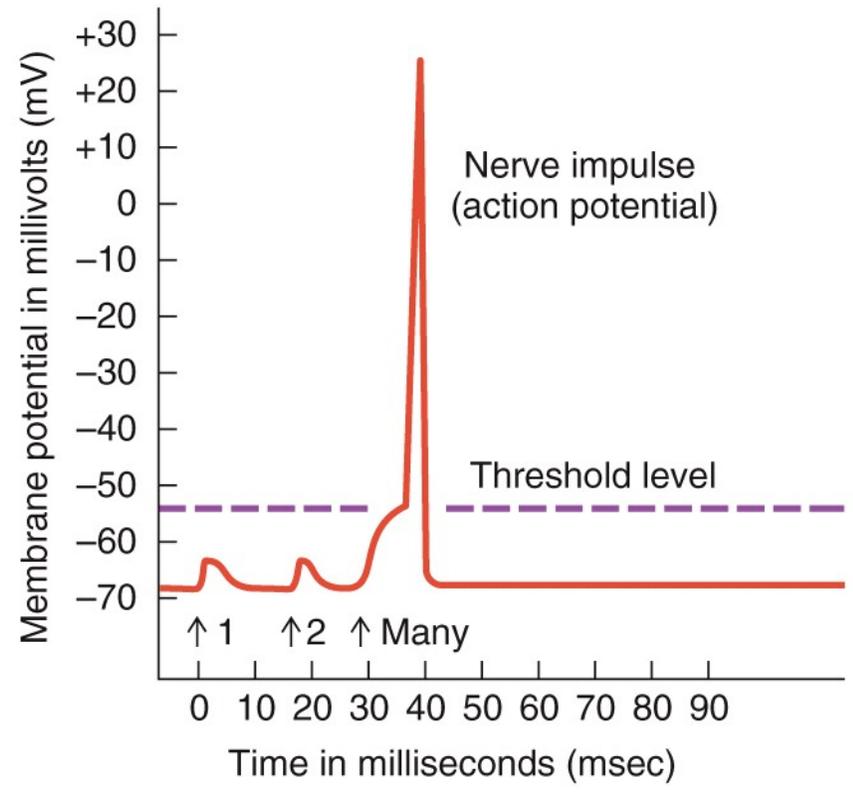
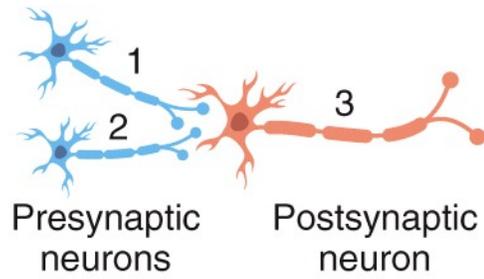
# Temporal and Spatial Summation



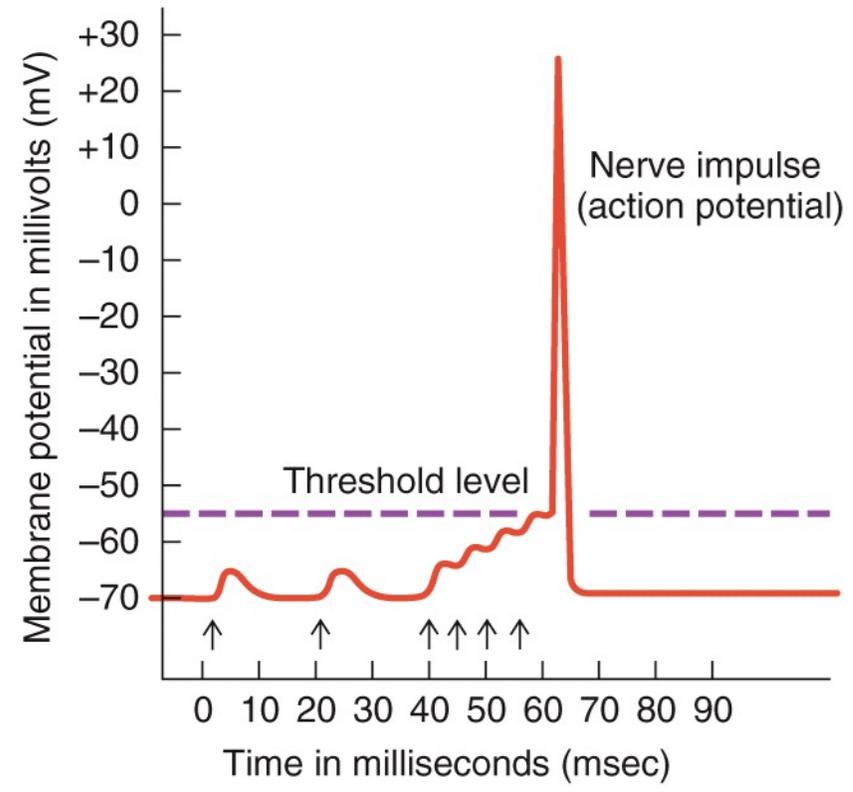
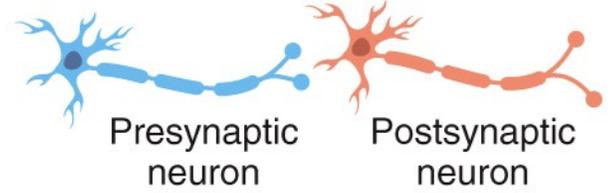
(a) Temporal summation



(b) Spatial summation



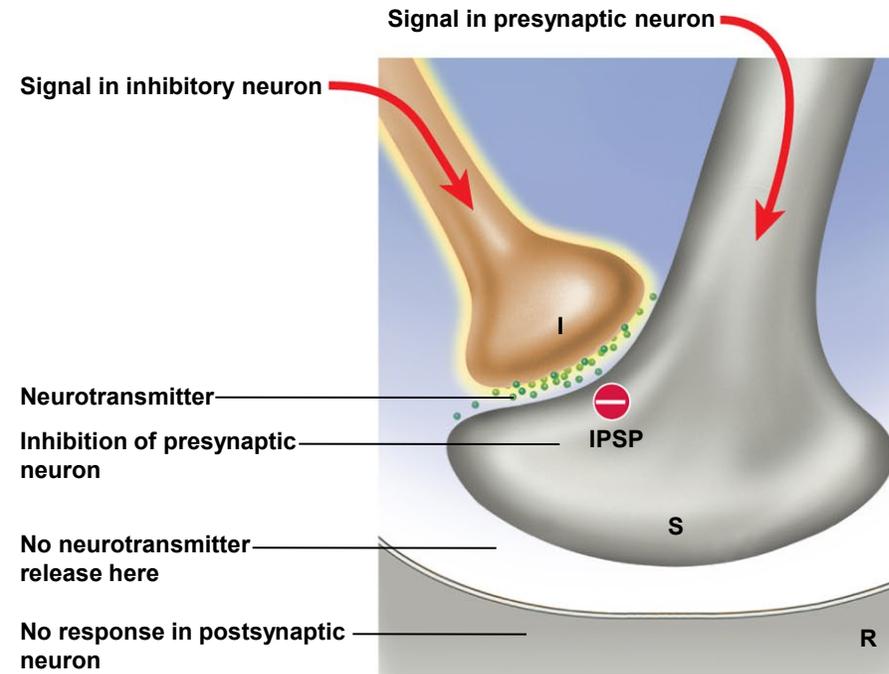
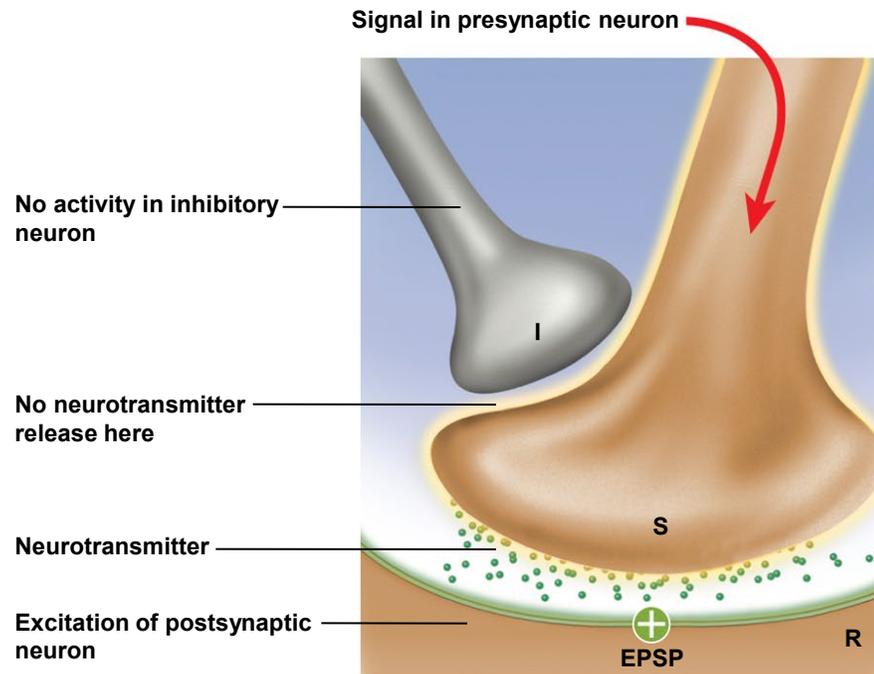
(a) Spatial summation



(b) Temporal summation

# Summation, Facilitation, and Inhibition

- neurons routinely work in groups to modify each other's action
- facilitation – a process in which one neuron enhances the effect of another one // combined effort of several neurons facilitates firing of postsynaptic neuron



# Summation, Facilitation, and Inhibition

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- Presynaptic inhibition – process in which one presynaptic neuron suppresses another one
- the opposite of facilitation // reduces or halts unwanted synaptic transmission
- neuron I releases inhibitory GABA // prevents voltage-gated calcium channels from opening in synaptic knob and presynaptic neuron releases less or no neurotransmitter

# Excitatory Postsynaptic Potentials - EPSP

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- neural integration is based on the postsynaptic potentials produced by neurotransmitters
- typical neuron has a resting membrane potential of -70 mV and threshold of about -55 mV
- **excitatory postsynaptic potentials (EPSP)**

–any voltage change in the direction of threshold that makes a neuron more likely to fire

–usually results from Na<sup>+</sup> flowing into the cell cancelling some of the negative charge on the inside of the membrane

–**glutamate and aspartate** are excitatory CNS (brain) neurotransmitters that produce EPSPs

## Inhibitory Postsynaptic Potentials - IPSP

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- Inhibitory postsynaptic potentials (IPSP)

–any **voltage change away from threshold** that makes a neuron less likely to fire

- neurotransmitter **hyperpolarizes** the postsynaptic cell and makes it more negative than the RMP making it less likely to fire

- produced by neurotransmitters that open ligand-regulated chloride gates // causing inflow of Cl<sup>-</sup> making the cytosol more negative

# Inhibitory Postsynaptic Potentials - IPSP

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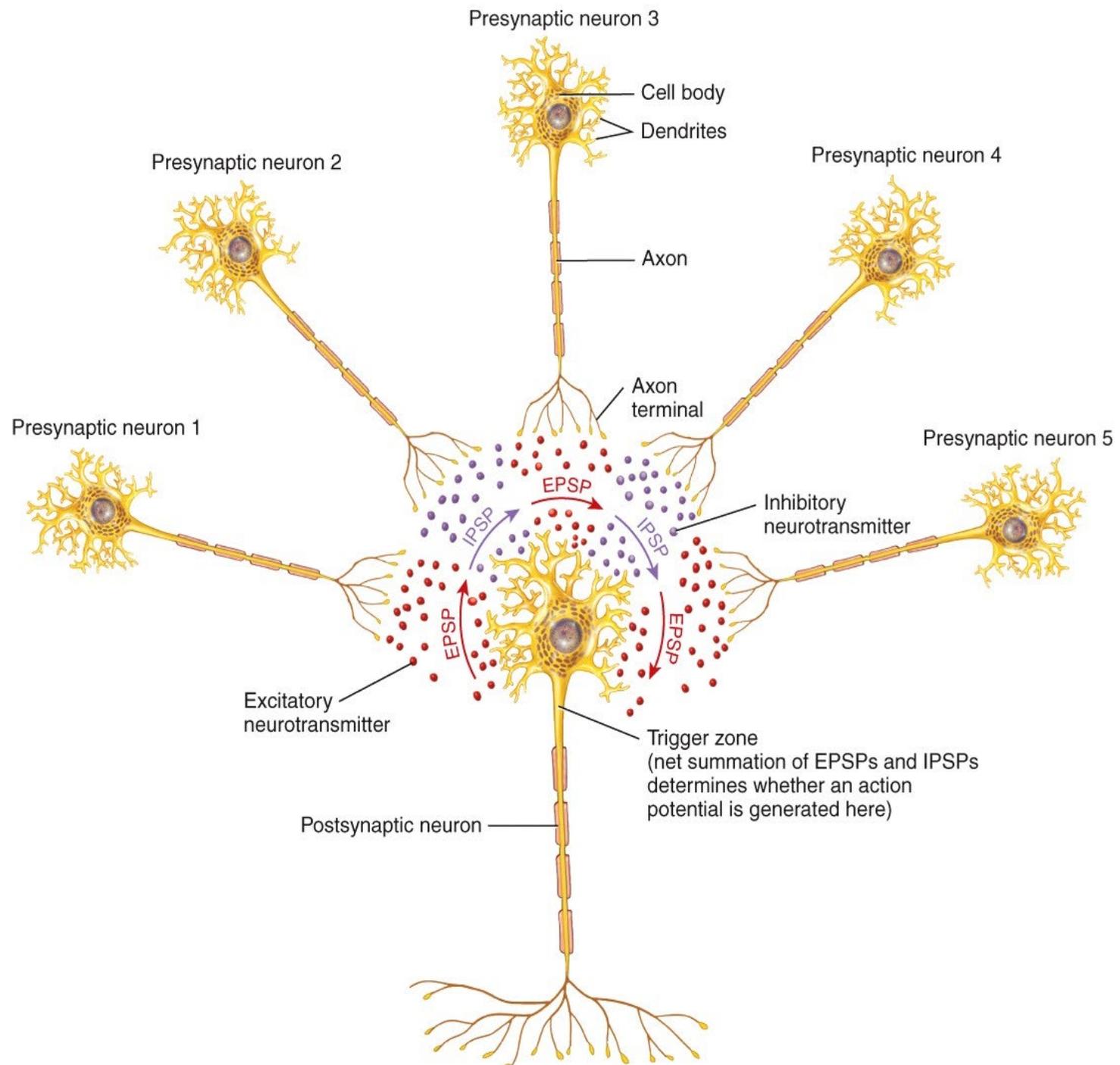
**Glycine and GABA** produce IPSPs /// move potential away from threshold /// inhibitory

–Acetylcholine (ACh) and norepinephrine are excitatory however for some cells (with different receptors) maybe inhibitory

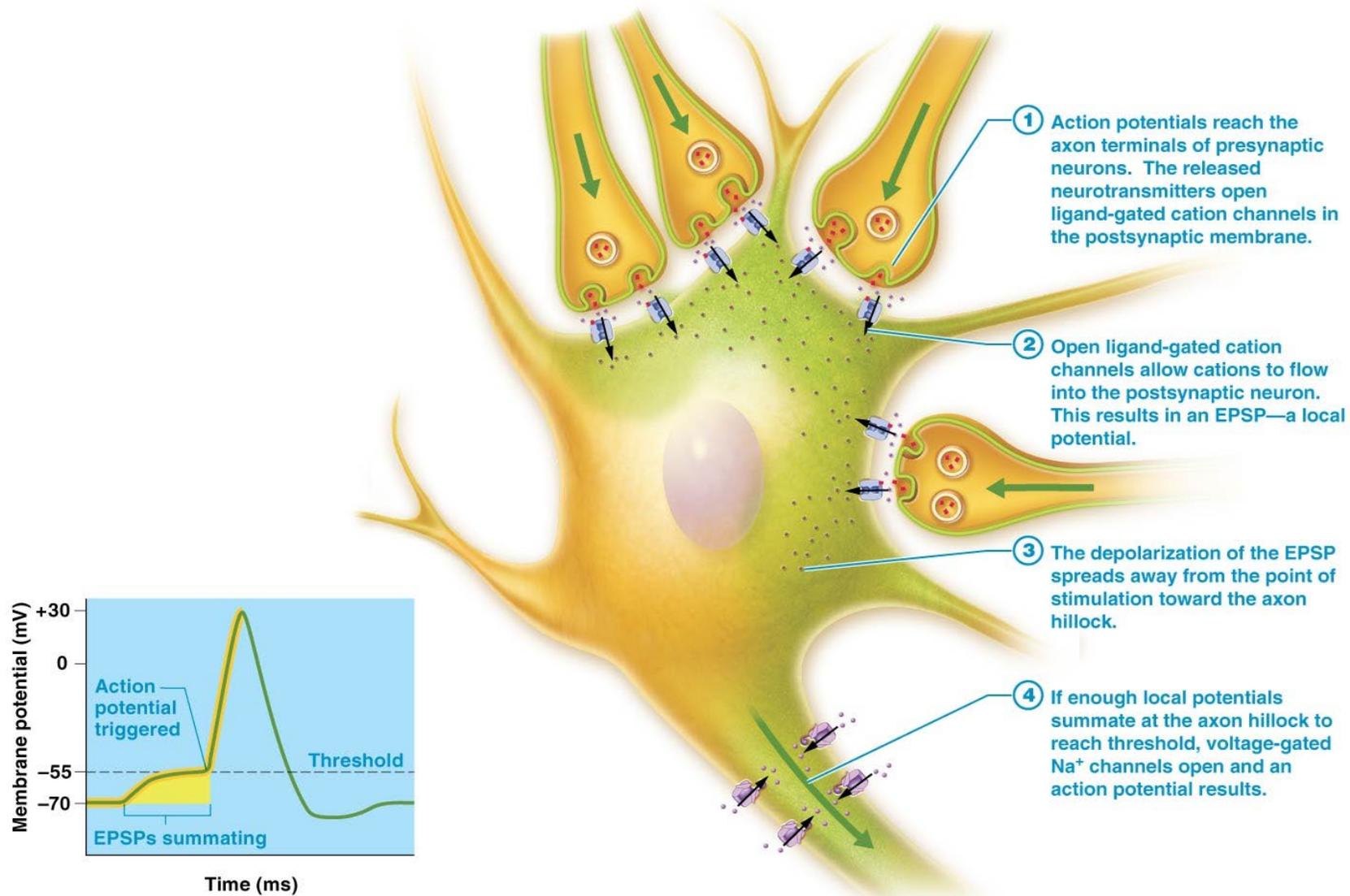
- depending on the type of receptors on the target cell

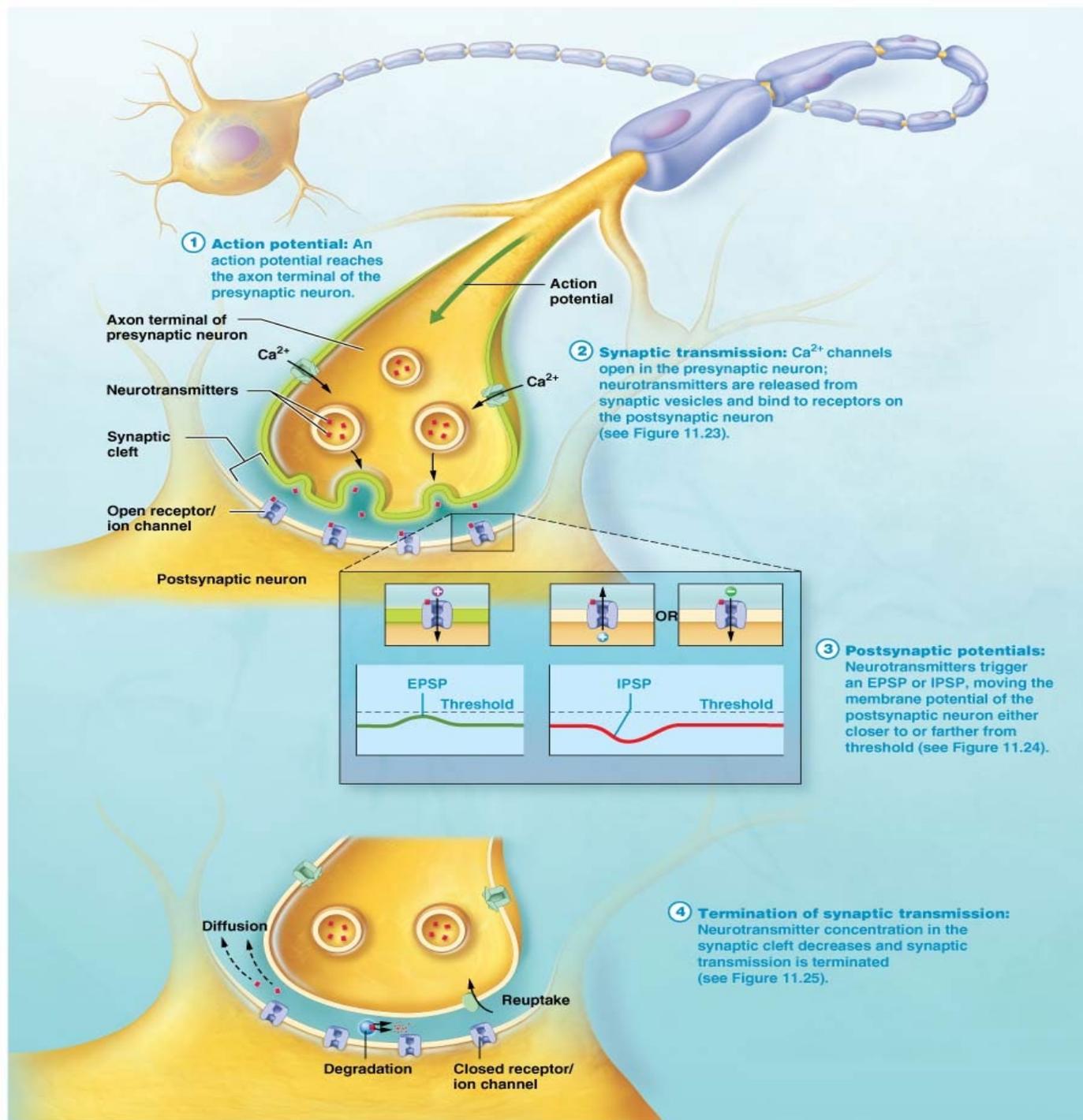
- It is the receptor that has final say on the outcome!

- Note: ACh excites skeletal muscle (ionotropic receptor), but inhibits cardiac muscle (metabotropic receptor) due to the different type of receptors**



# Local potentials summing and leading to an action potential.

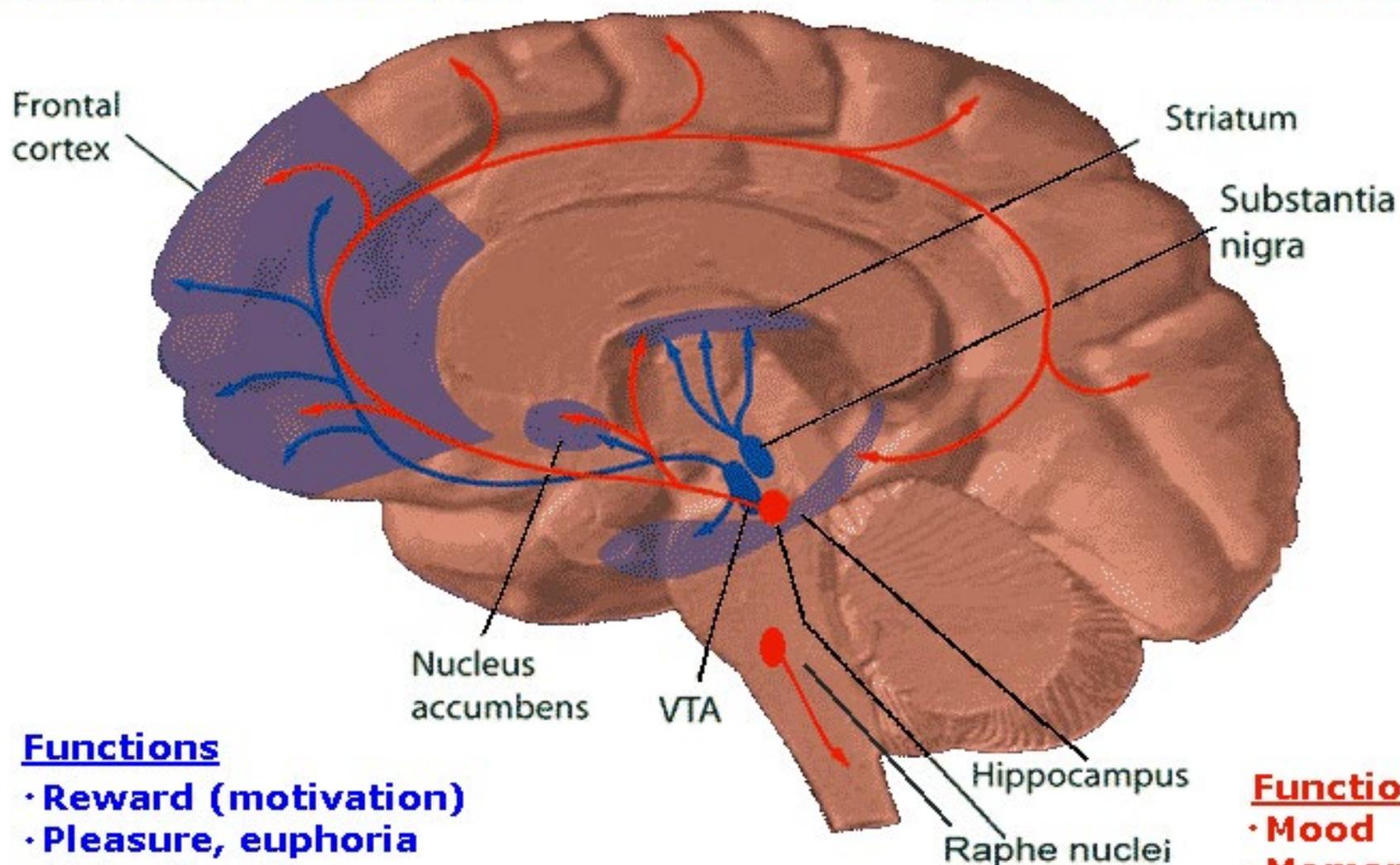




## The Big Picture of Chemical Synaptic Transmission.

## Dopamine Pathways

## Serotonin Pathways

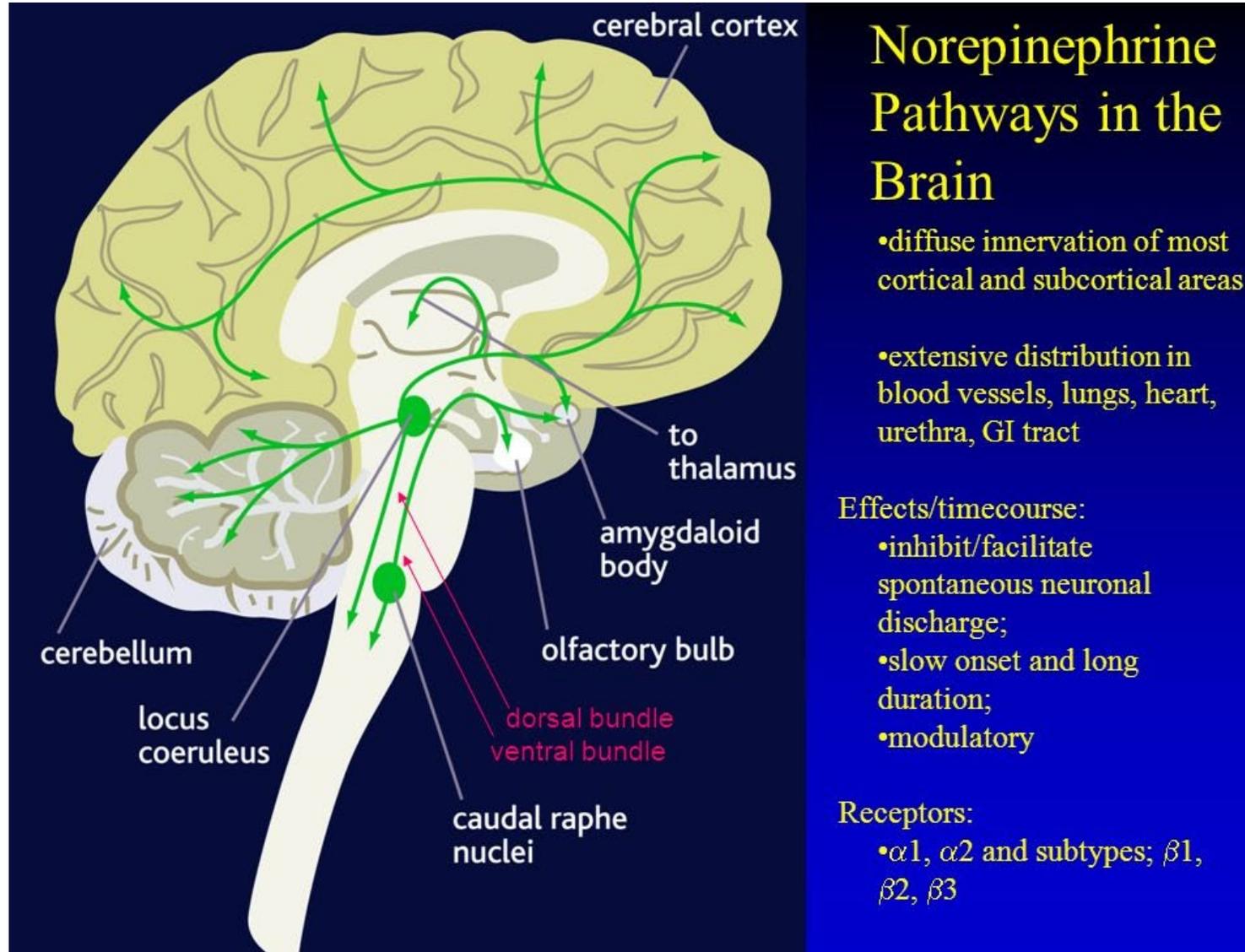


### Functions

- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine tuning)
- Compulsion
- Perseveration

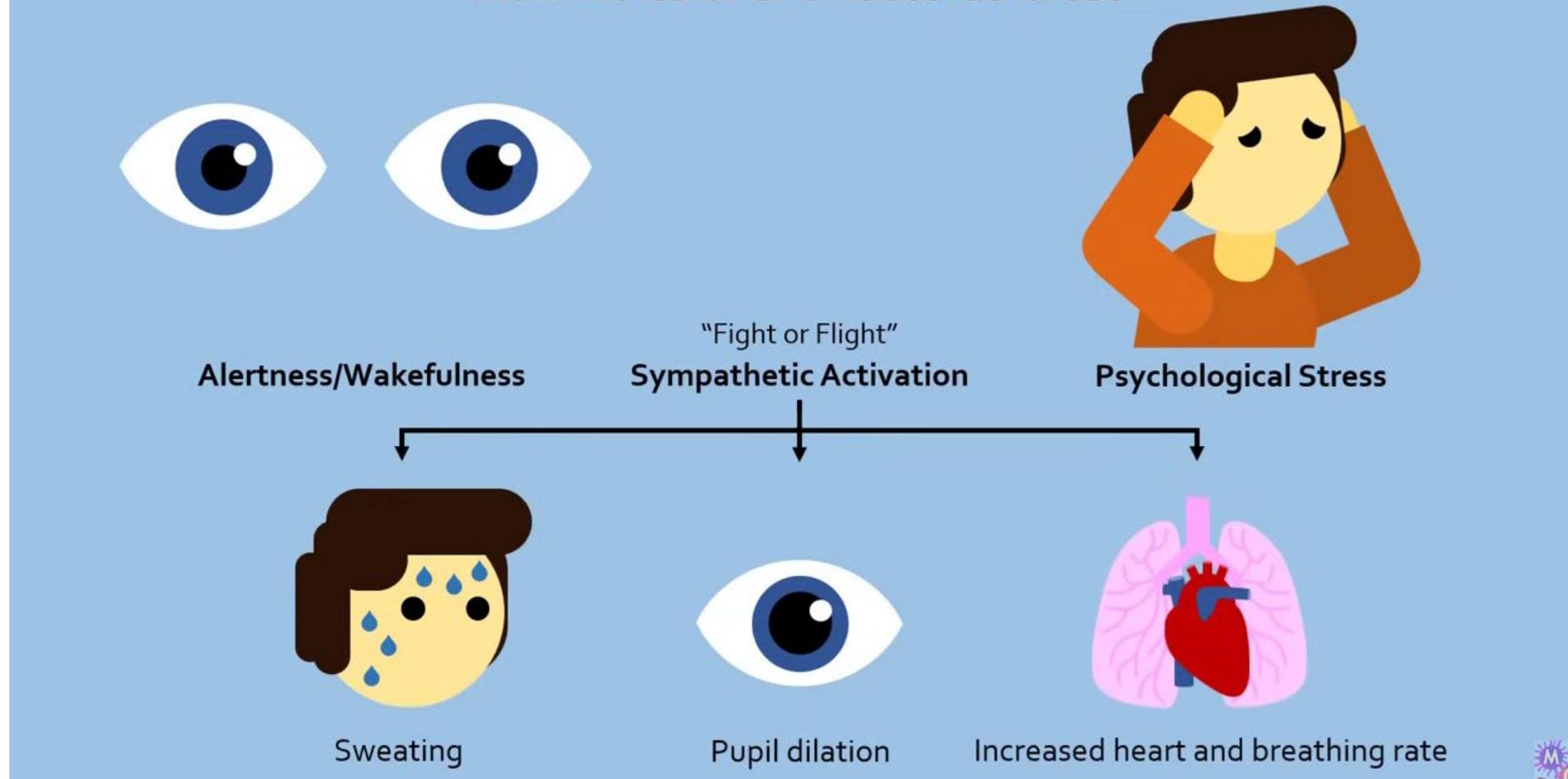
### Functions

- Mood
- Memory processing
- Sleep
- Cognition



Norepinephrinergic Neurons (secrete norepinephrine) project bilaterally (send signals to both sides of the brain) from the **locus coeruleus** along distinct pathways to many locations, including the cerebral cortex, limbic system, and the spinal cord, forming a neurotransmitter system.

## Main Roles of the Locus Ceruleus



Locus ceruleus is the main source for CNS noradrenaline. It projects this neurotransmitter throughout the brain and stimulates transmission between neurons.

# Main Roles of the Locus Ceruleus When opioids bind...

Opioid use symptoms are  
**OPPOSITE OF**  
normal Locus Ceruleus function



Drowsiness

"Rest and Digest"  
Parasympathetic Activation

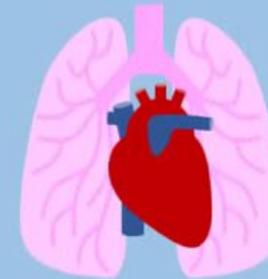
Sedation



Reduced sweating



Pupil constriction  
"Pinpoint pupils"



Decreased heart and breathing rate



# Main Roles of the Locus Ceruleus During Withdrawal...



Jitteriness/Insomnia

"Fight or Flight"  
Sympathetic Overactivation

Anxiety/Panic/Stress



Excessive sweating

Pupil dilation

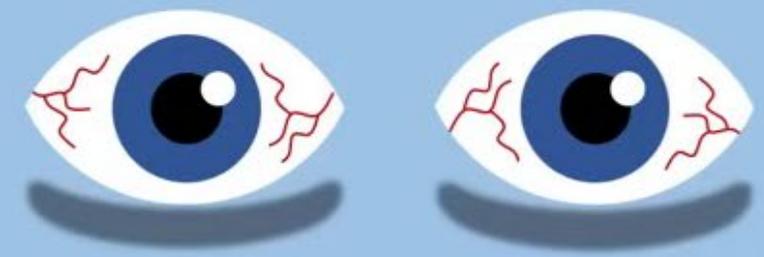
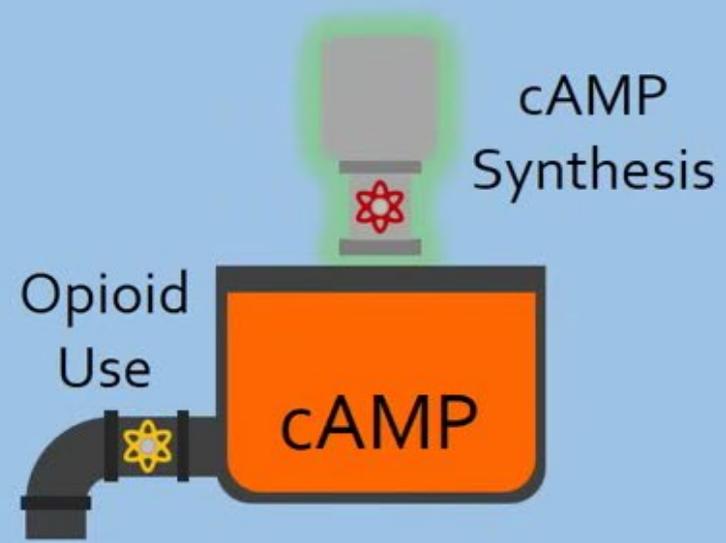
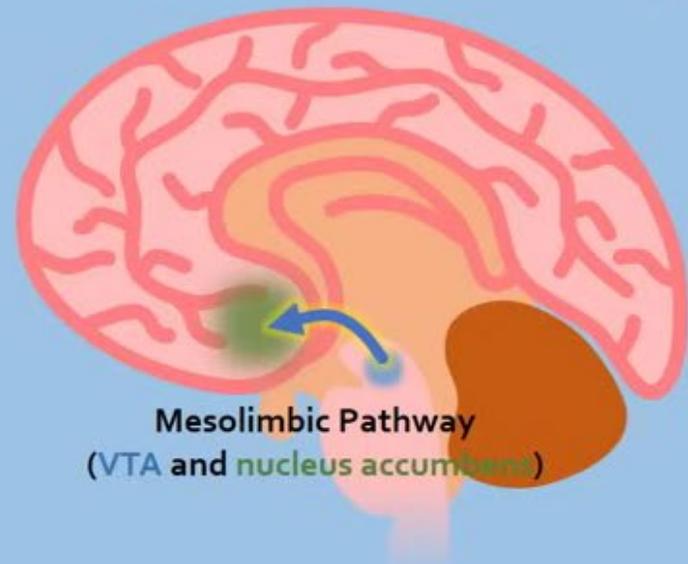
Increased heart and breathing rate

Opioid Mu receptors (DA 2R) are on locus ceruleus neurons. When opioid binds to the G protein linked receptor (second messenger/ metabotropic) it lowers the cytoplasmic cAMP and this then reduces locus ceruleus secretion of norepinephrine.

# Behavior



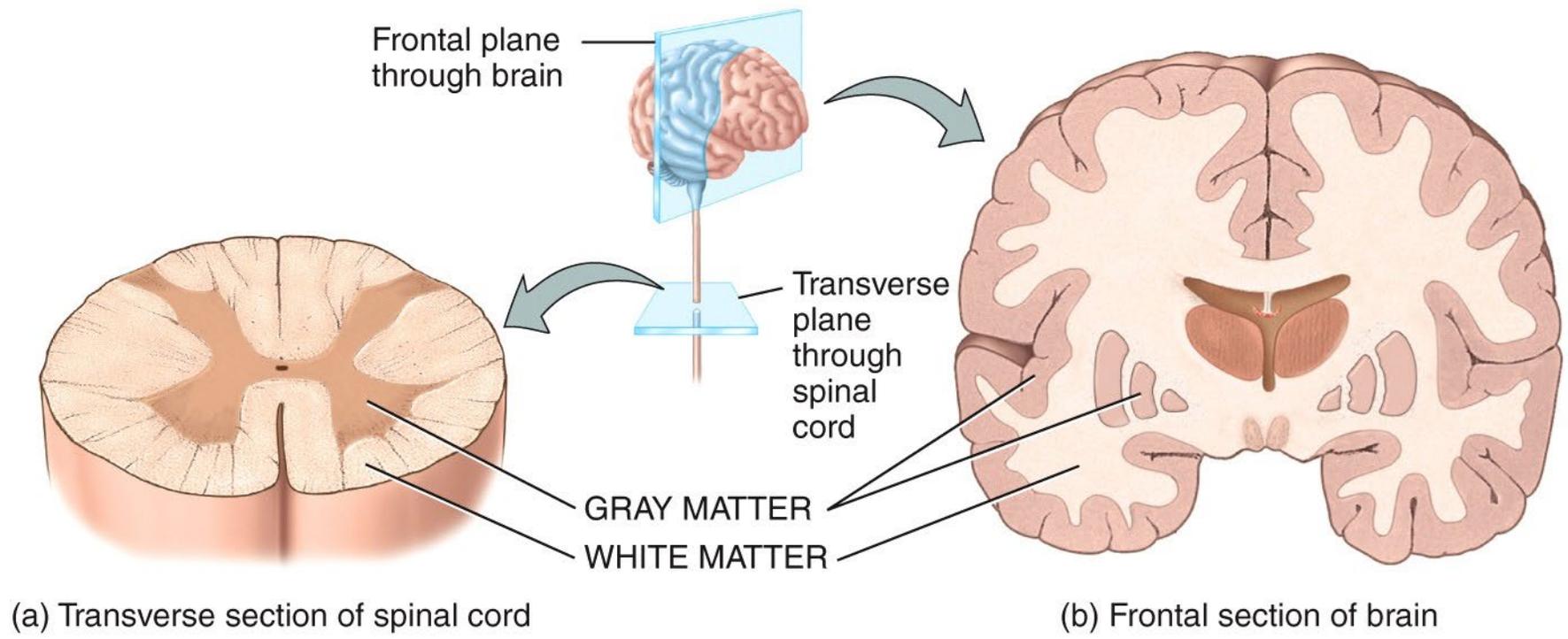
# Progression of Opioid Use Disorder



1. Association between drug and pleasure is formed after repeated opioid use

2. Tolerance results from preemptive cAMP increase due to repeated opioid use

3. Withdrawal symptoms prevent patient from stopping opioid use



# What is the difference between dopamine and serotonin?

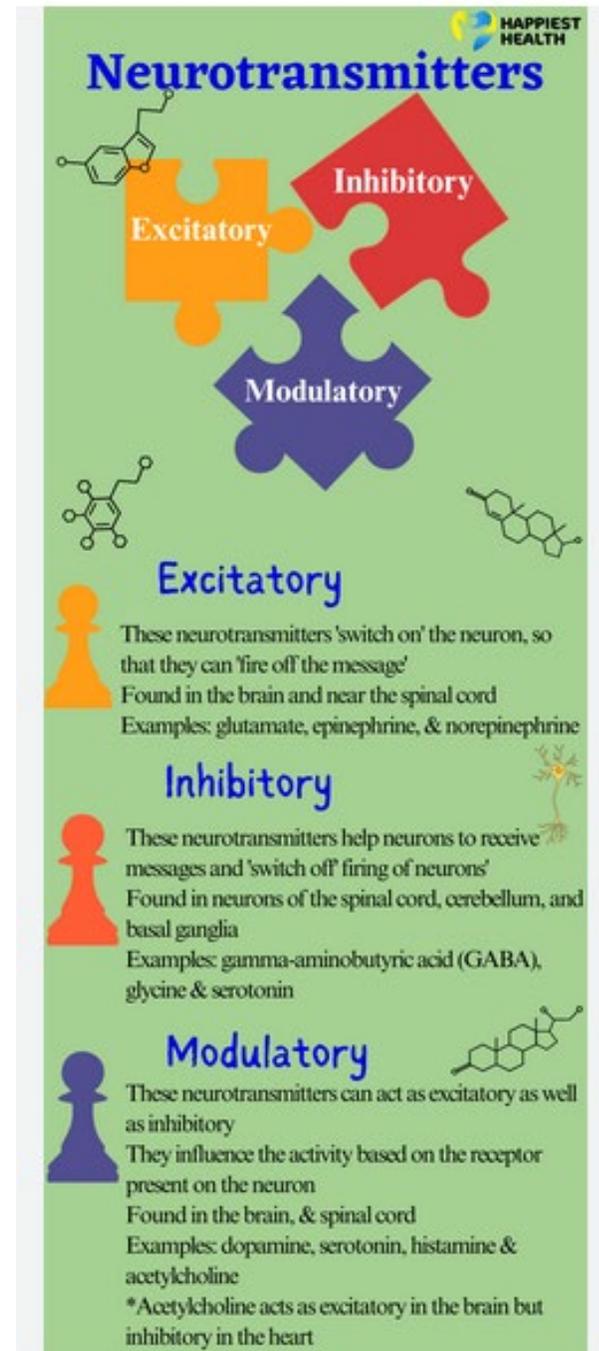
The brain says I like dopamine and I want more.  
Dopamine is pleasure.

The brain says I like serotonin, but I don't want more.  
Serotonin is happiness.

Pleasure and happiness are not the same.

Pleasure is achieved by taking something, like a substance. It is receiving something. You may get pleasure from gambling if you win.

Happiness is achieved by giving something. You may achieve happiness by attending helping someone or going to a birthday party.



# SEROTONIN

## TOO LITTLE

Sadness  
Fatigue  
Suicidal thoughts  
Anxiety  
Overeating  
Insomnia  
Increased pain  
sensation



Happiness  
Contentment  
Relaxed

## TOO MUCH

Irritability  
Agitation  
Restlessness  
Tremors  
Muscle spasms  
Rapid heartbeat  
High blood pressure  
Sweating

## Neurotransmitters

```
graph TD; A[Neurotransmitters] --> B[Inhibitory]; A --> C[Excitatory]; B --- B_list["GABA, Serotonin, Glycine, Taurine, Dopamine, Agmatine"]; C --- C_list["Glutamate, Epinephrine, Histamine, Aspartic Acid, Dopamine, Glycine, Norepinephrine, Phenylethylamine"];
```

### Inhibitory

GABA  
Serotonin  
Glycine  
Taurine  
Dopamine  
Agmatine

### Excitatory

Glutamate  
Epinephrine  
Histamine  
Aspartic Acid  
Dopamine  
Glycine  
Norepinephrine  
Phenylethylamine

Serotonin (5-HT) primarily acts as an **inhibitory neurotransmitter** within the central nervous system, helping to regulate mood, sleep, appetite, and pain by balancing excessive excitatory signals. While often classified as inhibitory, it can exert both excitatory and inhibitory responses depending on the specific receptor subtype (G-protein coupled receptors or ligand-gated ion channels). [Cleveland Clinic +3](#)

- **Inhibitory Function:** It is essential for curbing excessive nervous system activity, which helps regulate mood and anxiety.
- **Action Mechanism:** Serotonin acts on various receptors to cause either excitatory or inhibitory postsynaptic potentials.
- **Key Regulation:** It modulates excitatory and inhibitory inputs, frequently regulating GABAergic (inhibitory) neurotransmission.
- **Balance:** Serotonin works in conjunction with excitatory neurotransmitters to stabilize brain activity. [National Institutes of Health \(.gov\) +3](#)

In summary, while widely known for its inhibitory role in regulating mood and behavior, serotonin's effects are highly receptor-dependent. [National Institutes of Health \(.gov\)](#)

This is for informational purposes only. For medical advice or diagnosis, consult a professional. AI responses include mistakes. [Learn more](#)

Negative feedback

# NEUROTRANSMITTERS

## ADRENALINE fight or flight

produced in stressful situations. Increases heart rate and blood flow, leading to physical boost and heightened awareness.

## GABA calming

Calms firing nerves in the central nervous system. High levels improve focus, low levels cause anxiety. Also contributes to motor control and vision.

## NORADRENALINE concentration

affects attention and responding actions in the brain. Contracts blood vessels, increasing blood flow.

## ACETYLCHOLINE learning

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

## DOPAMINE pleasure

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

## GLUTAMATE memory

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

## SEROTONIN mood

contributes to well-being and happiness. Helps sleep cycle and digestive system regulation. Affected by exercise and light exposure.

## ENDORPHINS euphoria

Released during exercise, excitement and sex, producing well-being and euphoria, reducing pain