Advanced Cell Biology. Lecture 35

Alexey Shipunov

Minot State University

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Outline

Questions and answers

Cell communication

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Cell communication

Previous final question: the answer

How dynamite relates to Viagra?

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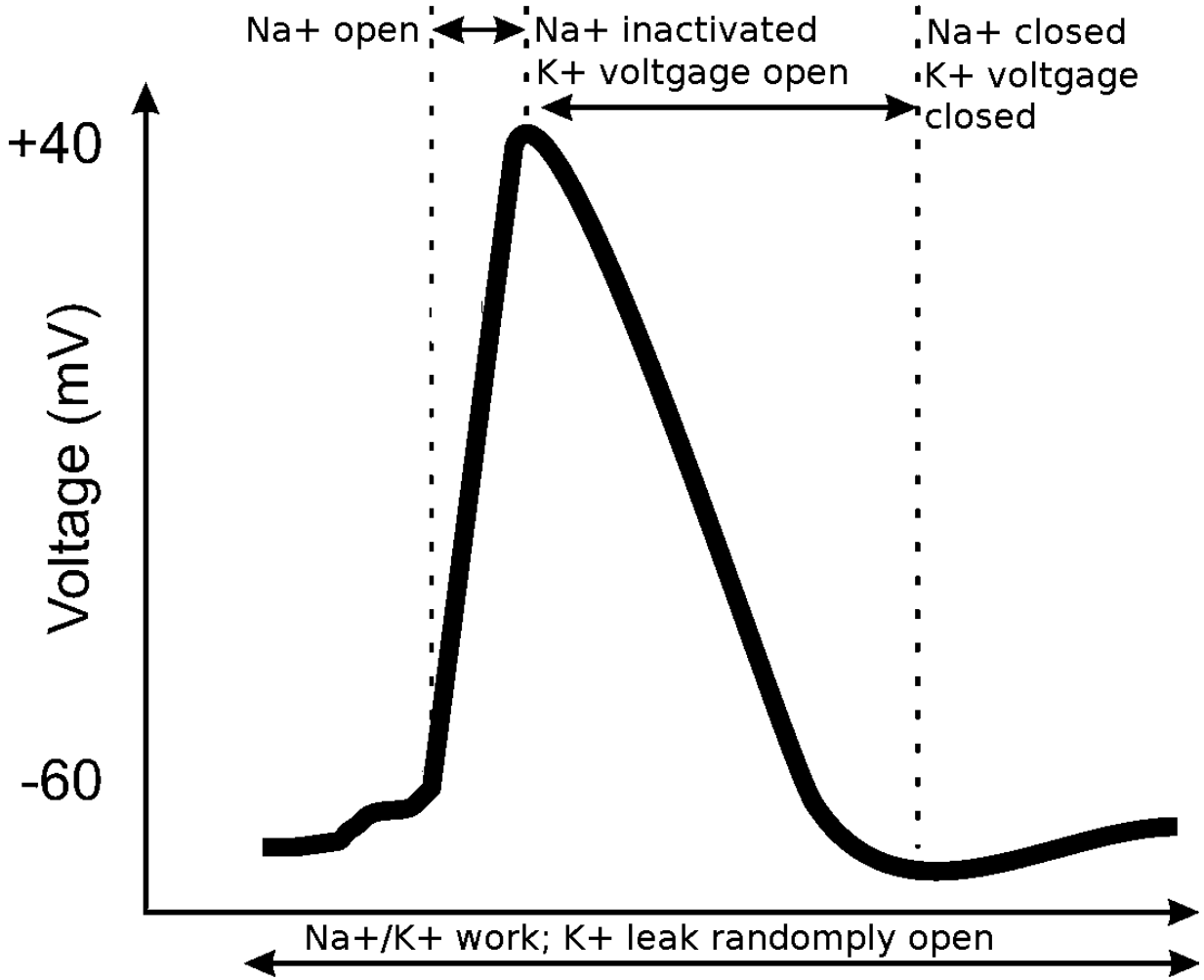
How dynamite relates to Viagra?

- Dynamite contains nitroglycerin, nitroglycerin releases nitric oxide, nitric oxide facilitates cyclic GMP synthesis
- Viagra also facilitates cyclic GMP synthesis

Action potential



Molecular switches

- Many ISPs have active and inactive states
- The switch between forms is due to phosphorylation of GTP binding
- Kinases (serine/threonine or tyrosine) attach phosphate, phosphatases detatch phosphate

Molecular switches

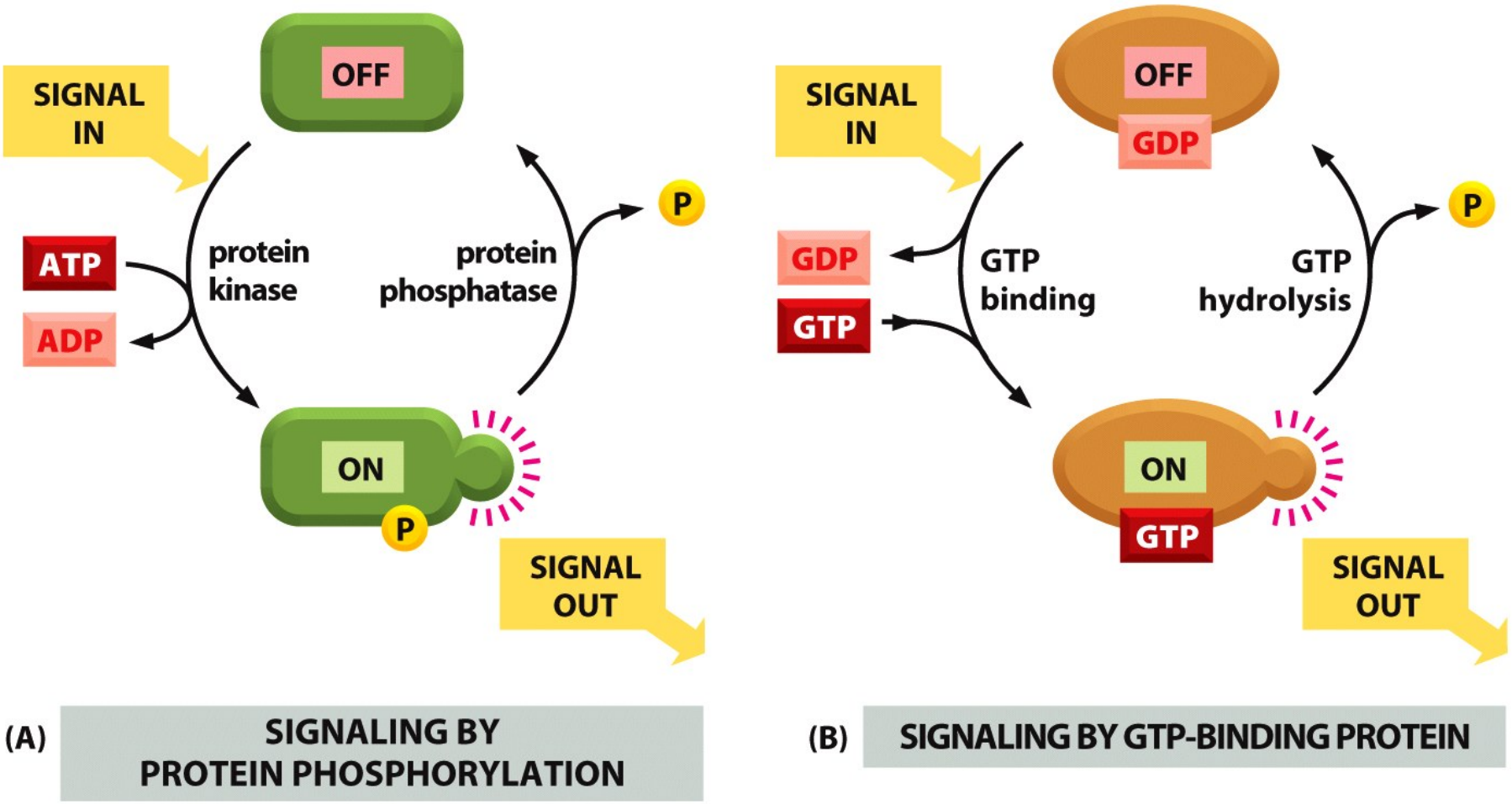


Figure 16-14 Essential Cell Biology 3/e (© Garland Science 2010)

Three classes of receptors

- Ion-channel-coupled receptors = ligand-gated channels: curare
- G-protein-coupled receptors (GPCR) have a mediator membrane protein, G-protein: morphine
- Enzyme-coupled receptors are proteins with enzymatic or enzyme-binding activity: many hormones

Ion-channel-coupled receptors

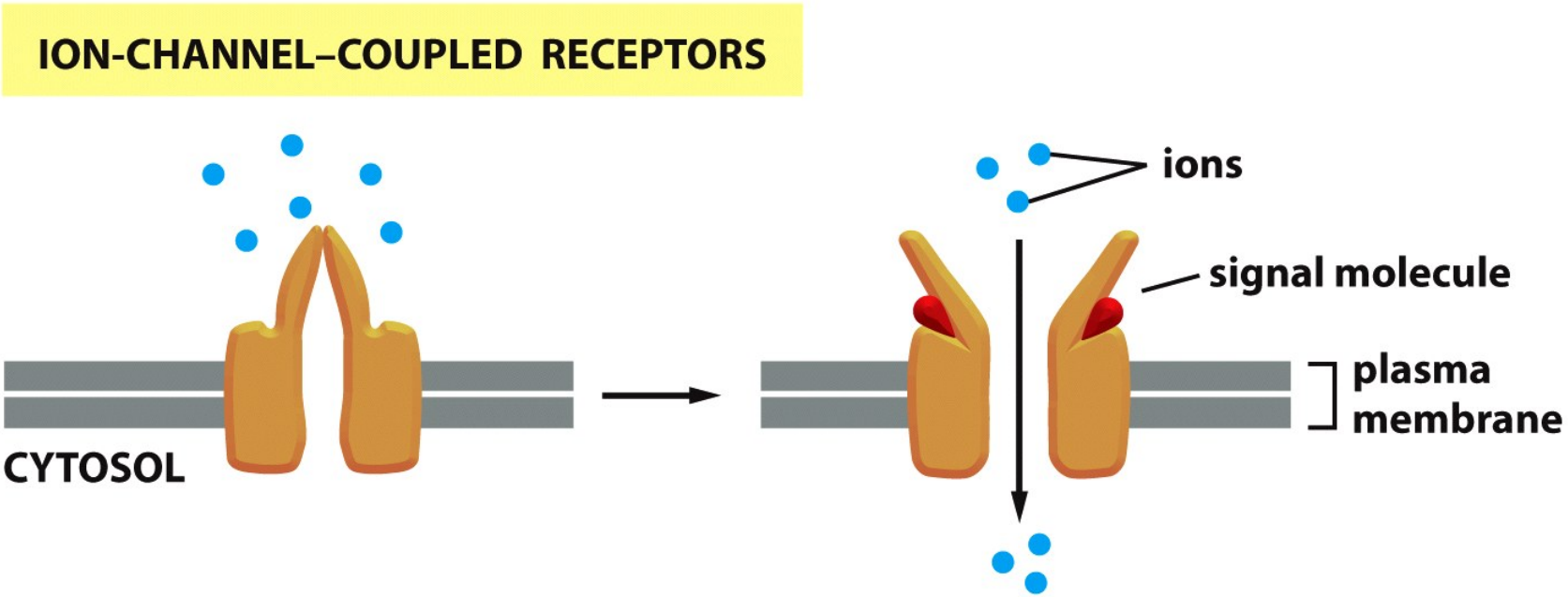


Figure 16-15a Essential Cell Biology 3/e (© Garland Science 2010)

Ca^{2+} receptor movie

GPCRs

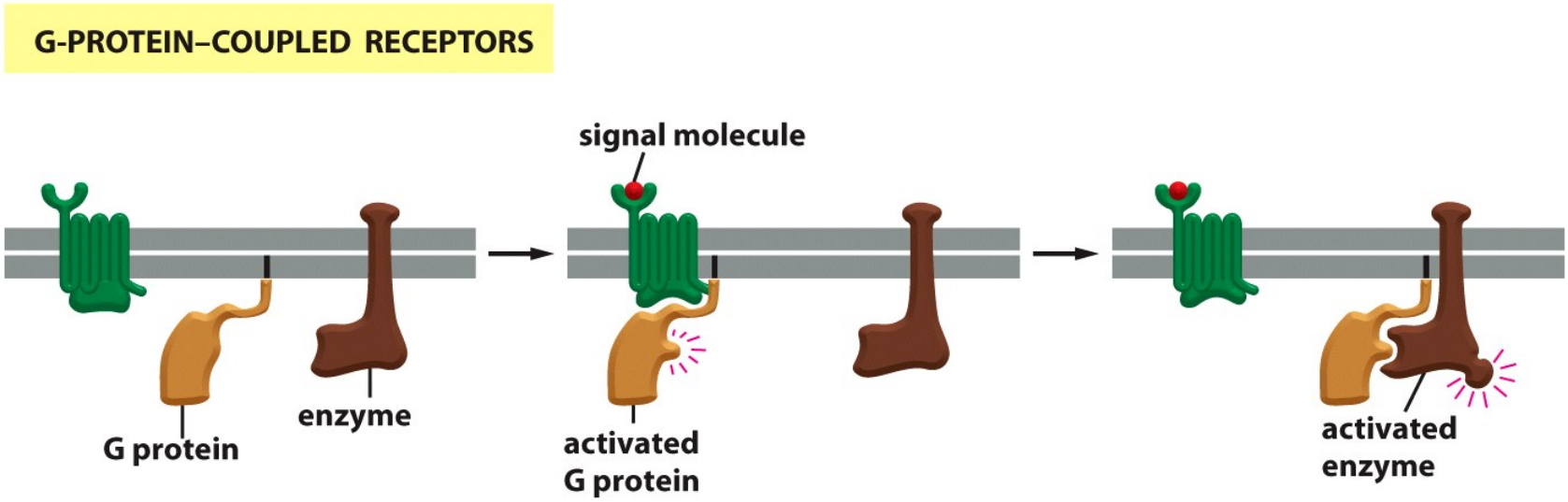
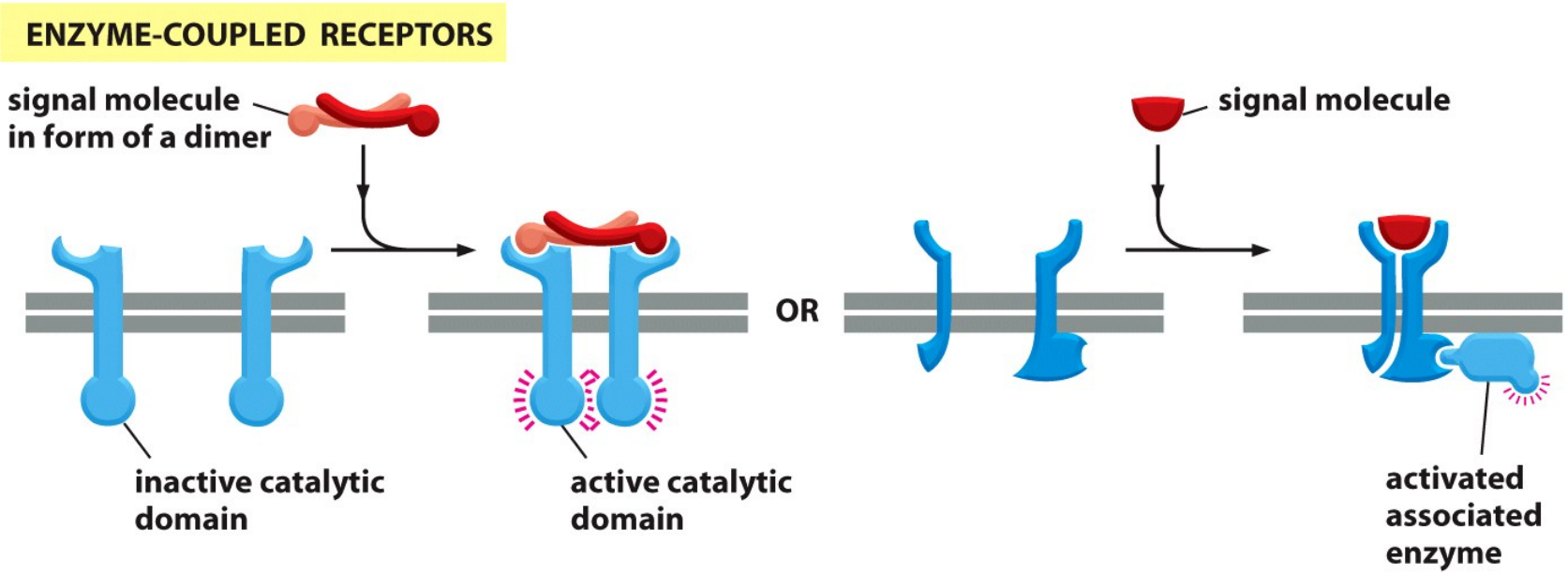


Figure 16-15b Essential Cell Biology 3/e (© Garland Science 2010)

Enzyme-coupled receptors



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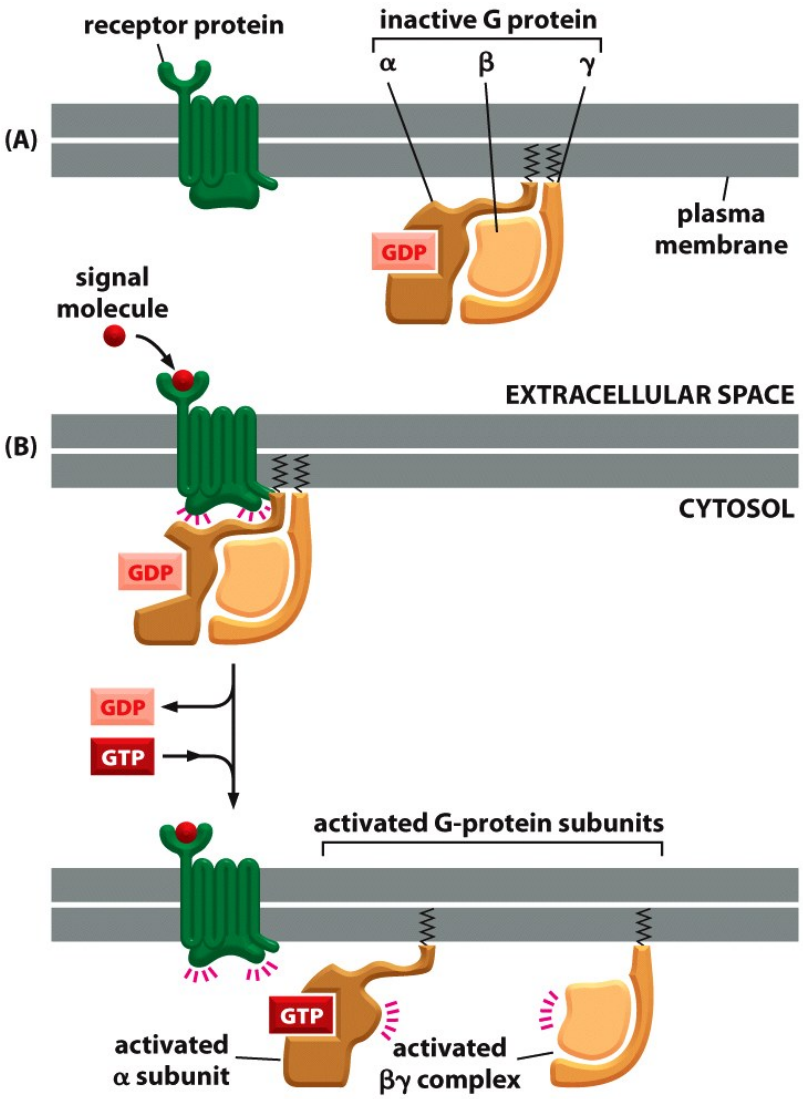
G-protein-coupled receptors (GPCRs)

- About 50% of known drugs are working with GPCRs
- They are seven-pass transmembrane proteins structurally similar to bacteriorhodopsin

Stimulation of GPCRs

- Signal facilitate conformational change of receptor
- Receptor will activate G protein
- In activated G protein, α subunit binds GTP, other two form $\beta\gamma$ complex
- α and/or $\beta\gamma$ bind to target protein
- α subunit will finally hydrolyze GTP and deactivate itself plus $\beta\gamma$ complex

Activation of GPCRs



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Deactivation of GPCRs

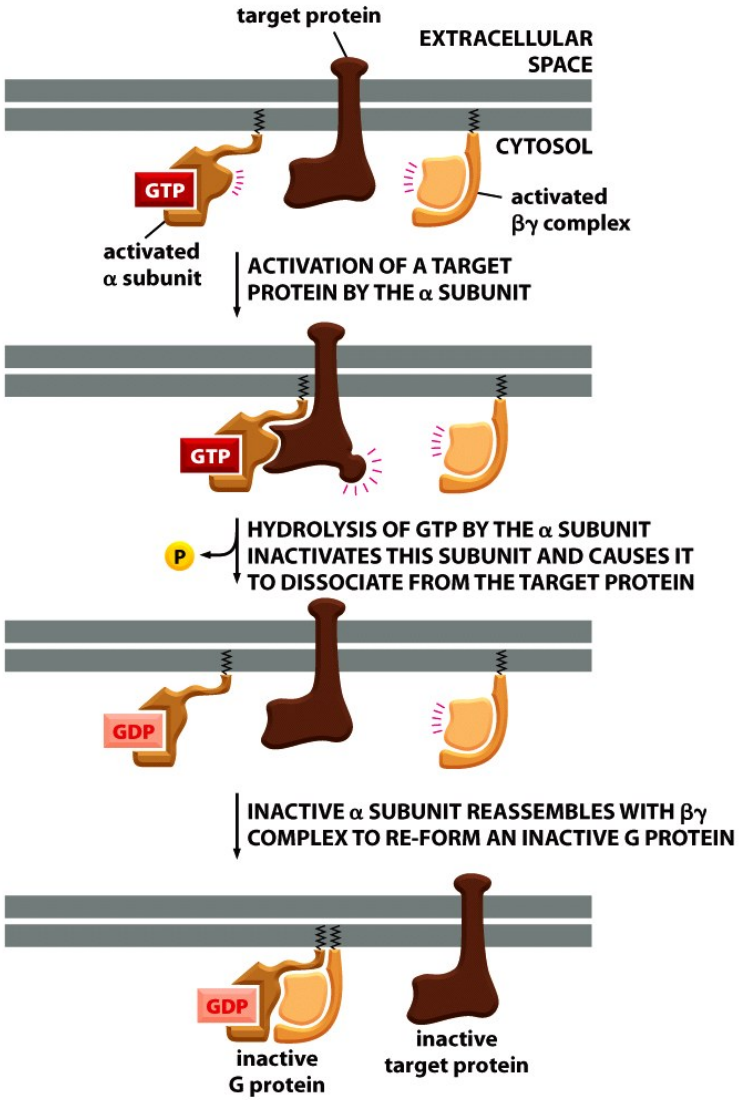


Figure 16-18 Essential Cell Biology 3/e (© Garland Science 2010)

Cholera and whooping cough (pertussis)

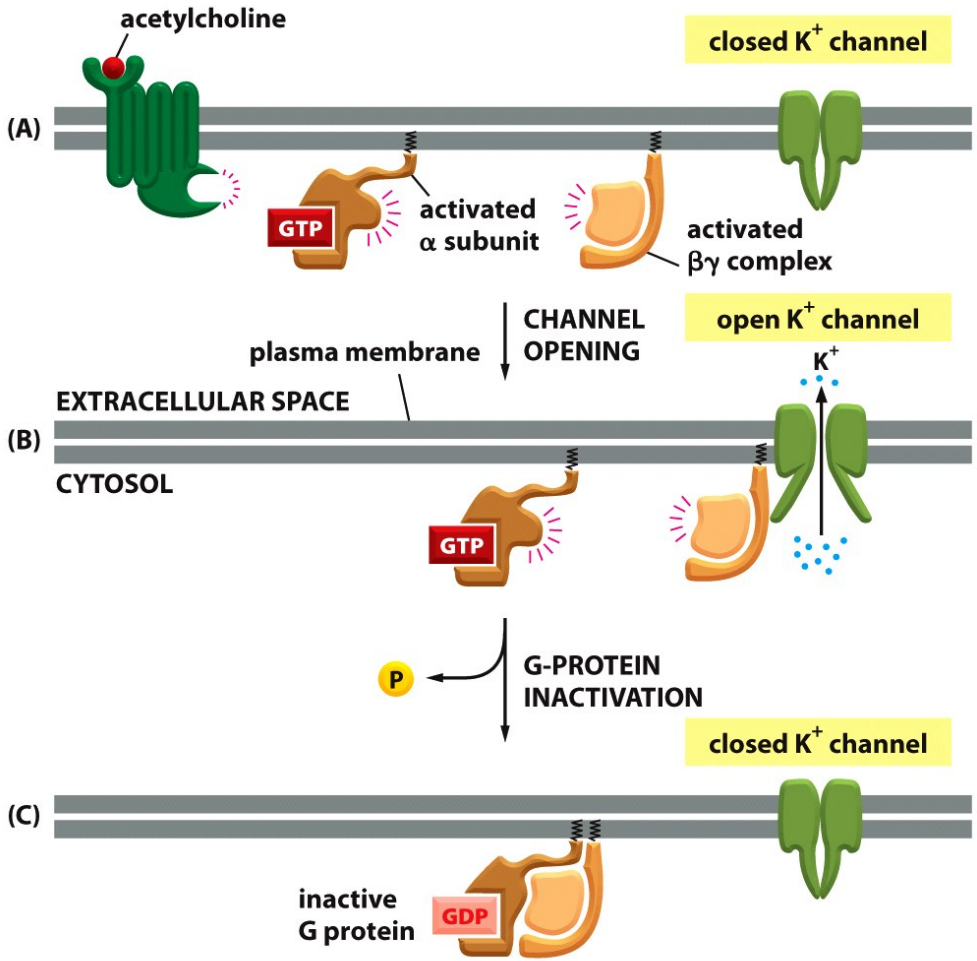
- Cholera toxin stops deactivation of particular G-protein; as a result, water and ions will not be absorbed in gut
- Pertussis toxin stops activation of inhibitory G-protein; as a result, prolonged signal is generated resulted in a cough

G-protein signalling movie

GPCRs as ion channels regulators in heart muscle cells

- Acetylcholine signal binds to GPCR of muscle cell membrane
- Activated $\beta\gamma$ complex facilitates K^+ ligand channels to open; as a result exitability is lowered

GPCRs as ion channel regulator



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GPCRs as membrane enzyme activators

- G-protein may activate either adenylyl cyclase, or phospholipase C
- Both are enzymes producing small molecules—second messengers
- Phospholipase C produces inositol triphosphate and diacylglycerol

GPCRs and cyclic AMP

- Adenylyl cyclase produces cyclic AMP
- In turn, cAMP activates PKA (AMP-dependent protein kinase)
- PKA may either catalyze cellular reactions (e.g., glycogen breakdown), or activate transcription regulators

cAMP

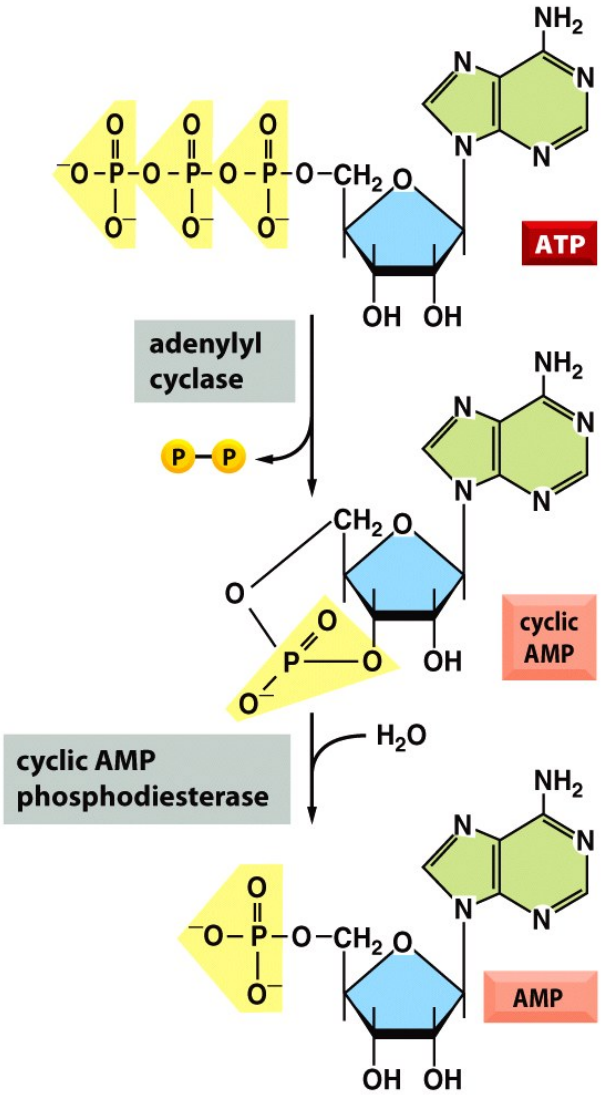

Figure 16-21 Essential Cell Biology 3/e (© Garland Science 2010)

Adrenaline

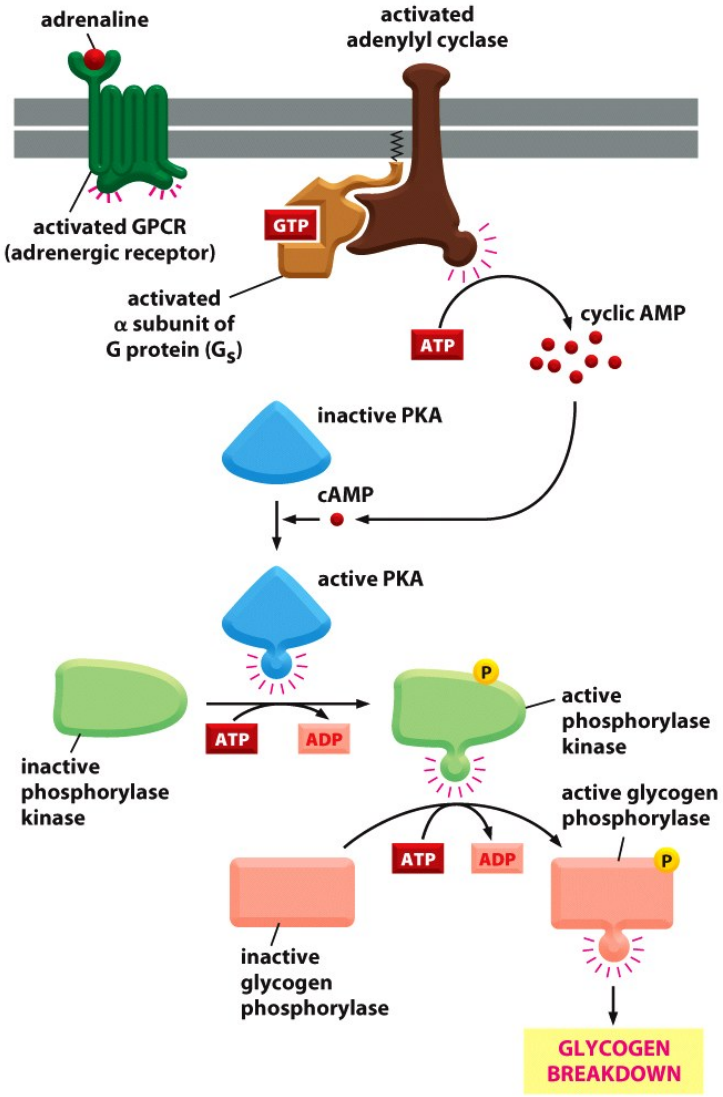

Figure 16-23 Essential Cell Biology 3/e (© Garland Science 2010)

cAMP transcription regulation

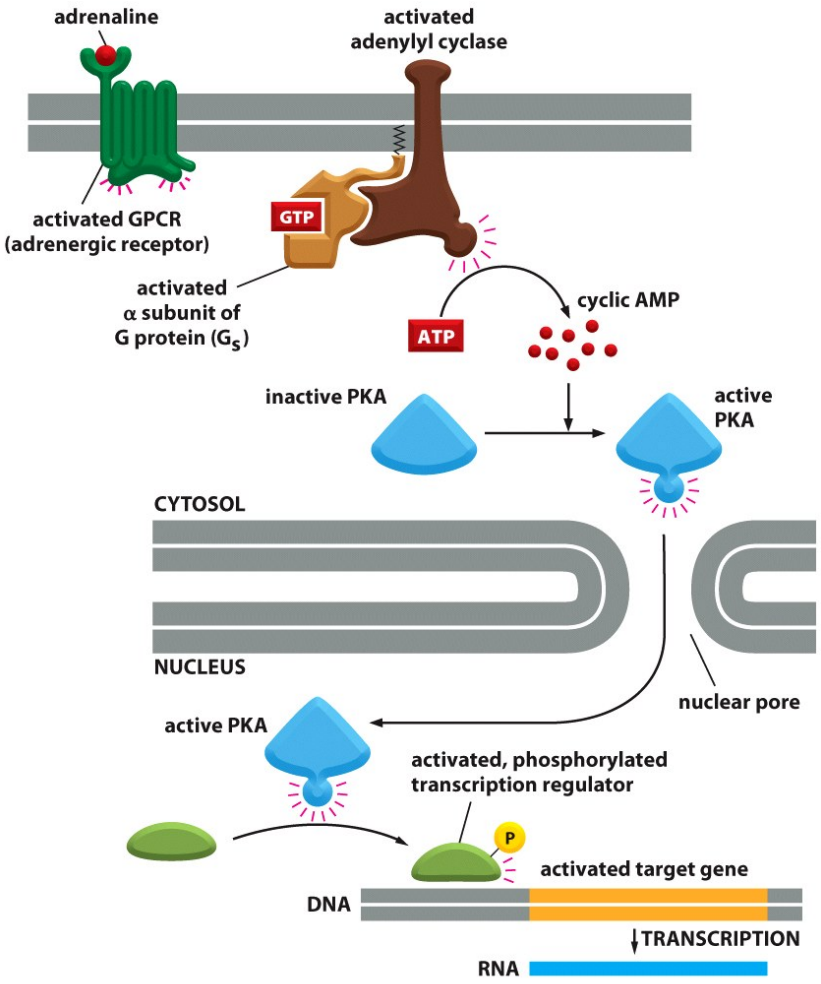

Figure 16-24 Essential Cell Biology 3/e (© Garland Science 2010)

cAMP movie

Final question (1 point)

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What is the functional difference between α subunit and $\beta\gamma$ complex of GPCR?

Summary

- Most signals need transduction with membrane receptors of three main classes: ion-channel-coupled, G-protein-coupled and enzyme-coupled
- G-protein-coupled receptors (GPCRs) may activate membrane ion channels or membrane enzyme proteins (e.g., adenynyl cyclase)

For Further Reading

A. Shipunov.
Advanced Cell Biology [Electronic resource].
2011—onwards.
Mode of access: http://ashipunov.info/shipunov/school/biol_250.

B. Alberts et al.
Essential Cell Biology. 3rd edition.
Garland Science, 2009.
Chapter 16: 541–551.