# Lecture 14. Insect nerve system (II)

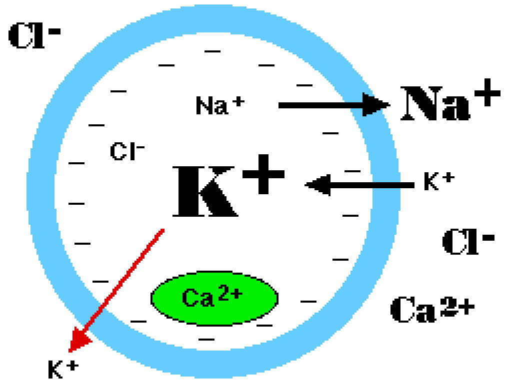
- Structures (Anatomy)
  - Cells
  - Anatomy
- How NS functions
  - Signal transduction
  - Signal transmission

# Overview

- More on neurons: ions, ion channel, ligand receptor
- Signal transduction: convert various incoming sense signals into electric signals
  - Chemotransduction: chemical signals (smell, taste)
  - Phototransduction: visual cues (see)
  - Mechanotransduction: mechanical signals (hear, feel touching)
- Signal transmission
  - Axon transmission
  - Synaptic transmission

# Neuron: ions and resting potential

- Asymmetrical distribution of ions: more Na+ (>10- fold), Ca2+ (10,000-fold), and Cl- but less K+ (<20-fold) outside the cell. EXCEPTION: some intracellular membrane-bounded compartments (ER) may have high Ca2+
- Two ion pumps (Na+/K+ ATPase, Ca2+ ATPase) and the presence of "leaky" K+ channels (red arrow): Na+/K+ ATPase pumps 3 Na+ out and 2K+ into the cell at the expense of 1 ATP; Ca2+ ATPase pump Ca2+ out the cell. http://highered.mcgraw-hill.com/olc/dl/120107/bio_a.swf
- A resting potential of about -70 millivolts (mv) for neurons: an electrical charge across the plasma membrane, with the interior of the cell negative with respect to the exterior.
- Cells are polarized



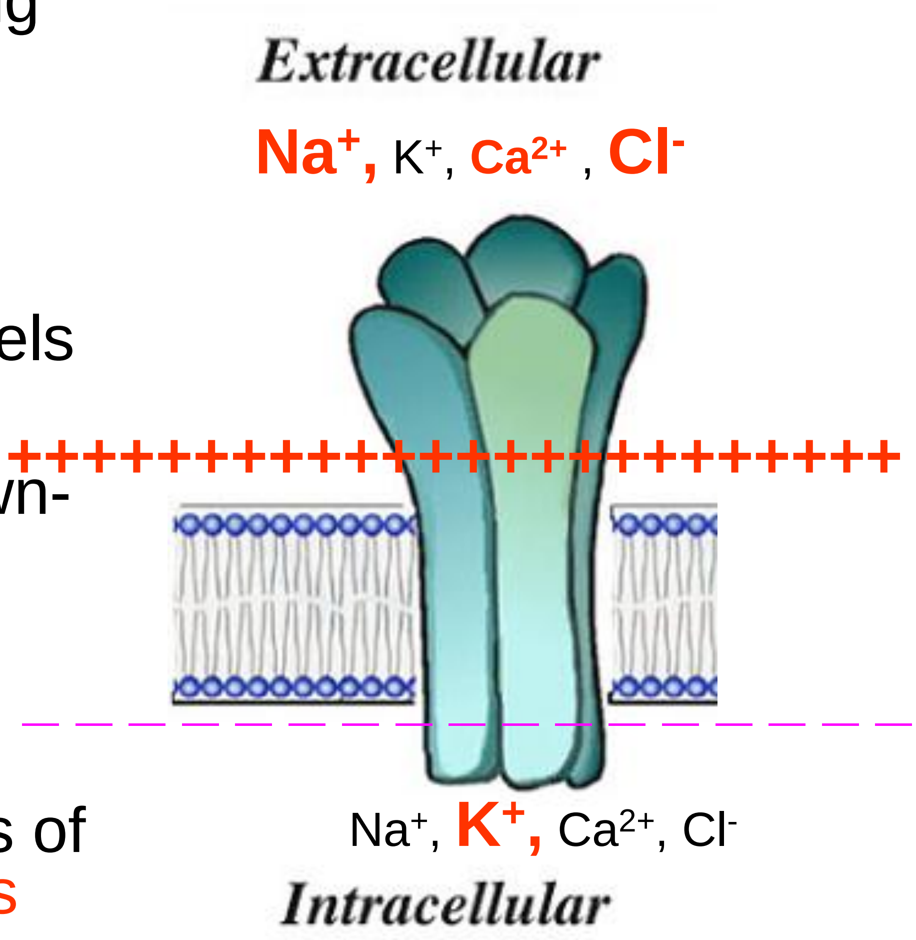
# Neuron: ion channels

- Ion Channels are pore-forming transmembrane proteins. Channels are closed at the resting state

- Stimulus can open ion channels

- Ions may flow in or out in down-hill directions when their corresponding channels are open

- Cross-membrane movements of ions lead to potential changes across membrane---electrical signals



# Ion channels: gating mechanisms

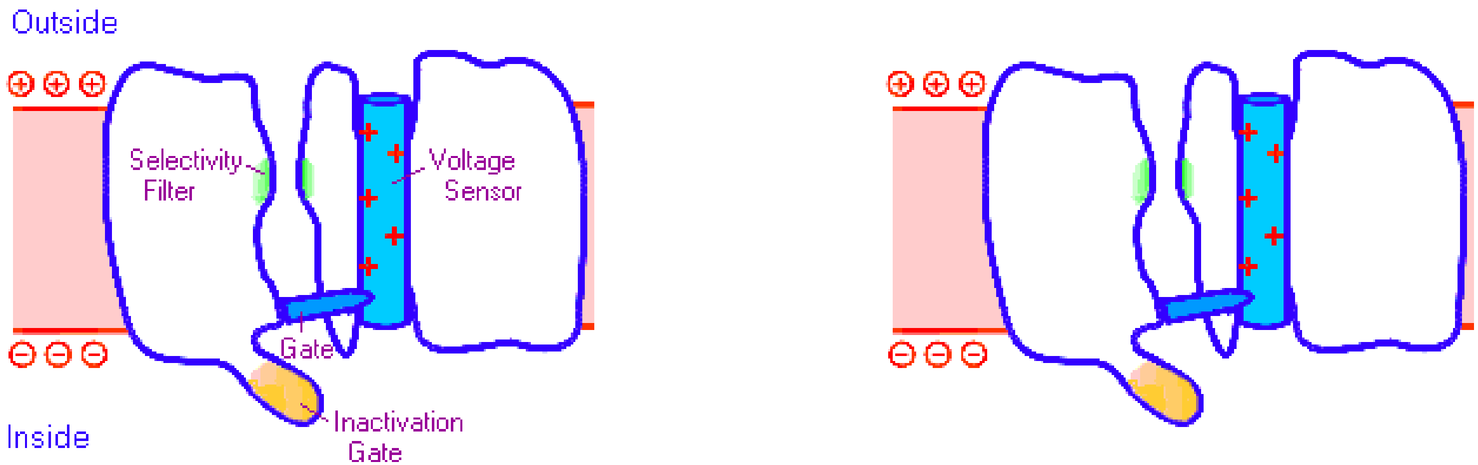
- Mechanically-gated channels: open or close in response to mechanical forces that arise from local stretching or compression of the membrane around them

- Voltage-gated ion channels: open in response to the transmembrane potential changes. E.g. voltage-gated Na+, K+ and Ca2+ chananels

- Ligand-gated channels (=receptor of ligand): open in response to a specific ligand molecule on the **external** face of the membrane.

- Second messenger-gated channels: open in response to internal second messengers (cAMP, cGMP, IP3, Ca2+) on the **internal** face of the membrane.

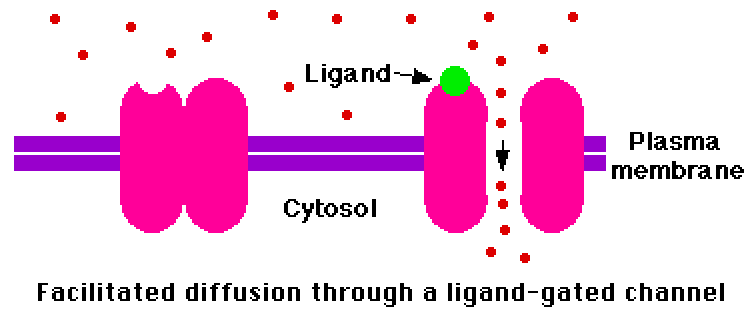
# Voltage-gated ion channel




1. Selectivity filter: Na+ only (Sodium channel).
2. Gate: closed at a resting potential (-70 mV)
3. Voltage sensor: when **depolarize** the membrane potential sufficiently (e.g., to -50 mV), the voltage sensor moves outward and the gate opens.
4. Inactivation gate: limits the period of time the channel remains open, despite steady stimulation

# Ligand-gated channel = ionotropic receptors

- Ligand-gated channel is the receptor of a ligand.
- Binding leads to immediate opening of channels and potential changes
- Nicotinic acetylcholine (Ach) receptor = Ach-gated cation (Na+ and Ca2+) channel
- γ -amino butyric acid (GABA) receptor: GABA-gated Cl- channel



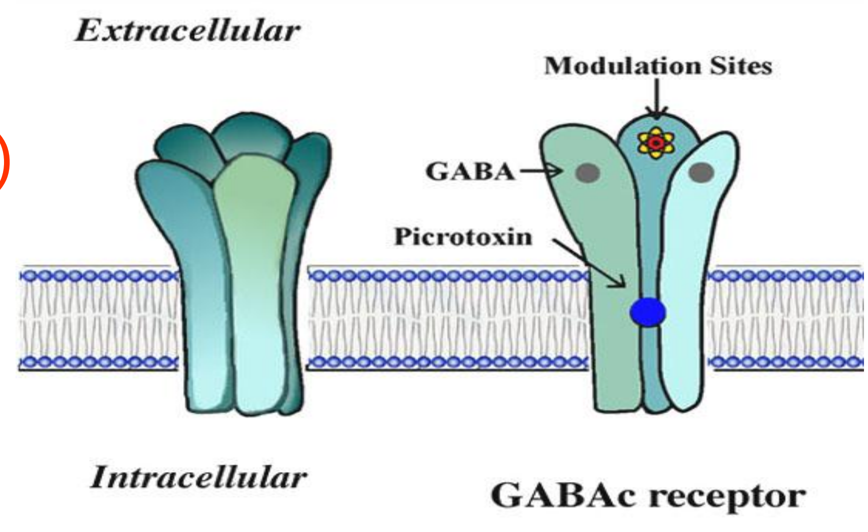
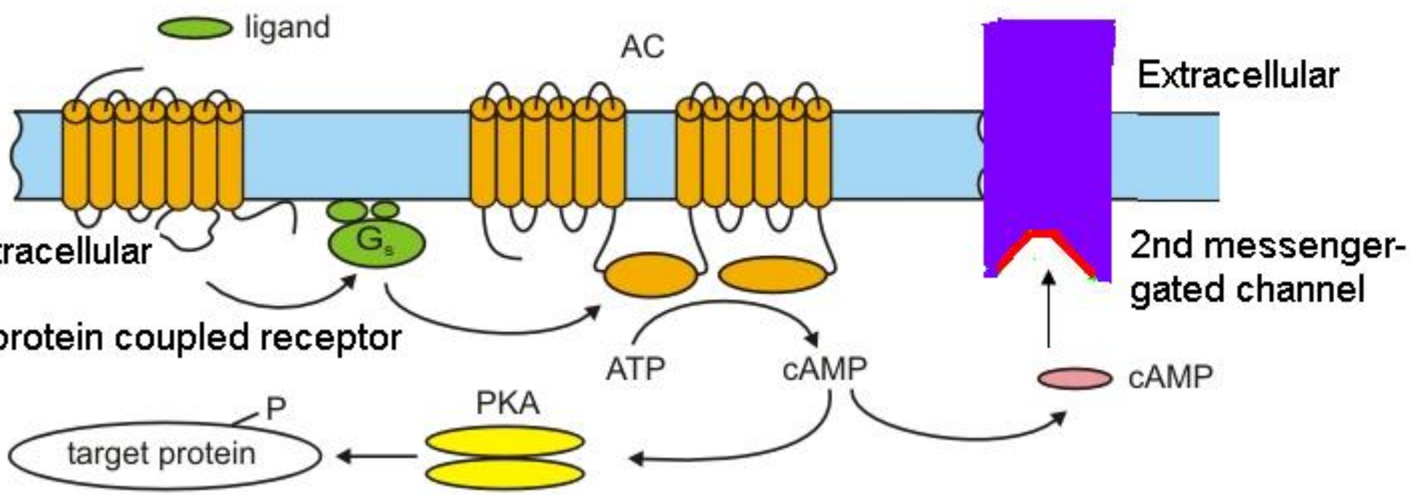



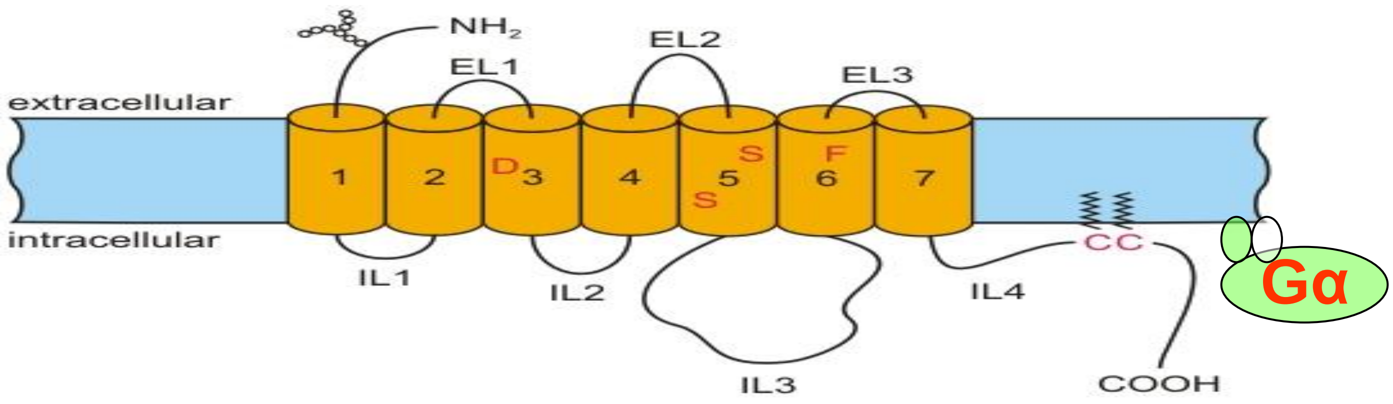

*Fig. 2. Schematic diagram of GABAc receptors. These receptors are formed by five subunits with an ionic channel in the middle of the receptor. On the extracellular side, the receptor contains the binding site for GABA, and several modulatory sites.*

# Second messenger-gated channels



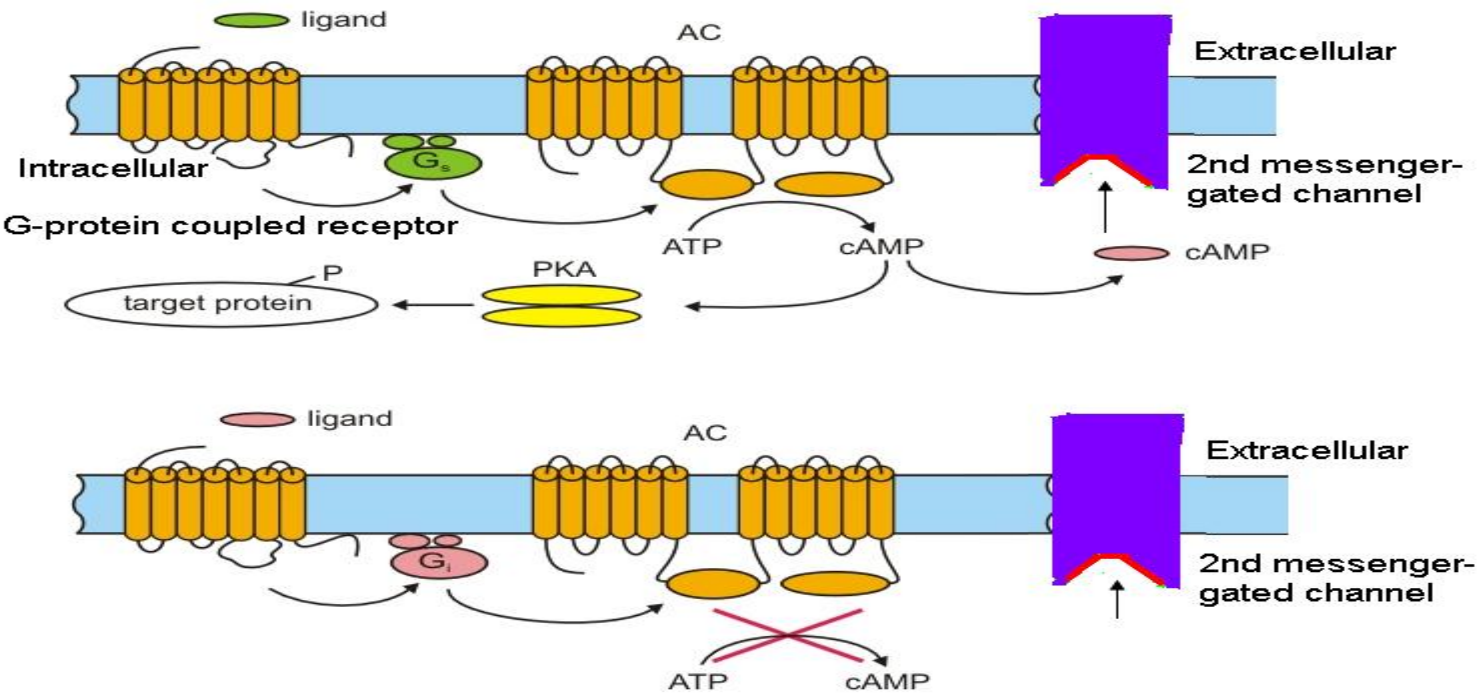

- The receptor of the extracellular ligand ≠ ion channel
- Metabotropic receptor = G-protein coupled receptor (GPCR)
- Ligand binding leads to G-protein activation and then increase or decrease of second messengers
- 2nd messengers bind to 2nd messenger-gated ion channels, channel open and potential changes. Thus 2nd messenger-gated channel = 2nd messenger receptor
- Slow potential changes

# GPCR: G-protein




- G-protein has three subunits: α, β,γ
- Alpha unit is critical in function
- Three important classes of alpha units
- $G_s$: stimulate adenyl cyclase (AC), cAMP increase
- $G_i$: inhibit AC, cAMP decrease
- $G_q$: stimulate phospholipase C (PLC), leading to increase of DAG (diacylglycerol), IP3 (inositol 1,4,5-triphosphate), and intracellular Ca2+

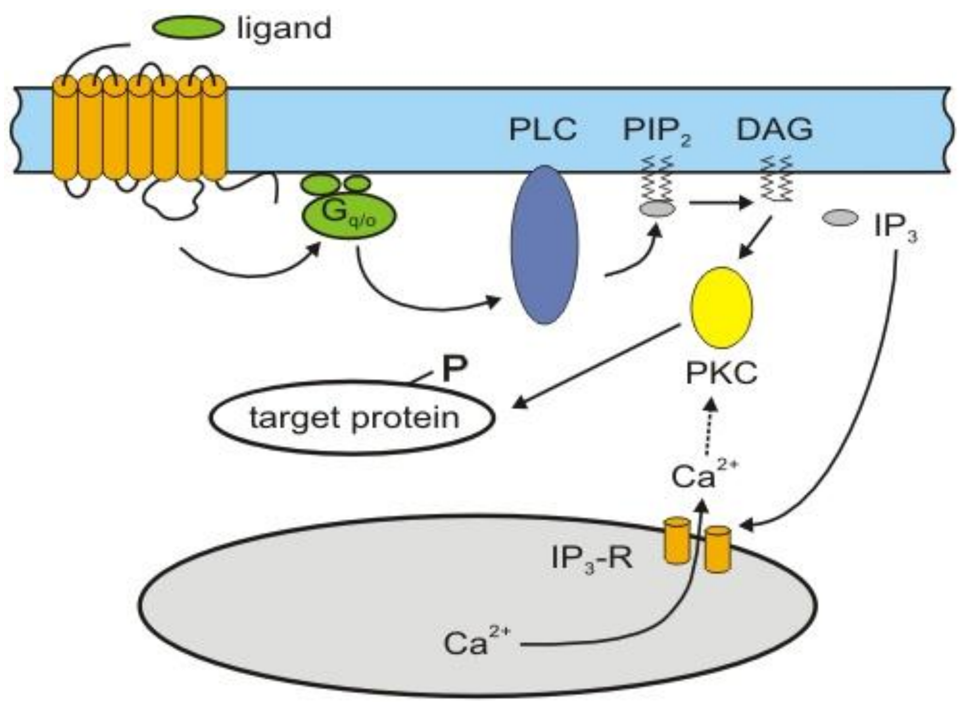
# GPCR signaling pathway: regulate AC and cAMP level




Examples

- Biogenic amine receptors in synaptic transmission
- Odorant receptors in chemotransduction

# GPCR signaling pathway: PLC activation & Ca2+ increase




Examples

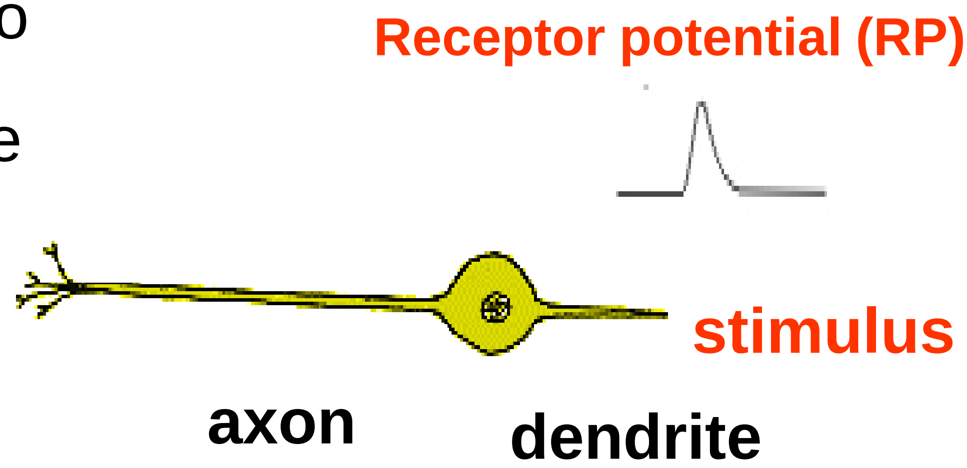
- Rhodopsin in phototransduction
- Odorant receptors in chemotransduction
- Muscarinic Ach receptor

# Signal transduction

- convert incoming sense (hear, see, smell, taste, touch) signals (visual, chemical, mechanical) to electric signals, namely, potential changes on the dendritic tip

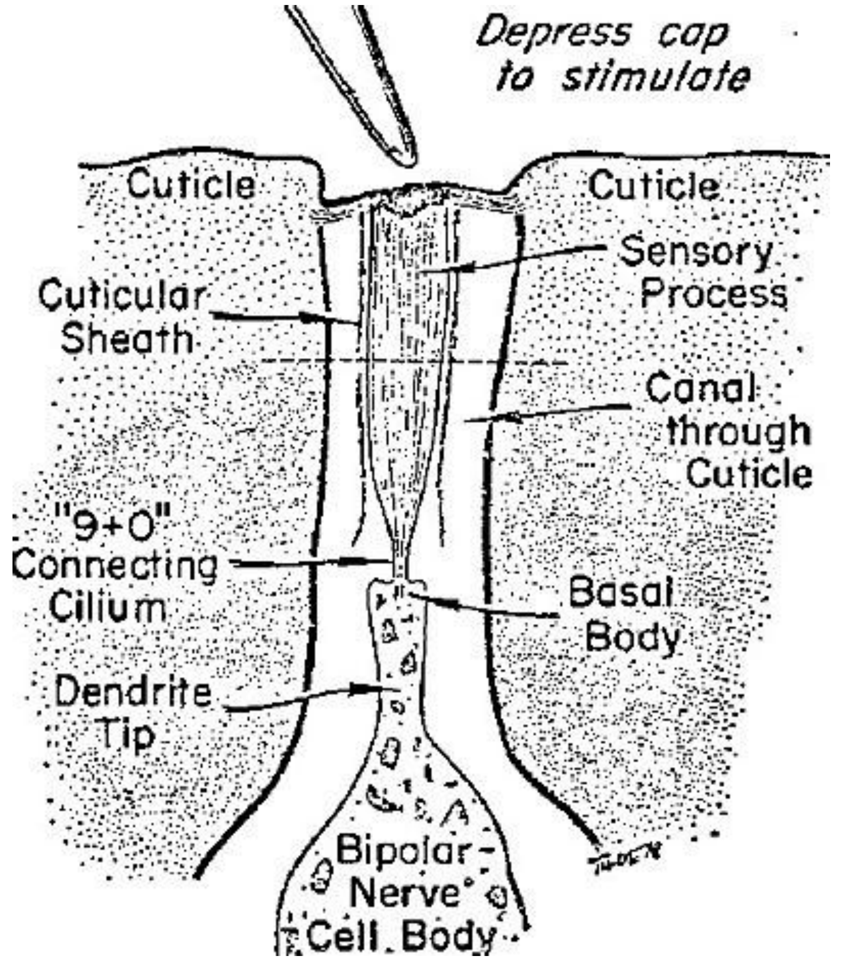
- The resulted potential changes is known as receptor potential.

- The amplitude of receptor potential is graded and vary with the intensity of stimuli



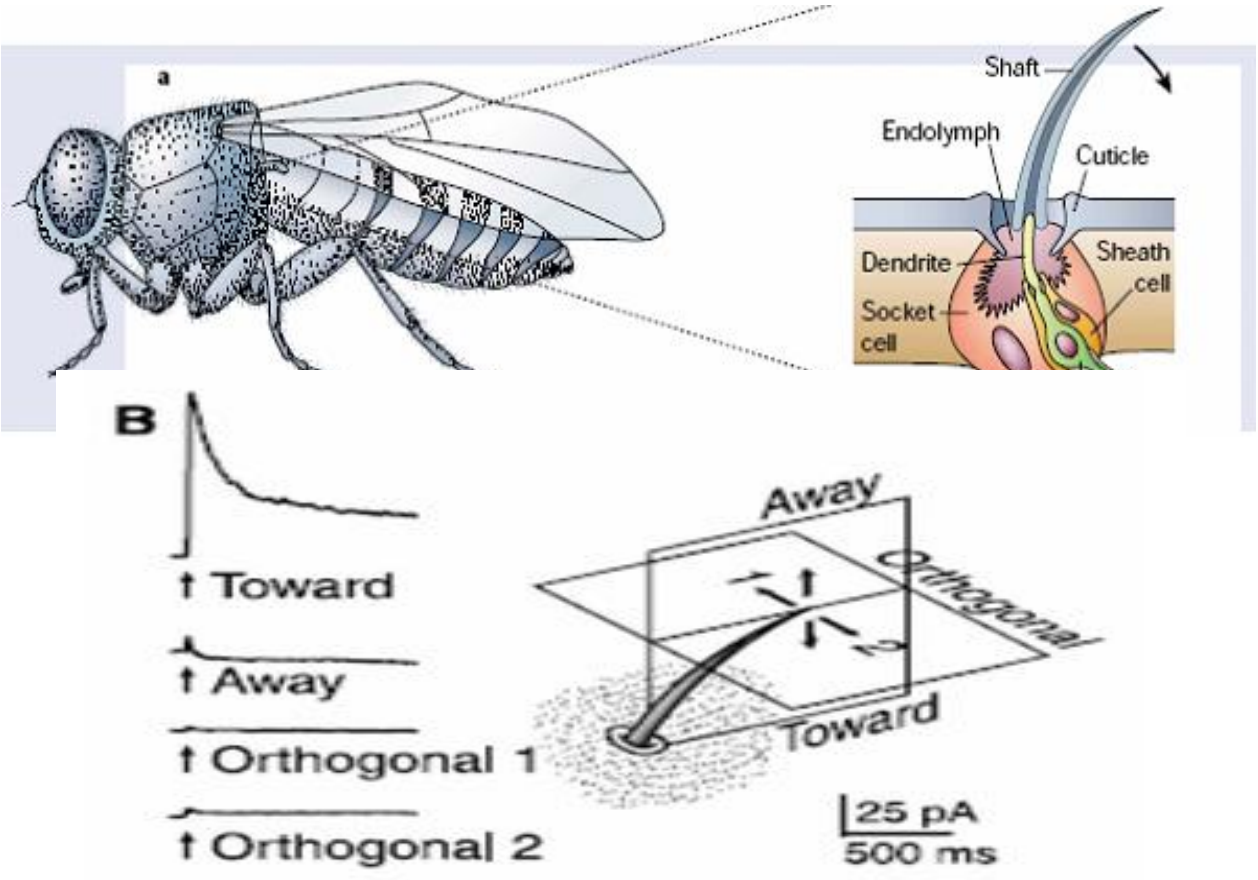
# Signal transduction: mechanotransduction

- Mechanosensory transduction: touch, balance, and hearing.
- The dendritic tip of sensory neuron is directly resided below the thin cuticle or hollow hair
- Various mechanical forces compress the dendritic tip and open the mechanically-gated ion channels that transduces sound, pressure, or movement into potential changes--receptor potential.




A campaniform sensillum

# Signal transduction: mechanotransduction




Directional sensitivity of a ventral notopleural bristle.
Walker et al., 2000. Science

# Signal transduction: chemotransduction

- Chemotransduction underlying smell and taste
- Airborne (smell) or water-borne chemical (taste) molecule directly bind to its receptor, i.e. GPCR in the dendrite membrane
- The coupled G protein regulates AC or PLC rather than directly open or close ion channels
- The resulted intracellular 2nd messengers (cAMP, IP3, Ca2+) then open 2nd messenger-gated cation channels--receptor potential

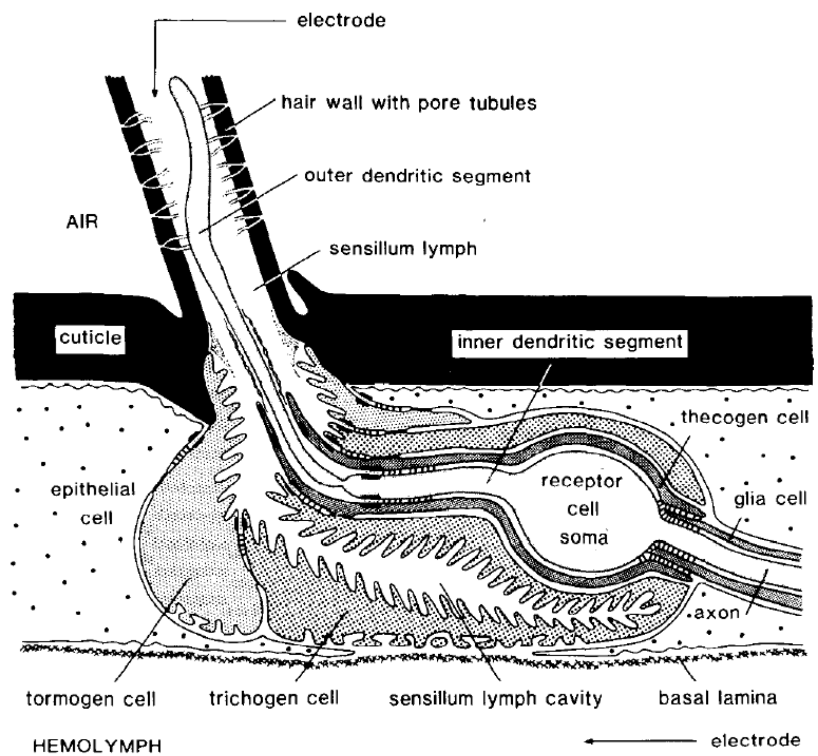
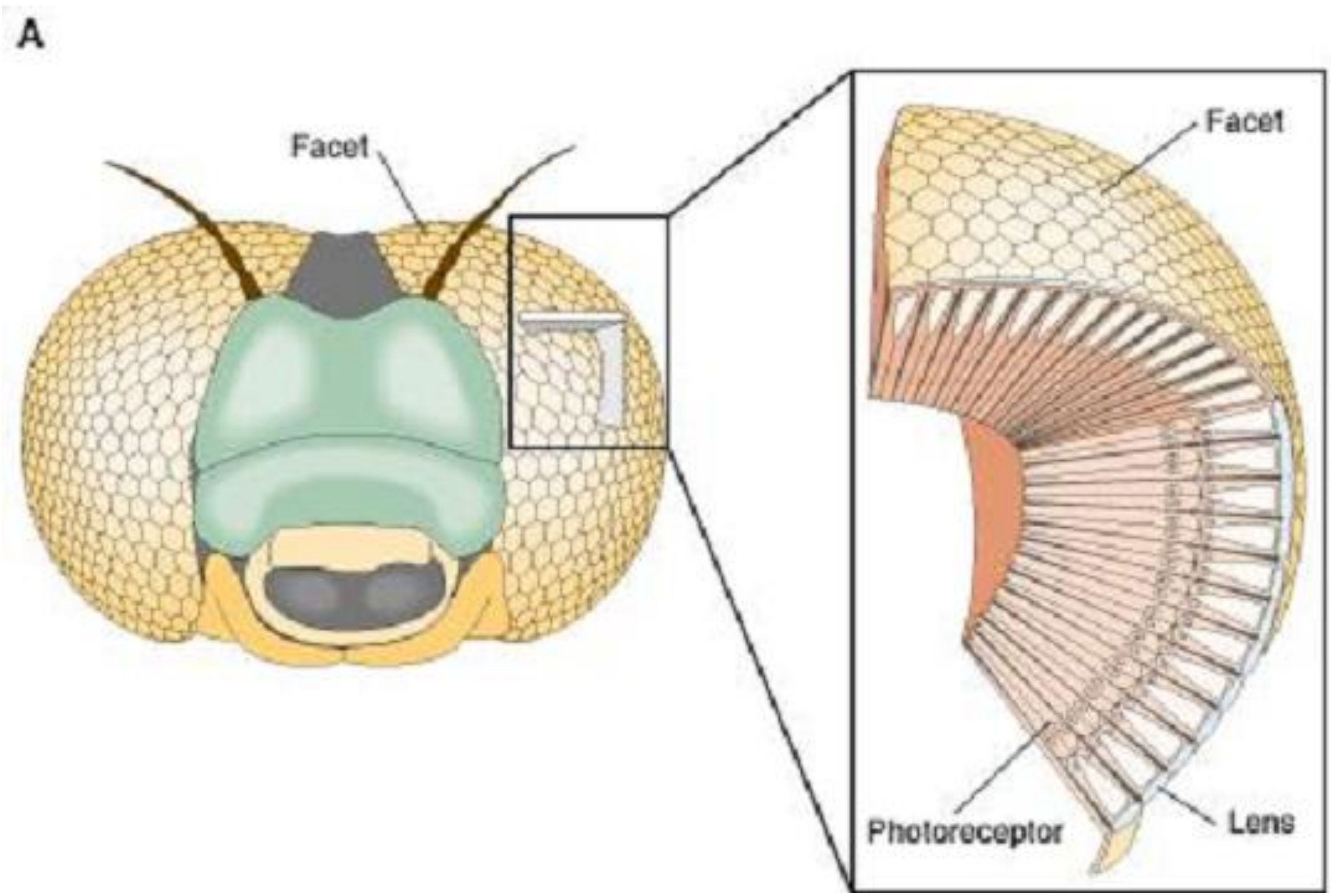



*Figure 1* Schematic diagram of an olfactory sensillum trichodeum with one receptor cell and three auxiliary cells. The cuticular hair is 5 $\mu$m thick and 300 $\mu$m long (by courtesy of T. A. Keil).

# Phototransduction: a compound eye



# Phototransduction: ommatidium

- **Typically contains 8 sensory neurons called retinal cells or visual cells**
- **Rhabdom: central photoreceptive region, formed of specialized portion of each retinal cell, called rhabdomere (dendrite?)**
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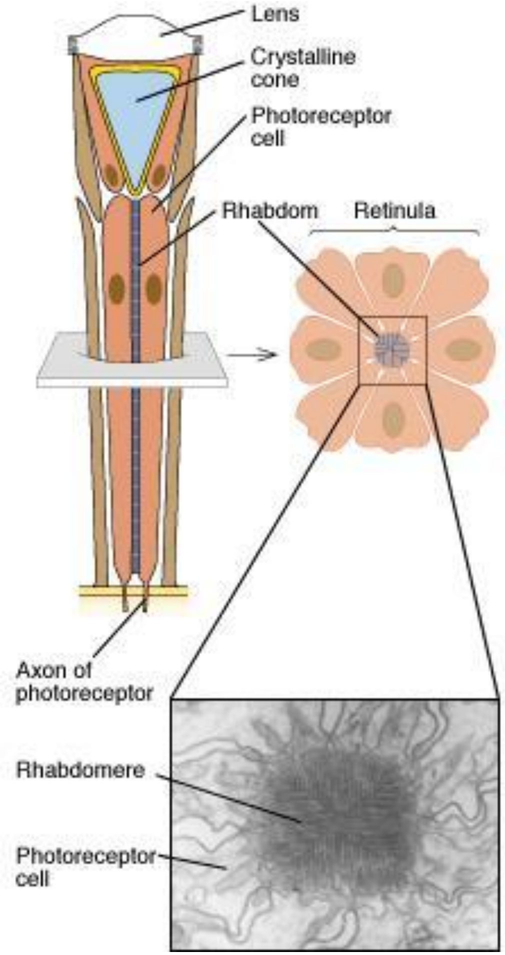
- **Rhabdom membrane contains photoreceptive pigments, Rhodopsin, the photon receptor protein**



# Rhodopsin is a G-protein coupled photo receptor

Rhodopsin
G-protein-coupled photopigment $\xleftrightarrow{\text{Light}}$ Metarhodopsin, active state

↓

G protein activation

↓

PLC (phospholipase C)

↓

PIP2

↓

IP3 and DAG

↓

Ca2+ channel, Ca2+ influx

↓

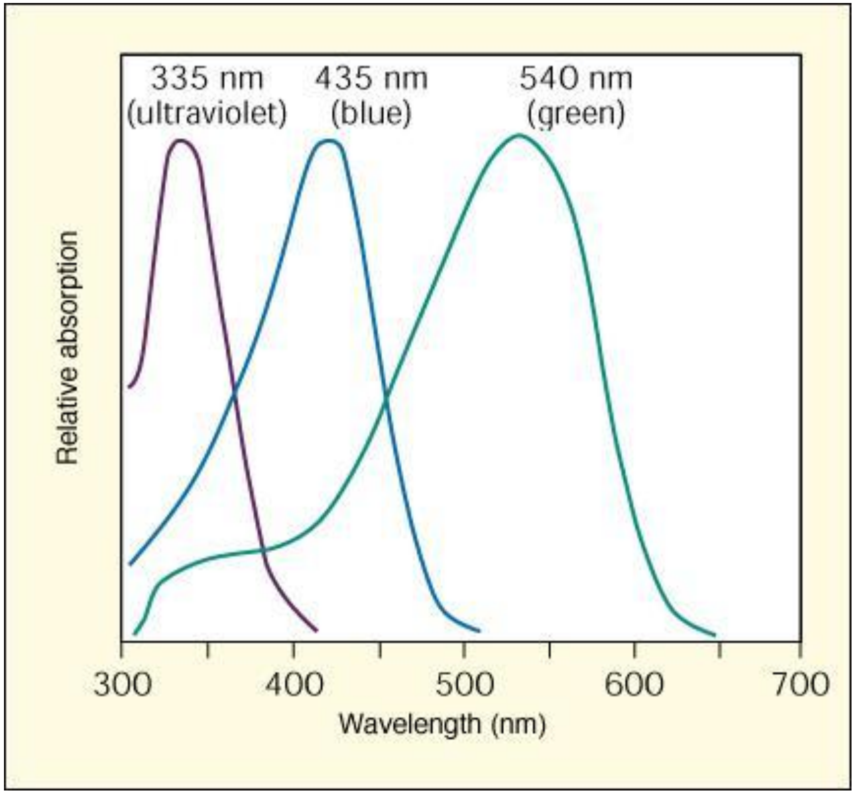
Receptor potential

IP3: inositol 1,4,5-triphosphate
DAG: diacylglycerol
PIP2: phosphatidylinositol
4,5-biphosphate

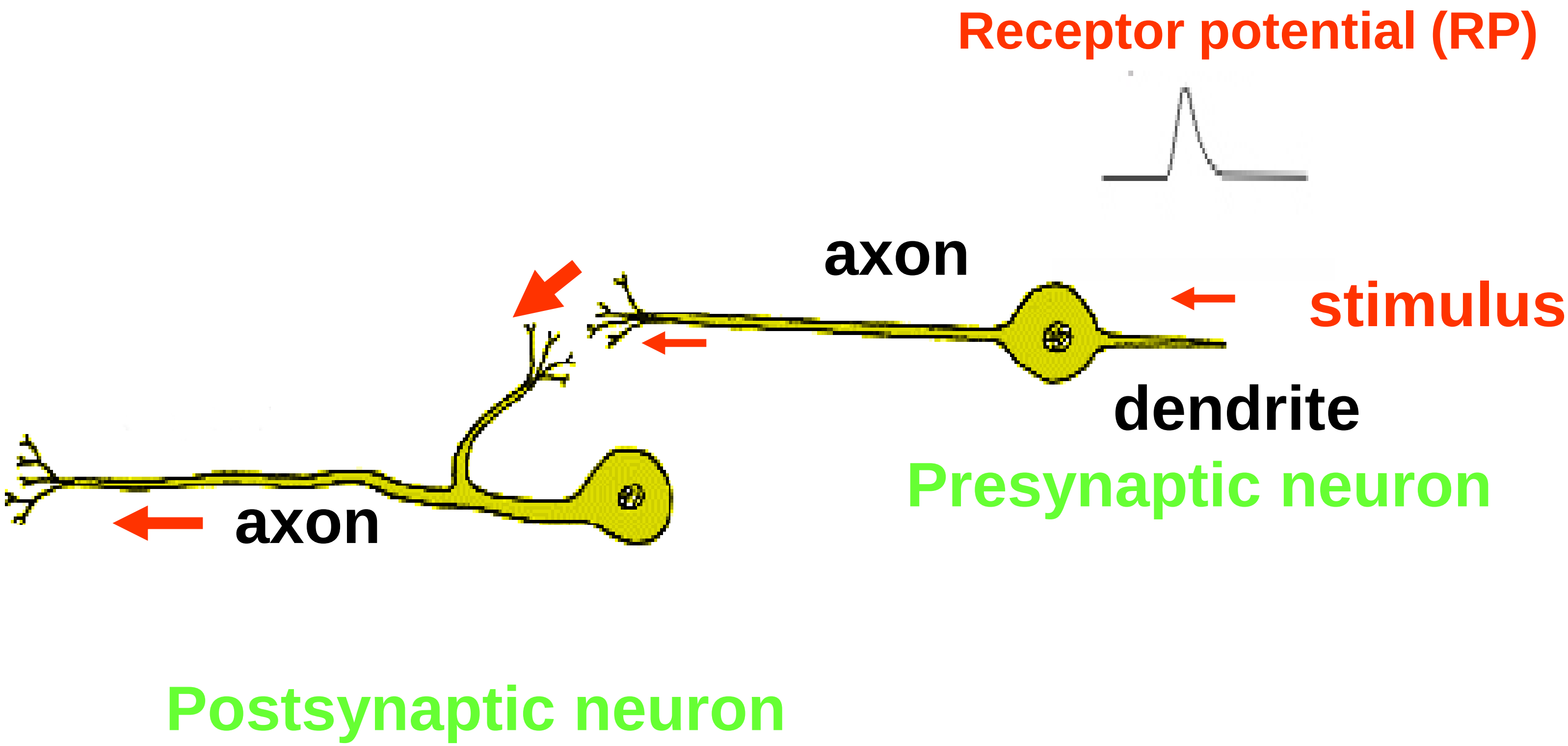
# Phototransduction: detection of colors

- **About 3 rhodopsins, each with different spectral sensitivity**

- **Insects can see ultra-violet, blue, green, yellow, but not red**



# Signal transmission: Axon transmission



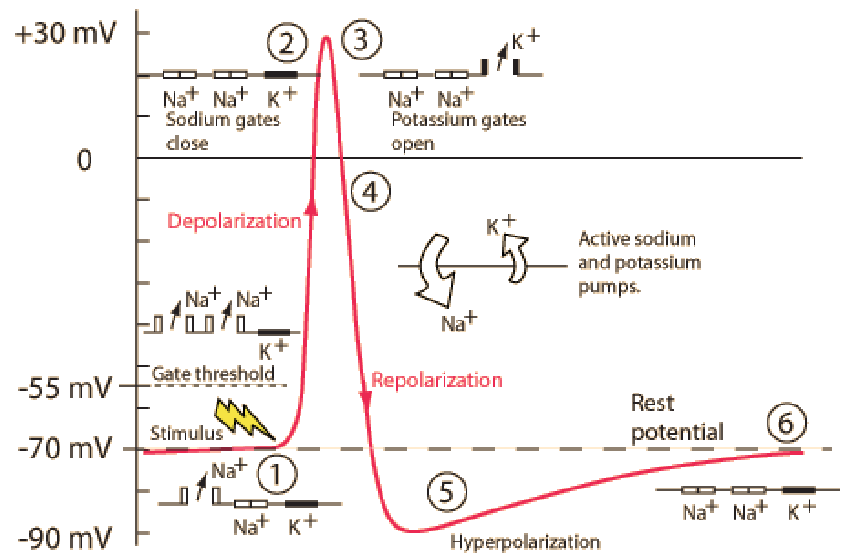

How is receptor potential transmitted to the terminal arborization of the axon in CNS?

Action potential

http://highered.mcgraw-hill.com/olc/dl/120107/anim0013.swf

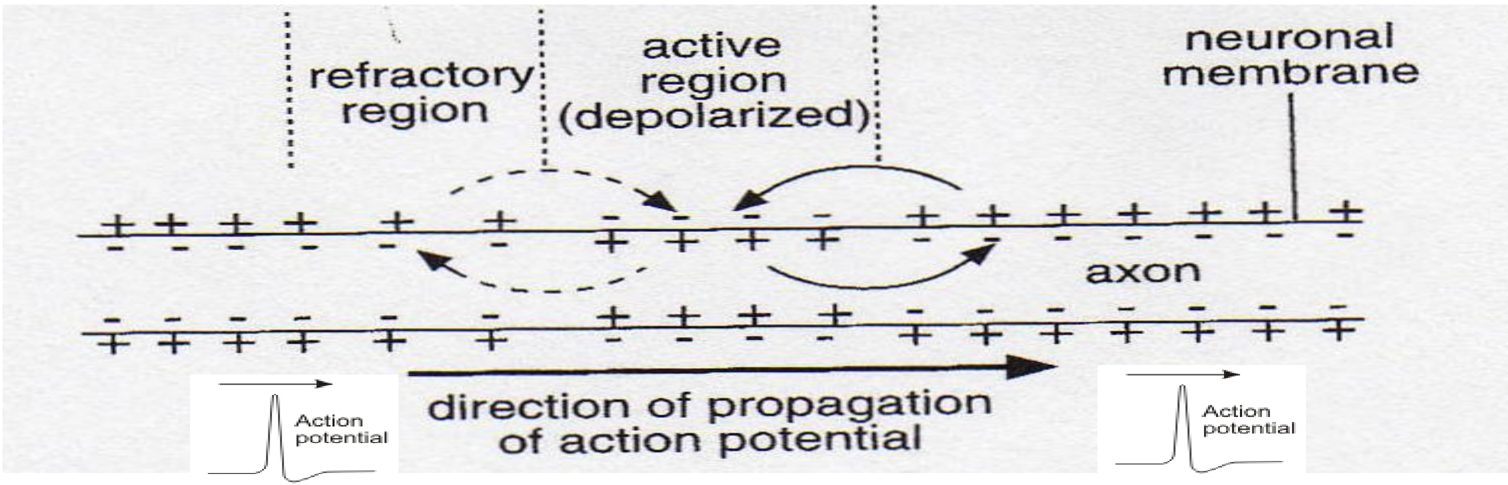
# Axon transmission: generation of action potentials

- If a RP > Na+ gate threshold, Na+ channels open
- Na+ rush into  the axon depolarizing it further, the membrane potential becomes positive (+ve) very rapidly, producing a spike
- The Na spike does not last long. Two things bring the voltage back to negative values (repolarization)
  1. Na+ channels close when +ve
  2. K+ channels open when +ve. K+  flows outward making the membrane potential more negative
- Hyperpolarization = negative afterpotential




Action Potential (AP)

# Axon transmission: propagation of action potential




- A local current flows away from the AP point in both direction
- This current results in a potential change sufficient to trigger another AP at the next point. In the same way, a AP wave is produced towards the axon terminal
- But this current can not trigger an AP at the point that AP has just passed through because of inactivation of Na+ channel and hyperpolarization. http://highered.mcgraw-hill.com/olc/dl/120107/bio_d.swf

# Axon transmission: AP is conducted in an All-or-None manner

- The "none" part:  if RP<Na+ gate threshold, there will be a little local electrical disturbance, but no action potential

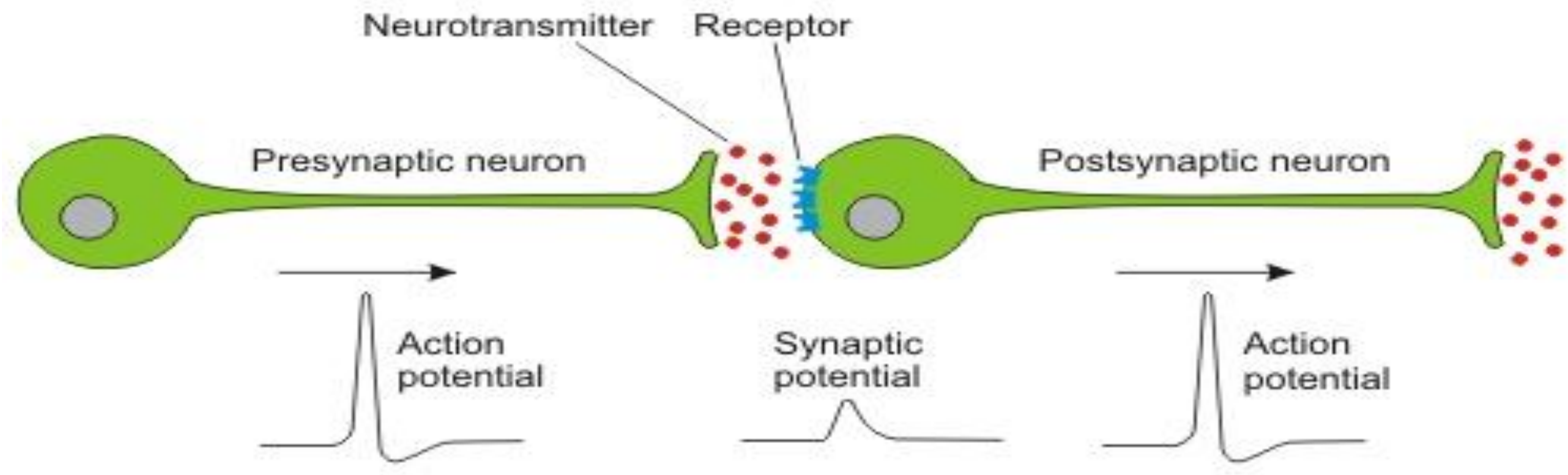
- The “all” part: if RP> Na+ gate threshold, an action potential of the same size--it does not get larger for stronger stimuli. So how do axons indicate stronger stimulus?

- Higher frequency: more action potentials per second

- As the action potential travels along the axon it does not die out, but stays the same size

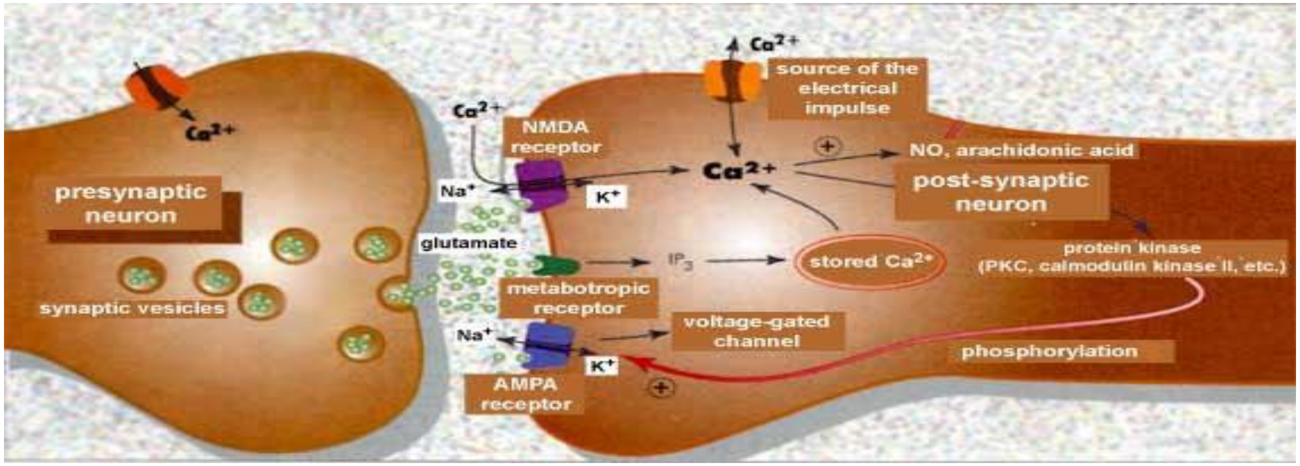
- This is called the all-or-none law

# Signal transmission: Synaptic transmission



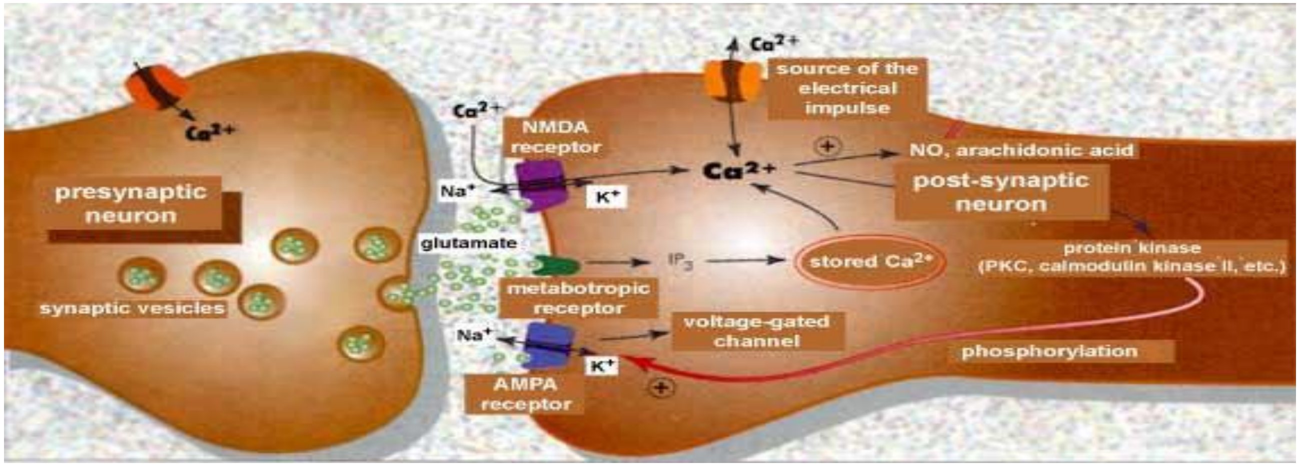

- At the synaptic gap the action potential ends
- In most cases further transmission of the signal requires a chemical transmitter. Only a few electrical synapses
- Synapses delay the signal: chemical transmission is slower than electrical transmission

# Synaptic transmission: transmitter release



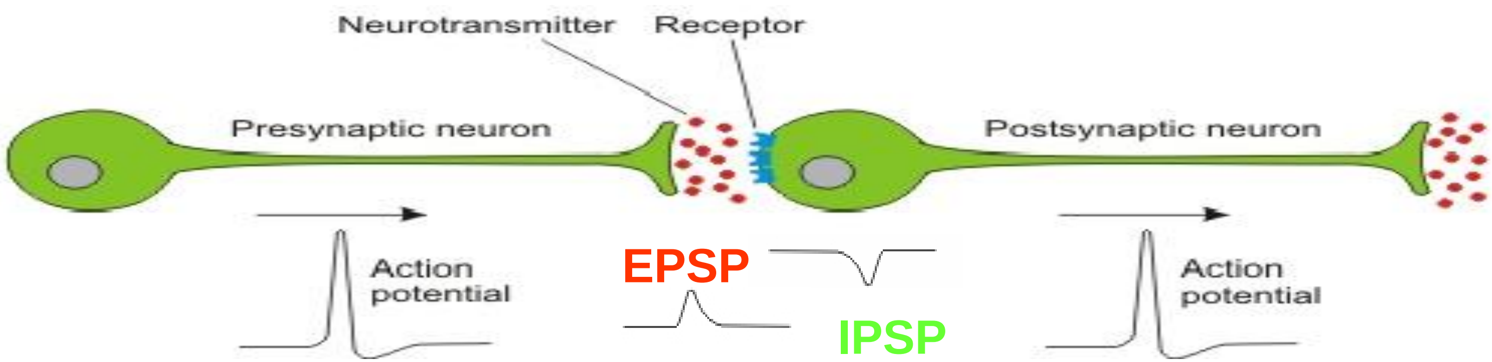

- Neurotransmitters are stored in membrane bound vesicles
- Arrival of action potential leads to opening of voltage-gated $Ca^{2+}$ channels at the presynaptic terminal
- Influx of $Ca^{2+}$ cause vesicles to fuse to the membrane, open up, and release transmitters

# Synaptic transmission: transmitters diffuses across the synaptic cleft




- Travel across the gap by simple diffusion
- Part of molecules reach the postsynaptic membrane and bind to specific receptors, which may be ionotropic (transmitter-gated ion channels) and metabotropic (GPCR)

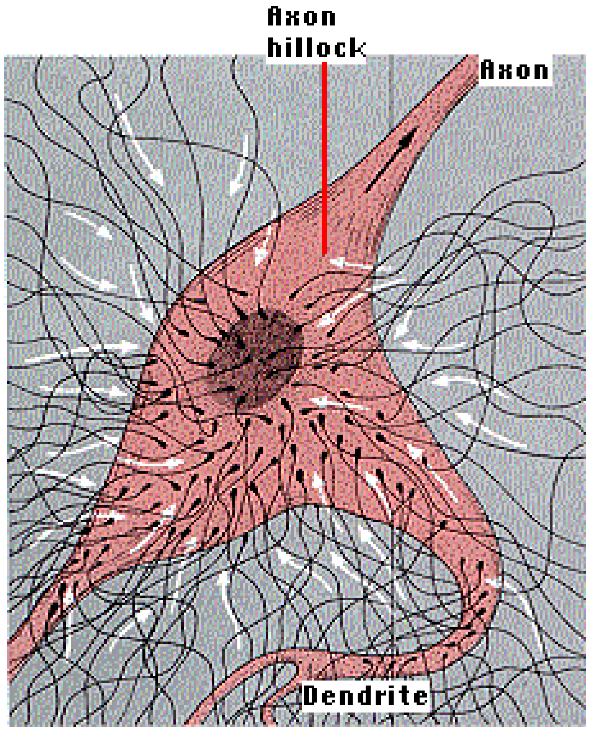
# Synaptic transmission: EPSP or IPSP



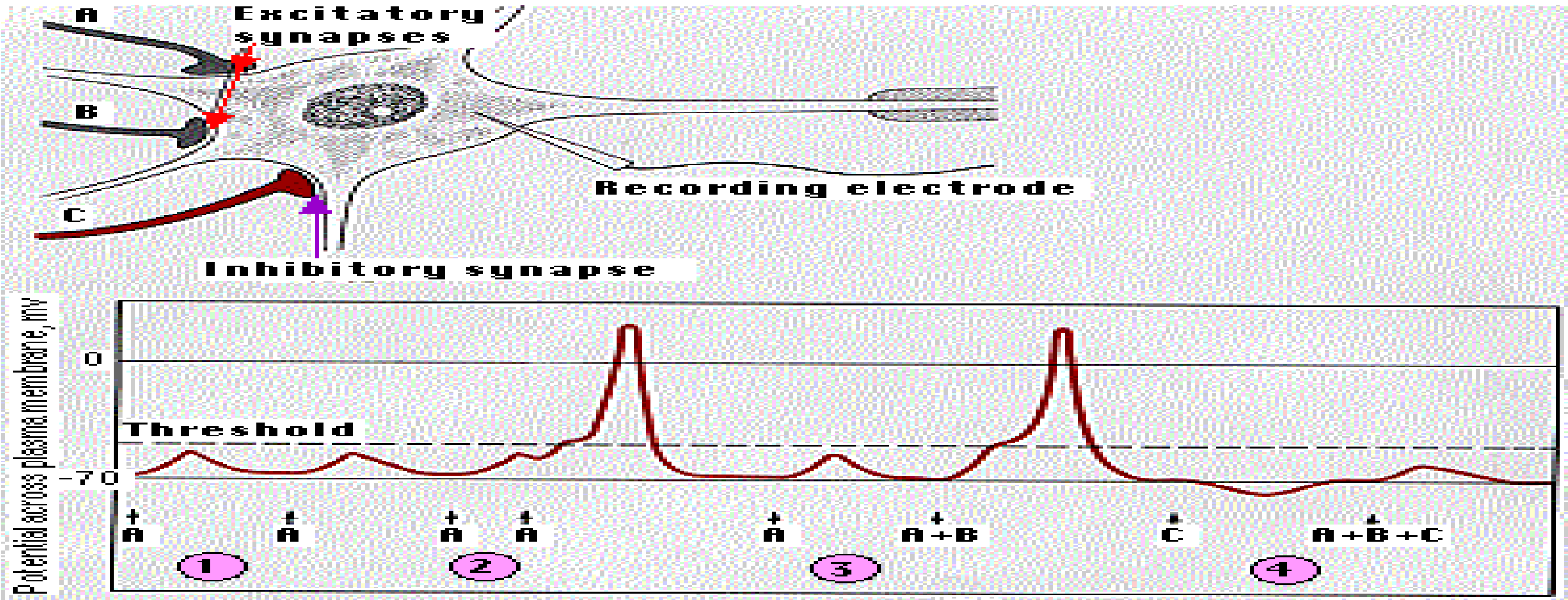

- Binding of ionotropic receptors leads to Fast opening of ion channels and influx of $Na^+$, $Ca^{2+}$ or $Cl^-$ or outflow of $K^+$
- Binding of GPCRs leads to production of 2nd messenger (e.g. cAMP, IP3, or Ca2+), which then open ion channel--Slow
- Influx of $Na^+$ and $Ca^{2+}$ produces an **e**xcitatory **p**ost**s**ynaptic **p**otential (EPSP)
- Influx of Cl- or outflow of $K^+$ produces an **i**nhibitory **p**ost**s**ynaptic **p**otential (IPSP)
- Postsynaptic potential is graded and vary with the number of transmitter molecules released which in turn rely on the presynaptic AP frequency

# Synaptic transmission: Axon hillock

- Axon hillock: locate at the beginning of axons and is the site for postsynaptic AP generation
- has no synapses of its own and thus is able to evaluate the total picture of EPSPs and IPSPs created in the dendrites
- It has a **lower Na+ gate threshold** than elsewhere on the cell.
- Only if ∑EPSPs -∑IPSPs ≥ Na+ gate threshold will an action potential be generated.

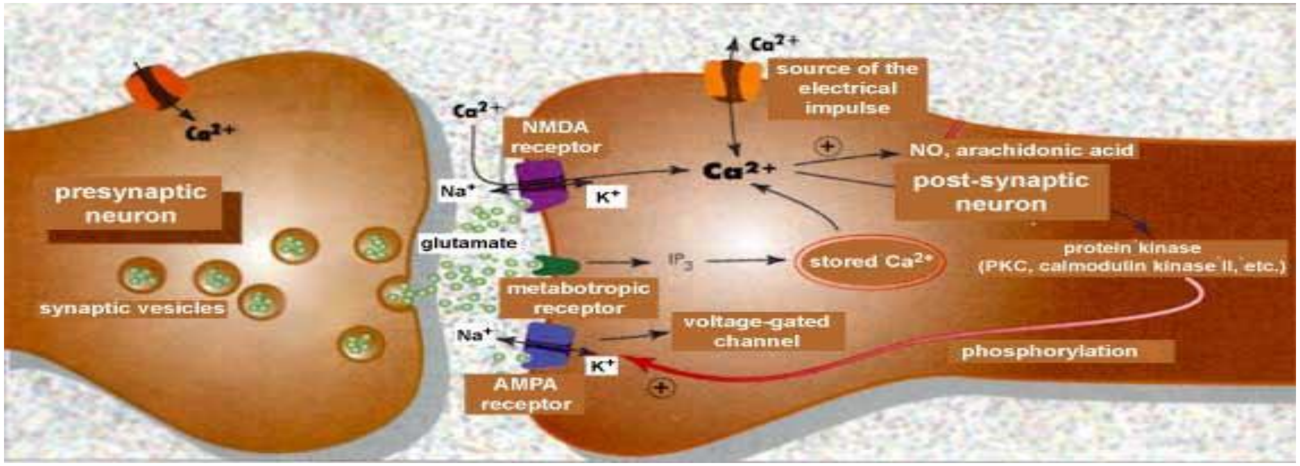


# Synaptic transmission: integration of EPSPs and IPSPs




- IPSPs make the membrane potential more negative (hyperpolarization) and cancel out EPSPs

# Synaptic transmission: breaking down and recycling of transmitters




- The transmitter must be removed once the signal is delivered
- Broken down by an enzyme. e.g. acetylcholinesterase (**AchE**) breaks down acetylcholine (Ach) to acetate and choline .
- recycled--transported back into the presynaptic neuron
- Combine enzyme degradation and recycling
  - http://highered.mcgraw-hill.com/olc/dl/120107/bio_c.swf

# Diversity of chemical synapses

| Groups | Neurotransmitter | Receptor & Channel | Function |
|---|---|---|---|
| Acetylcholine (Ach) | Acetylcholine | Nicotinic : Ach-gated Na + channel<br><br>Muscarinic: GPCR, IP3-gated Ca2+ channel | Fast Excitatory<br><br>Slow excitatory |
| Biogenic amines | Dopamine | GPCR, cAMP-gated channel | Excitatory or inhibitory (salivary gland, mushroom body, learning and memory) |
| | octopamine | GPCR, cAMP-gated cation channel, Ca2+ release | Excitatory (learning and behavior) |
| | tyramine | GPCR, cAMP-gated cation channel | inhibitory |
| | Serotonin (5-HT) | GPCR, cAMP-gated cation channel | Excitatory or inhibitory |
| | Histamine | GPCR, ? | ? |
| Amino acids | glutamate | Glutamate-gated cation or Cl- channel | Excitatory or inhibitory (nerve-musle) |
| | γ -Amino butyric acid (GABA) | GABA-gated Cl- channel | Inhibitory (both nerve-nerve and nerve-muscle) |