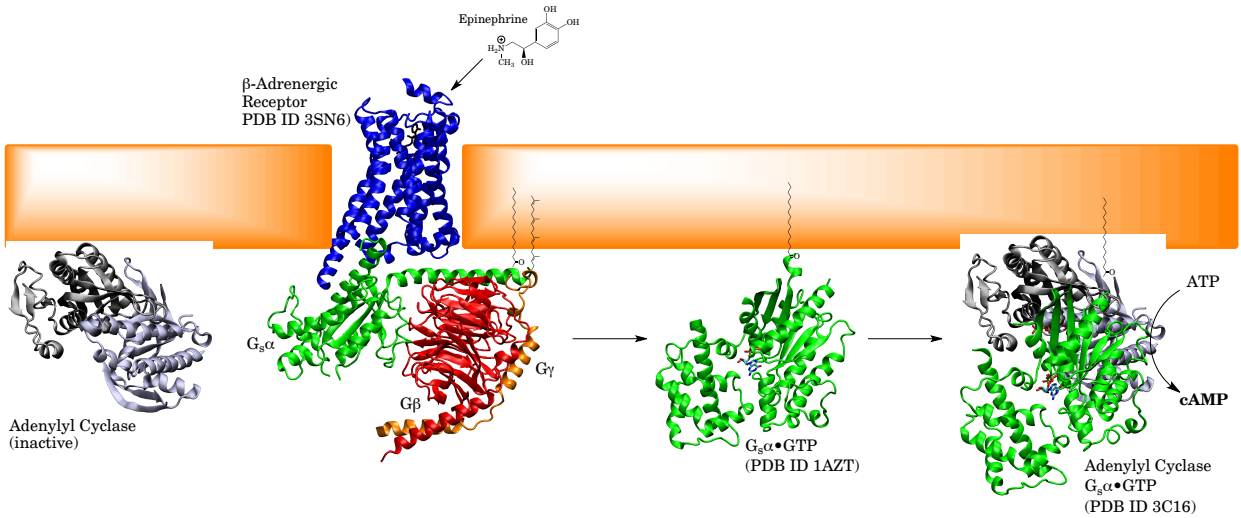
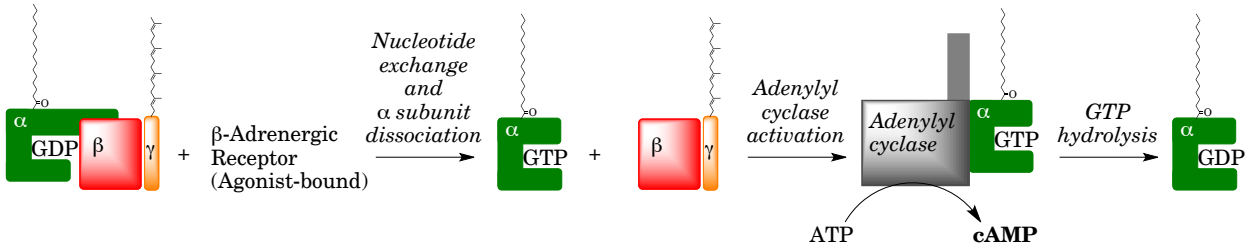
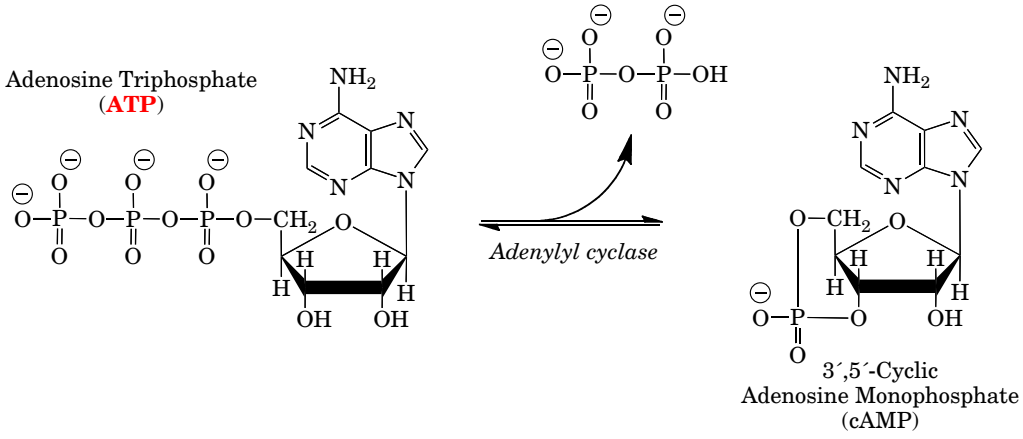
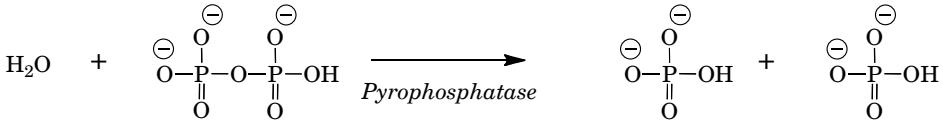
G-Protein Coupled Receptors (GPCR, 7-TM)









G proteins

Heterotrimeric G Proteins

$G\alpha$

$G\beta$

$G\gamma$

G_s

G_{olf}

G_i

G_t

G_q

G_{13}

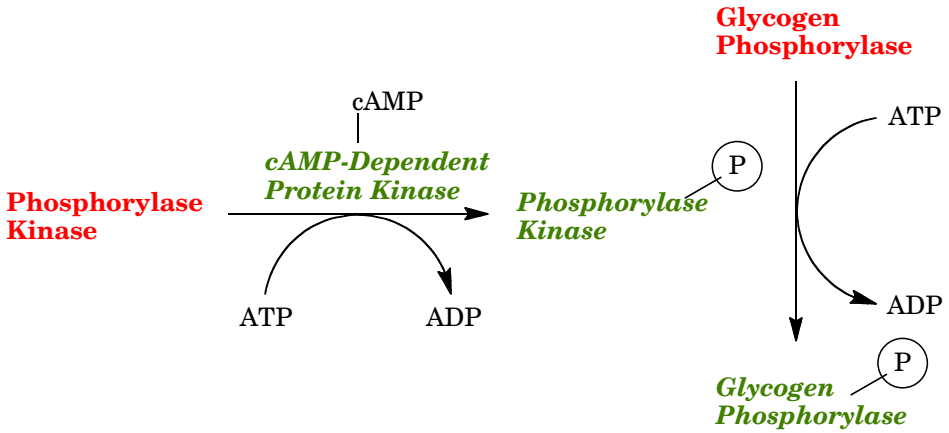
Monomeric G proteins

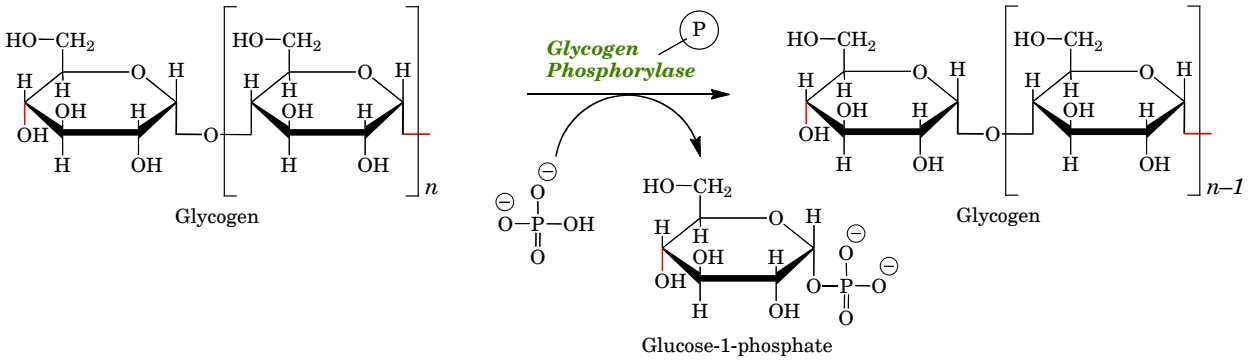
GAP

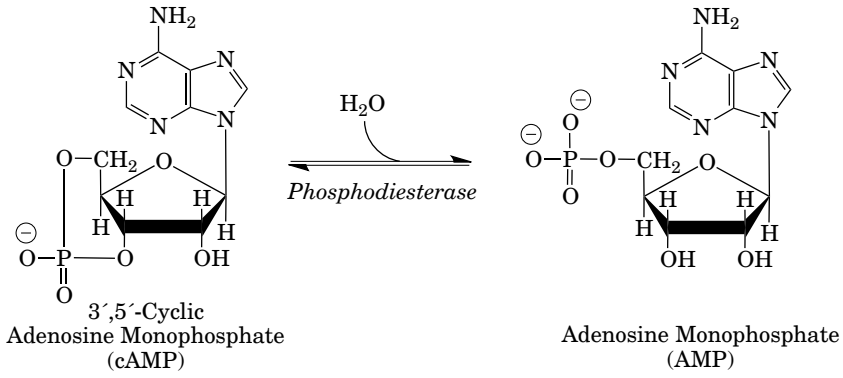
GEF

GDI

Signaling Pathway Example



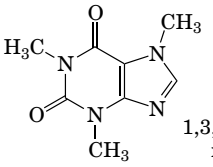




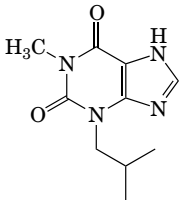
3′,5′-Cyclic Adenosine Monophosphate (cAMP)

Adenosine Monophosphate (AMP)

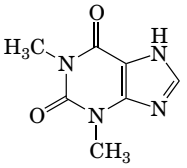
Studying cAMP-based processes



1,3,7-trimethyl xanthine

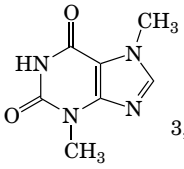


3-Isobutyl-1-methyl xanthine (IBMX)



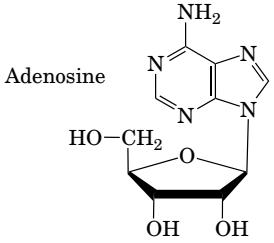
Theophylline

1,3-dimethyl xanthine

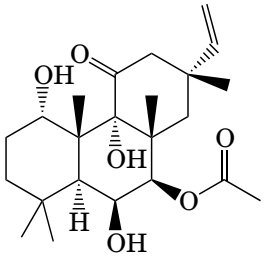


Theobromine

3,7-dimethyl xanthine

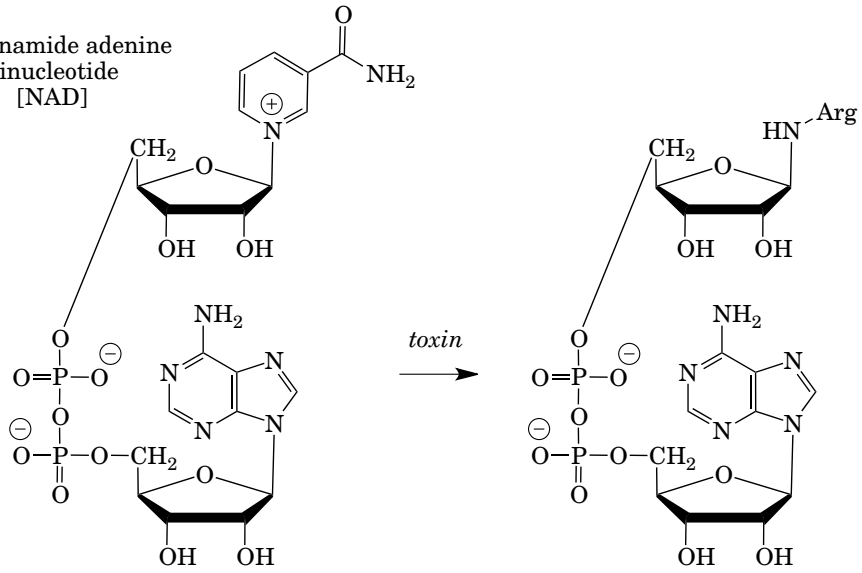


Adenosine



Forskolin

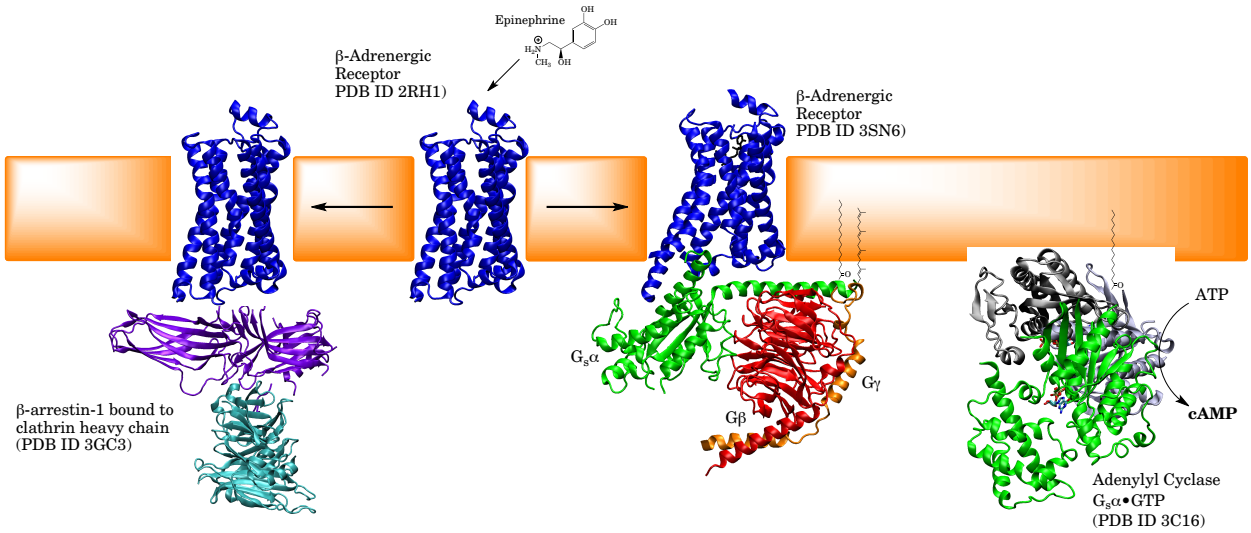
Nicotinamide adenine dinucleotide [NAD]

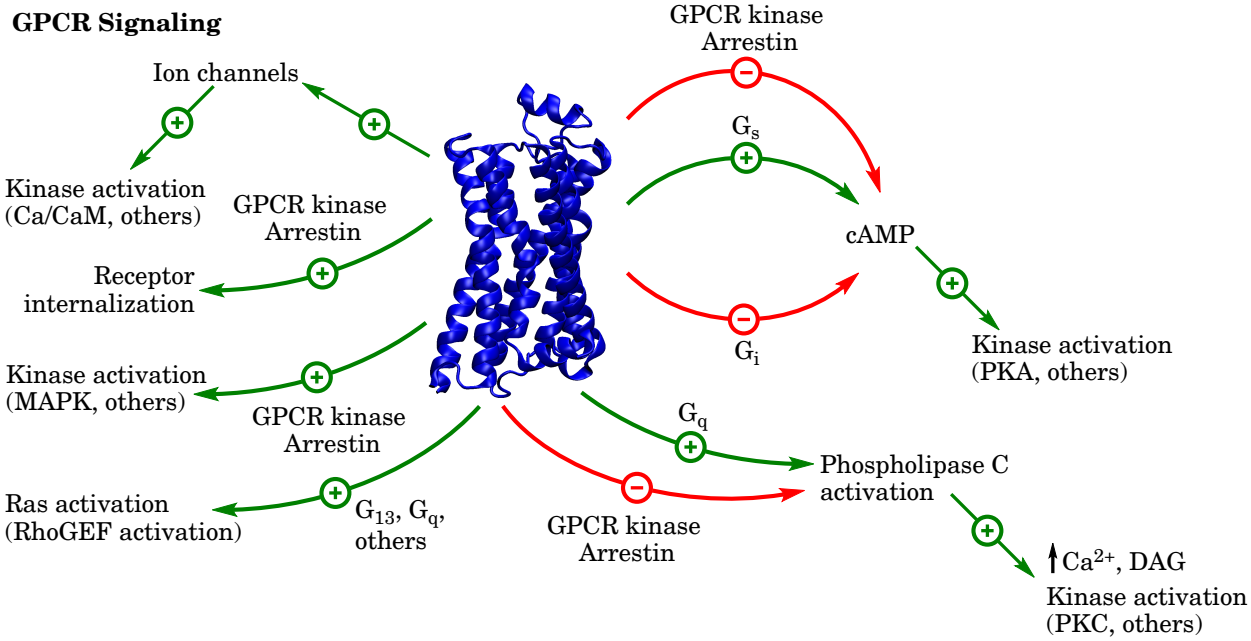


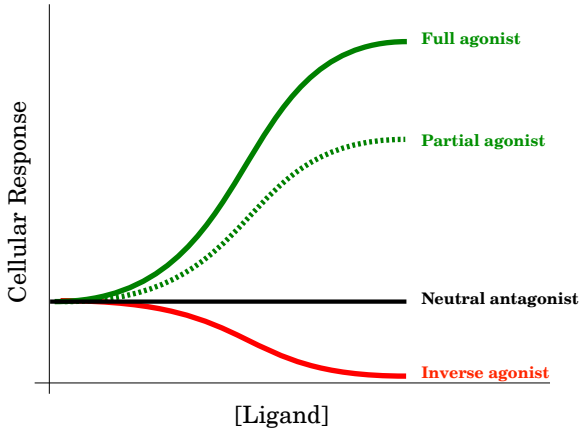
Cholera toxin (*Vibrio cholerae*)

Pertussis toxin (*Bordetella pertussis*)

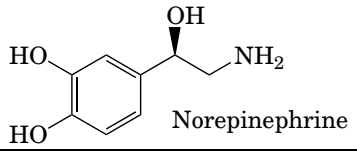
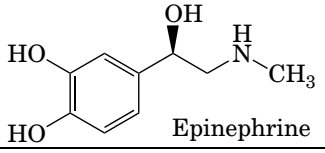
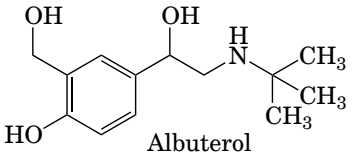
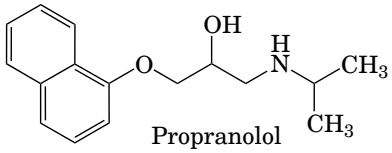
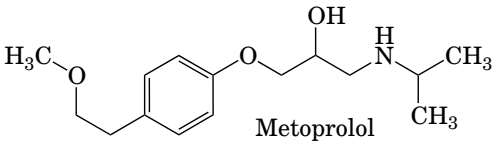
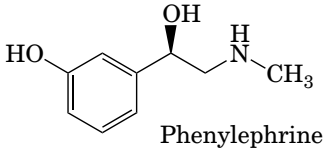
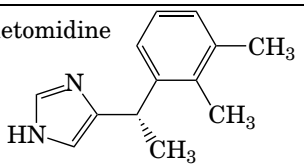
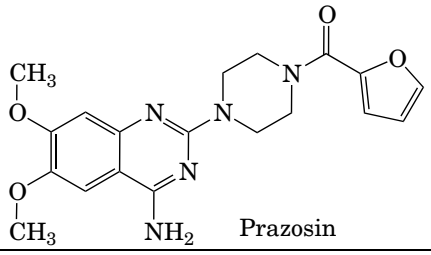
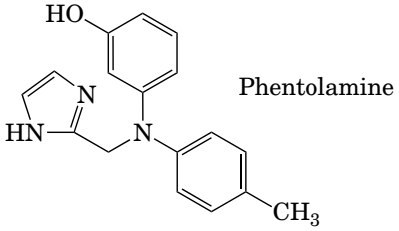
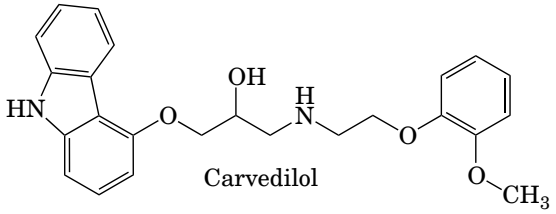
G-Protein Coupled Receptor Signaling







Selected Adrenergic Receptor Ligands

 Norepinephrine	 Epinephrine
β_2-agonist Bronchodilator, smooth muscle relaxant (especially uterus)	 Albuterol
β-antagonist (non-selective) Anti-hypertensive, anti-anxiety	 Propranolol
β_1-antagonist Anti-hypertensive	 Metoprolol
α_1-agonist Decongestant	 Phenylephrine
α_2-agonist Sedative, hypotensive	Dexmedetomidine 
α_1-antagonist Hypotensive – vasodilator in peripheral tissues	 Prazosin
α-antagonist (non-selective) Vasodilator	 Phentolamine
β-agonist/antagonist (agonist via arrestin pathway only) Anti-hypertensive	 Carvedilol

Classification of G-protein coupled receptors

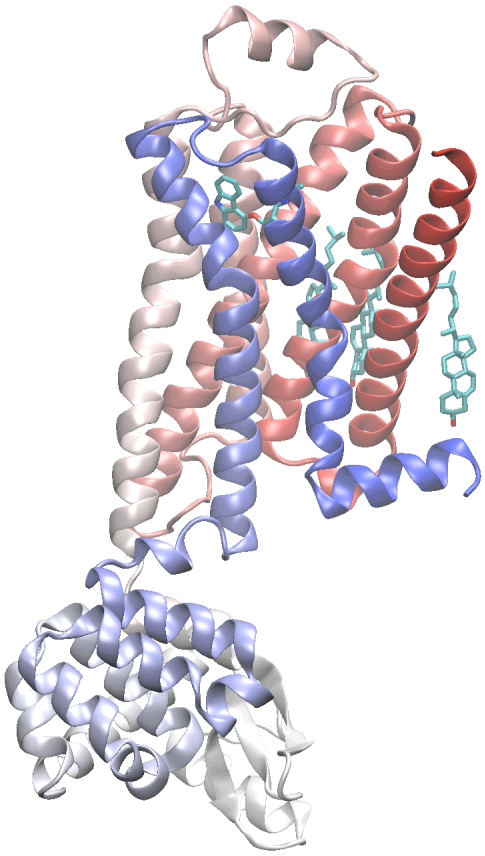
GRAFS
Glutamate (Class C)

Rhodopsin (Class A)

Adhesion (Class B)

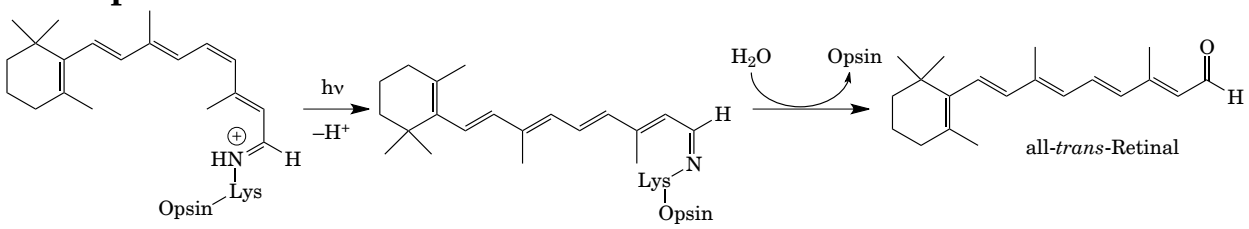
Frizzled/Taste2

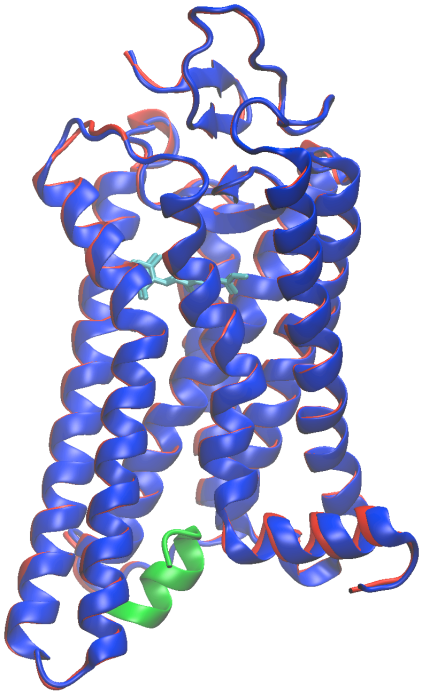
Secretin (Class B)



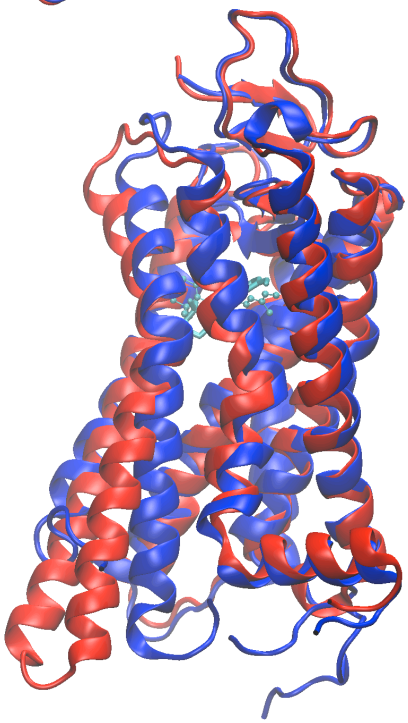
β-adrenergic receptor (pdb ID 2RH1)

Rhodopsin



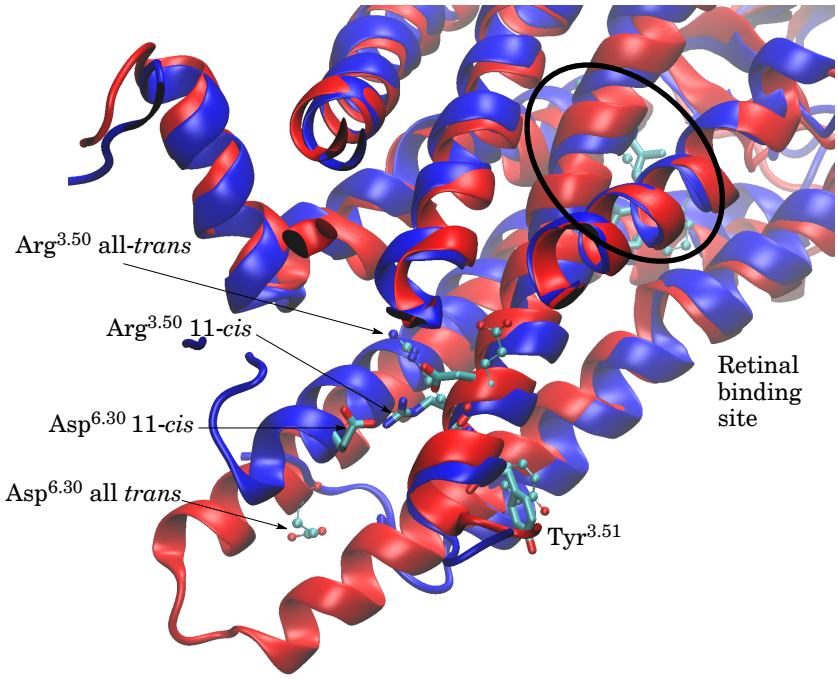


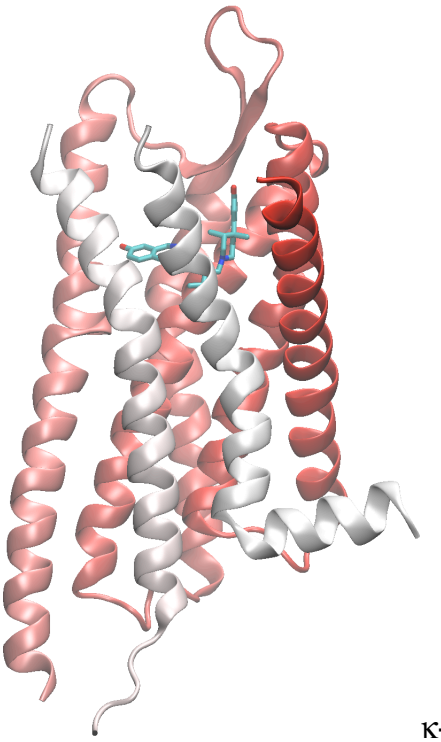
all-*trans*-retinal bound rhodopsin (pdb ID 3PQR with and 3PXO without G-protein peptide)



red 3PXO
blue 1F88

Conformational Changes





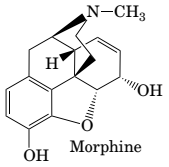
κ-opioid receptor (pdb ID 4DJH)

Opioid Receptors

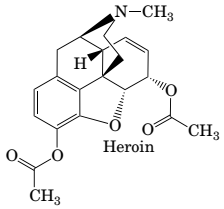
μ receptor

Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe-Lys-Asn-Ala-Ile-Ile-Lys-Asn-Ala-Tyr-Lys-Lys-Gly-Glu

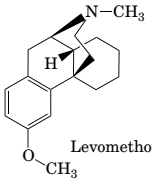
β-endorphin



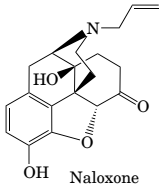
Morphine



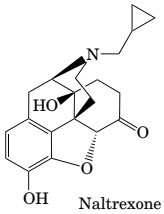
Heroin



Levomethorphan



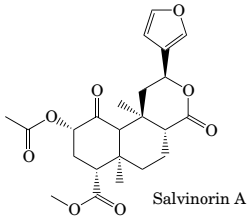
Naloxone



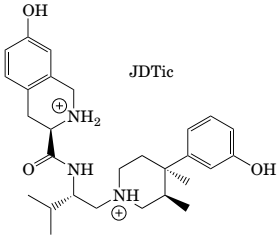
Naltrexone

κ receptor

Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Ile-Arg-Pro-Lys-Leu-Lys Dynorphin A



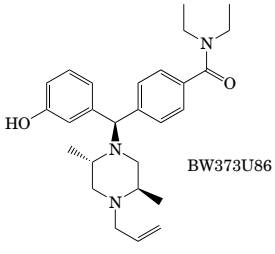
Salvinorin A



JDTic

δ receptor

Tyr-Gly-Gly-Phe-Met (Met-enkephalin) Tyr-Gly-Gly-Phe-Leu (Leu-enkephalin)



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