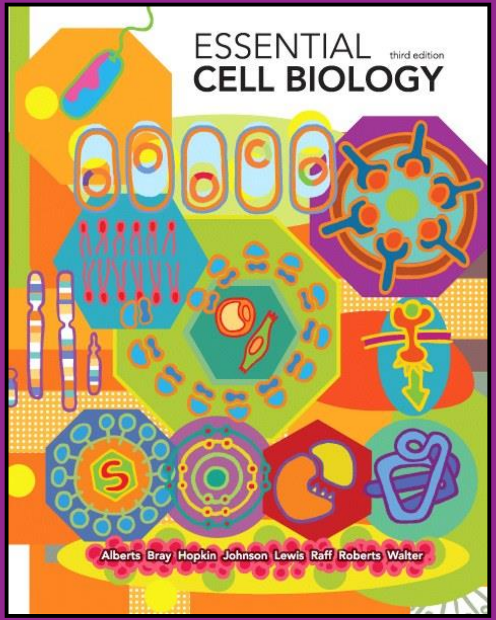
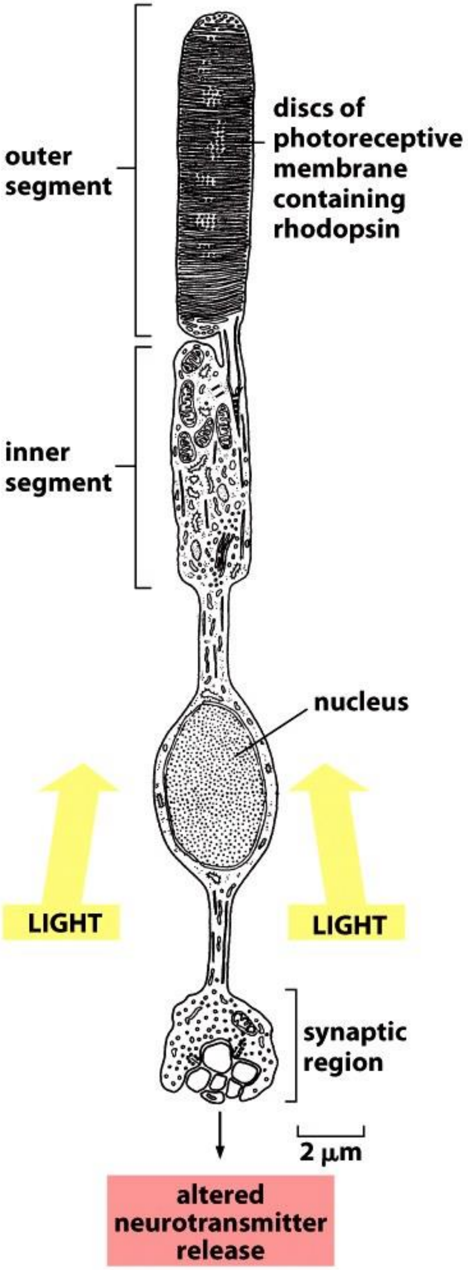


Essential Cell Biology

Third Edition

Chapter 16
Cell Communication



آبشارهای پیام‌رسانی درون‌سلولی، می‌توانند با سرعت، حساسیت و سازش‌پذیری حیرت‌آوری عمل کنند

توضیح مراحل آبشارهای پیام‌رسانی مرتبط با گیرنده‌های وابسته به پروتئین G بسیار وقت‌گیر است، ولی این وقایع فقط ظرف چند ثانیه روی می‌دهند. توجه کنید که چگونه هیجان ناگهانی می‌تواند ضربان قلب شما را سریع‌تر کند (آدرنالین، گیرنده‌های وابسته به پروتئین G را در سلول‌های ماهیچه‌ای تحریک می‌کند و ضربان قلب را افزایش می‌دهد)، یا چگونه رایحه‌ی یک غذا به‌سرعت بزاق دهان شما را افزایش می‌دهد (این عمل از طریق گیرنده‌های وابسته به پروتئین G مربوط به بوهاست که در بینی شما وجود دارند و همچنین گیرنده‌های وابسته به پروتئین G موجود در سلول‌های بزاقی که با استیل‌کولین تحریک می‌شوند). از جمله سریع‌ترین پاسخ‌ها که به‌واسطه‌ی گیرنده‌های وابسته به پروتئین G می‌باشند، پاسخ چشم به نور است، به‌طوری‌که تنها بیست هزارم ثانیه طول می‌کشد تا سلول‌های گیرنده‌ی نوری شبکیه (گیرنده‌های نوری مخروطی که مسئول دید رنگی در روشنایی هستند) نسبت به یک لحظه‌ی نوردهی، پاسخ دهند.

Smell and Vision Depend on GPCRs That Regulate Ion Channels

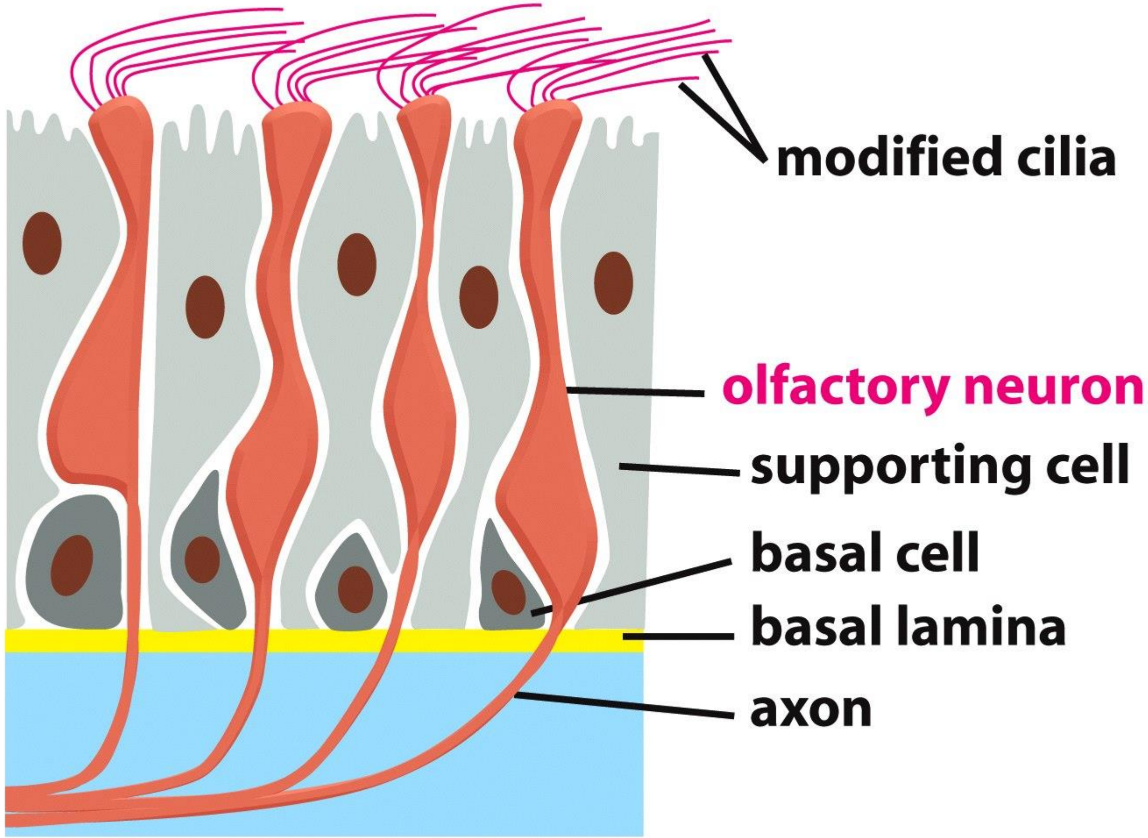
- Humans can distinguish more than 10,000 distinct smells, which they detect using specialized **olfactory receptor neurons in the lining of the nose**.

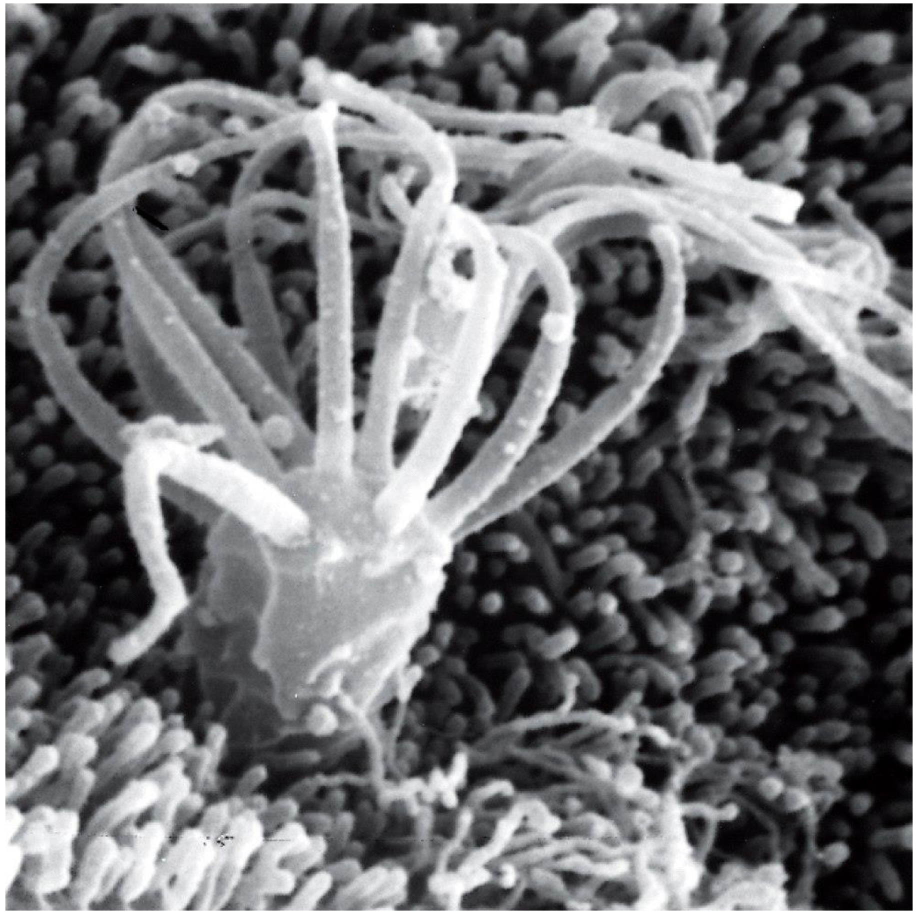
- These cells use specific GPCRs called **olfactory receptors** to recognize odors; the receptors are displayed on the surface of the **modified cilia** that extend from each cell (Figure 15–36).

- The receptors act through **cAMP**. When stimulated by odorant binding, they activate an **olfactory-specific G protein** (known as G_{olf}), which in turn activates **adenylyl cyclase**. The resulting increase in cAMP opens cyclic-AMP-gated cation channels, thereby allowing an **influx of Na^+,** which **depolarizes** the olfactory receptor neuron and initiates a **nerve impulse** that travels along its axon to the brain.

- There are about **1000** different olfactory receptors in a mouse and about **350** in a human, each encoded by a different gene and each recognizing a different set of odorants.

- Each olfactory receptor neuron produces only one of these receptors; the neuron responds to a specific set of odorants by means of the specific receptor it displays, and each **odorant** activates its own characteristic set of olfactory receptor neurons.





Olfactory receptor neurons.

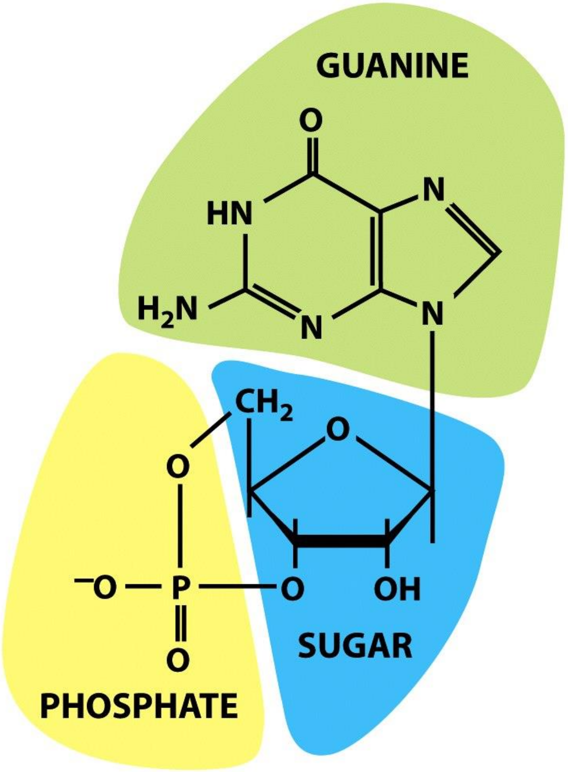
(A) A section of olfactory epithelium in the nose. Olfactory receptor neurons possess **modified cilia**, which project from the surface of the epithelium and contain the **olfactory receptors**, as well as the **signal transduction machinery**. The axon, which extends from the opposite end of the receptor neuron, conveys electrical signals to the brain when an odorant activates the cell to produce an action potential. In rodents, at least, the basal cells act as stem cells, producing new receptor neurons throughout life, to replace the neurons that die.

(B) A scanning electron micrograph of the cilia on the surface of an olfactory neuron.

Smell and Vision Depend on GPCRs That Regulate Ion Channels

Vertebrate vision employs a similarly elaborate, highly sensitive, signal-detection process. **Cyclic-nucleotide-gated ion channels** are also involved, but the crucial cyclic nucleotide is cyclic GMP rather than cAMP.

As with cAMP, a continuous rapid synthesis (by **guanylyl cyclase**) and rapid degradation (by **cyclic GMP phosphodiesterase**) controls the concentration of cyclic GMP in the cytosol.



Smell and Vision Depend on GPCRs That Regulate Ion Channels

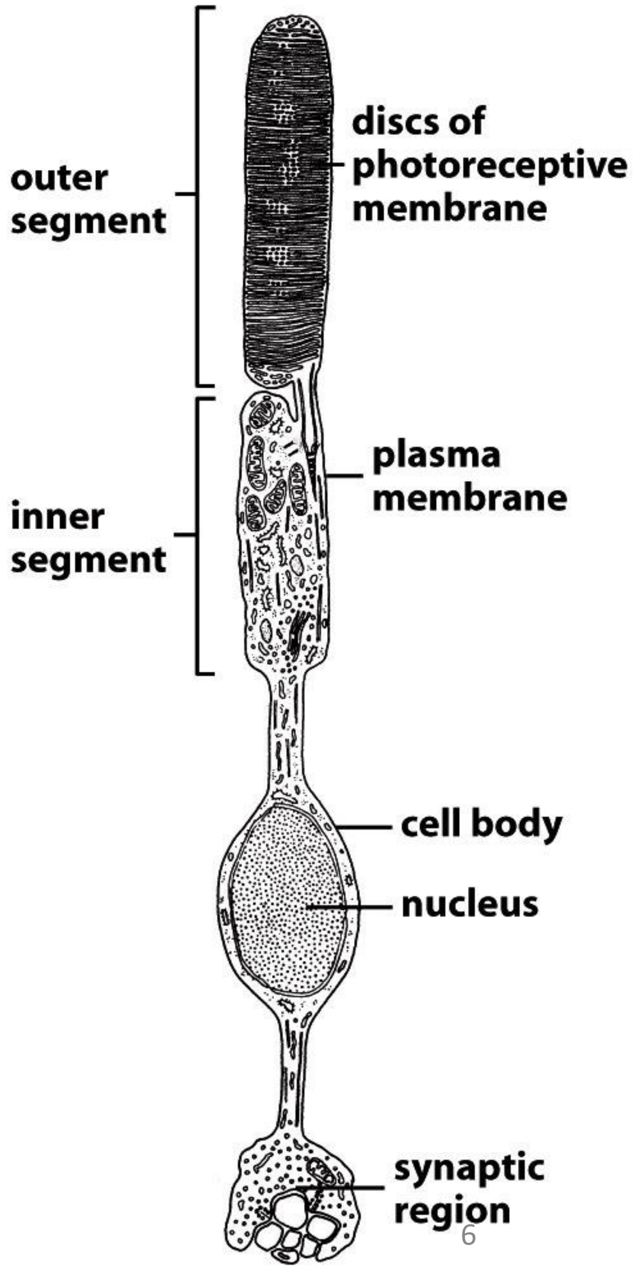
- In visual transduction responses, which are the **fastest G-protein-mediated responses** known in vertebrates, **the receptor activation stimulated by light causes a fall rather than a rise in the level of the cyclic nucleotide**.

- The pathway has been especially well studied in **rod photoreceptors (rods)** in the vertebrate retina.

- Rods are responsible for **noncolor vision in dim light**, whereas **cone photoreceptors (cones)** are responsible for **color vision in bright light**.

- A rod photoreceptor is a highly specialized cell with outer and inner segments, a cell body, and a synaptic region where the rod passes a chemical signal to a retinal nerve cell.

- This nerve cell relays the signal to another nerve cell in the retina, which in turn relays it to the brain.



Smell and Vision Depend on GPCRs That Regulate Ion Channels

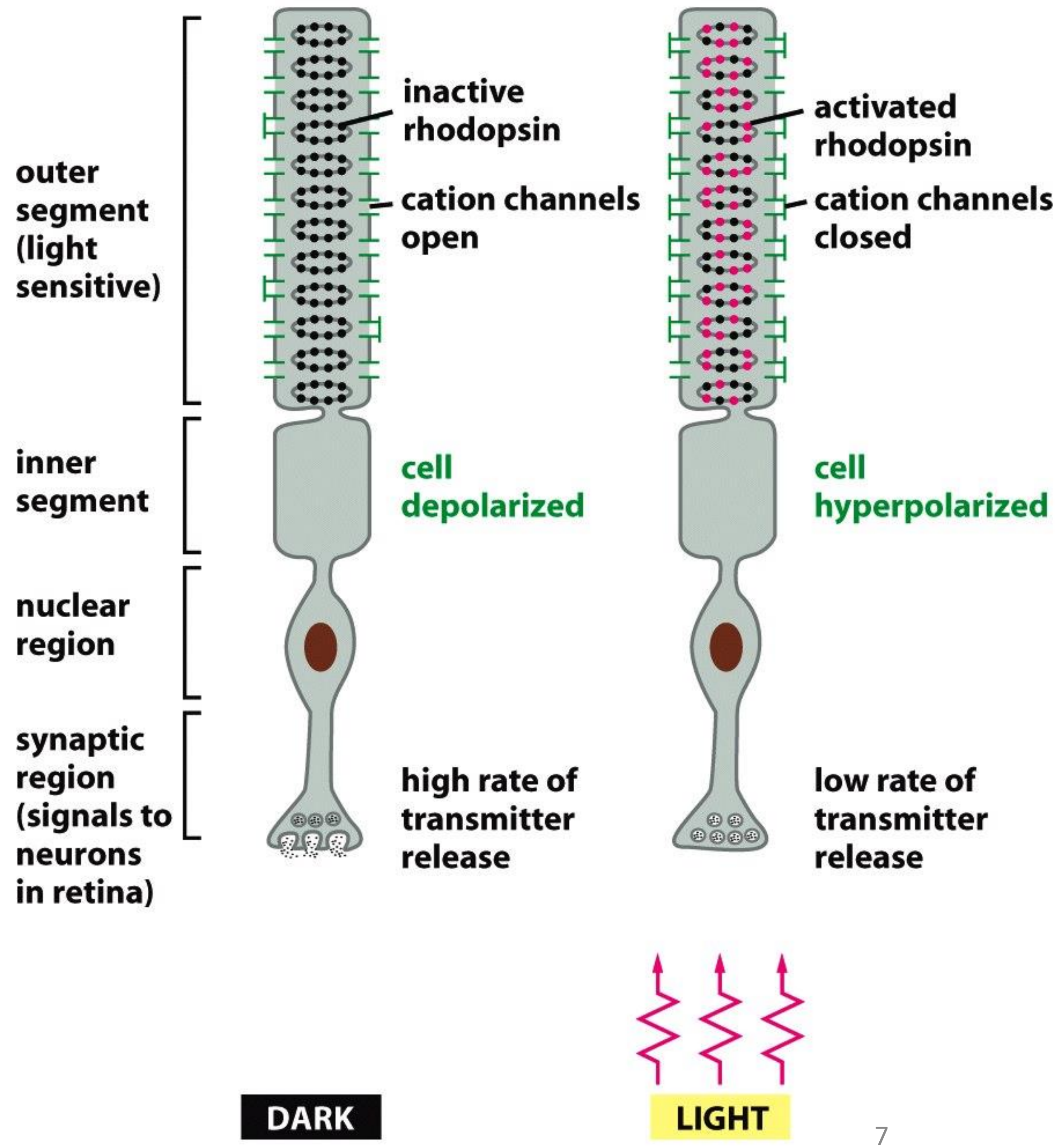
- The **phototransduction apparatus** is in the outer segment of the rod, which contains a stack of discs, each formed by a closed **sac of membrane** that is densely packed with **photosensitive rhodopsin molecules**.

- The plasma membrane surrounding the outer segment contains **cyclic-GMP-gated cation channels**.

- Cyclic GMP bound to these channels keeps them **open in the dark**.

- Paradoxically, light causes a **hyperpolarization** (which inhibits synaptic signaling) rather than a depolarization of the plasma membrane (which would stimulate synaptic signaling).

- Hyperpolarization (that is, the membrane potential moves to a **more negative** value) results because the light-induced activation of rhodopsin molecules in the disc membrane decreases the cyclic GMP concentration and closes the cation channels in the surrounding plasma membrane.



Smell and Vision Depend on GPCRs That Regulate Ion Channels

Rhodopsin is a member of the GPCR family, but the activating extracellular signal is not a molecule but a photon of light.

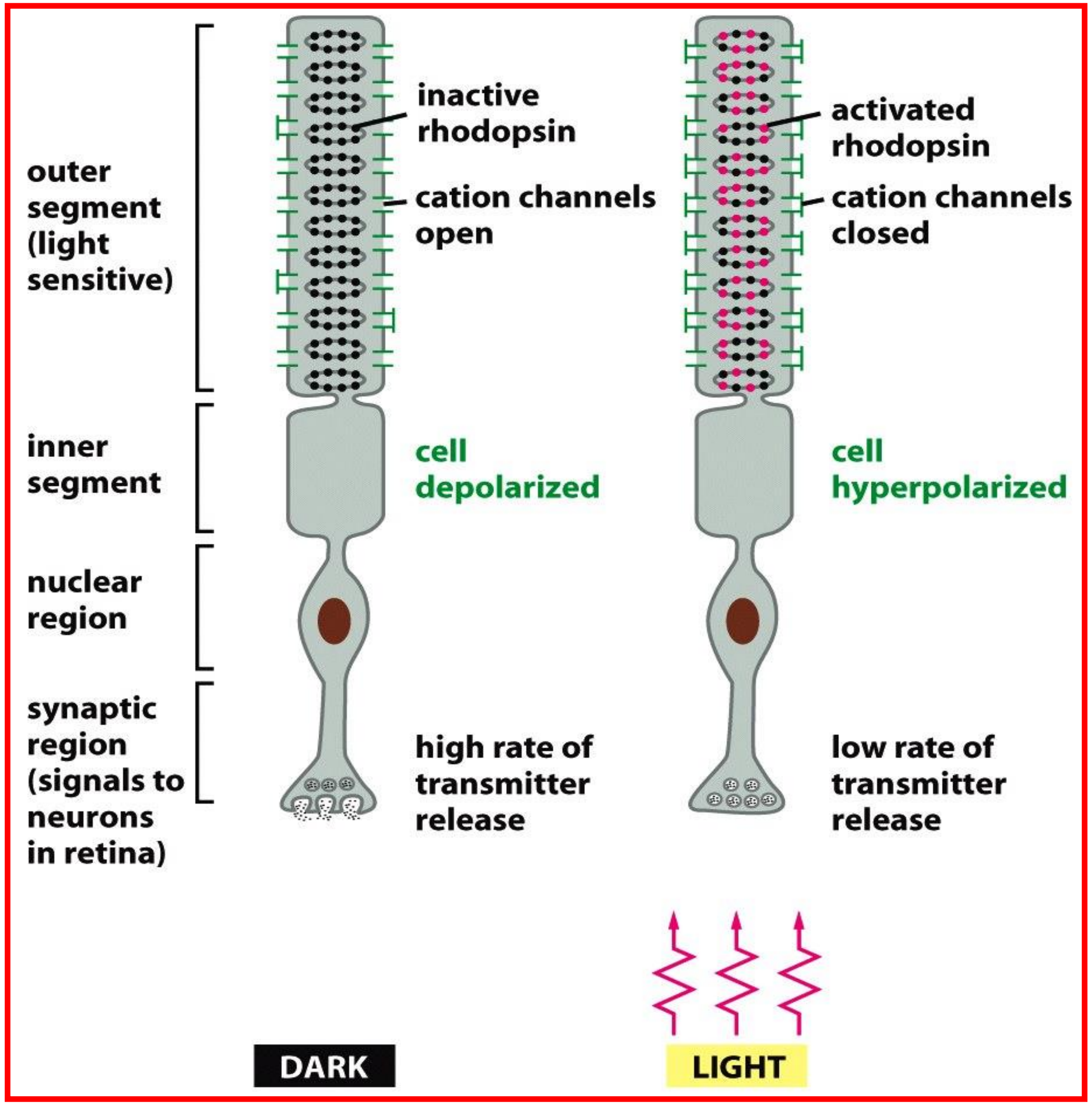
1. Each rhodopsin molecule contains a covalently attached chromophore, **11-cis retinal**, which isomerizes almost instantaneously to **all-trans retinal** when it absorbs a single photon. The isomerization alters the shape of the retinal, **forcing a conformational change in the protein (opsin)**.

2. The activated rhodopsin molecule then alters the conformation of the **G protein transducin (G_t),** causing the transducin α subunit to activate **cyclic GMP phosphodiesterase**.

3. The phosphodiesterase then hydrolyzes cyclic GMP, so that cyclic GMP levels in the cytosol fall.

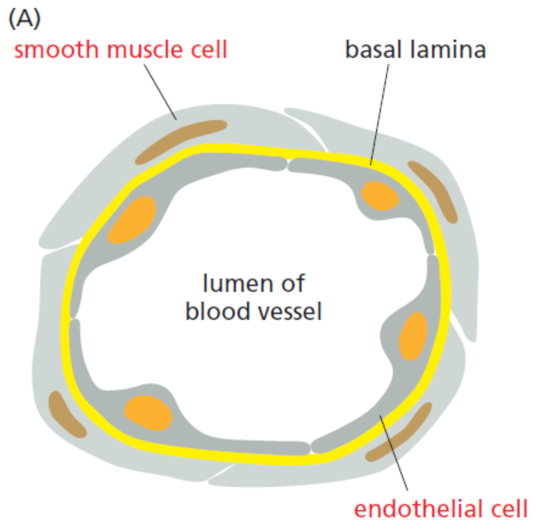
4. This drop in cyclic GMP concentration decreases the amount of cyclic GMP bound to the plasma membrane cation channels, allowing more of these cyclic-GMP-sensitive channels to close.

In this way, the signal quickly passes from the disc membrane to the plasma membrane, and a light signal is converted into an electrical one, through a hyperpolarization of the rod cell plasma membrane.



Nitric Oxide Is a Gaseous Signaling Mediator That Passes Between Cells

- Signaling molecules like **cyclic nucleotides** and **calcium** are hydrophilic small molecules that generally act within the cell where they are produced.
- Some signaling molecules, however, are hydrophobic enough, small enough, or both, to pass readily across the plasma membrane and carry signals to nearby cells like gas **nitric oxide (NO)**, which acts as a signal molecule in many tissues of both animals and plants.

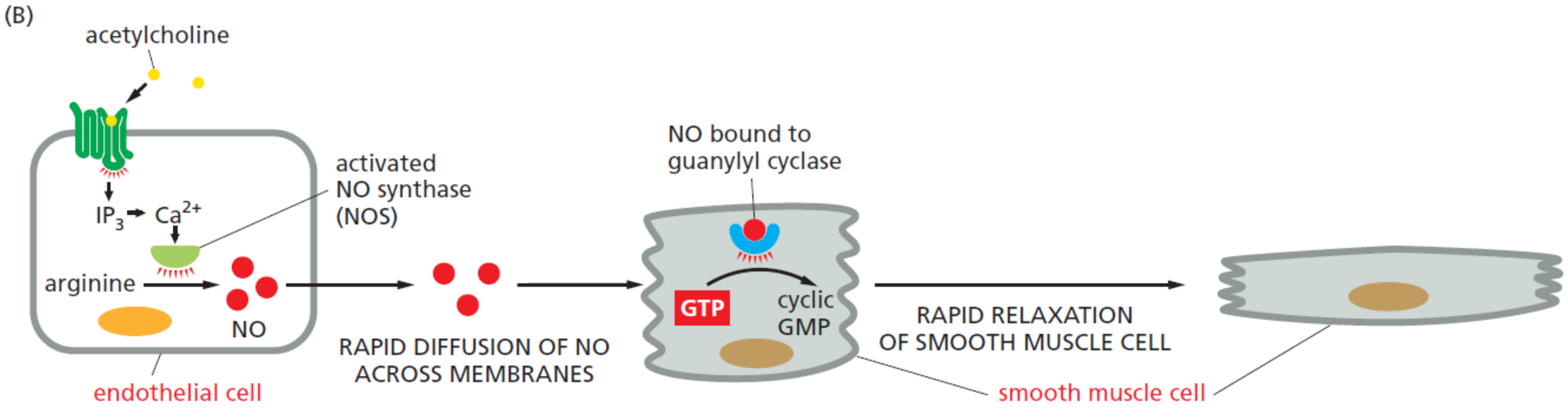


In mammals, one of NO's many functions is to **relax smooth muscle in the walls of blood vessels**:

1.The neurotransmitter **acetylcholine** stimulates NO synthesis by activating a GPCR on the membranes of the endothelial cells that line the interior of the vessel.

2.The activated receptor triggers IP3 synthesis and Ca2+ release, leading to stimulation of an **enzyme that synthesizes NO**.

3.Because dissolved NO passes readily across membranes, it diffuses out of the cell where it is produced and into **neighboring smooth muscle cells**, where it causes muscle relaxation and thereby vessel dilation.



Nitric Oxide Is a Gaseous Signaling Mediator That Passes Between Cells

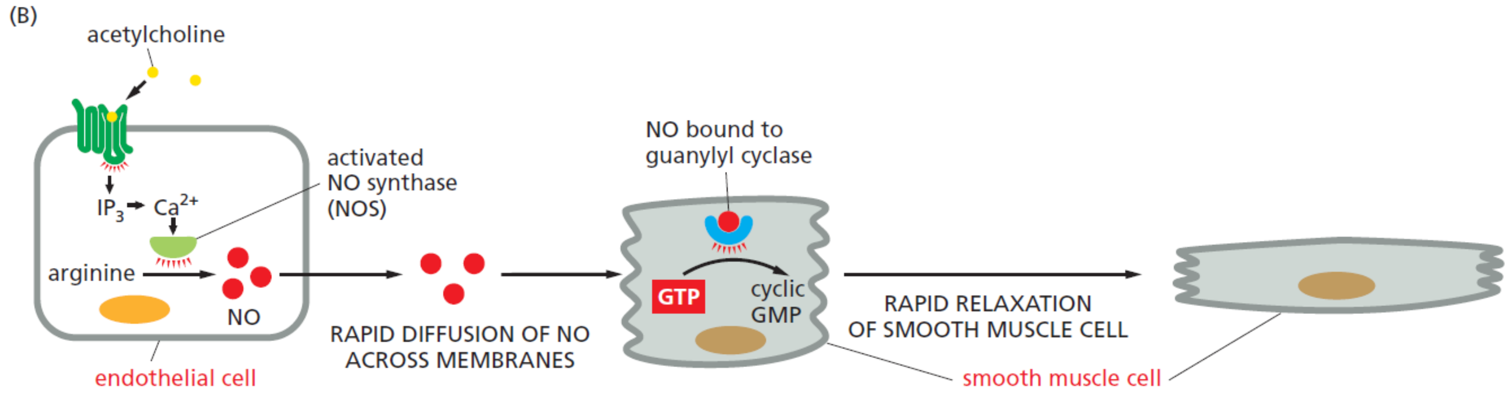
- It acts only locally because it has a ***short half-life***—about 5–10 seconds—in the extracellular space before oxygen and water convert it to nitrates and nitrites.
- The effect of NO on blood vessels provides an explanation for the mechanism of action of **nitroglycerine**, which has been used for about 100 years to treat patients with angina (pain resulting from inadequate blood flow to the heart muscle).
The nitroglycerine is converted to NO, which relaxes blood vessels.

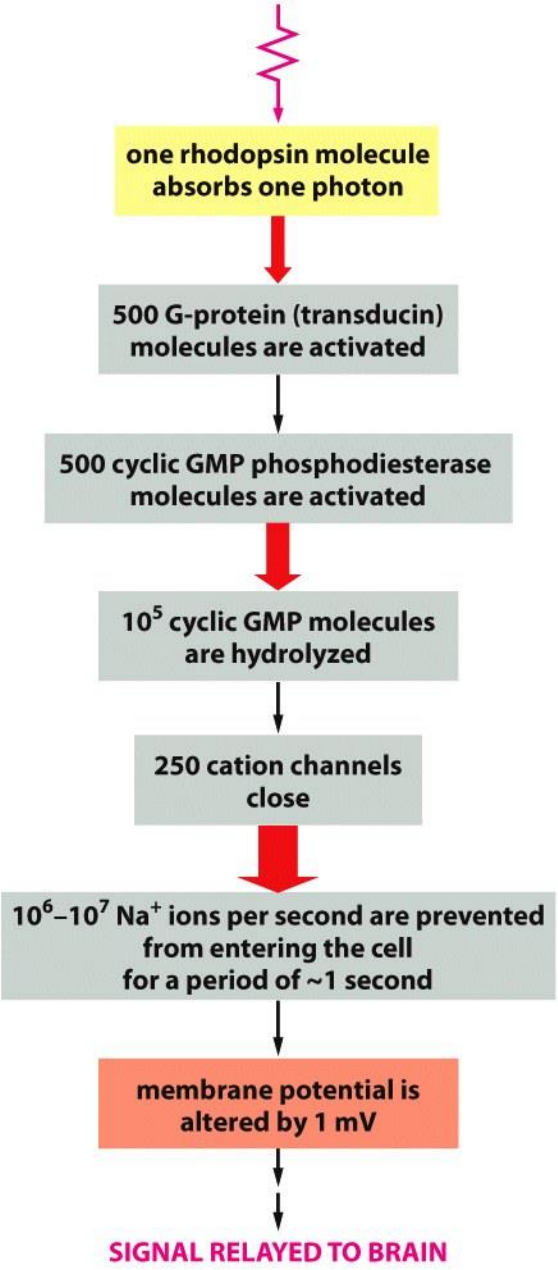
This reduces the workload on the heart and, as a consequence, reduces the oxygen requirement of the heart muscle.

- NO is made **by the deamination of the amino acid arginine, catalyzed by enzymes called NO synthases (NOS)** .

- In some target cells, including smooth muscle cells, NO binds reversibly to **iron in the active site of guanylyl cyclase**, stimulating synthesis of cyclic GMP.
- NO can increase cyclic GMP in the cytosol within seconds, because the normal rate of turnover of cyclic GMP is high: rapid degradation to GMP by a phosphodiesterase constantly balances the production of cyclic GMP by guanylyl cyclase.
- The **cyclic GMP triggers** a response that causes the smooth muscle cells to relax, increasing blood flow through the vessel

- NO can also signal cells independently of cyclic GMP. It can, for example, alter the activity of an intracellular protein by covalently nitrosylating thiol (–SH) groups on specific cysteines in the protein.





آبشارهای پیام‌رسانی درون‌سلولی، می‌توانند با سرعت، حساسیت و سازش‌پذیری حیرت‌آوری عمل کنند

همچنان که پیام از این مسیر رله می‌شود، مکرراً تشدید می‌گردد (شکل ۲۹-۱۶). با ضعیف‌تر شدن شرایط نوری (نظیر شب بدون ماه)، مقدار تشدید به‌شدت افزایش می‌یابد و حتی چند فوتون هم که جذب شبکیه شوند، می‌توانند سبب بروز یک پیام ارسالی به مغز شوند. اما در نور خورشید، وقتی که هر سلول گیرنده‌ی نوری در هر ثانیه در معرض میلیاردها فوتون قرار می‌گیرد، آبشار پیام‌رسانی سازش می‌یابد و میزان تشدید بیش از ده

هزار برابر کاهش می‌یابد، به‌گونه‌ای که سلول‌های گیرنده‌ی نوری اشباع نمی‌شود و باز هم می‌توانند کاهش یا افزایش نور را ثبت کنند. سازش‌پذیری به پس‌خورد منفی بستگی دارد، به‌طوری‌که پاسخ قوی در یک سلول گیرنده‌ی نوری، یک پیام درون‌سلولی (تغییر غلظت Ca^{2+}) تولید می‌کند و این پیام از فعالیت آنزیم‌های مسئول تشدید پیام جلوگیری می‌نماید.

در مسیرهای پیام‌رسانی که به پیام‌های شیمیایی پاسخ می‌دهند، نیز سازش‌پذیری وجود دارد و این امر سلول را قادر می‌سازد که نسبت به تغییرات شدید پیام در مقابل گستره‌ی وسیعی از تحریکات زمینه، حساس باقی بماند. به‌عبارت دیگر، سازش‌پذیری سبب می‌شود که سلول هم نسبت به پیام‌های ضعیف و هم نسبت به پیام‌های قوی پاسخ دهد.