Chem 452 - Lecture 10
Signal Transduction
111128

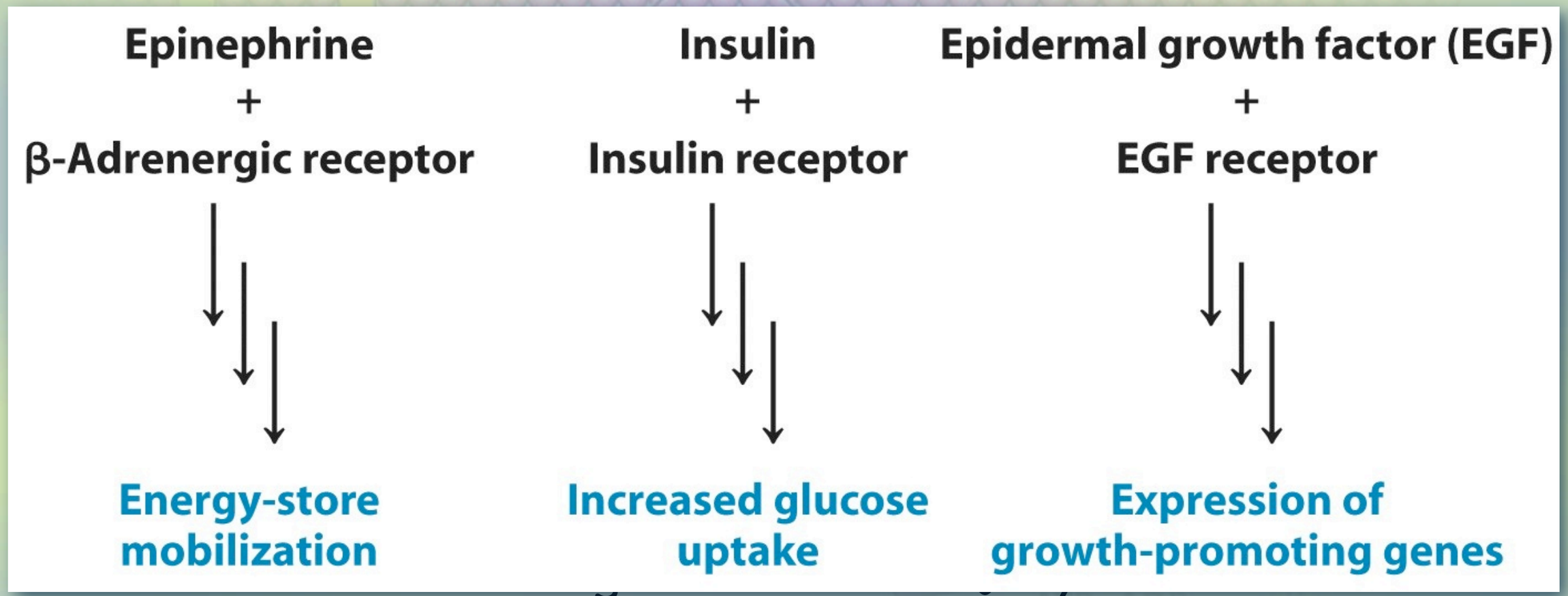
Here we look at the movement of a signal from the outside of a cell to its inside, where it elicits changes within the cell. These changes are usually mediated by protein kinases, which phosphorylate enzymes to turn them on or off. We will focus on three examples; the β-adrenergic receptor, which is involved in the "flight or fight response, the insulin receptor, which is involved in regulating blood glucose levels, and the epidermal growth factor (EGF) receptor, which triggers cell growth in response to injury. Each example presents common themes such as secondary messengers, the amplification of a signal, and the activation of protein kinases. These signal pathways also provide examples of how multiple proteins can work together in complex ways to produce a concerted result.

Introduction

- Signal transduction involves the changing of a cell's metabolism or gene expression in response to an external stimulus.
- We will focus on three examples
  - The hormone **epinephrine** (adrenalin)
    - Regulates the "flight or fight response"
  - The hormone **insulin**
    - Regulates blood glucose levels after a meal
  - The hormone **epidermal growth factor** (EGF)
    - Stimulates cell growth after injury

Introduction

- Signal transduction involves the changing of a cell's metabolism or gene expression in response to an external stimulus.

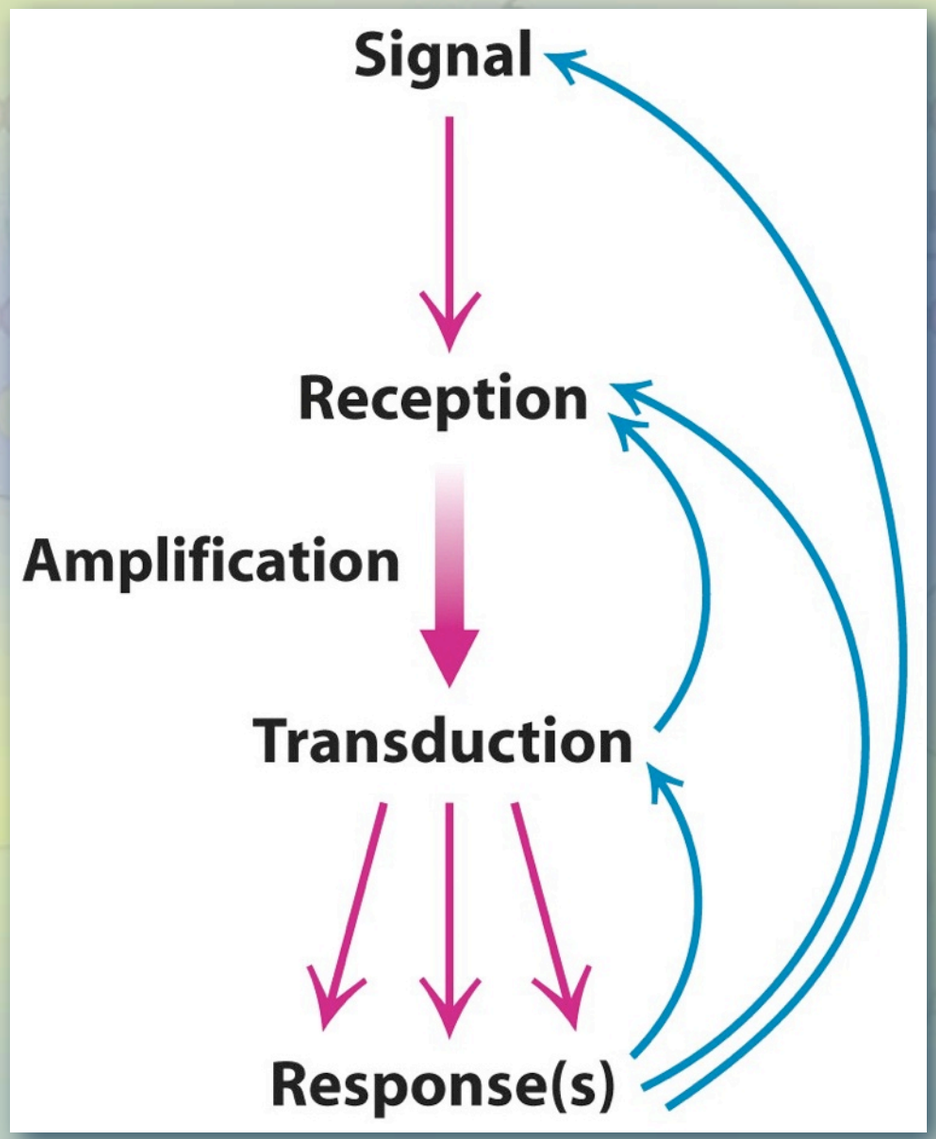


Introduction

- Signal transduction involves the changing of a cell's metabolism or gene expression in response to an external stimulus.
- We will focus on three examples
  - The hormone **epinephrine** (adrenalin)
    - Regulates the "flight or fight response"
  - The hormone **insulin**
    - Regulates blood glucose levels after a meal
  - The hormone **epidermal growth factor** (EGF)
    - Stimulates cell growth after injury

Introduction

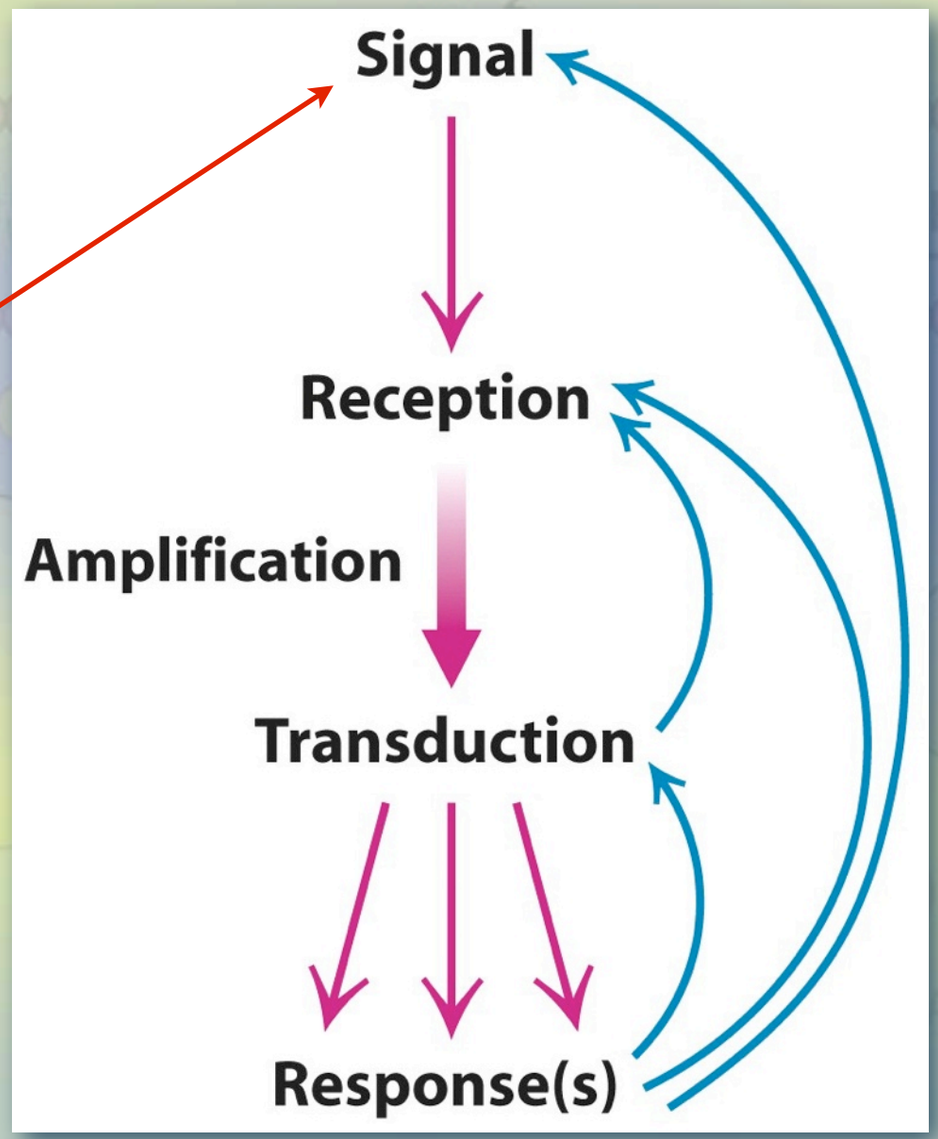
- All three examples will present common themes



Introduction

- All three examples will present common themes

Signal

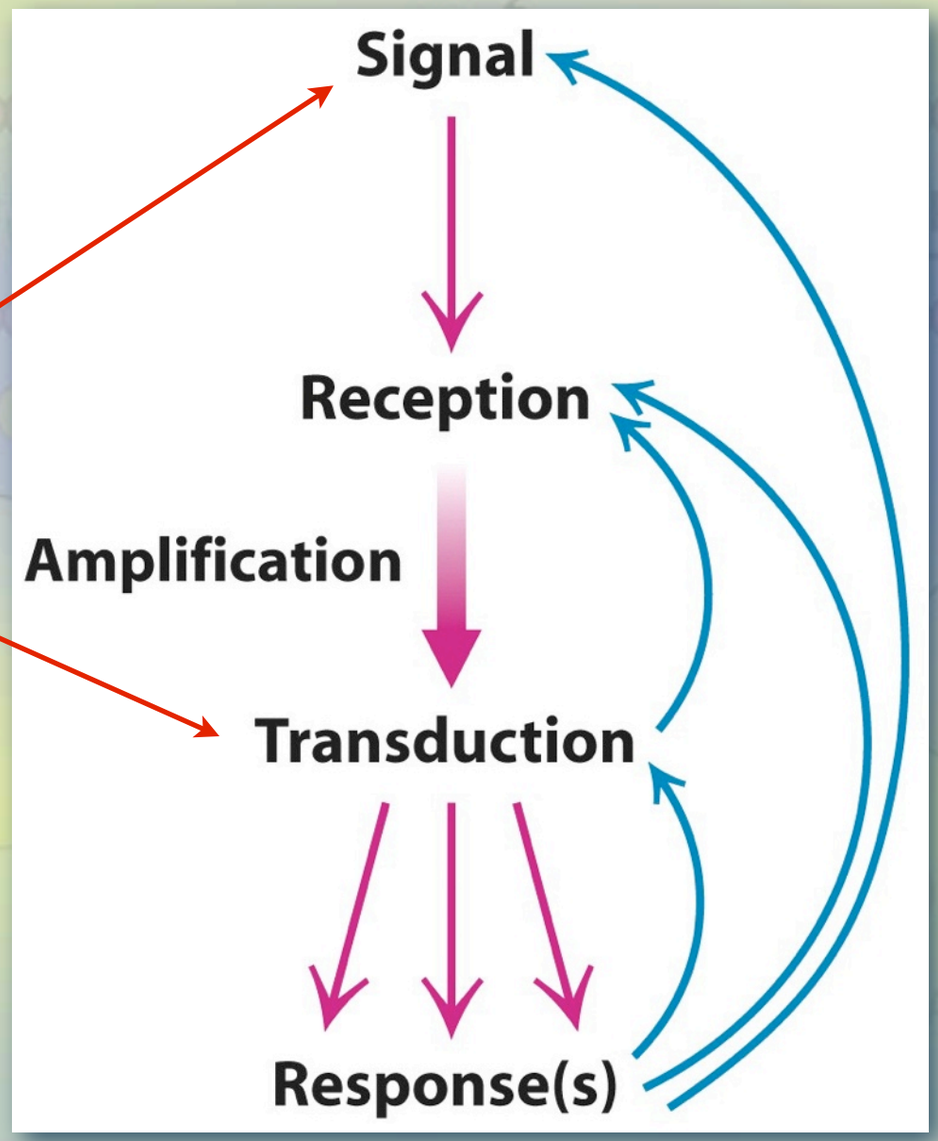


Introduction

- All three examples will present common themes

Signal

Transduction

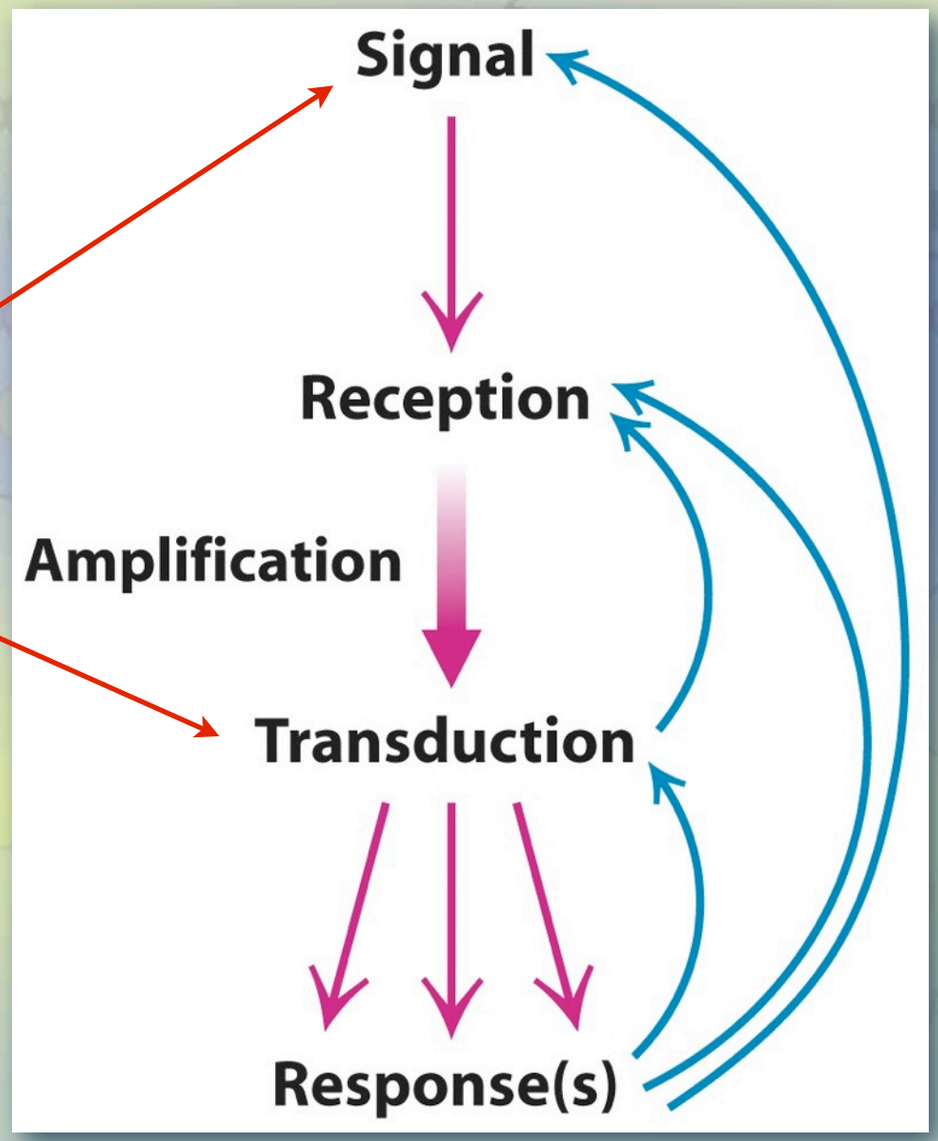


Introduction

- All three examples will present common themes

Signal

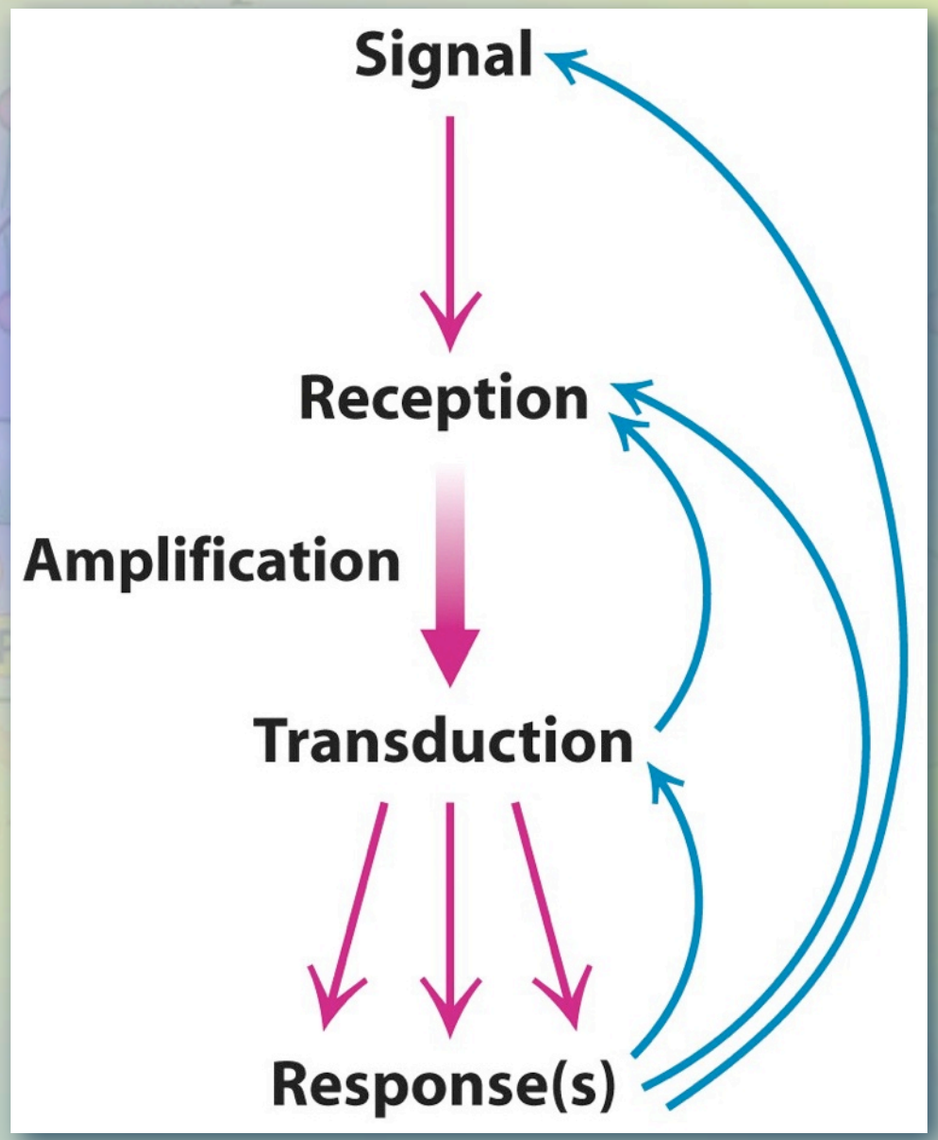
Transduction



Feedback
Regulation

Introduction

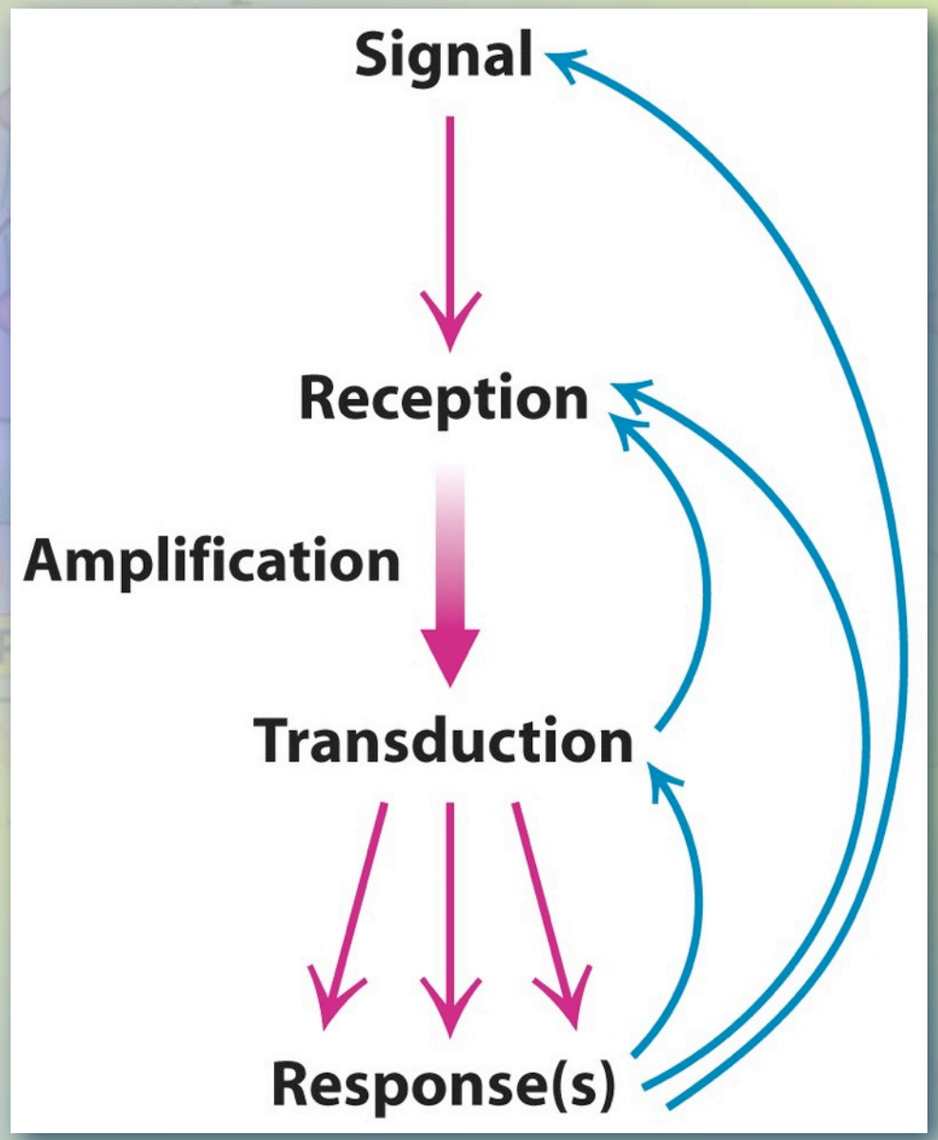
- All three examples will present common themes



Introduction

- All three examples will present common themes

1. Release of primary messenger

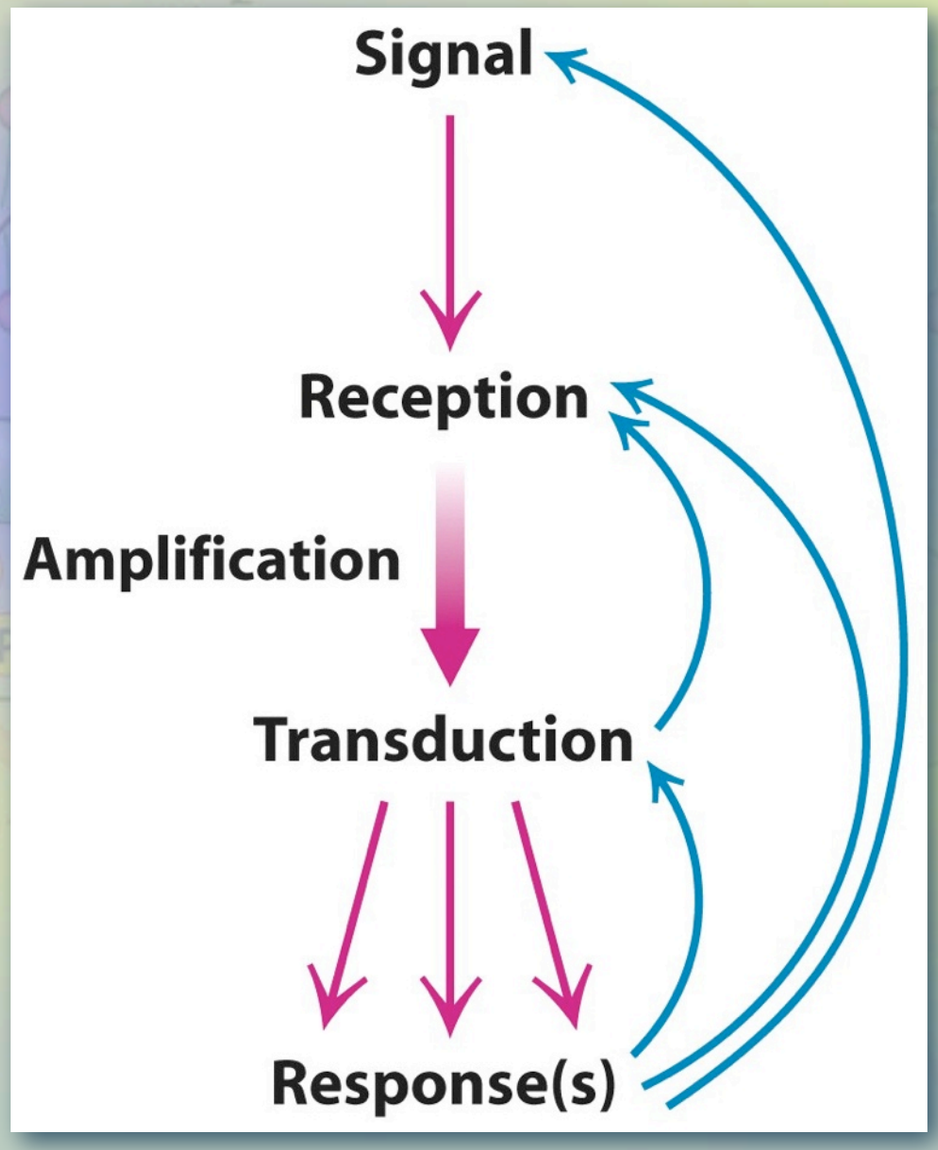


Introduction

- All three examples will present common themes

1. Release of primary messenger

2. Reception of the primary messenger



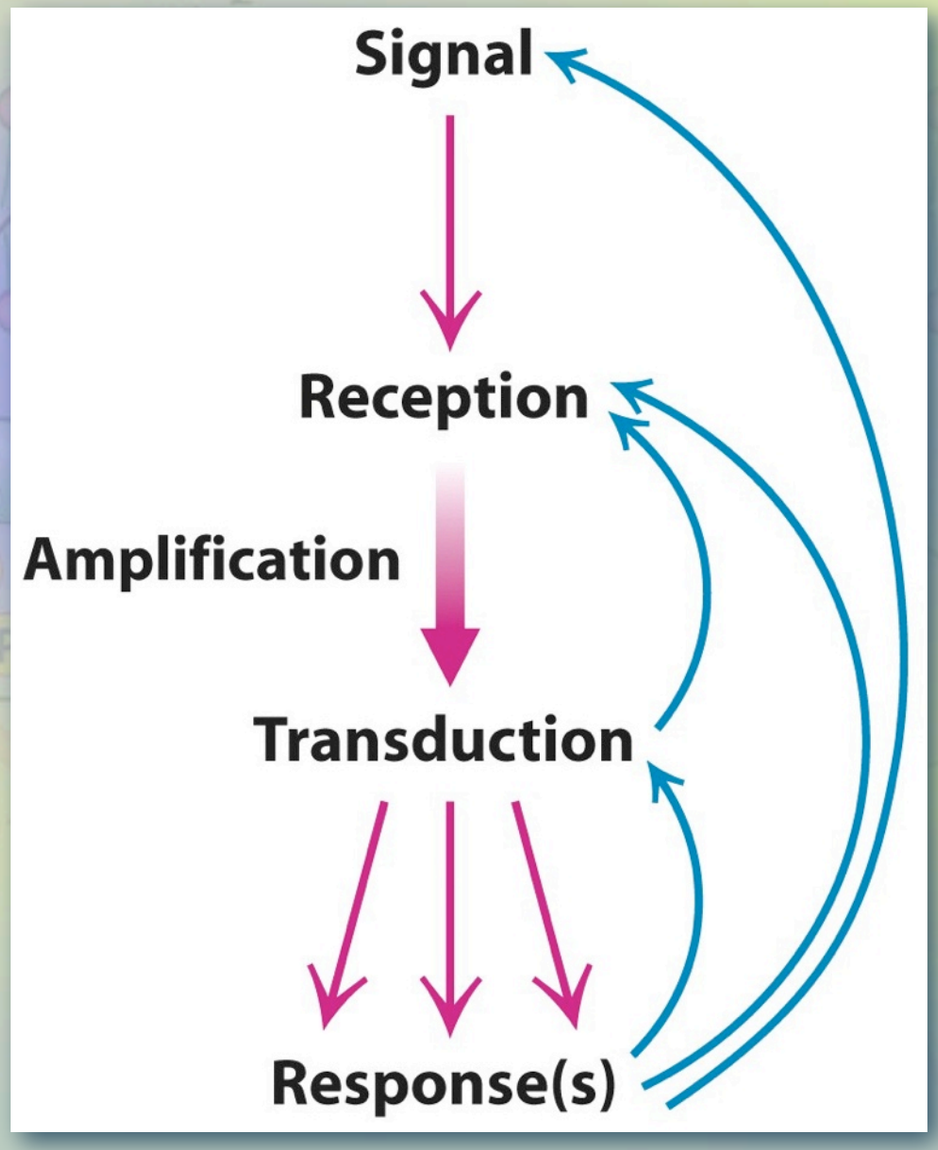
Introduction

- All three examples will present common themes

1. Release of primary messenger

2. Reception of the primary messenger

3. Delivery of message to cell interior by secondary messenger



Introduction

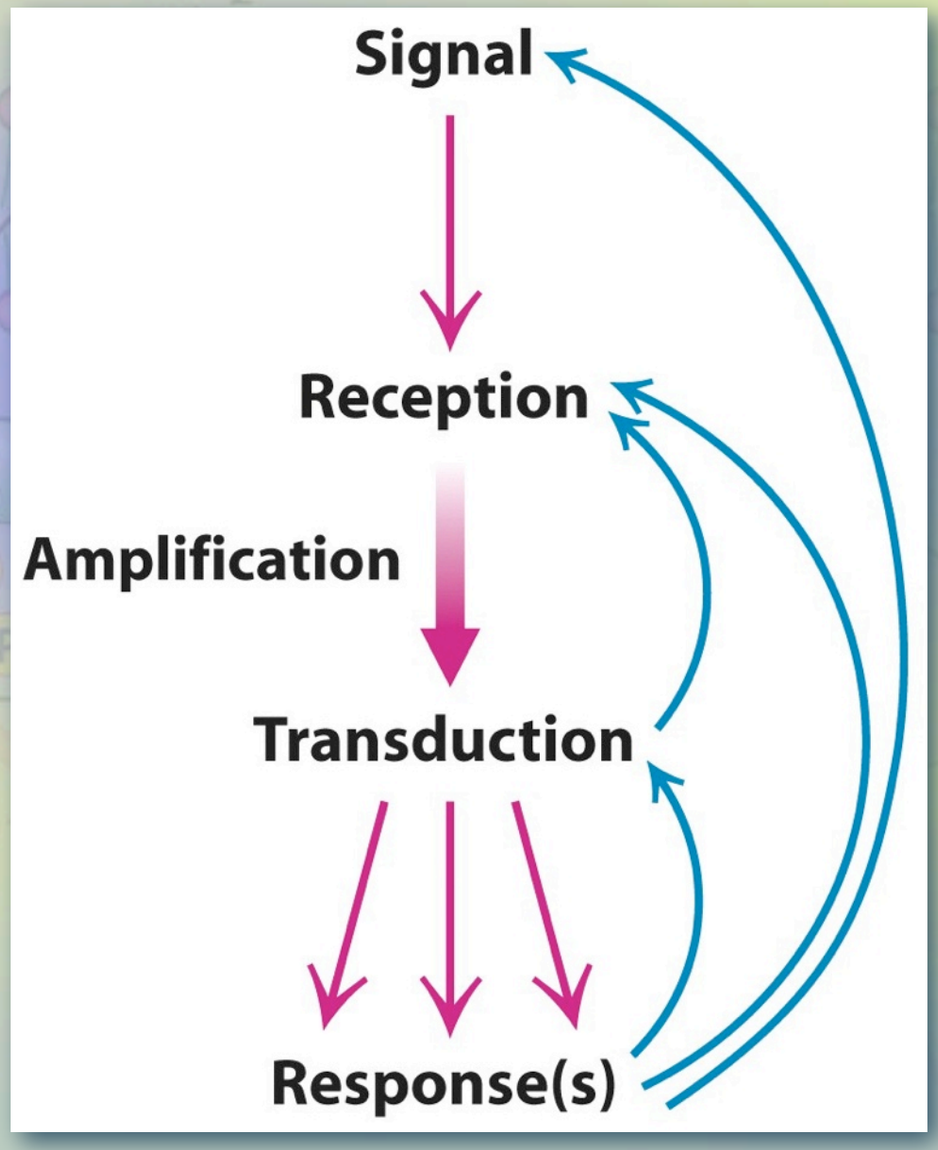
- All three examples will present common themes

1. Release of primary messenger

2. Reception of the primary messenger

3. Delivery of message to cell interior by secondary messenger

4. Activation of effectors



Introduction

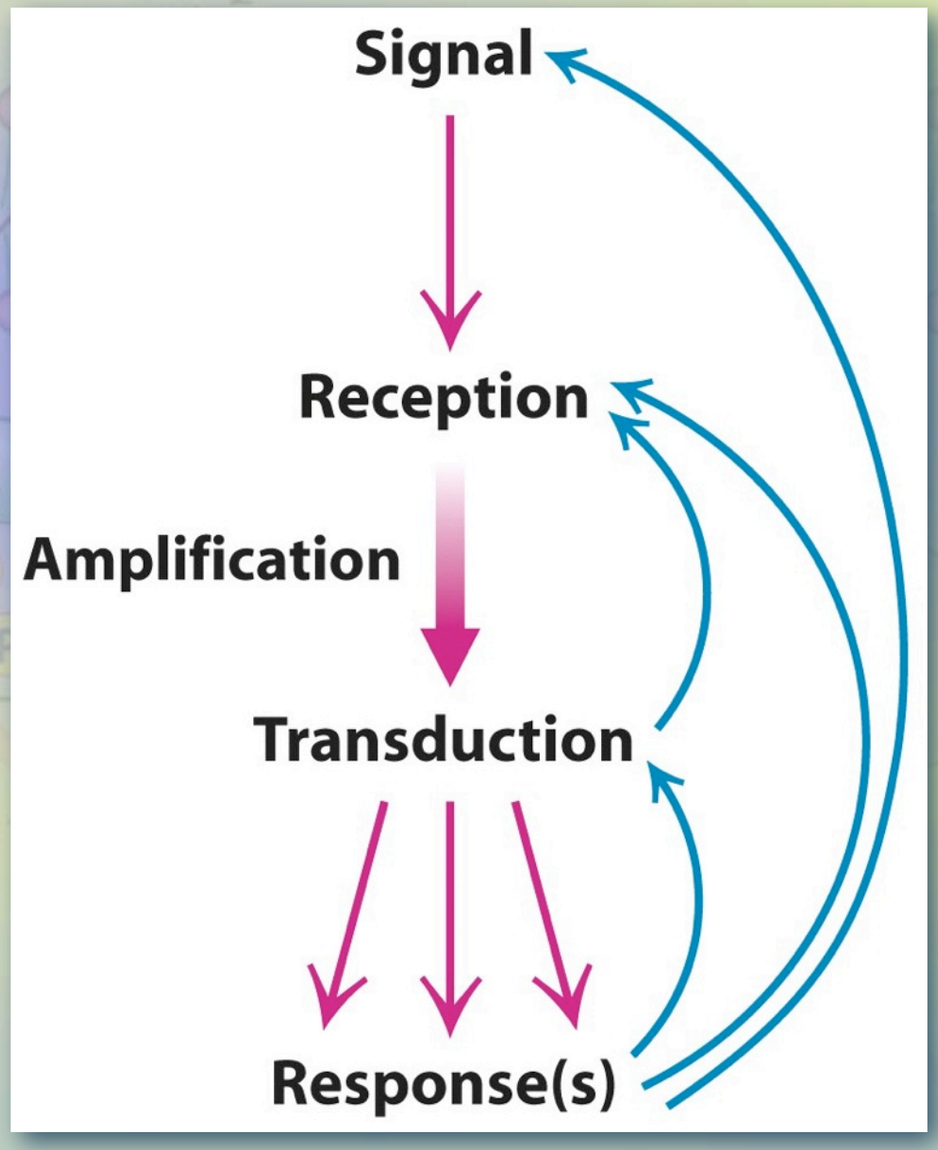
- All three examples will present common themes

1. Release of primary messenger

2. Reception of the primary messenger

3. Delivery of message to cell interior by secondary messenger

4. Activation of effectors



5. Termination of signal

Introduction

- All three examples will present common themes

1. Releas

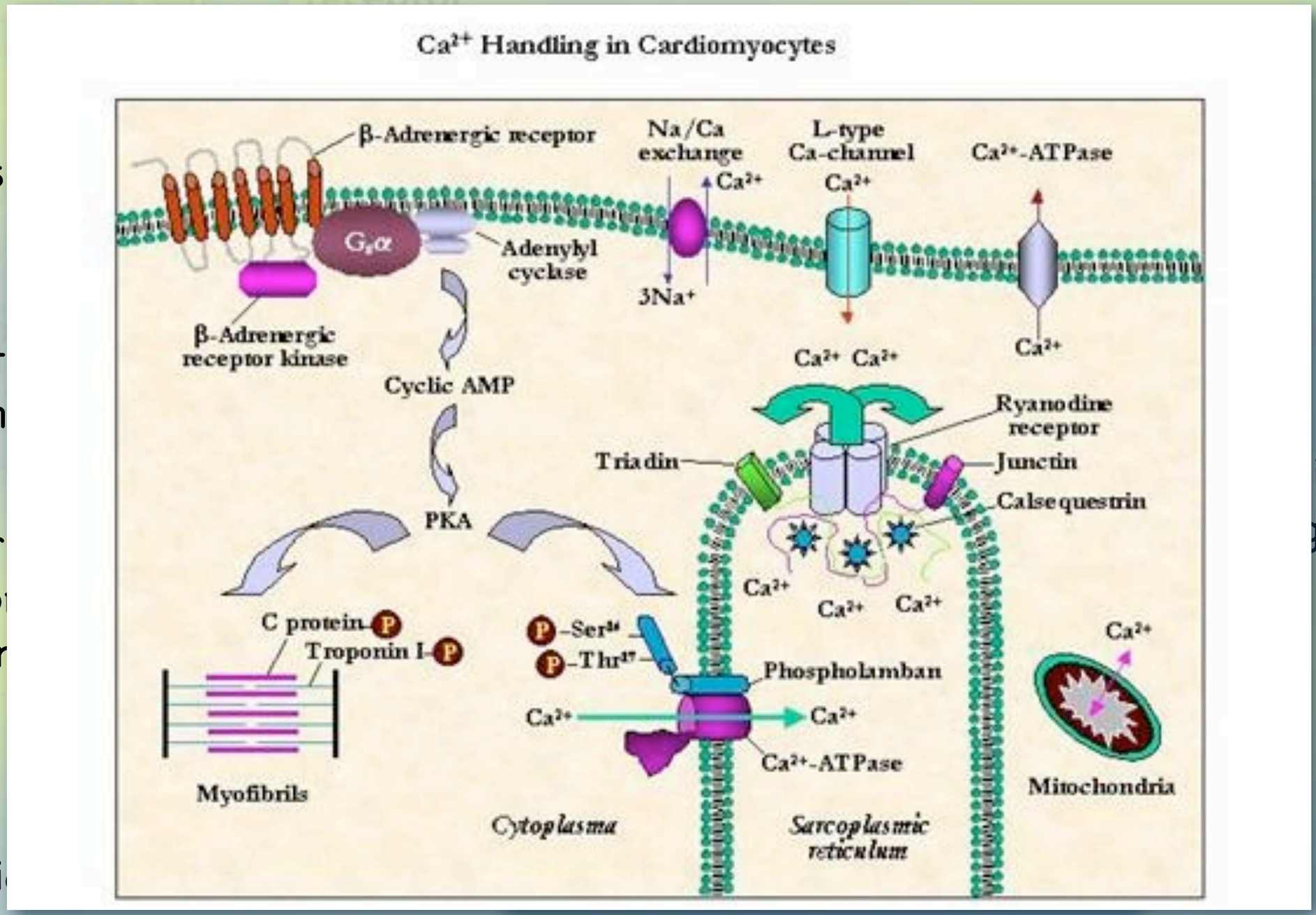
2. Recept
messen

3. Deliver
interio
messer

4. Activati

ination

gnal



Introduction

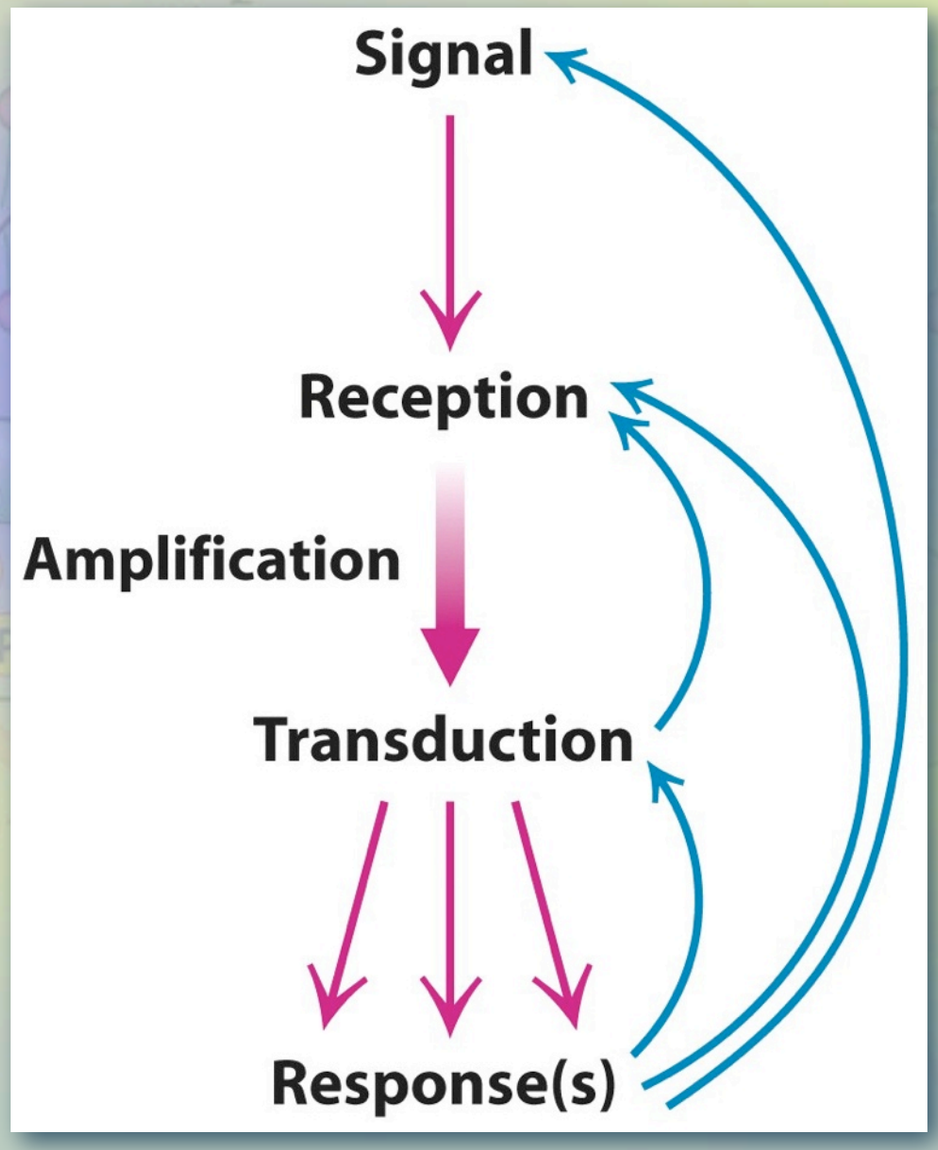
- All three examples will present common themes

1. Release of primary messenger

2. Reception of the primary messenger

3. Delivery of message to cell interior by secondary messenger

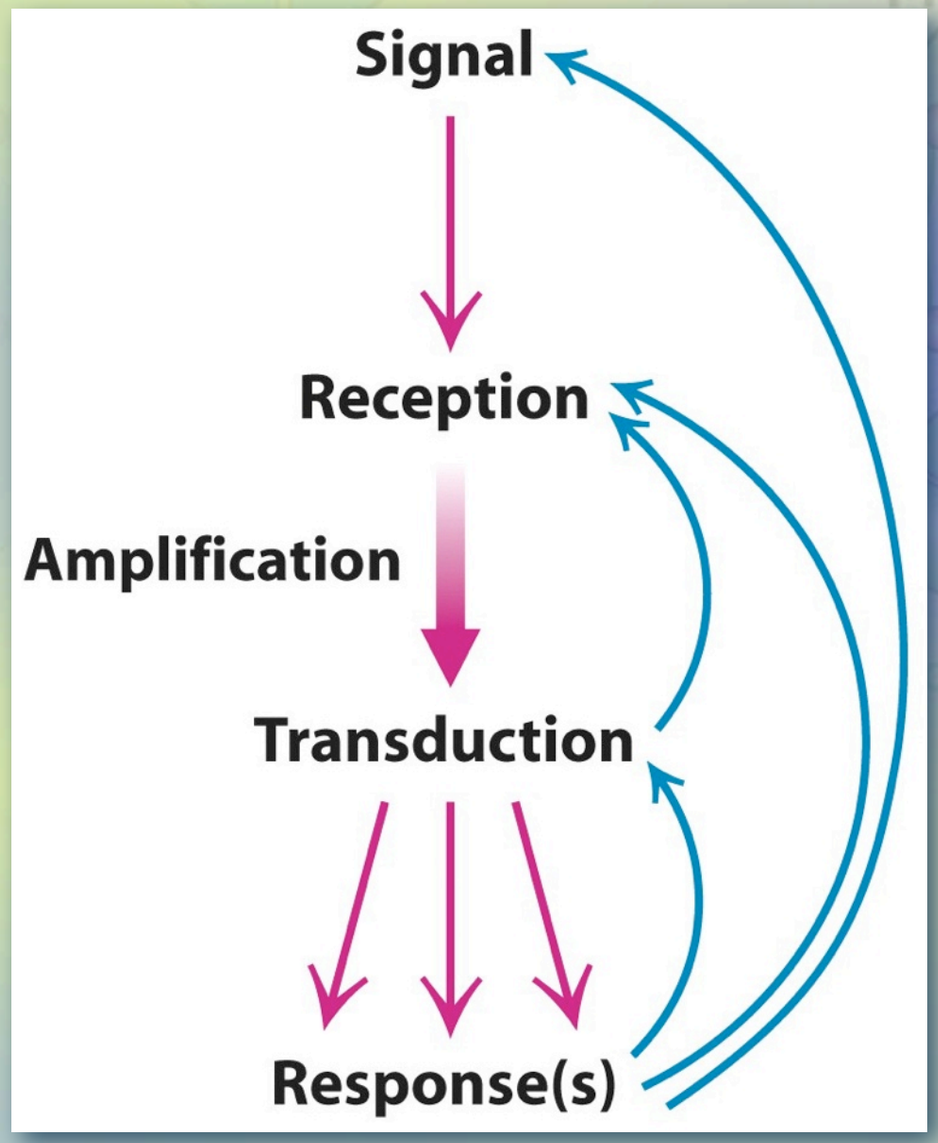
4. Activation of effectors



5. Termination of signal

Introduction

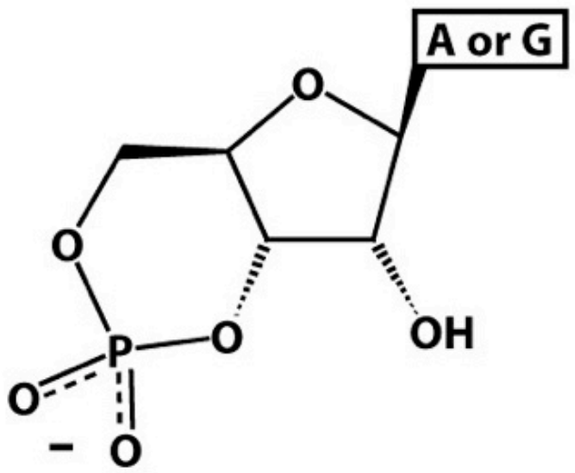
- All three examples will present common themes



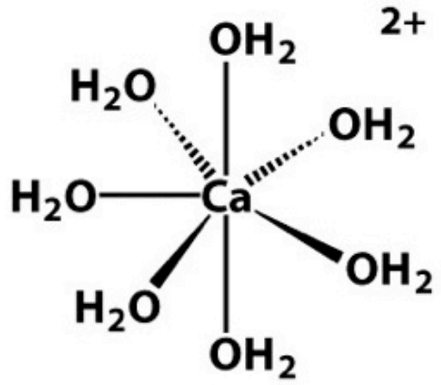
- Release of primary messenger
  - epinephrine
  - insulin
  - EGF
- Reception of primary message
- Delivery of message inside the cell
  - cAMP
  - Ca^{2+}
  - inositol 1,4,5-triphosphate (IP_3)
  - diacylglycerol (DAG)
- Activation of effectors
- Termination of the Signal

Introduction

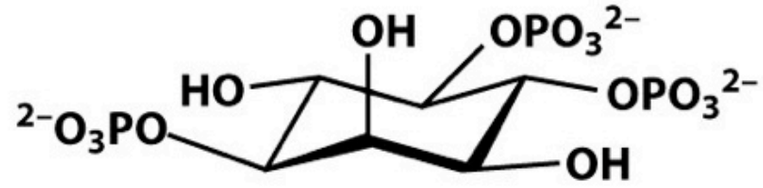
- All three examples will present common themes



cAMP, cGMP

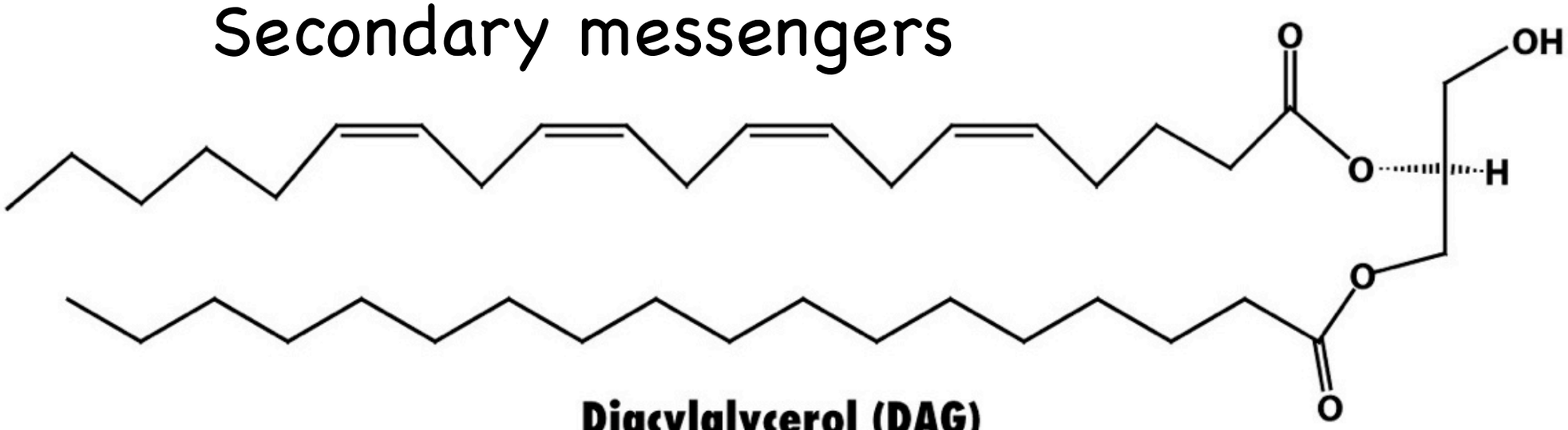


Calcium ion



Inositol 1,4,5-trisphosphate (IP_3)

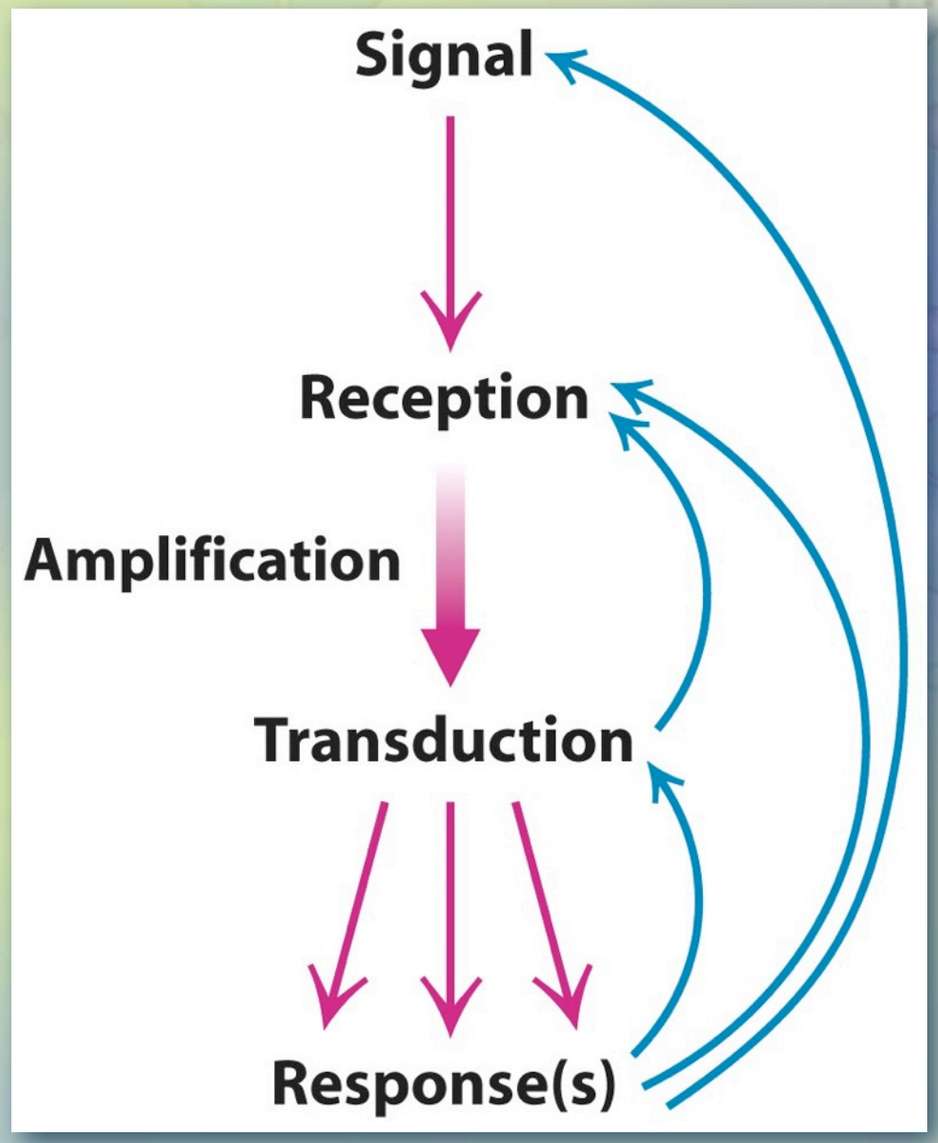
Secondary messengers



Diacylglycerol (DAG)

Introduction

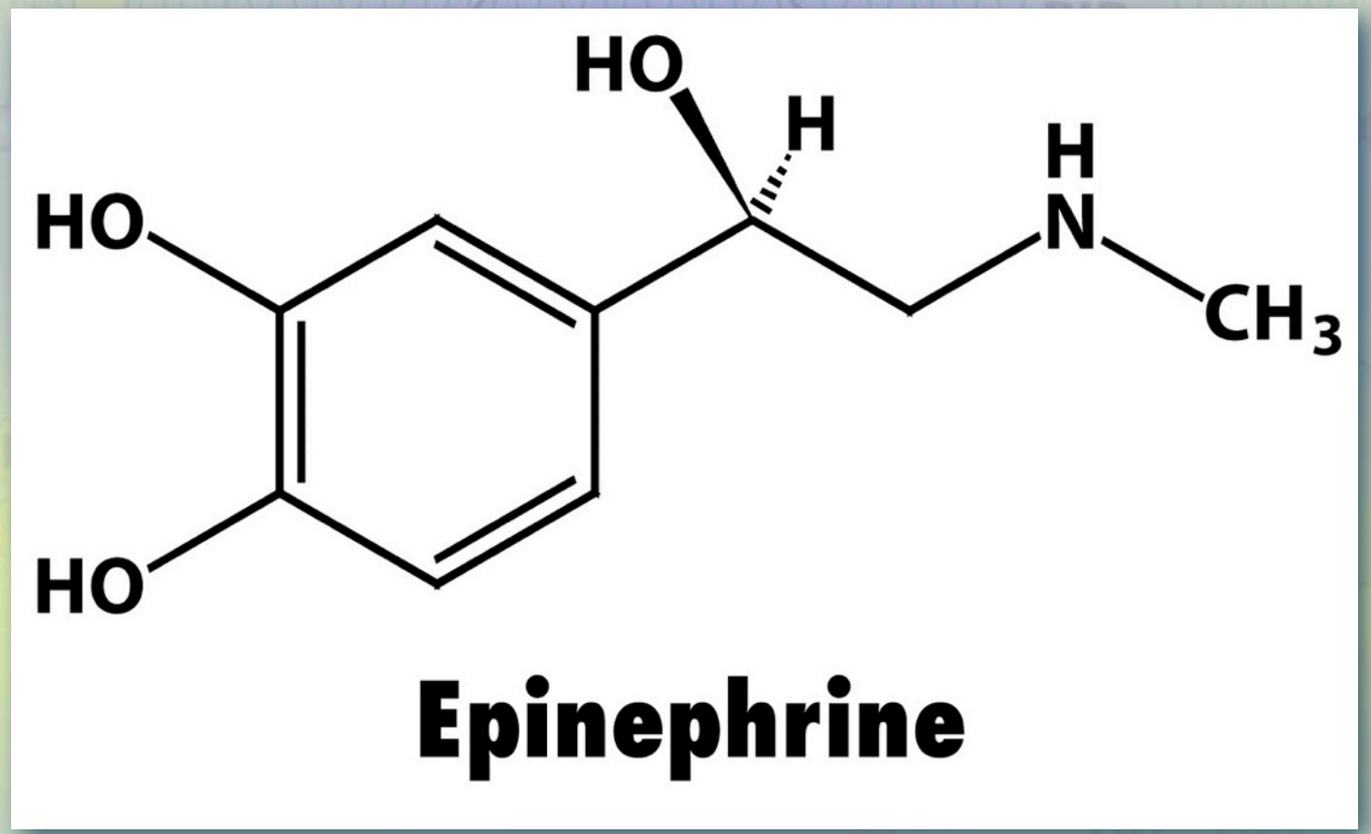
- All three examples will present common themes



- Release of primary messenger
  - epinephrine
  - insulin
  - EGF
- Reception of primary message
- Delivery of message inside the cell
  - cAMP
  - Ca^{2+}
  - inositol 1,4,5-triphosphate (IP_3)
  - diacylglycerol (DAG)
- Activation of effectors
- Termination of the Signal

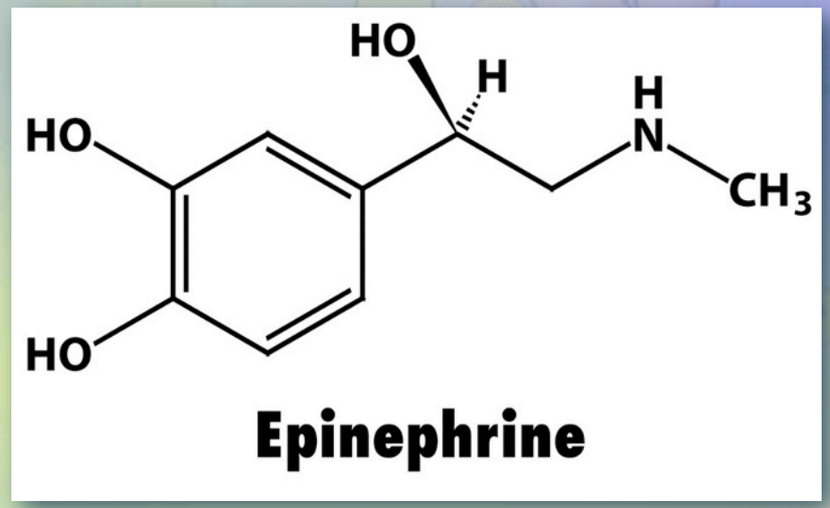
G-Protein Receptors

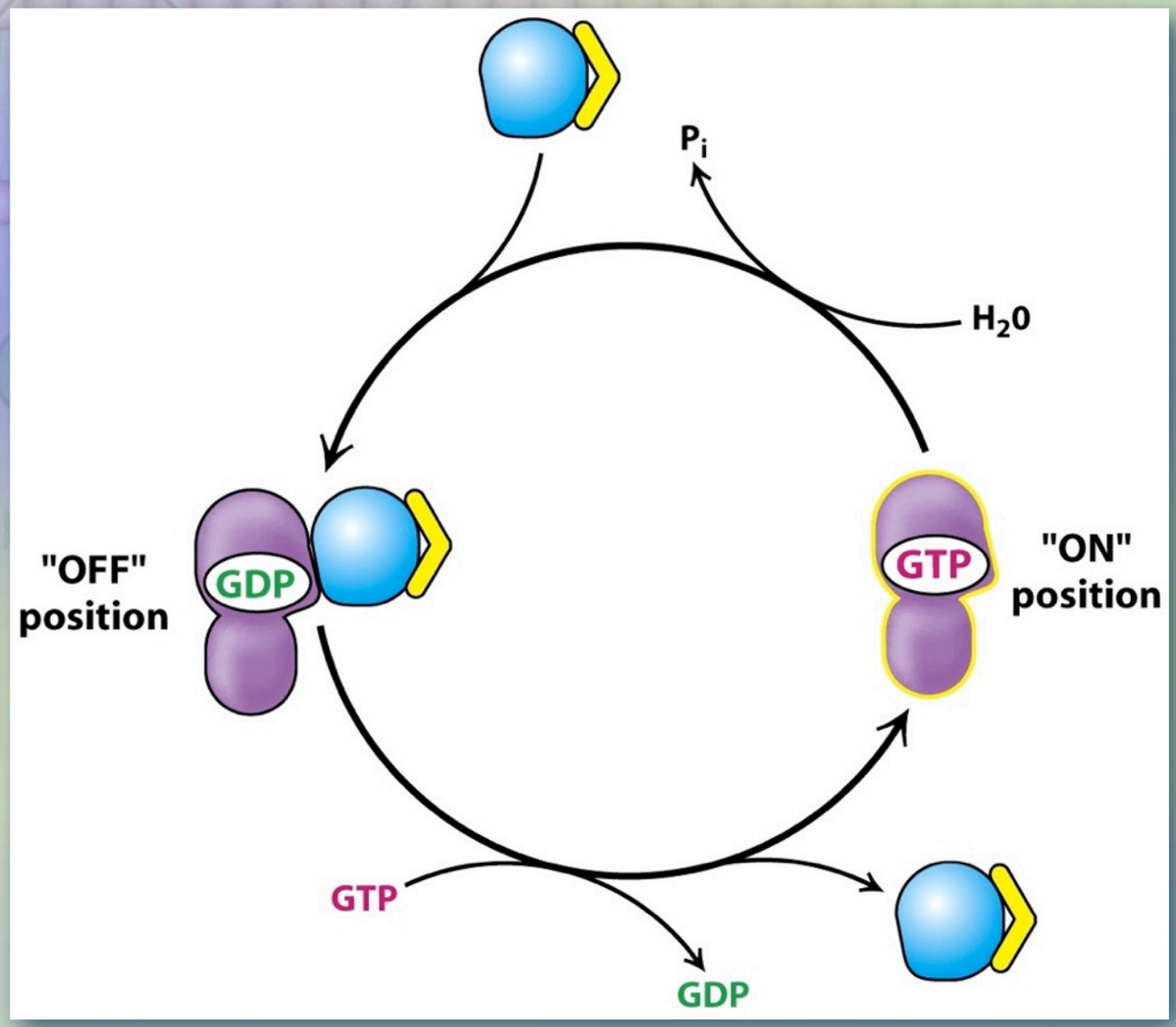
- The receptors for epinephrine (β-adrenergic receptors) provide and example for a class of receptors called G-proteins.



G-Protein Receptors

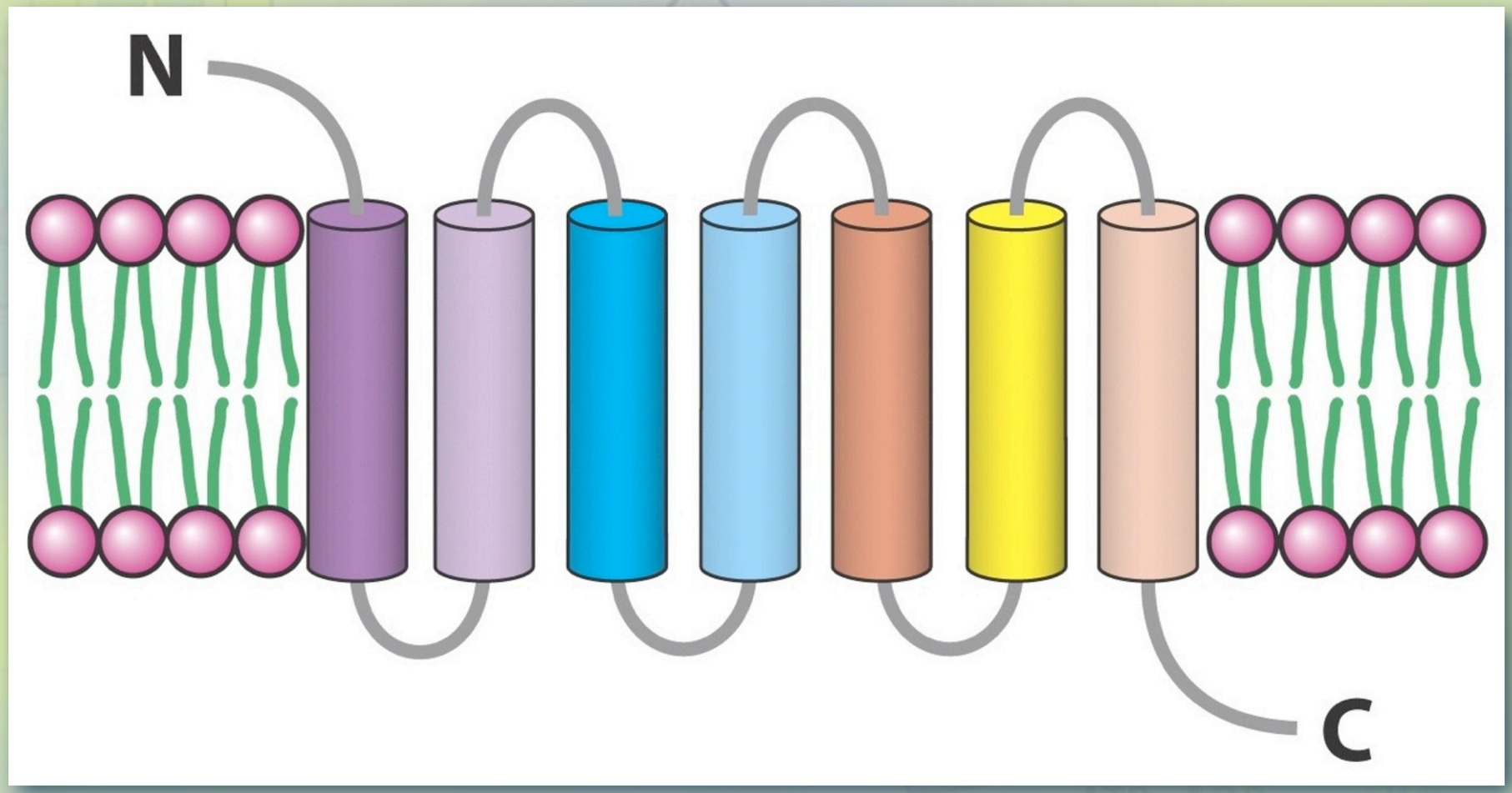
- The receptors for epinephrine (β-adrenergic receptors) provide and example for a class of receptors called G-proteins.





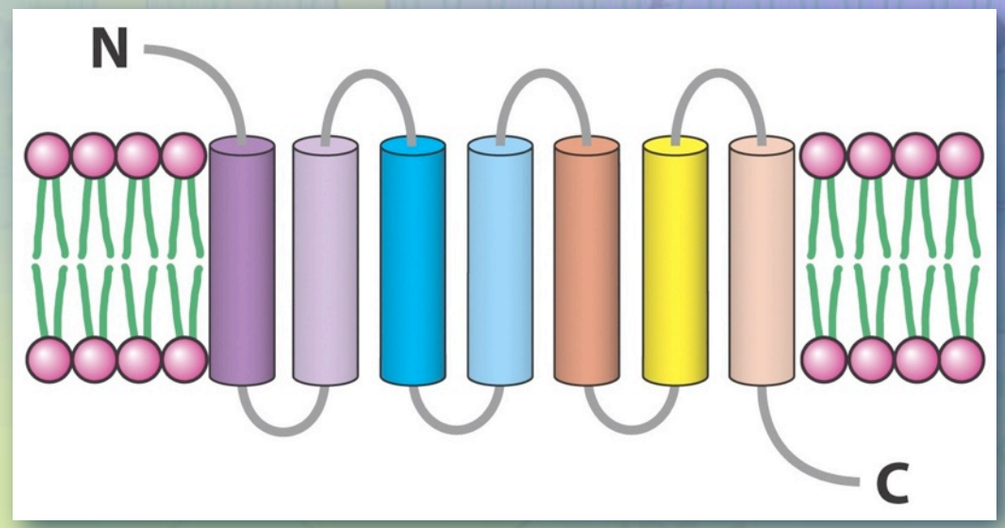
G-Protein Receptors

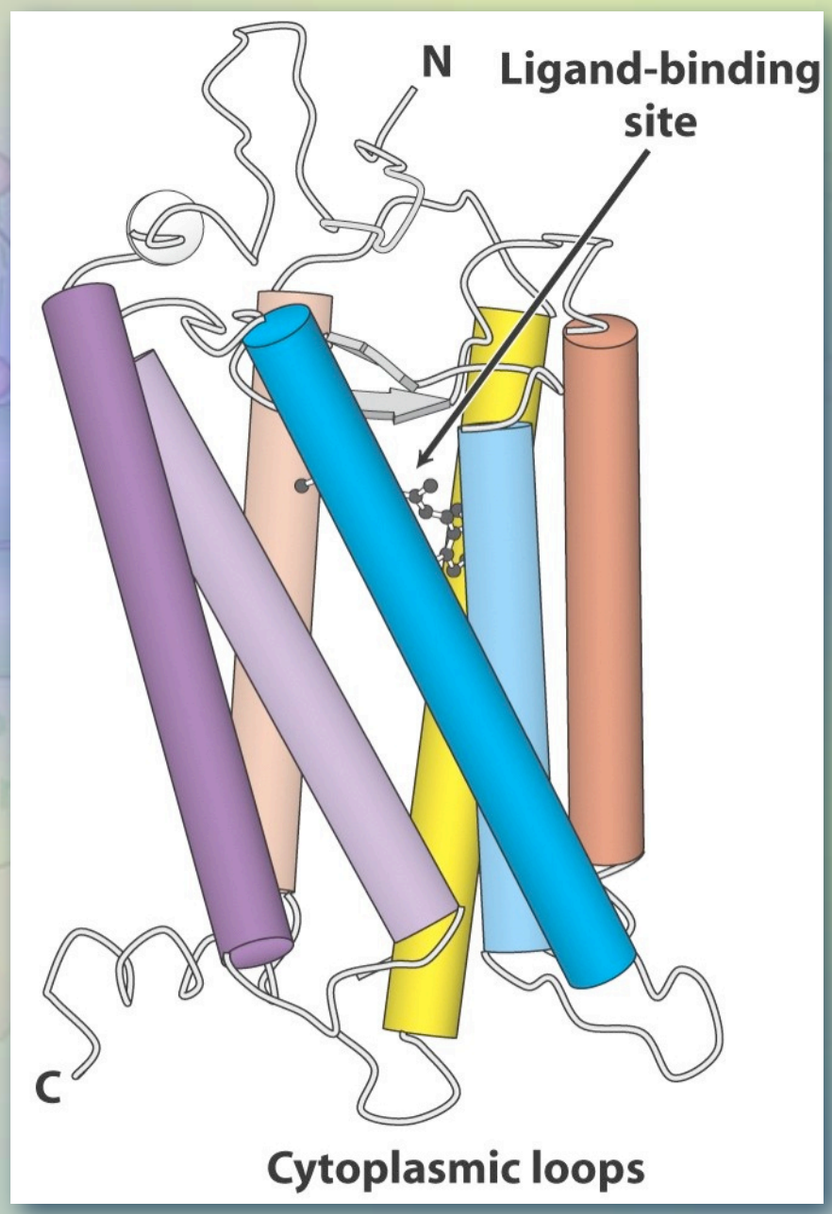
- G-protein receptors involve a 7-transmembrane receptor (7TM) protein.



G-Protein Receptors

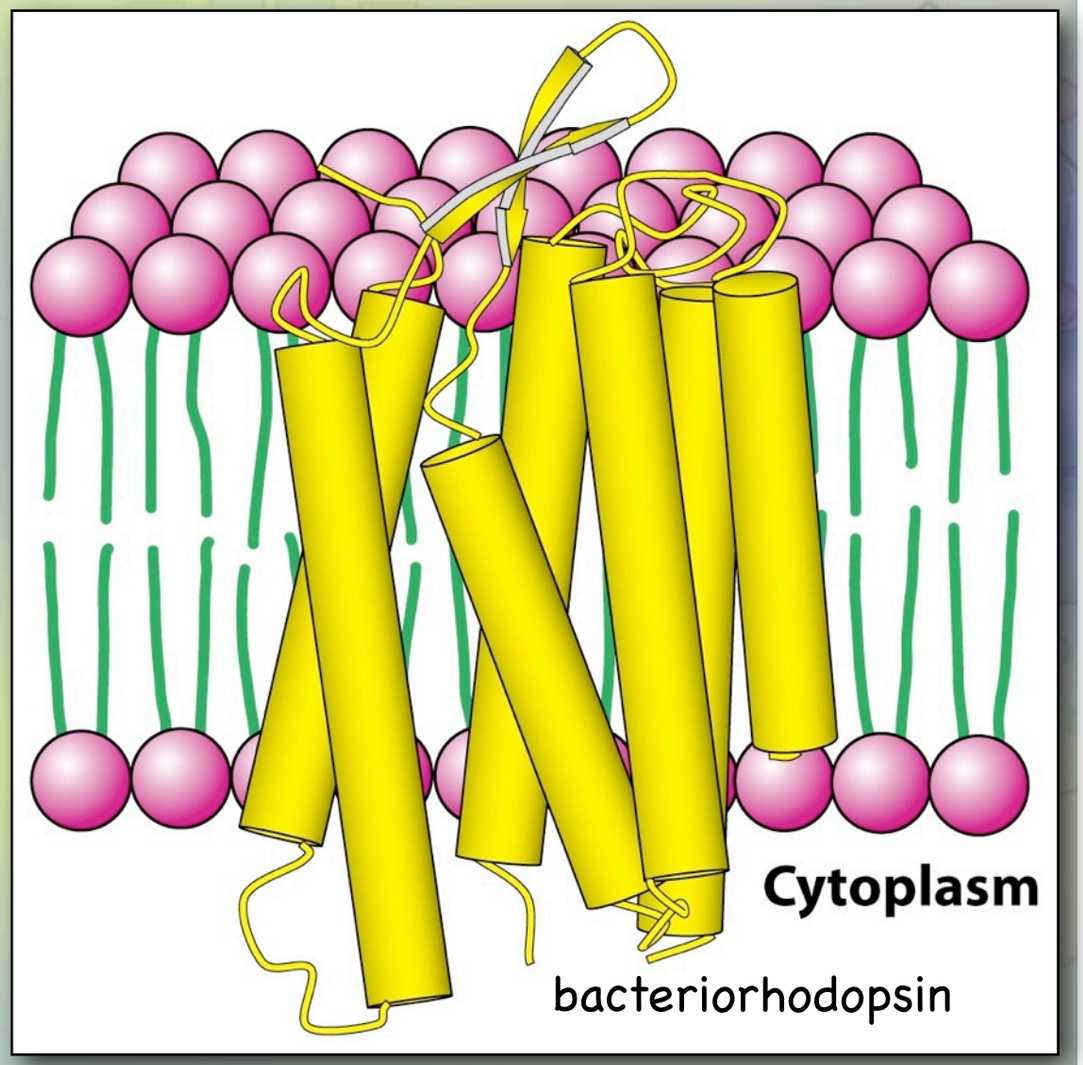
- G-protein receptors involve a 7-transmembrane receptor (7TM) protein.

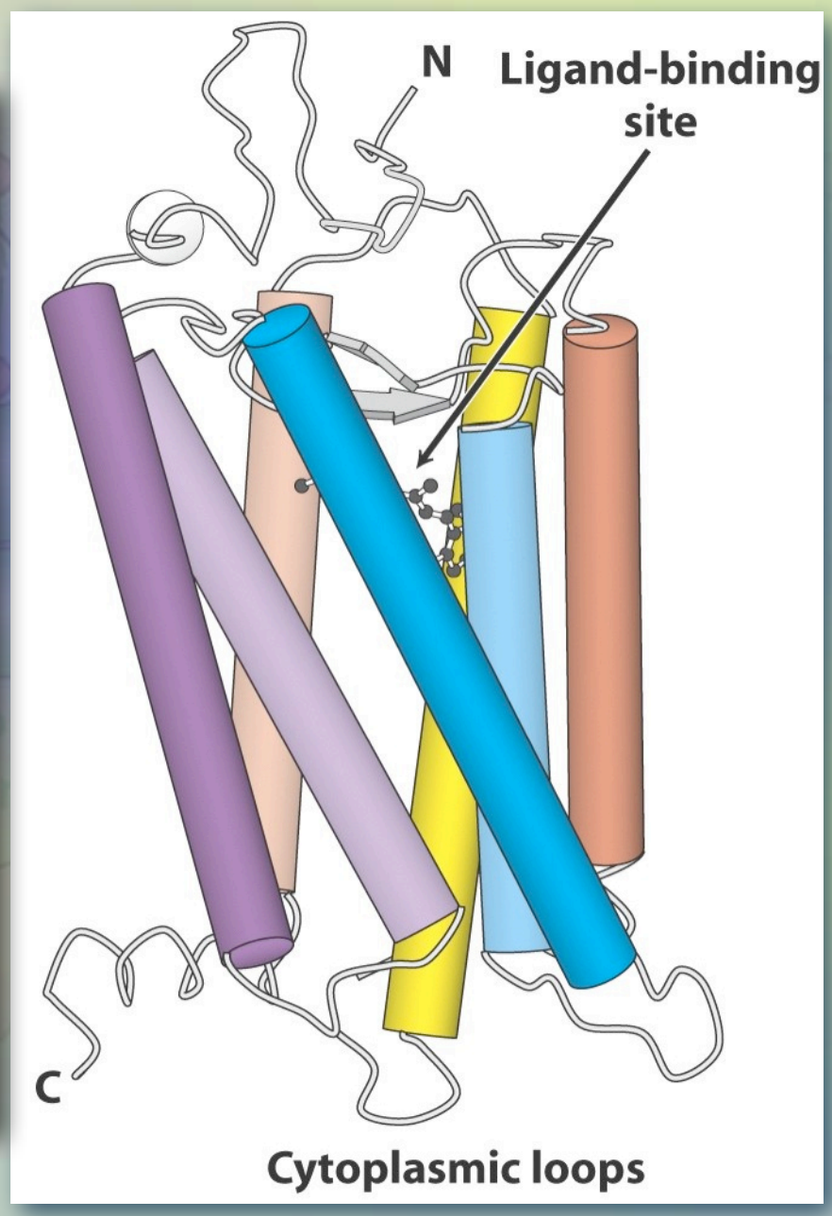




G-Protein Receptors

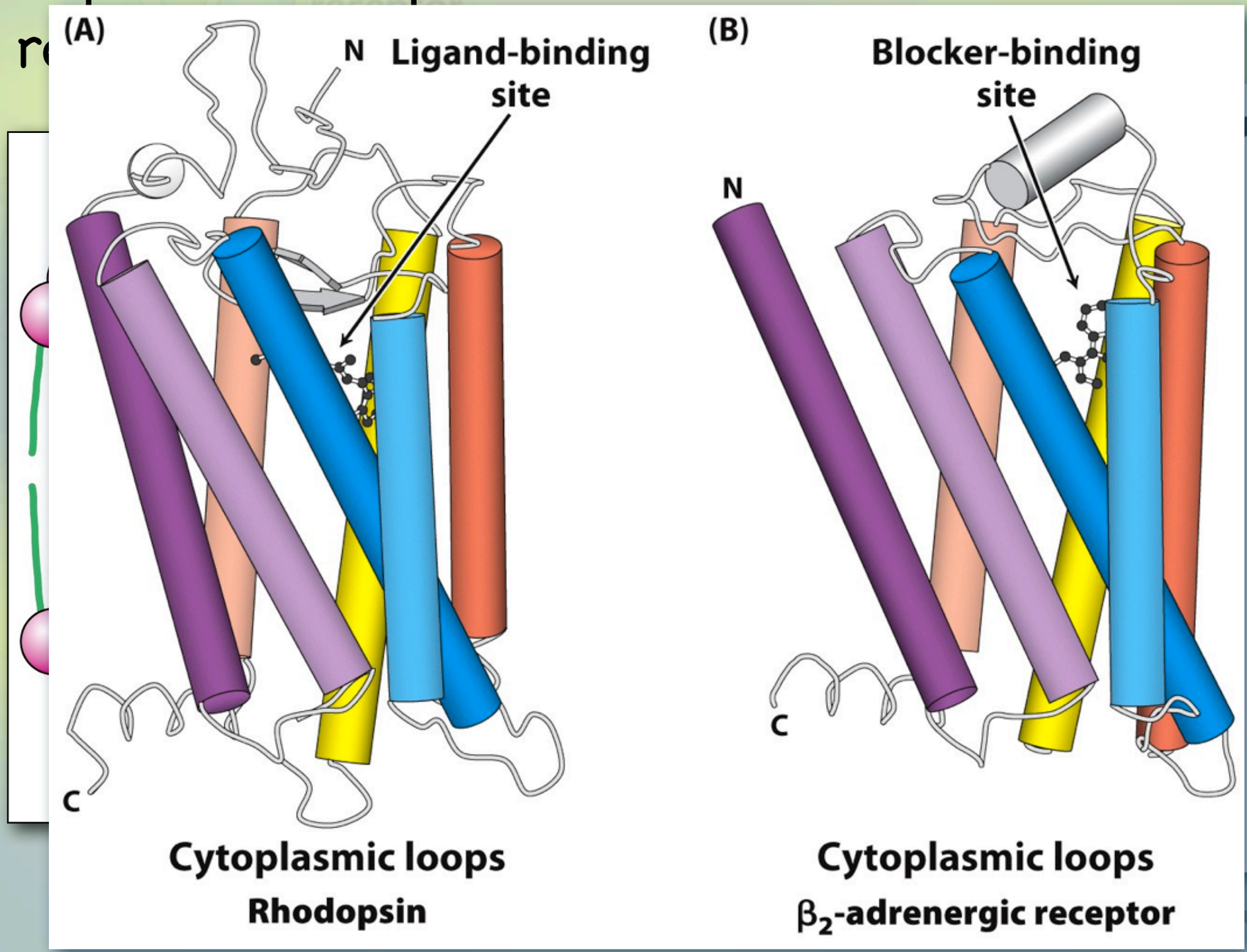
- G-protein receptors involve a 7-transmembrane receptor (7TM) protein.





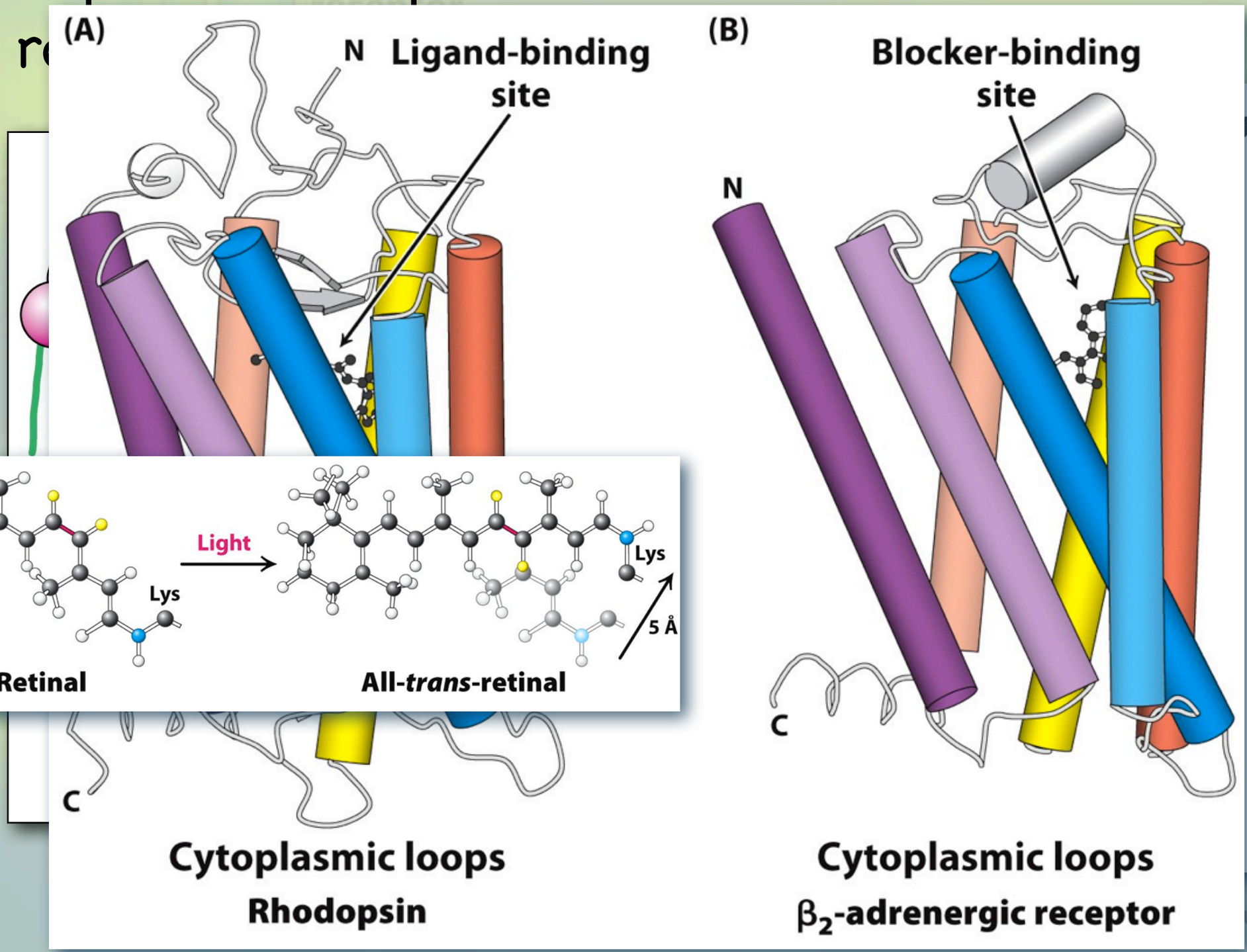
G-Protein Receptors

- G-protein receptors involve a 7-transmembrane r



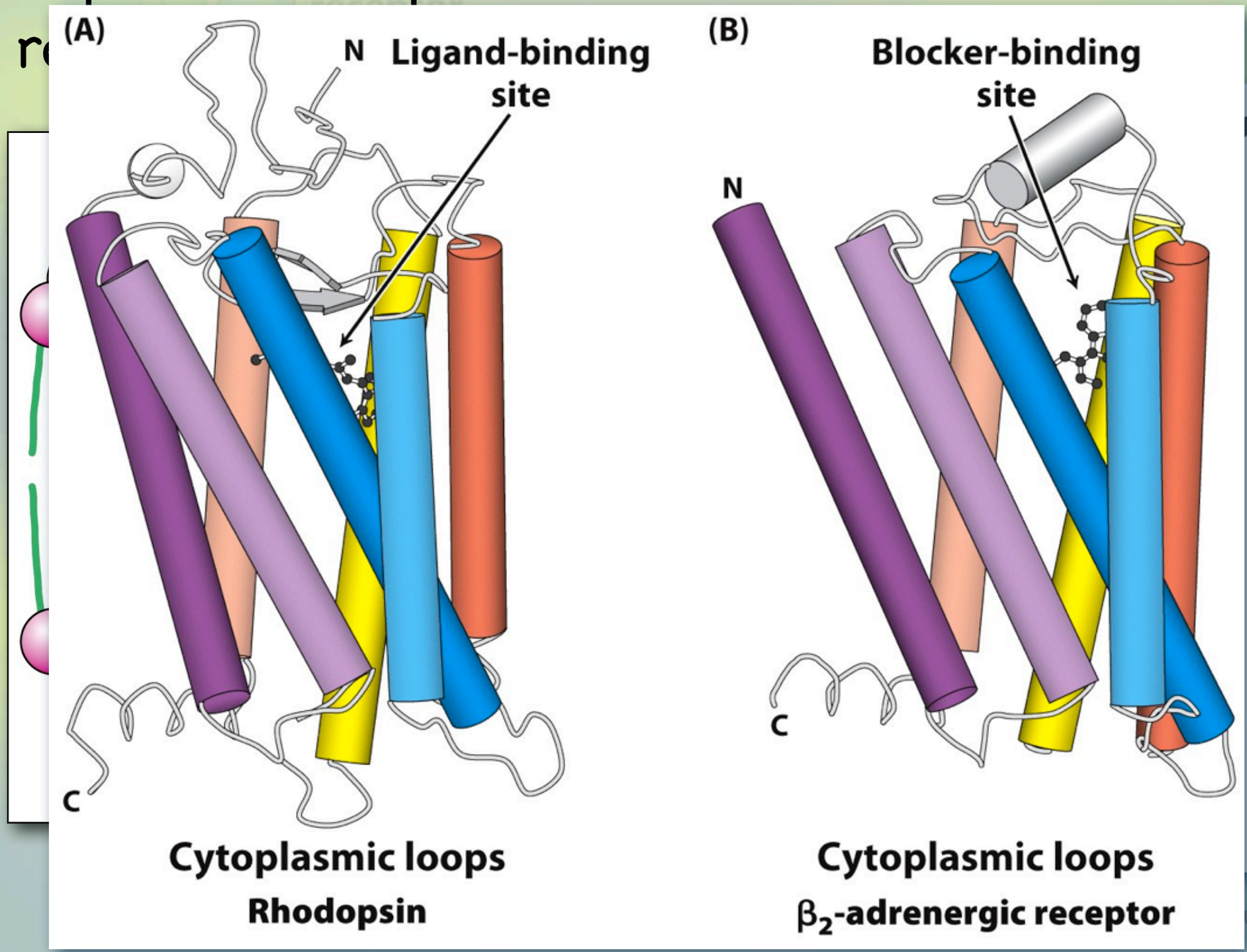
G-Protein Receptors

- G-protein receptors involve a 7-transmembrane r



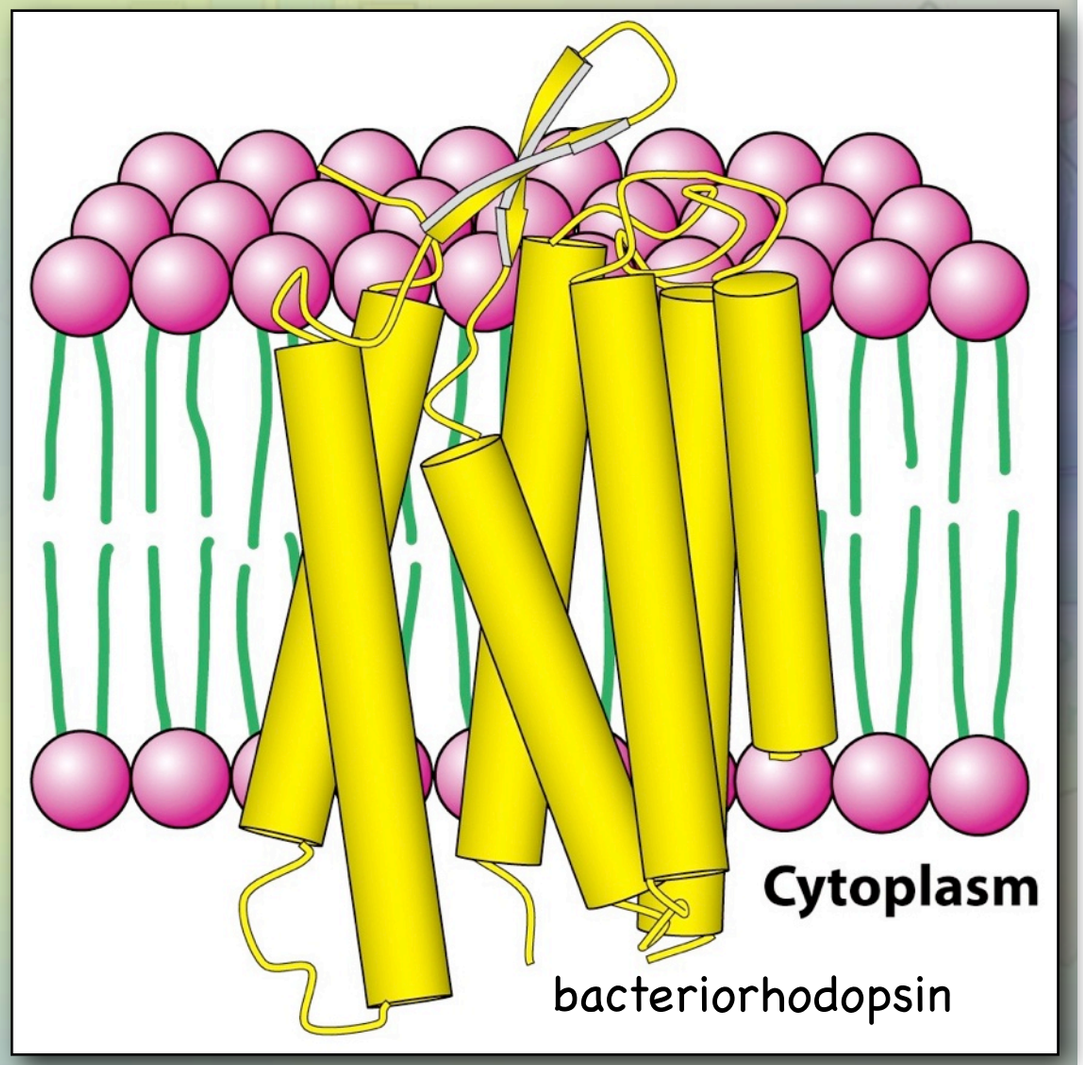
G-Protein Receptors

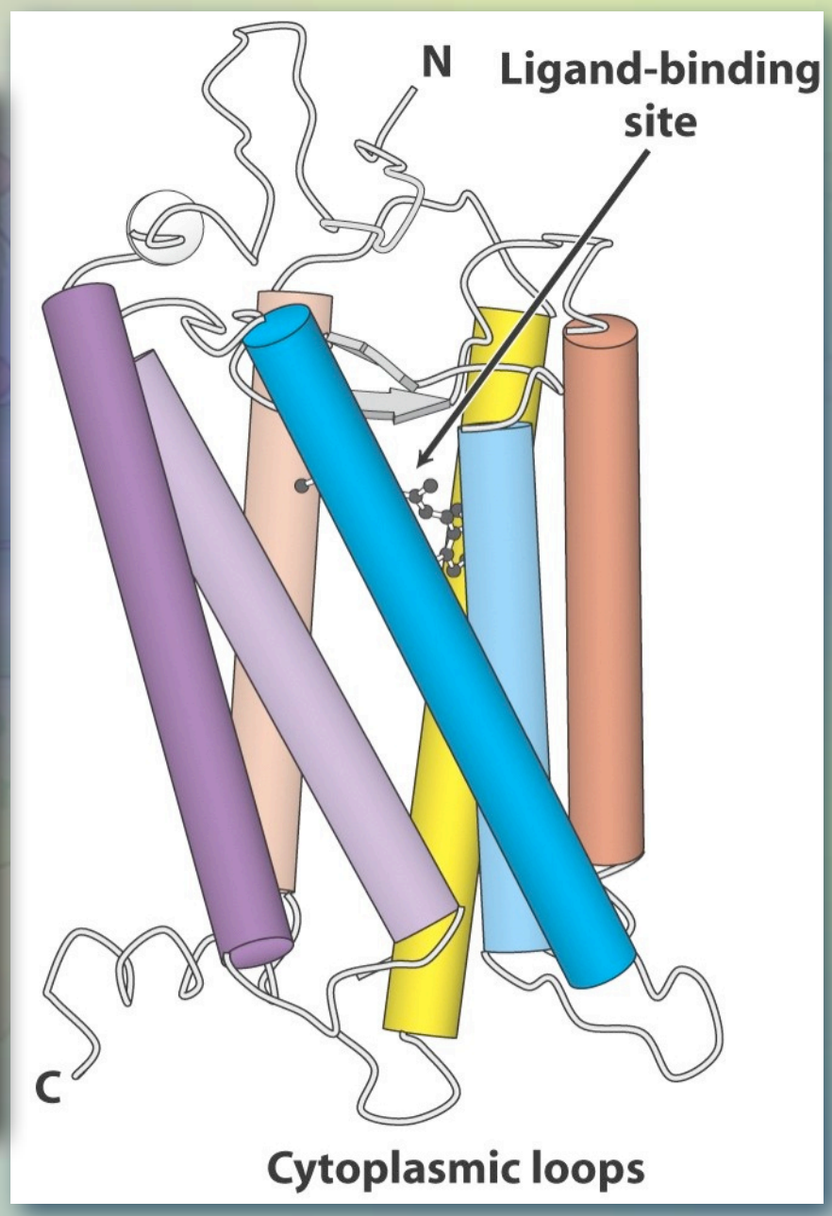
- G-protein receptors involve a 7-transmembrane r



G-Protein Receptors

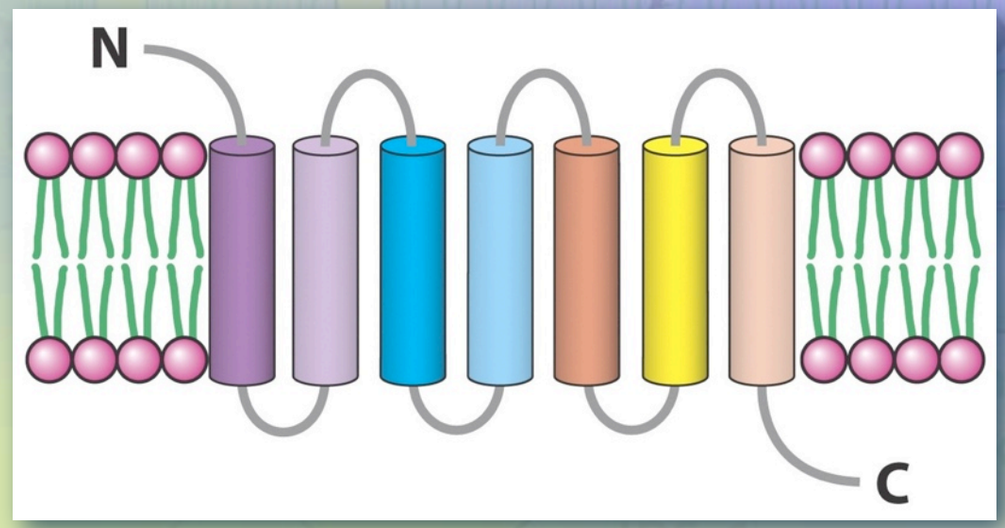
- G-protein receptors involve a 7-transmembrane receptor (7TM) protein.

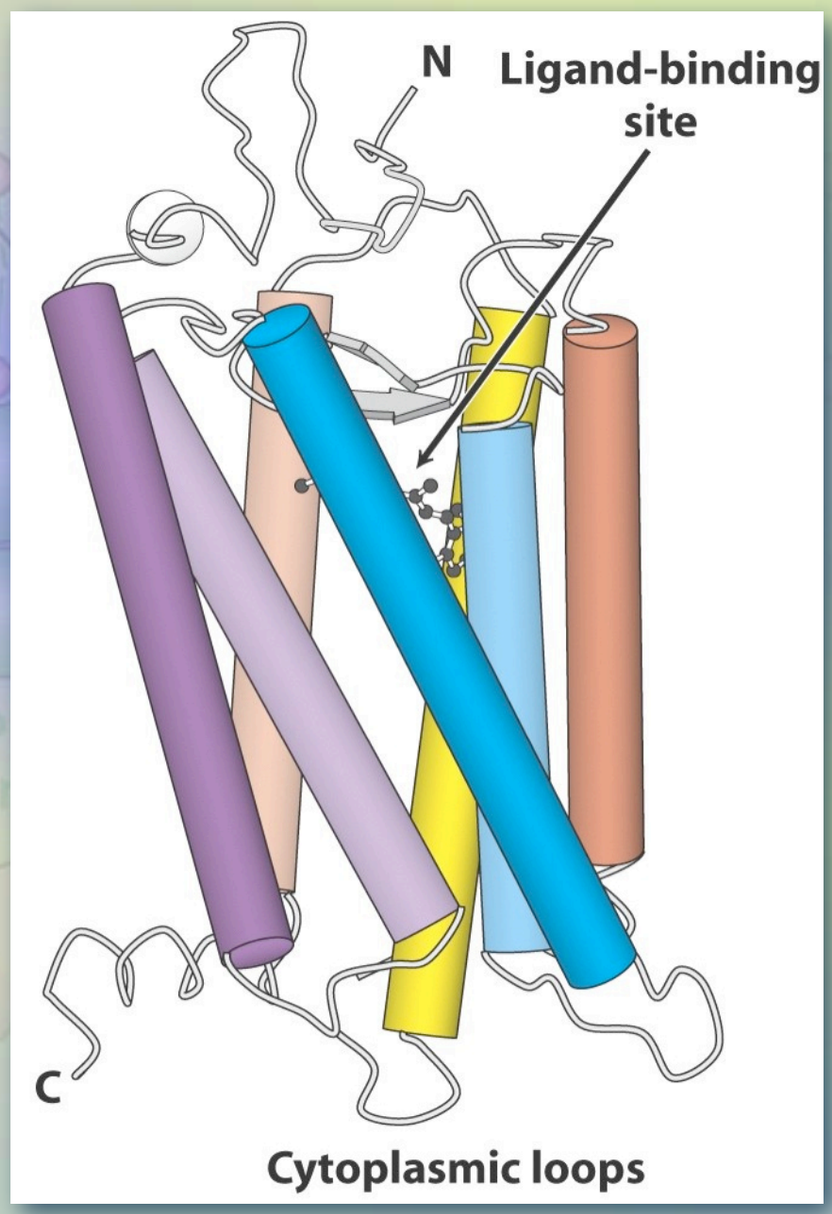




G-Protein Receptors

- G-protein receptors involve a 7-transmembrane receptor (7TM) protein.





G-Protein Receptors

- G-protein receptors involve a 7-transmembrane receptor (7TM) protein.

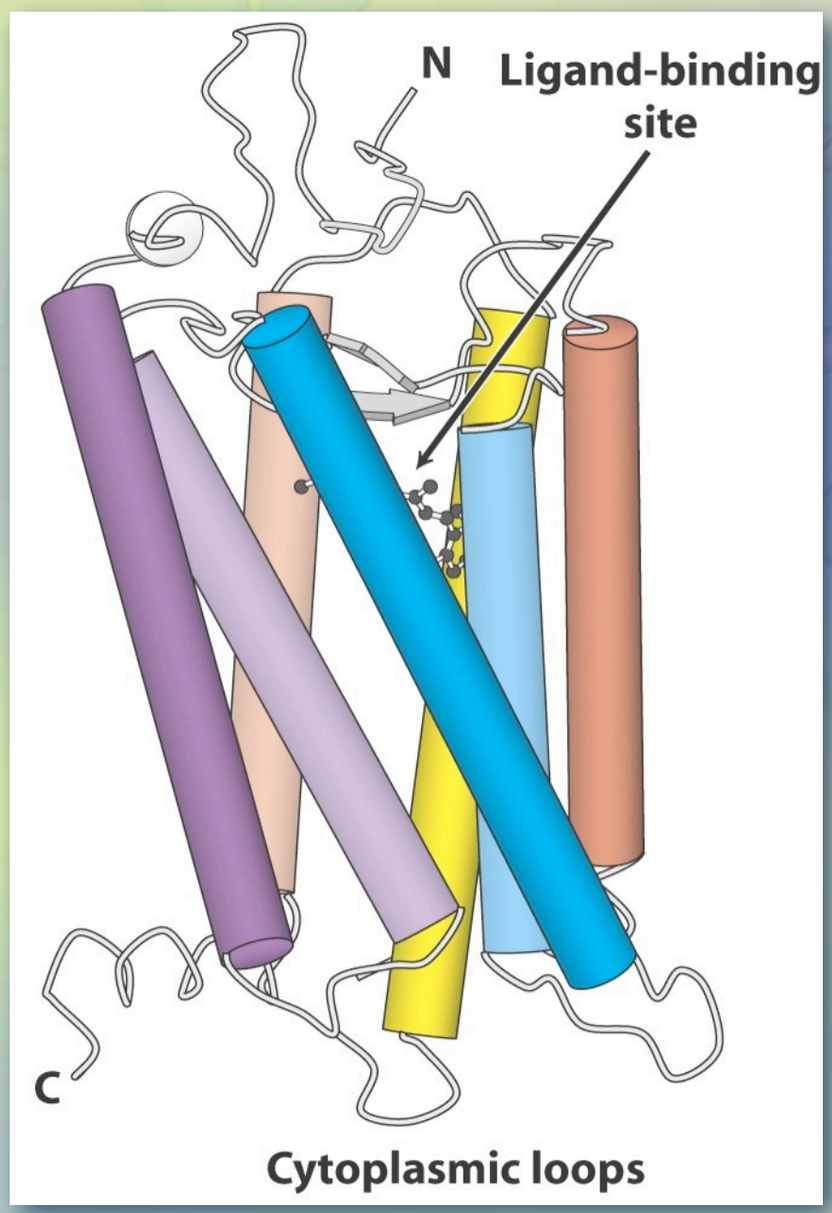


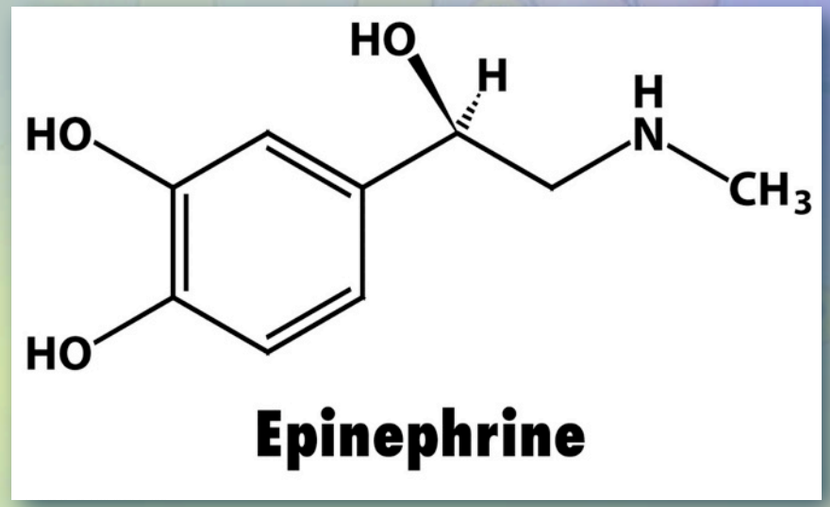
TABLE 14.1 Biological functions mediated by 7TM receptors

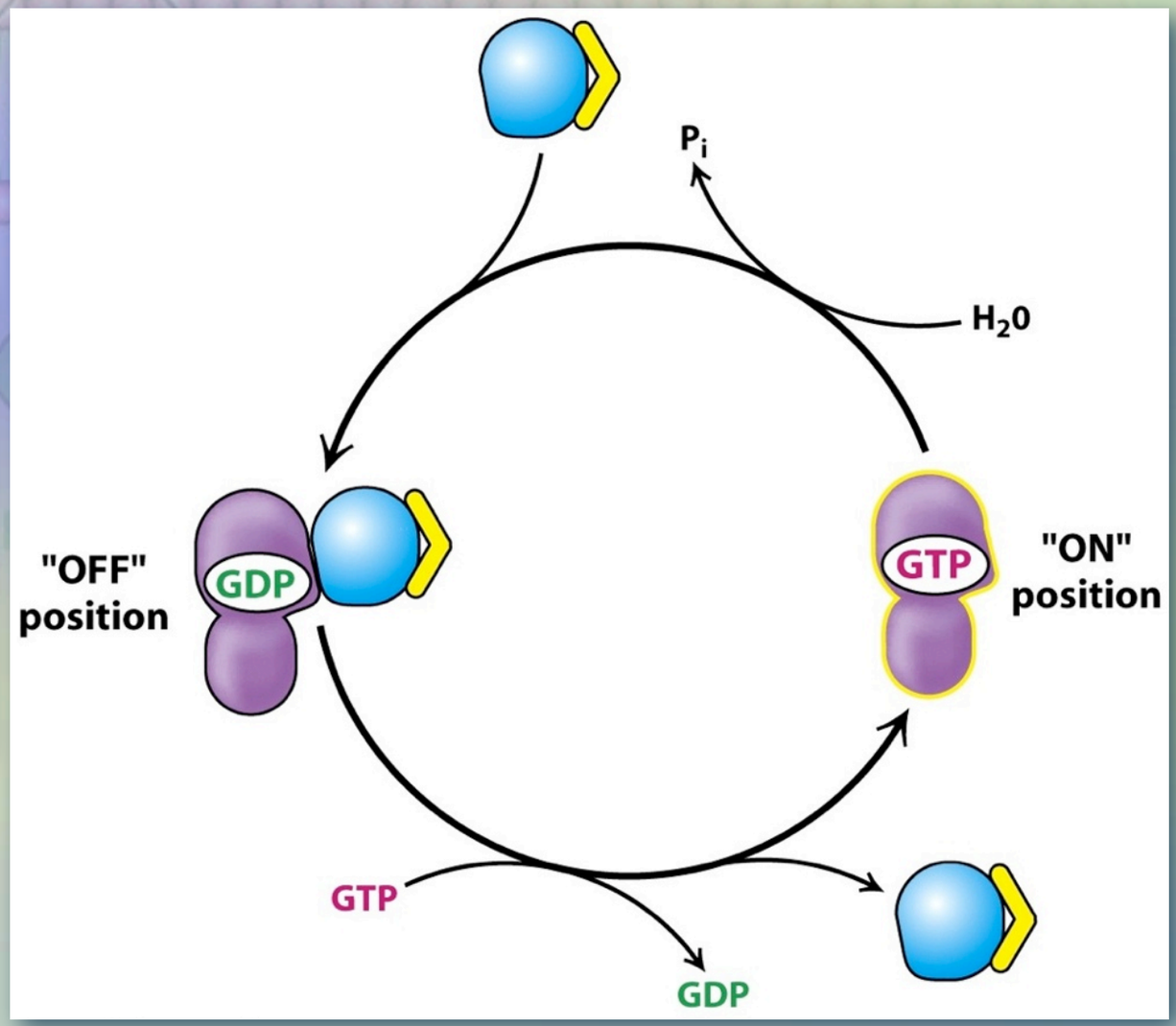
- Hormone action
- Hormone secretion
- Neurotransmission
- Chemotaxis
- Exocytosis
- Control of blood pressure
- Embryogenesis
- Cell growth and differentiation
- Development
- Smell
- Taste
- Vision
- Viral infection

Source: After J. S. Gutkind, *J. Biol. Chem.* 273(1998): 1839–1842.

G-Protein Receptors

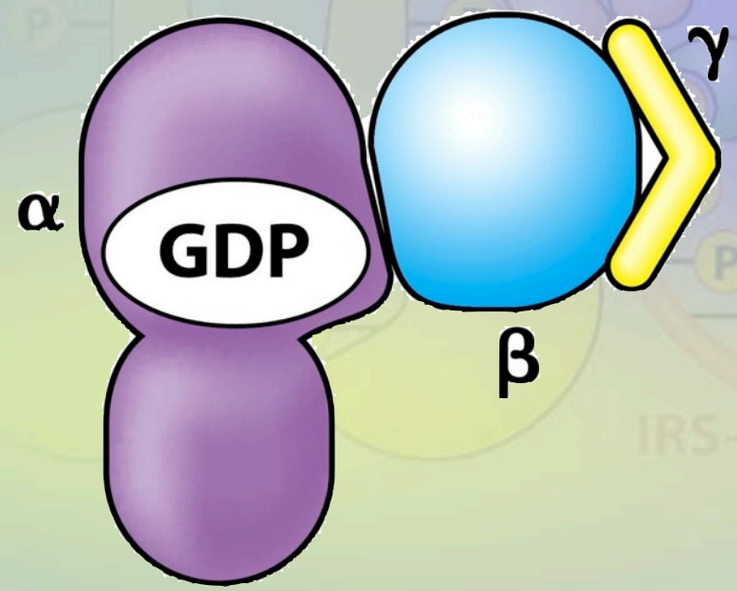
- The receptors for epinephrine (β-adrenergic receptors) provide and example for a class of receptors called G-proteins.

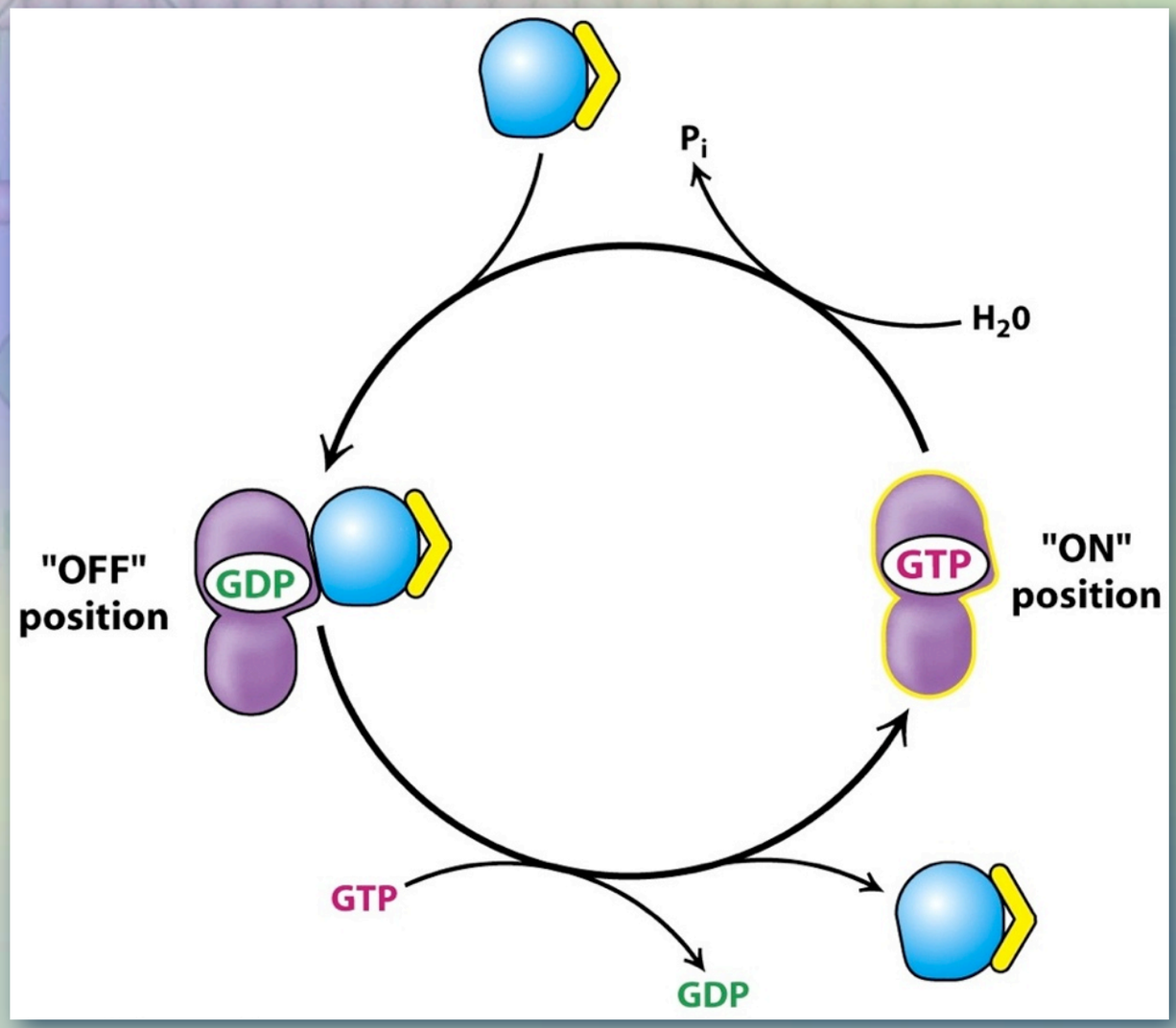




G-Protein Receptors

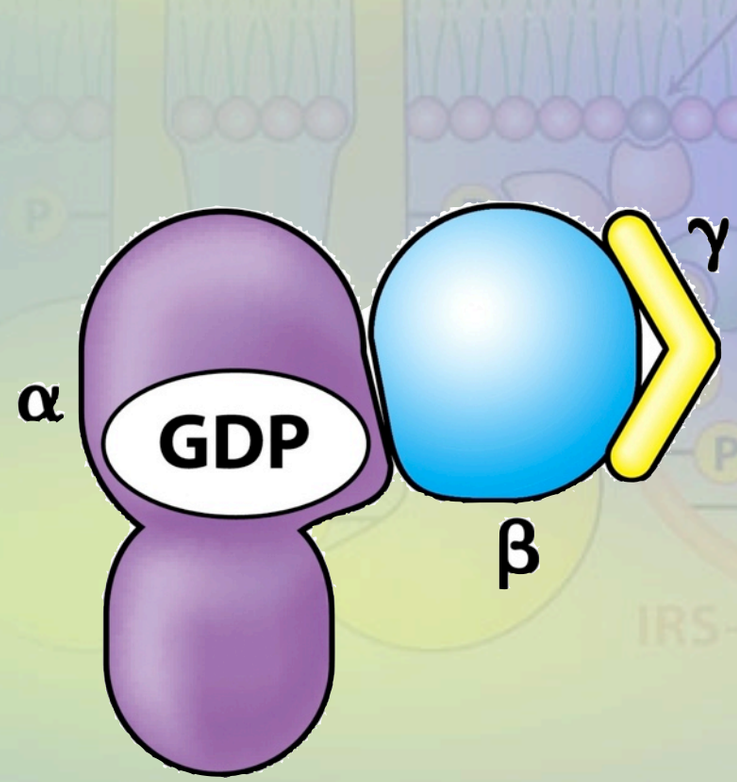
- The receptors for epinephrine (β-adrenergic receptors) provide and example for a class of receptors called G-proteins.

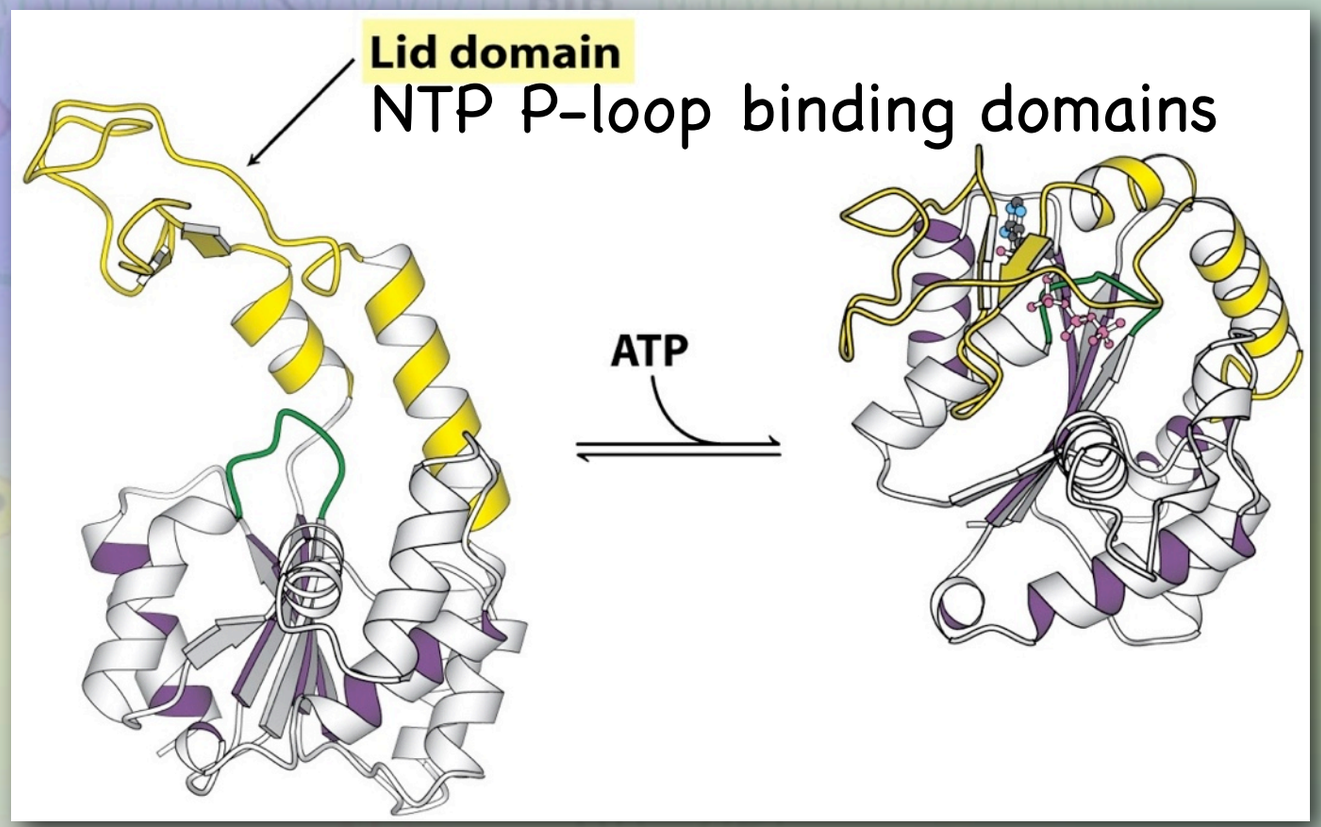




G-Protein Receptors

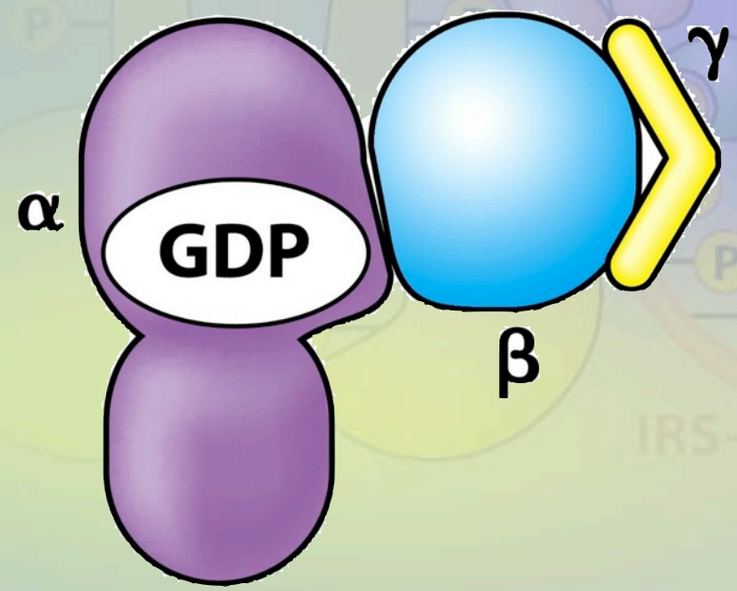
- The receptors for epinephrine (β-adrenergic receptors) provide and example for a class of receptors called G-proteins.

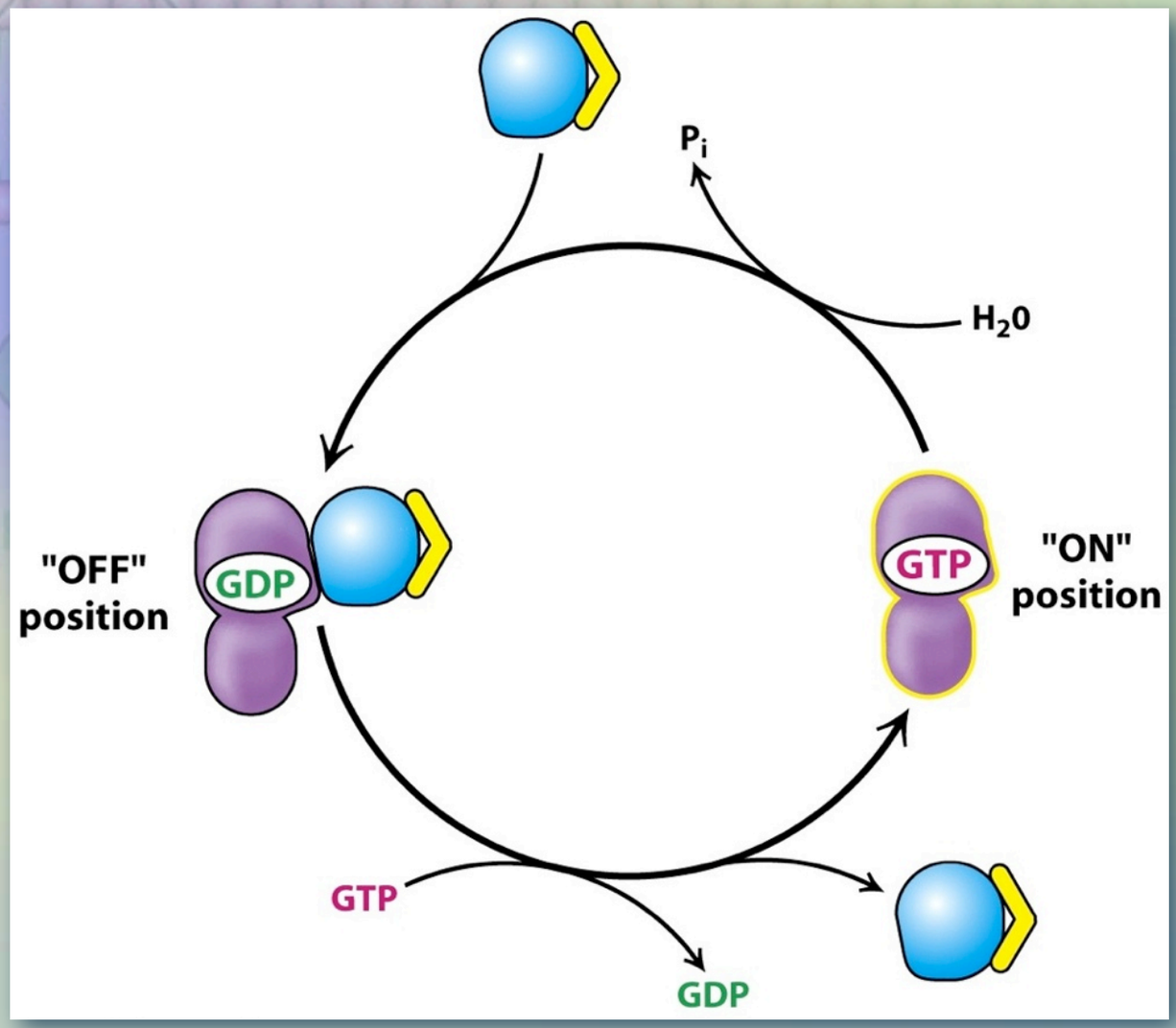




G-Protein Receptors

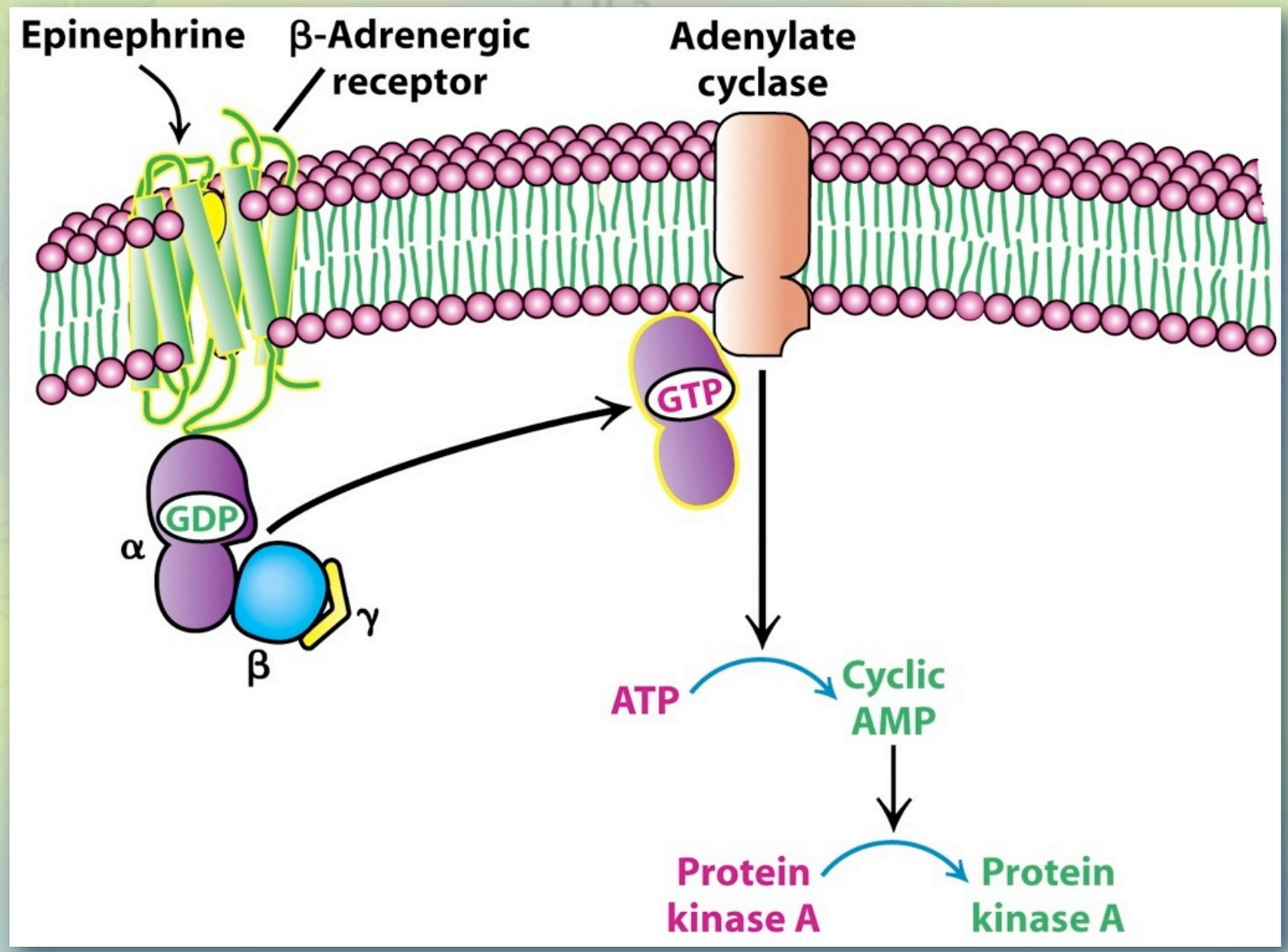
- The receptors for epinephrine (β-adrenergic receptors) provide and example for a class of receptors called G-proteins.





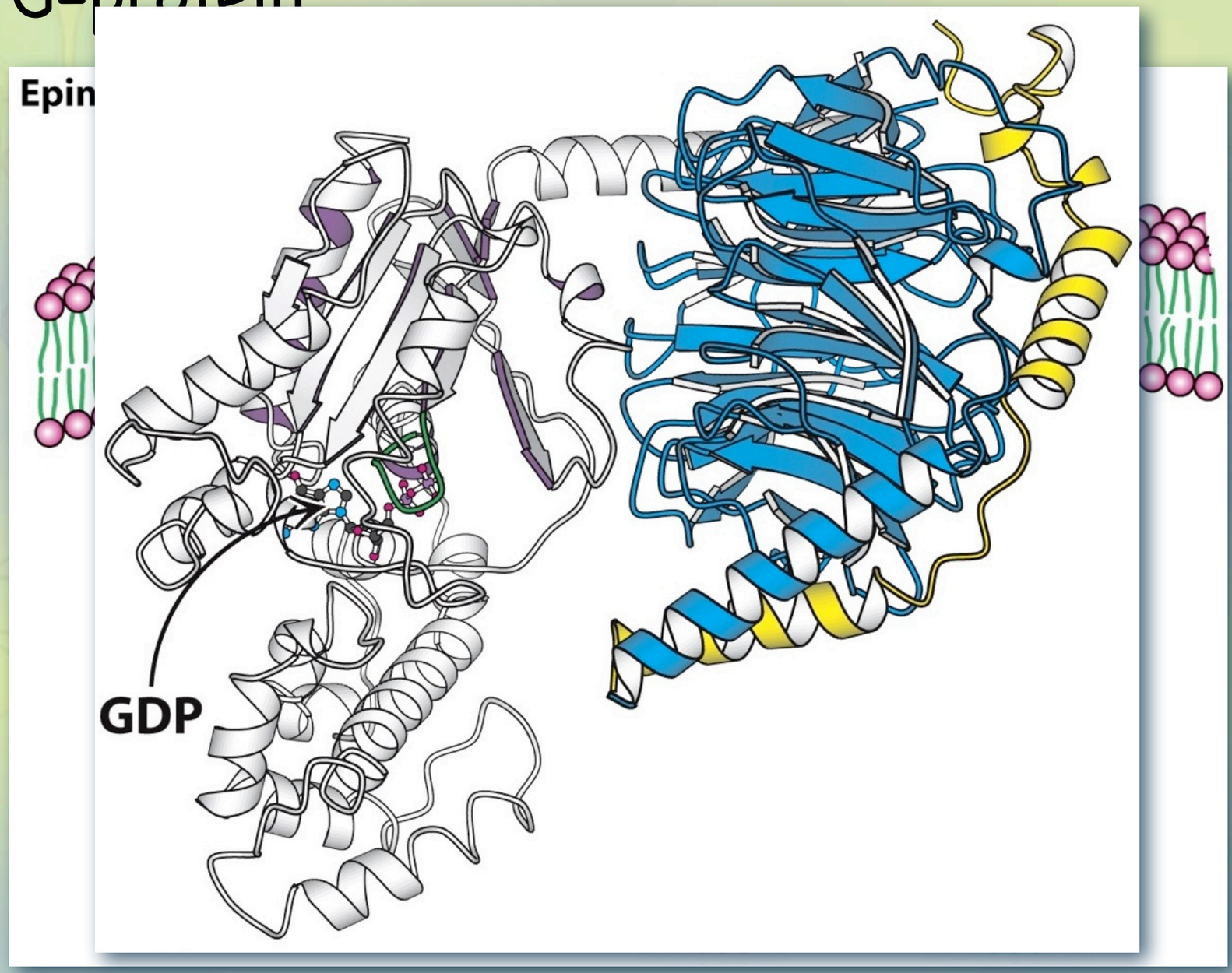
G-Protein Receptors

- Ligand Binding to the 7TM receptor activates the G-protein.



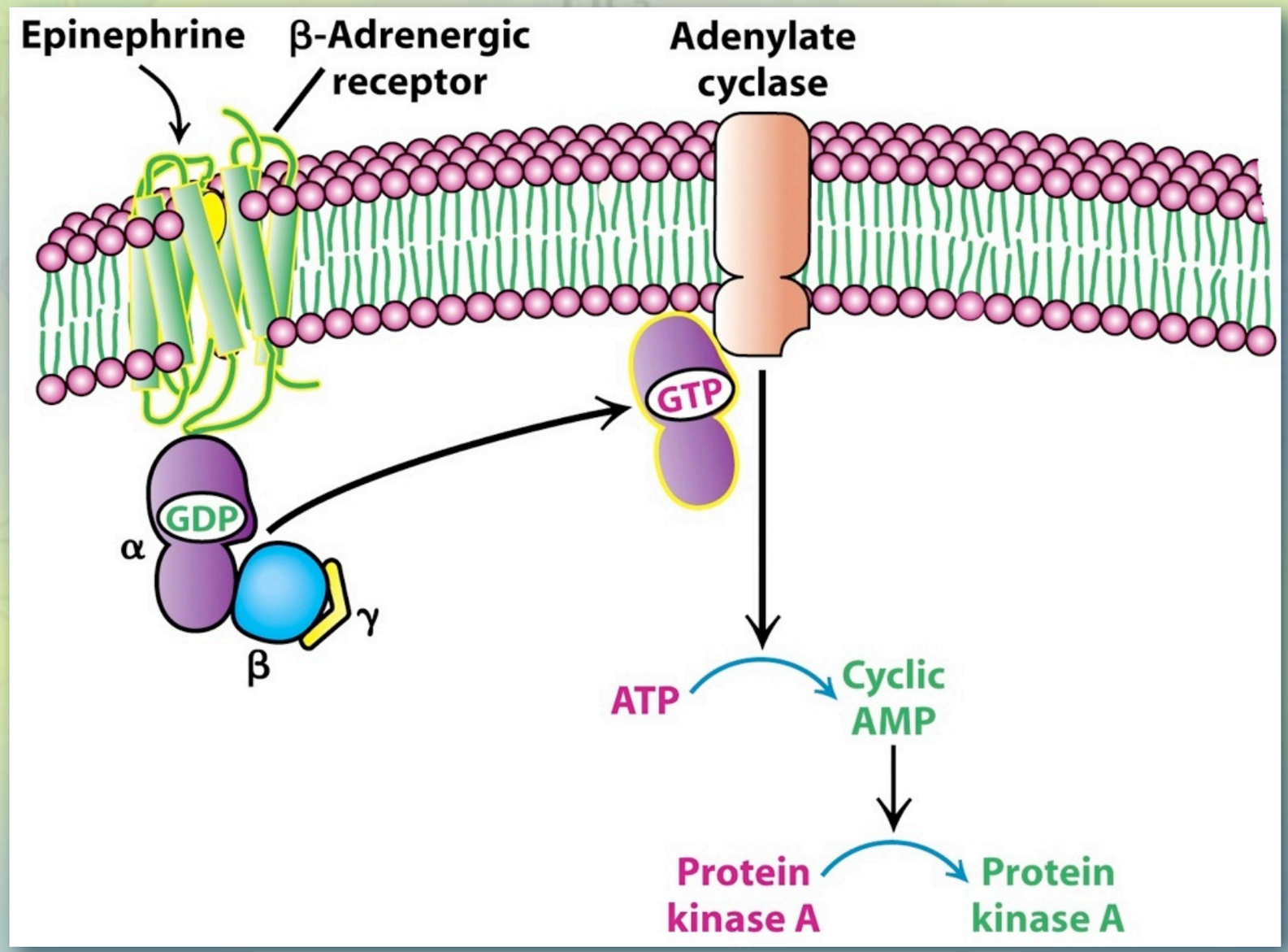
G-Protein Receptors

- Ligand Binding to the 7TM receptor activates the G-protein



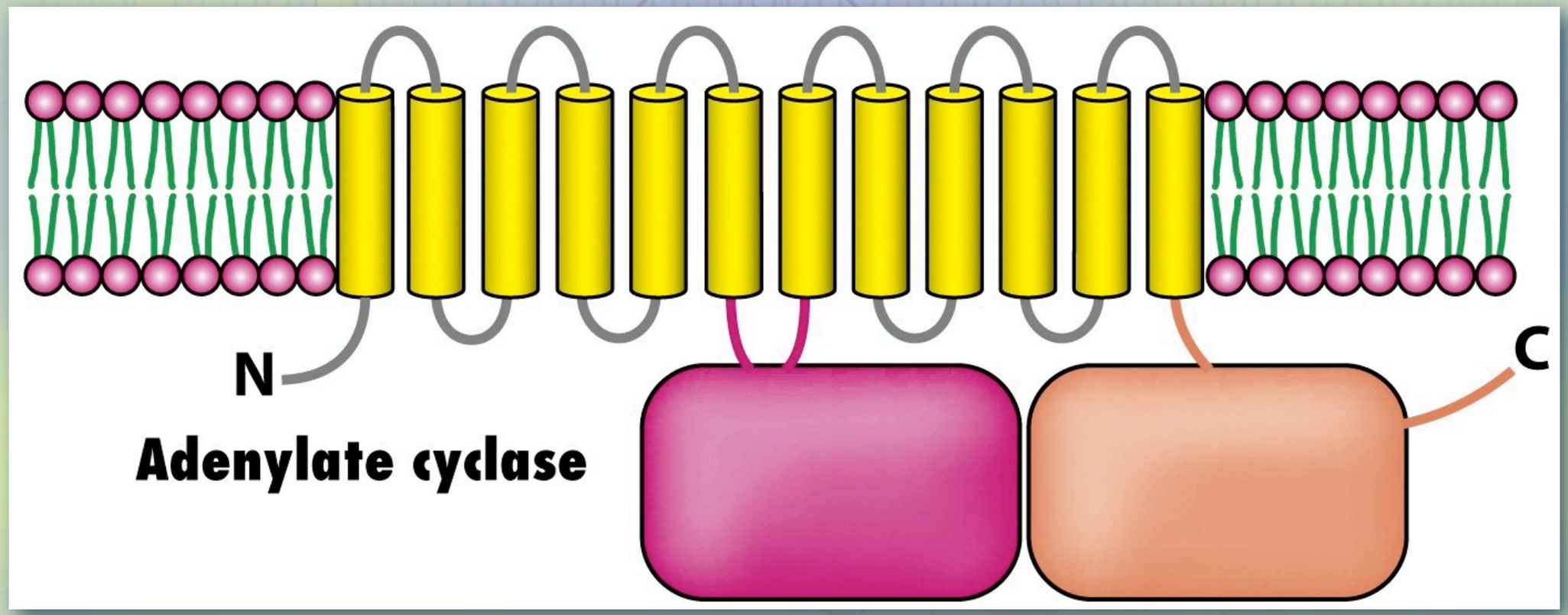
G-Protein Receptors

- Ligand Binding to the 7TM receptor activates the G-protein.



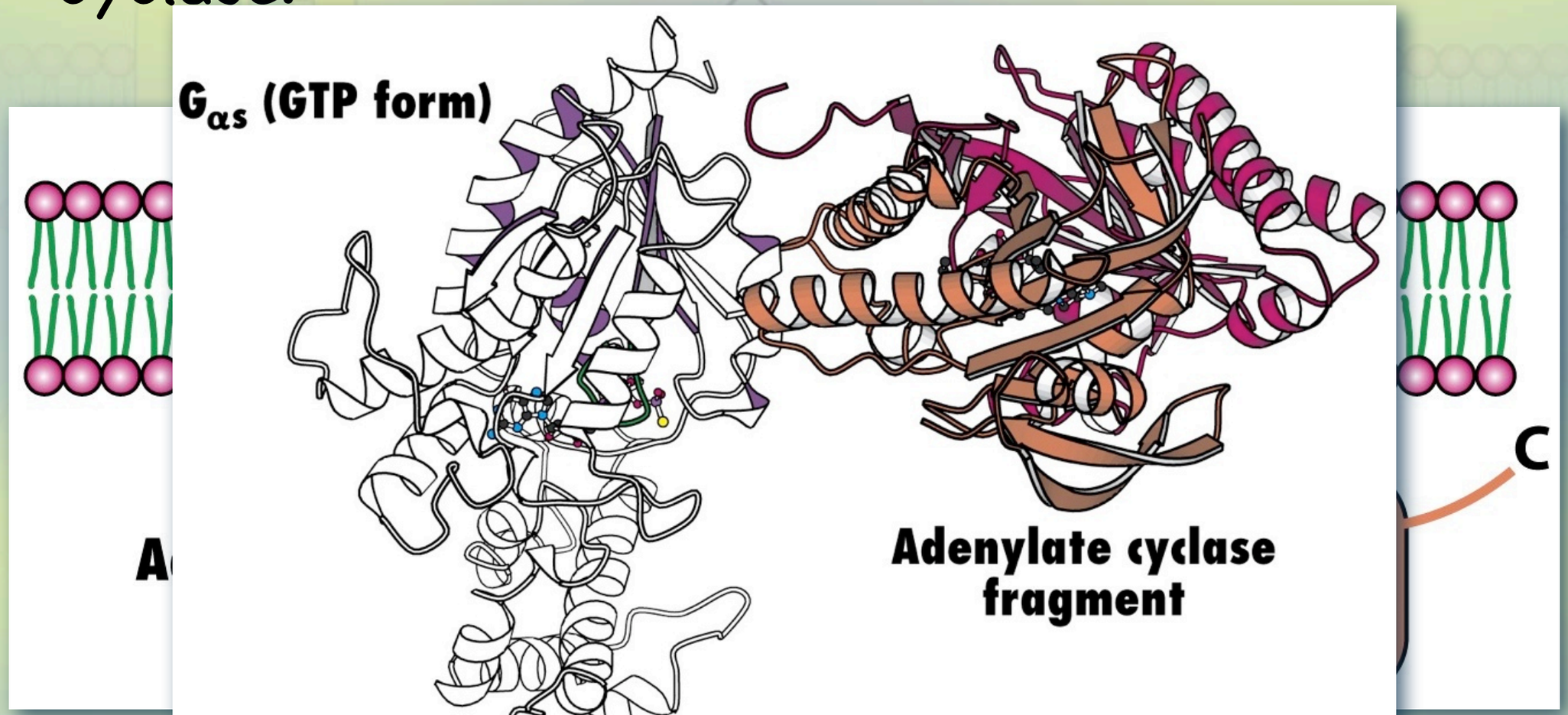
G-Protein Receptors

- The activated G-protein ($G_{\alpha s}$) goes on to activate the membrane bound enzyme adenylate cyclase.



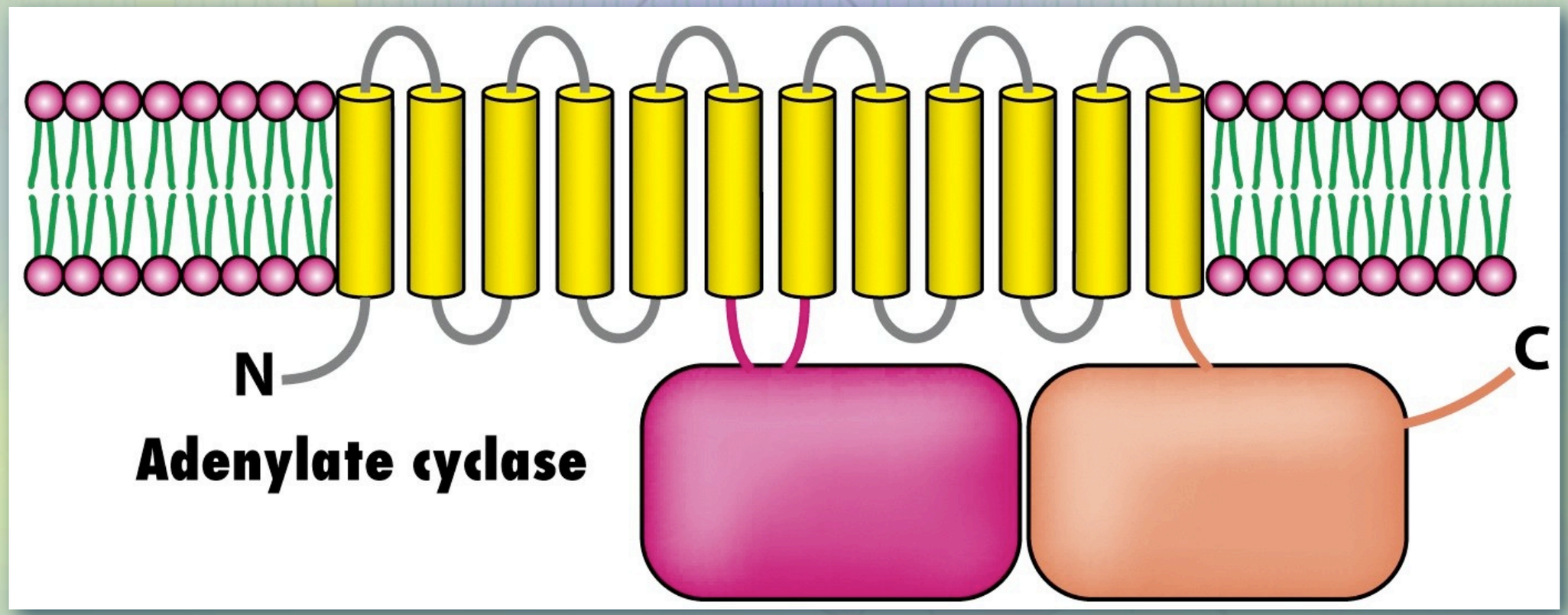
G-Protein Receptors

- The activated G-protein ($G_{\alpha s}$) goes on to activate the membrane bound enzyme adenylate cyclase.

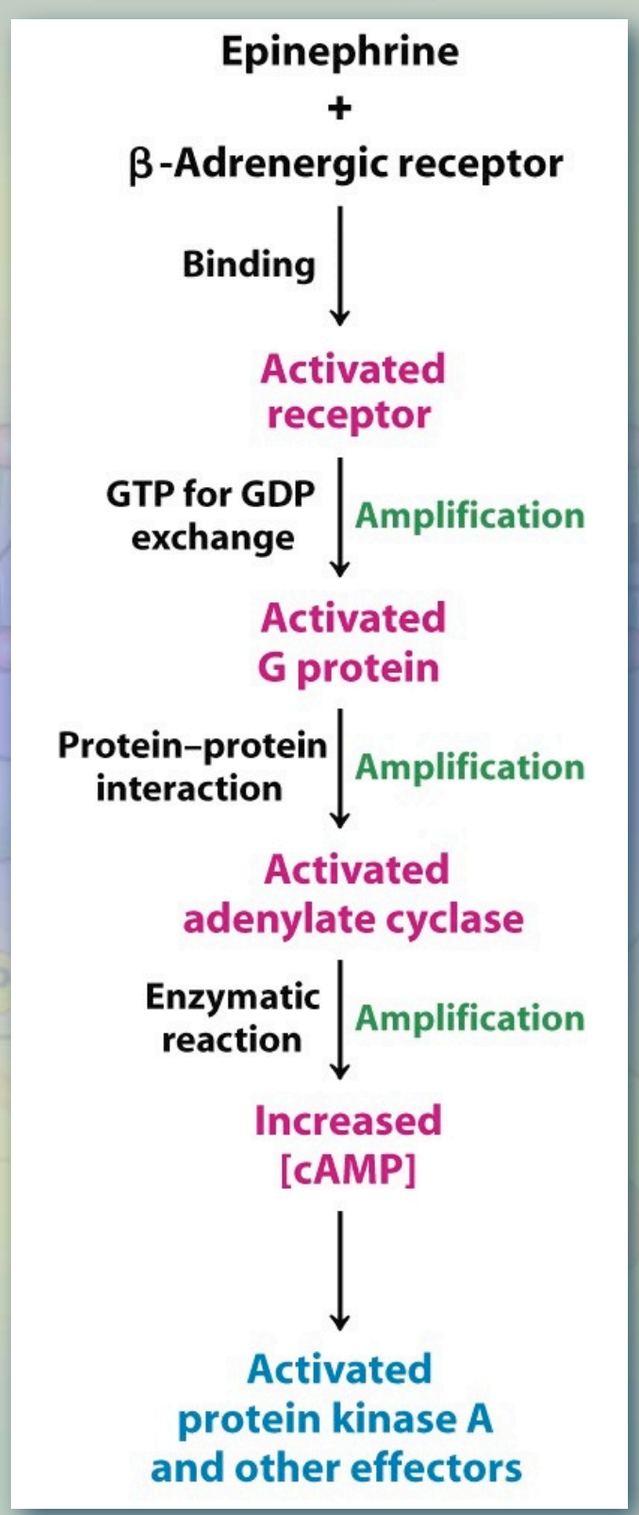


G-Protein Receptors

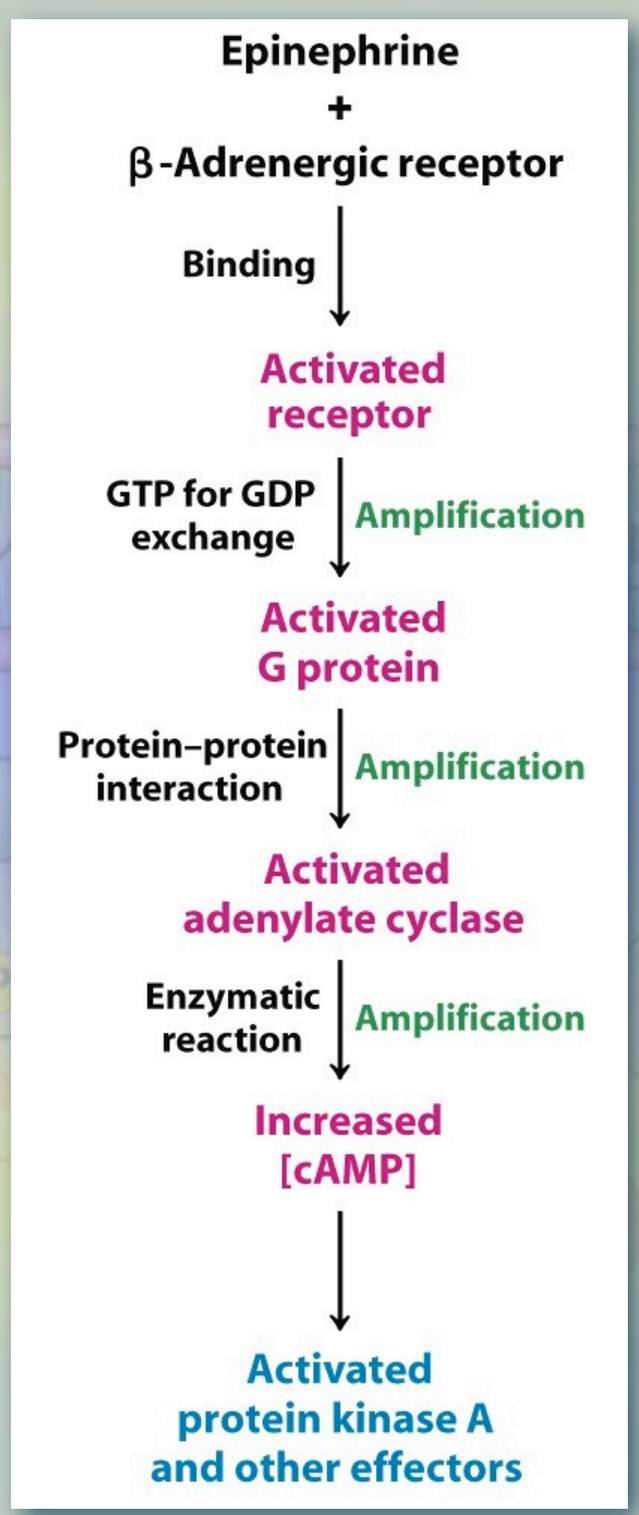
- The activated G-protein ($G_{\alpha s}$) goes on to activate the membrane bound enzyme adenylate cyclase.

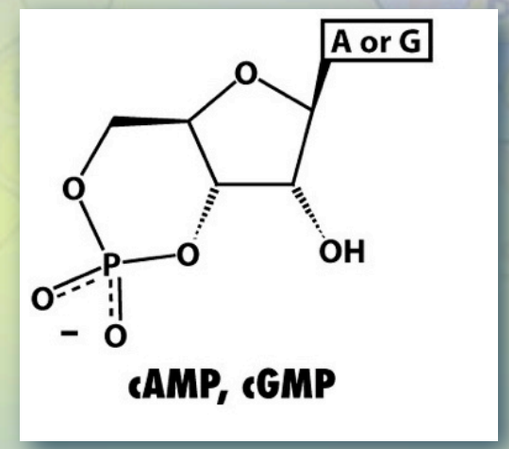


G-Protein Receptors

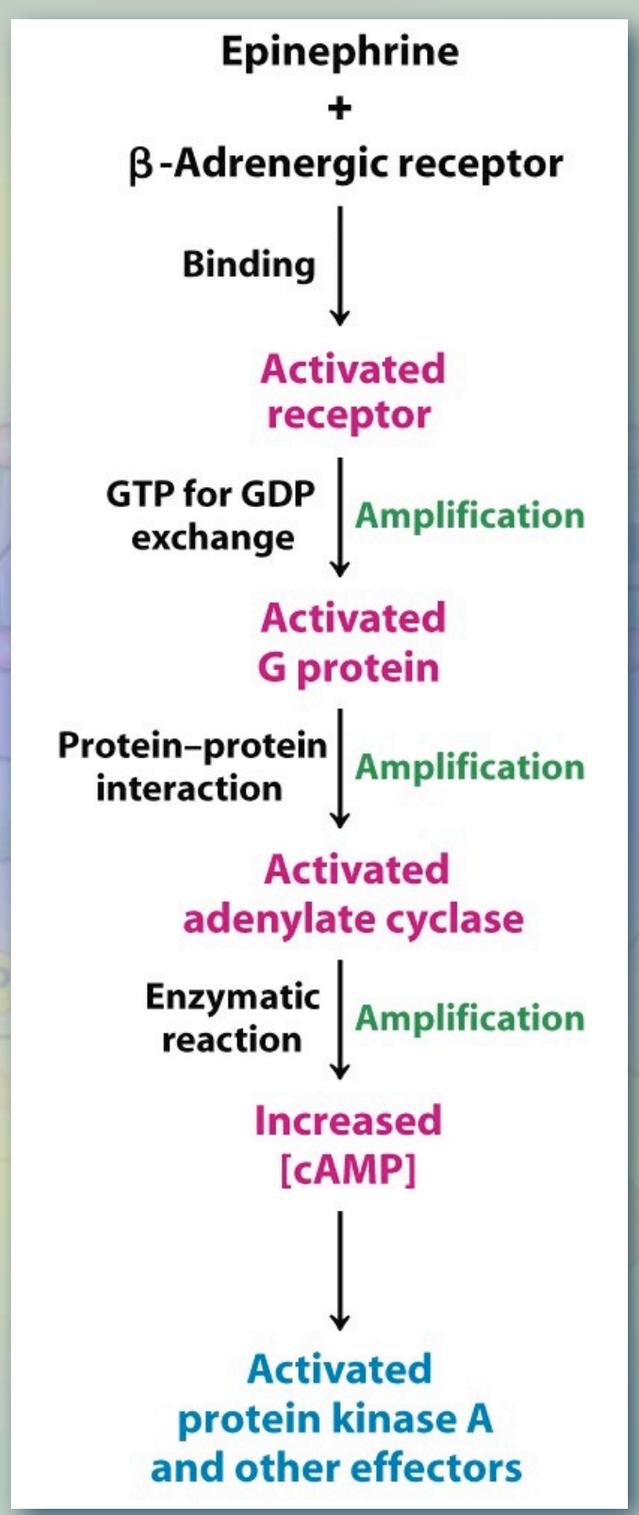


G-Protein Receptors





G-Protein Receptors

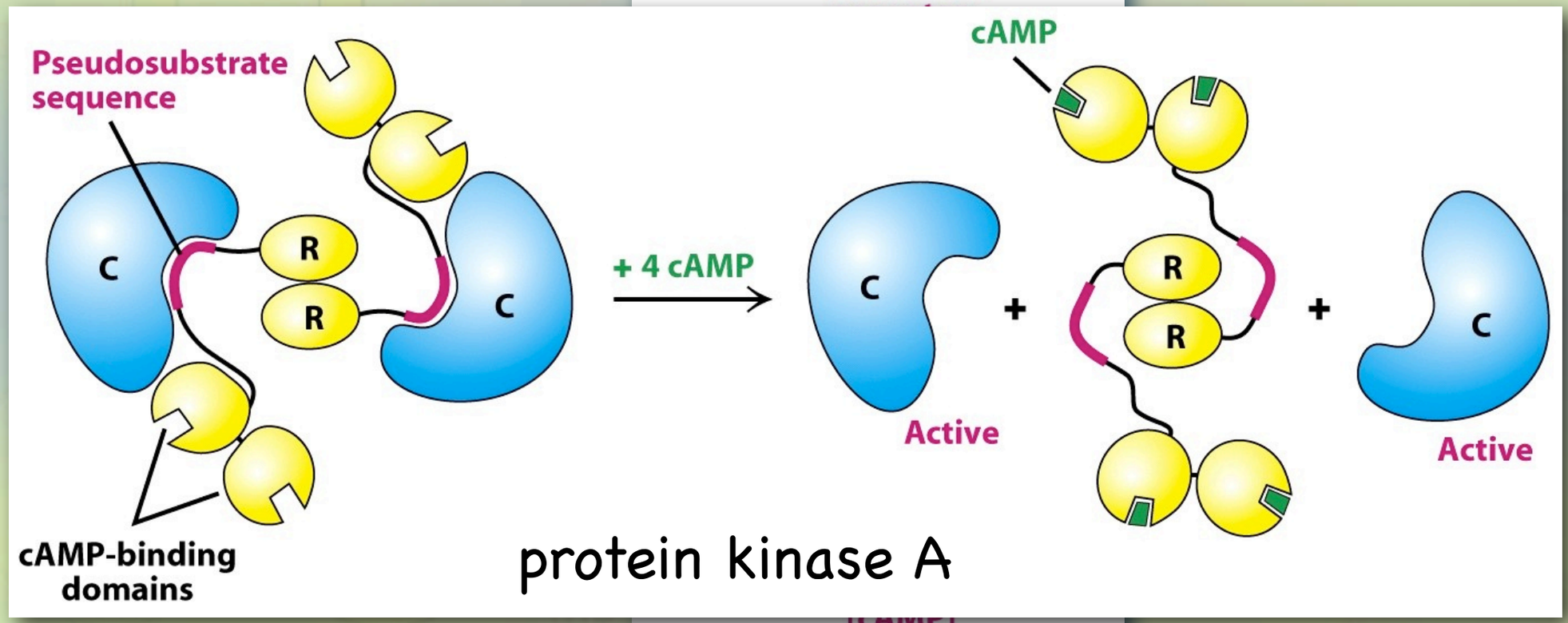


G-Protein Receptors

Epinephrine
+
β-Adrenergic receptor

Binding ↓

Activated



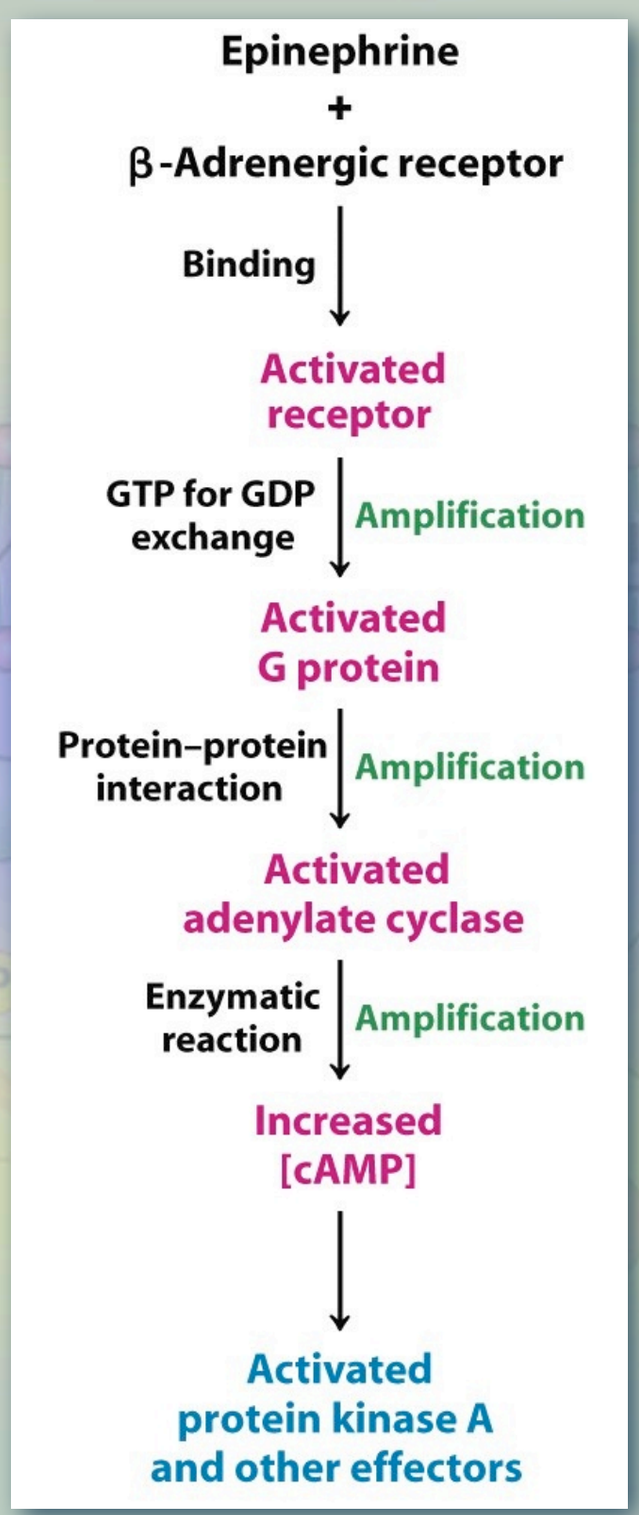
protein kinase A

[cAMP]

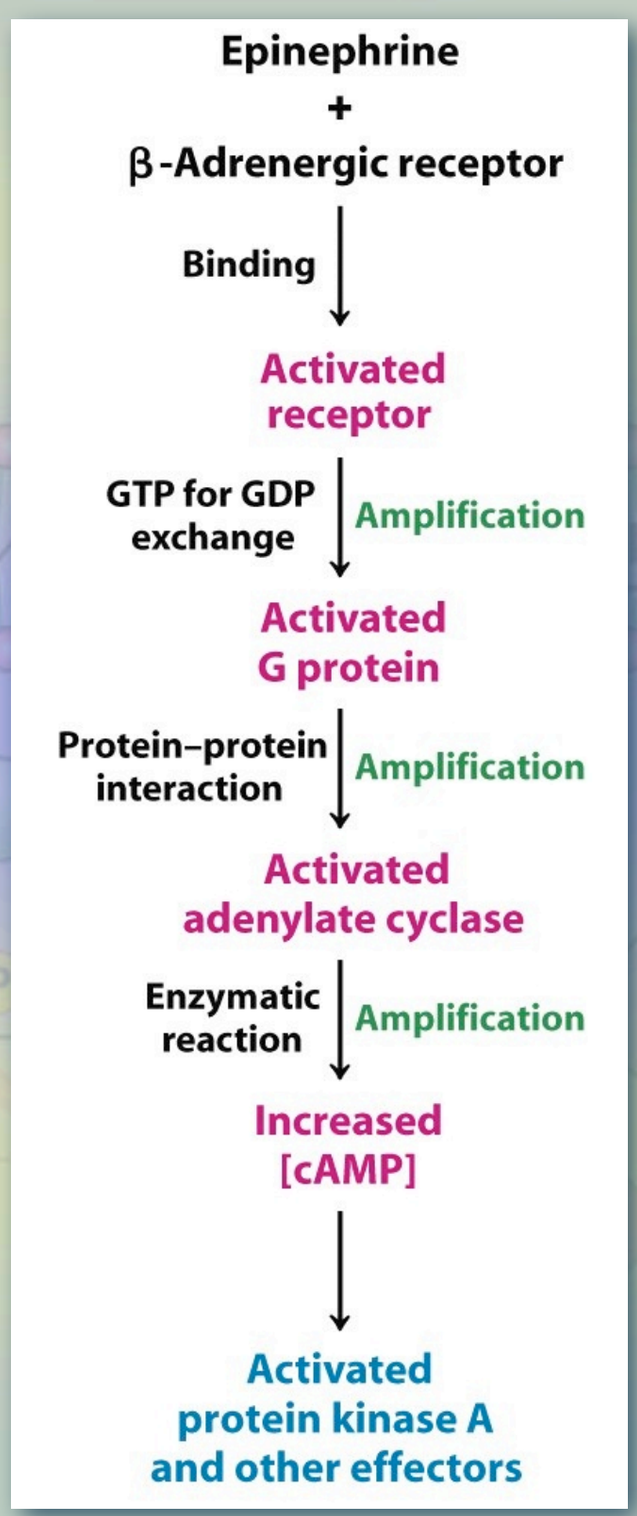
↓

Activated
protein kinase A
and other effectors

G-Protein Receptors



G-Protein Receptors



- Glycogen breakdown
- Stimulates transcription factors (CREB)
- Modulates muscular contractions
- Degradation of stored fuels
- Secretion of acid by gastric mucosa
- Dispersion of melanin granules
- Opening of chloride channels

G-Protein Receptors

- Glycogen breakdown

nscription

scular

f stored

cid by

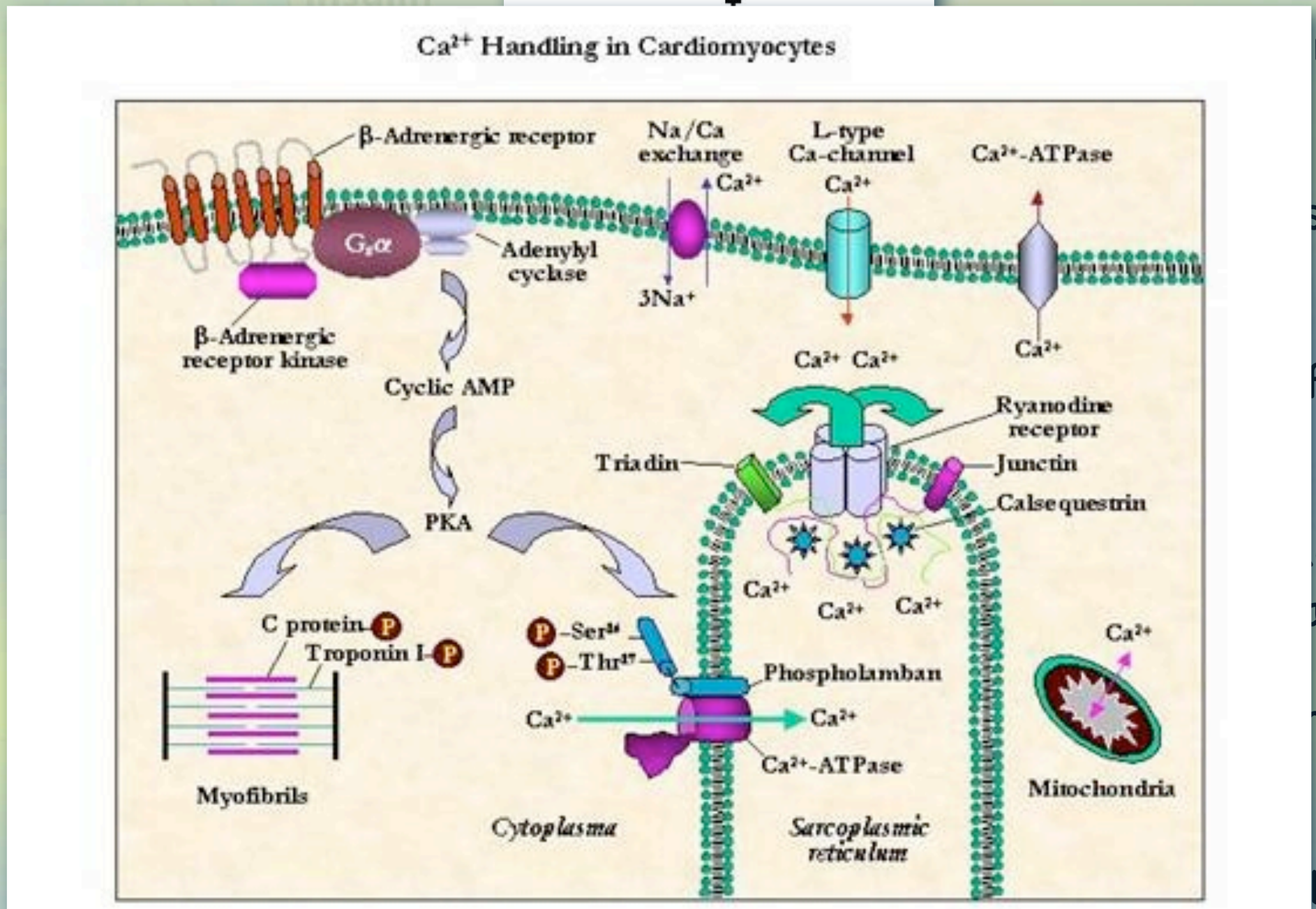
melanin

loride

channels

Epinephrine

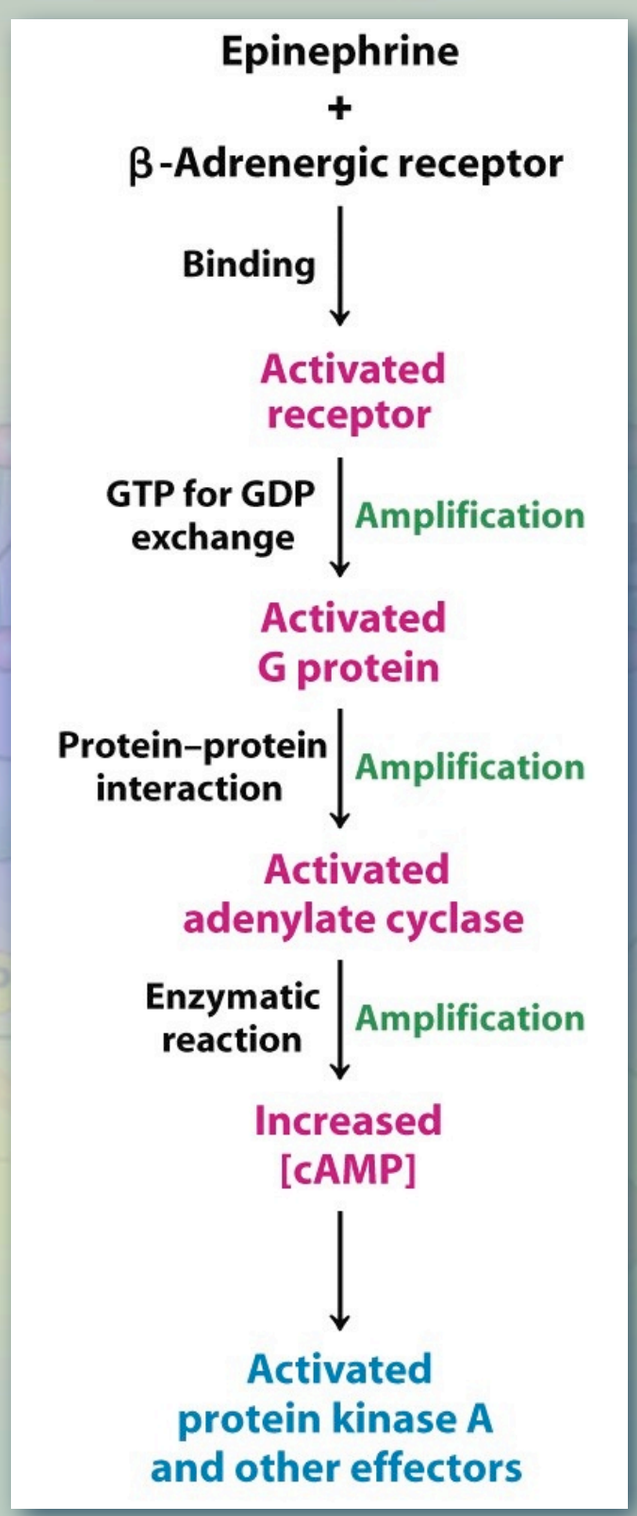
+



protein kinase A

and other effectors

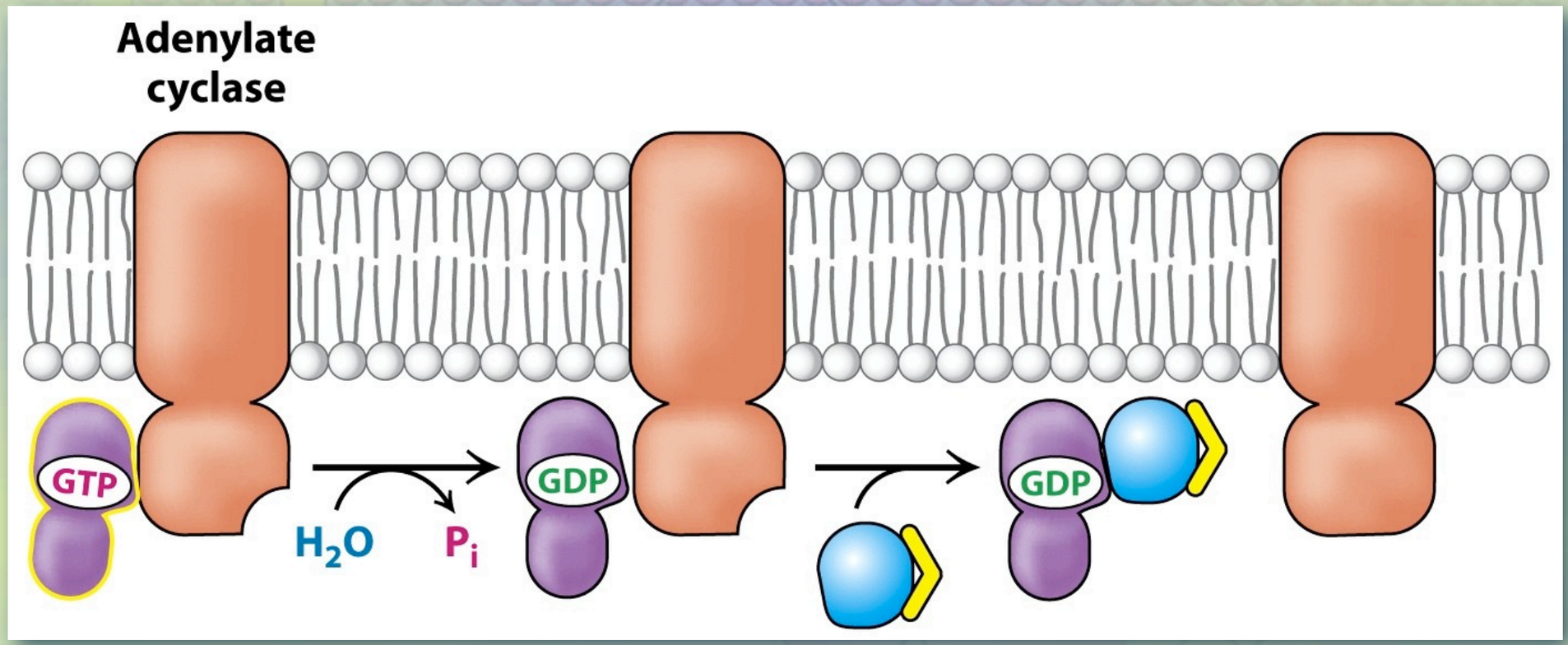
G-Protein Receptors



- Glycogen breakdown
- Stimulates transcription factors (CREB)
- Modulates muscular contractions
- Degradation of stored fuels
- Secretion of acid by gastric mucosa
- Dispersion of melanin granules
- Opening of chloride channels

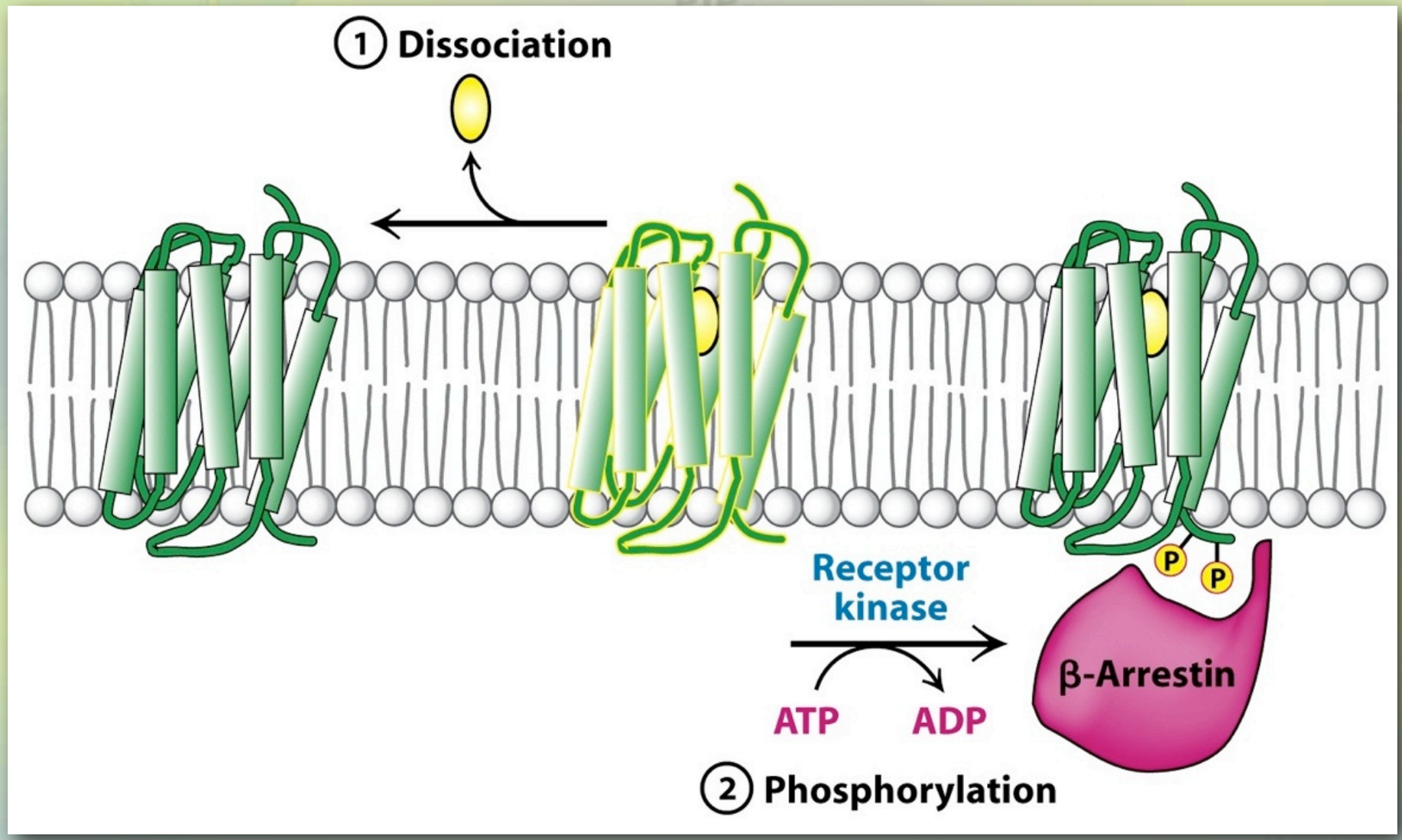
G-Protein Receptors

- Hydrolysis of GTP to GDP resets the activated G-protein.



G-Protein Receptors

- Resetting the receptor.



Next up

- Lecture 10, Signal Transduction (con'd). (Chapter 14)