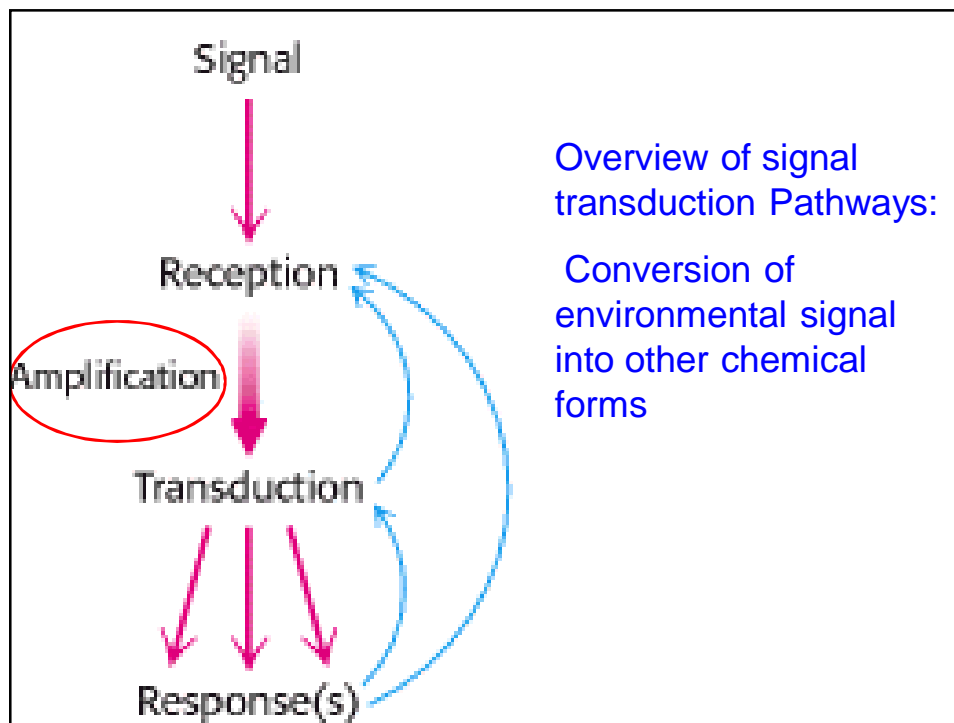


Transduction of hormone signal

Detection, amplification of external signals
and generation of cellular response

Stryer, Biochemistry Ch 15. pubmed.

<http://www.ncbi.nlm.nih.gov>



Membrane associated receptor transfers the information

- Most signals are polar and large
- Few of the signals are nonpolar
- Receptors are intrinsic membrane proteins
- Extracellular and intracellular domains
- Interaction of the signal with the extracellular domain → structural changes with transmission to intracellular domain

Second messengers relay information

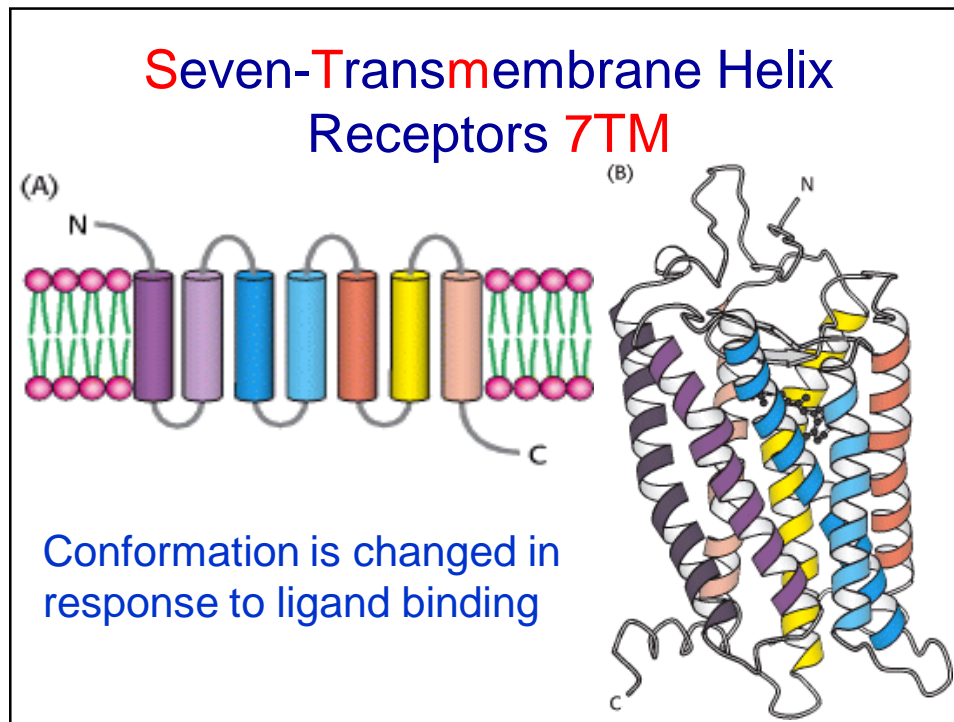
- Ability to diffuse to other cellular compartments
- Amplification of the signal
 - Enzyme activation
 - Membrane channels
- Some second messengers are common in multiple signaling pathways
Permits fine tuning but can pose problems

Protein phosphorylation is a common means of information transfer

- Many second messengers elicit responses by activating protein kinases
- Phosphorylation of proteins results in conformation changes
- Last longer than changes in concentrations of second messengers
- Reversible

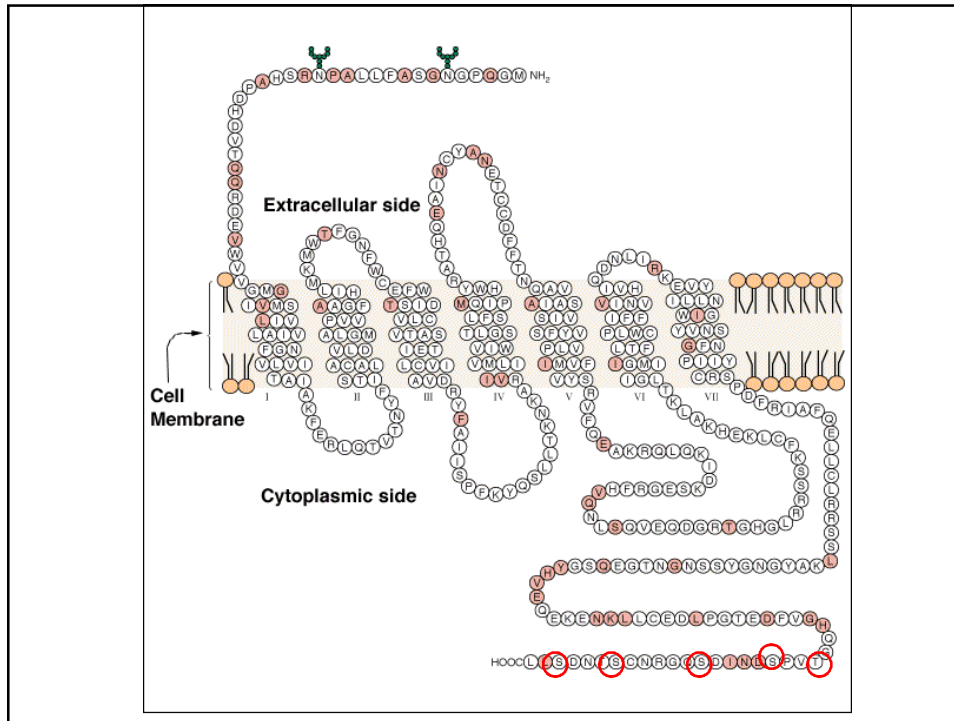
Termination of the signal.

- Keeps cells responsive to new signals
- Failure of termination may cause problems (uncontrolled cell growth....
 - Degradation of the second messenger
 - Dephosphorylation by hydrolysis



Biological Functions Mediated by 7TM

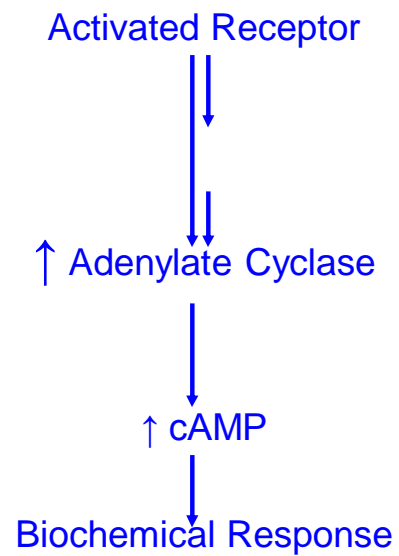
- Smell, Taste, Vision
- Neurotransmission
- Hormone Secretion
- Chemotaxis
- Exocytosis
- Cell Growth, Development
- Viral Infection



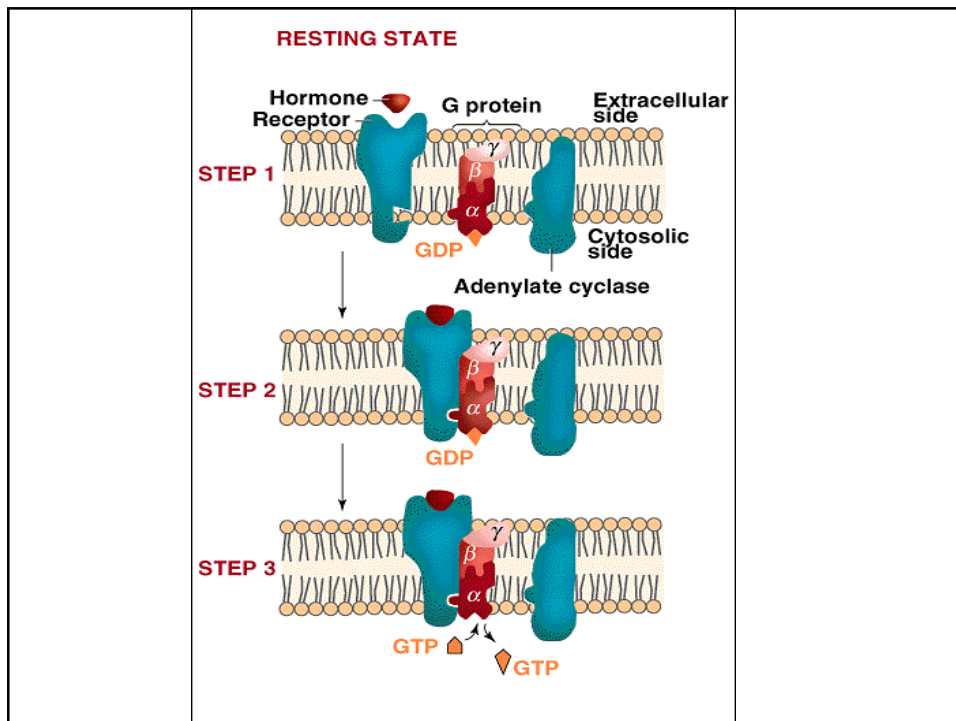
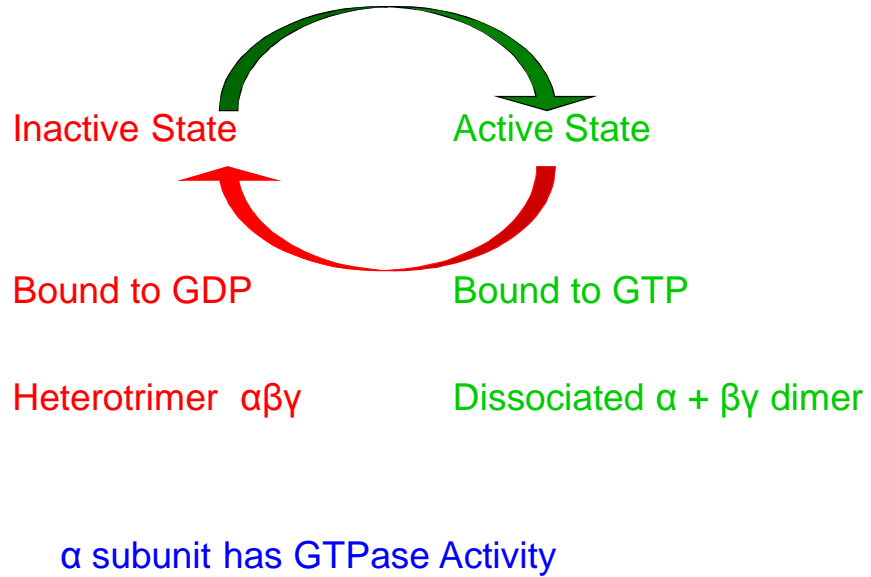
cAMP and G Proteins

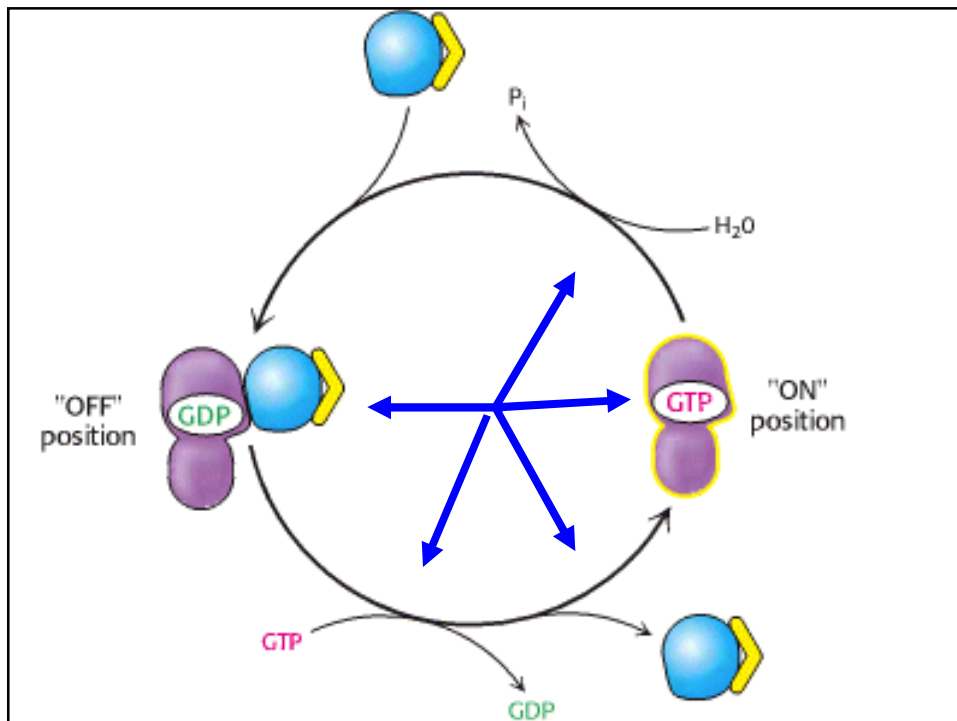
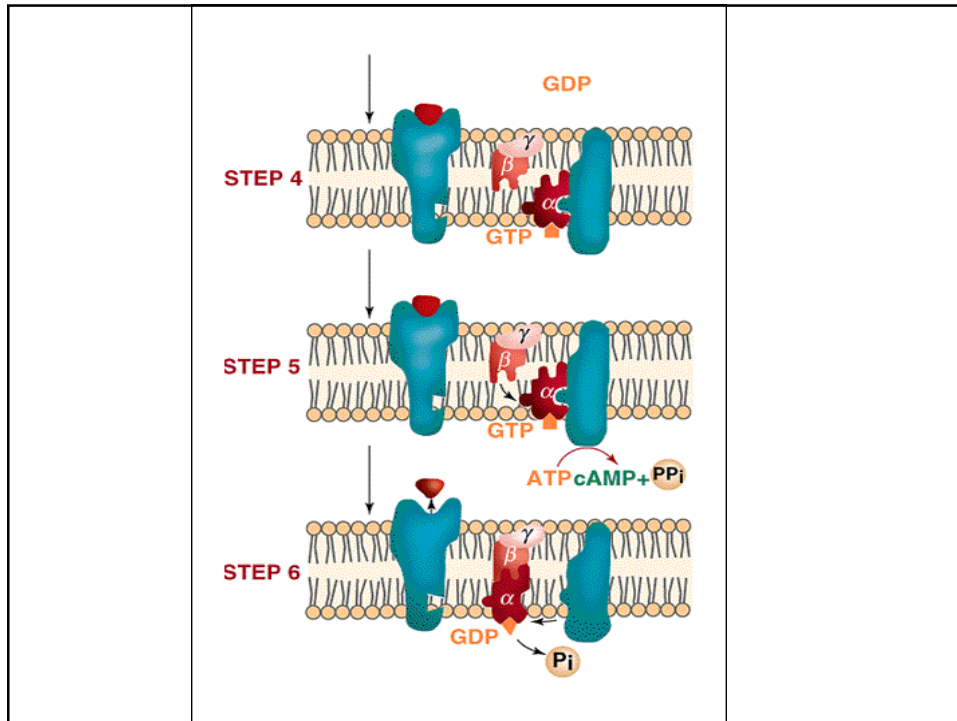
- GTP is essential for responding to Hormones
- Hormone Binding stimulates GTP hydrolysis

↓
Discovery of
G Protein



G Protein cycles between two forms





G Proteins (cont.)

- α and γ Subunits have covalently attached fatty acid
- α and $\beta\gamma$ can interact with other proteins
- Many G Protein molecules can be activated by one signal-bound receptor.
- All 7TM receptors appear to be coupled to G proteins **GPCRs**
- Many different G protein exist.

G Proteins transduce many activities

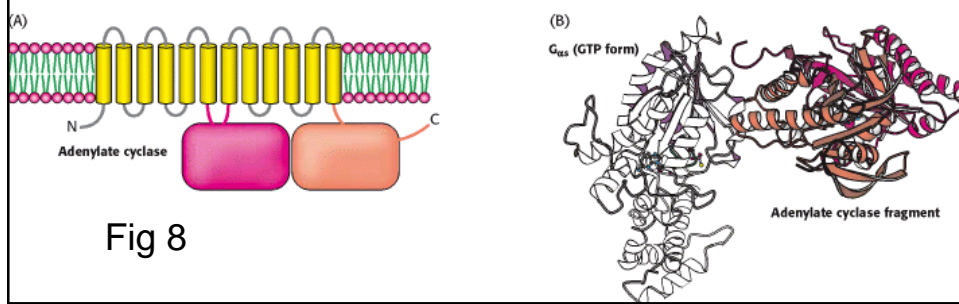
G_s	↑ Adenylate Cyclase
G_{olf}	↑ Adenylate Cyclase
Transducin	↑ cGMP Phosphodiesterase
G_i	↓ Adenylate Cyclase
G_o	Ca^{2+} Channels
G_q	↑ Phospholipase C

Adenylate Cyclase

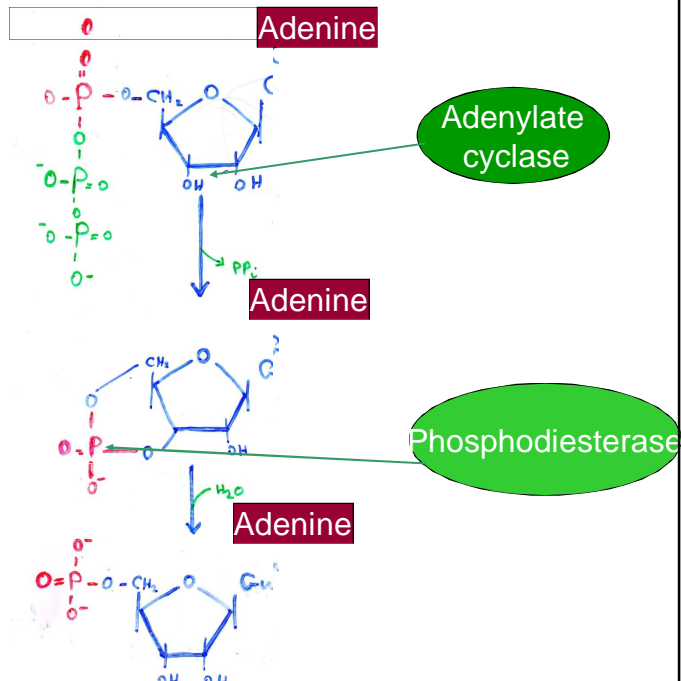
Membrane protein

12 helices

Two large intracellular domains

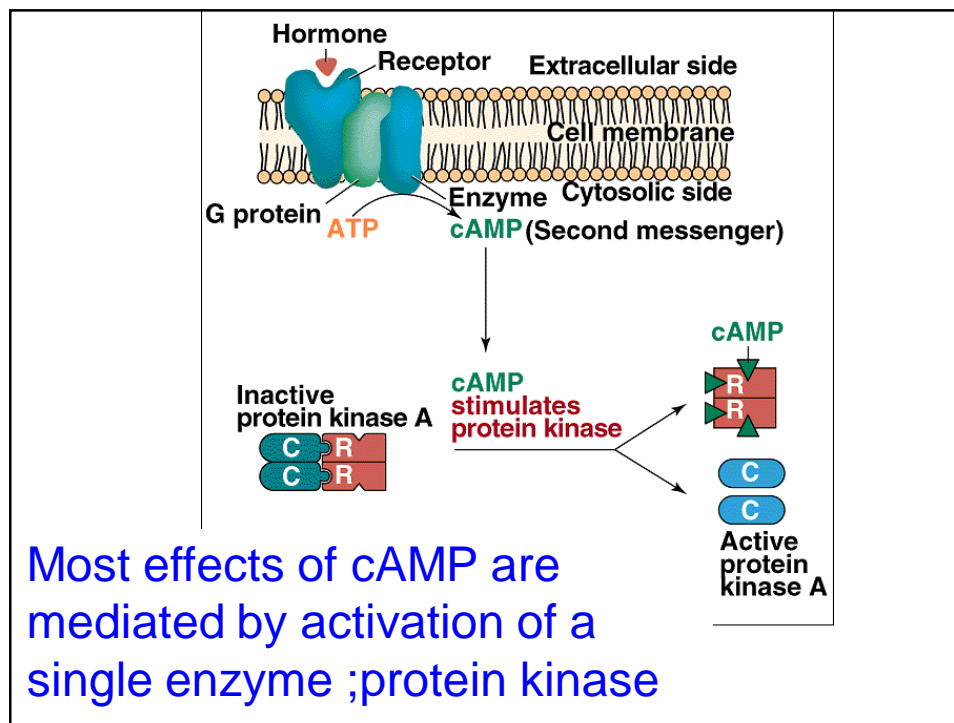


Synthesis and degradation of cAMP



cAMP can affect a wide range of cellular processes

- ↑ degradation of storage fuels
- ↑ secretion of acid by gastric mucosa
- Dispersion of melanin pigment granules
- ↓ aggregation of blood platelets.
- Opening of chloride channels



cAMP can affect gene expression

- Phosphorylation of a transcriptional factor
- cAMP Response Element Binding Protein (CREB)
- Phosphorylated CREB moves to nucleus and binds to a DNA region called CRE

Switching off the signal initiated by hormone binding to 7TM

- Dissociation of the hormone
- Phosphorylation of the hormone bound-receptor followed by binding to arrestin
- GTPase activity of G α subunit
- Hydrolysis of cAMP

