Cell Communication

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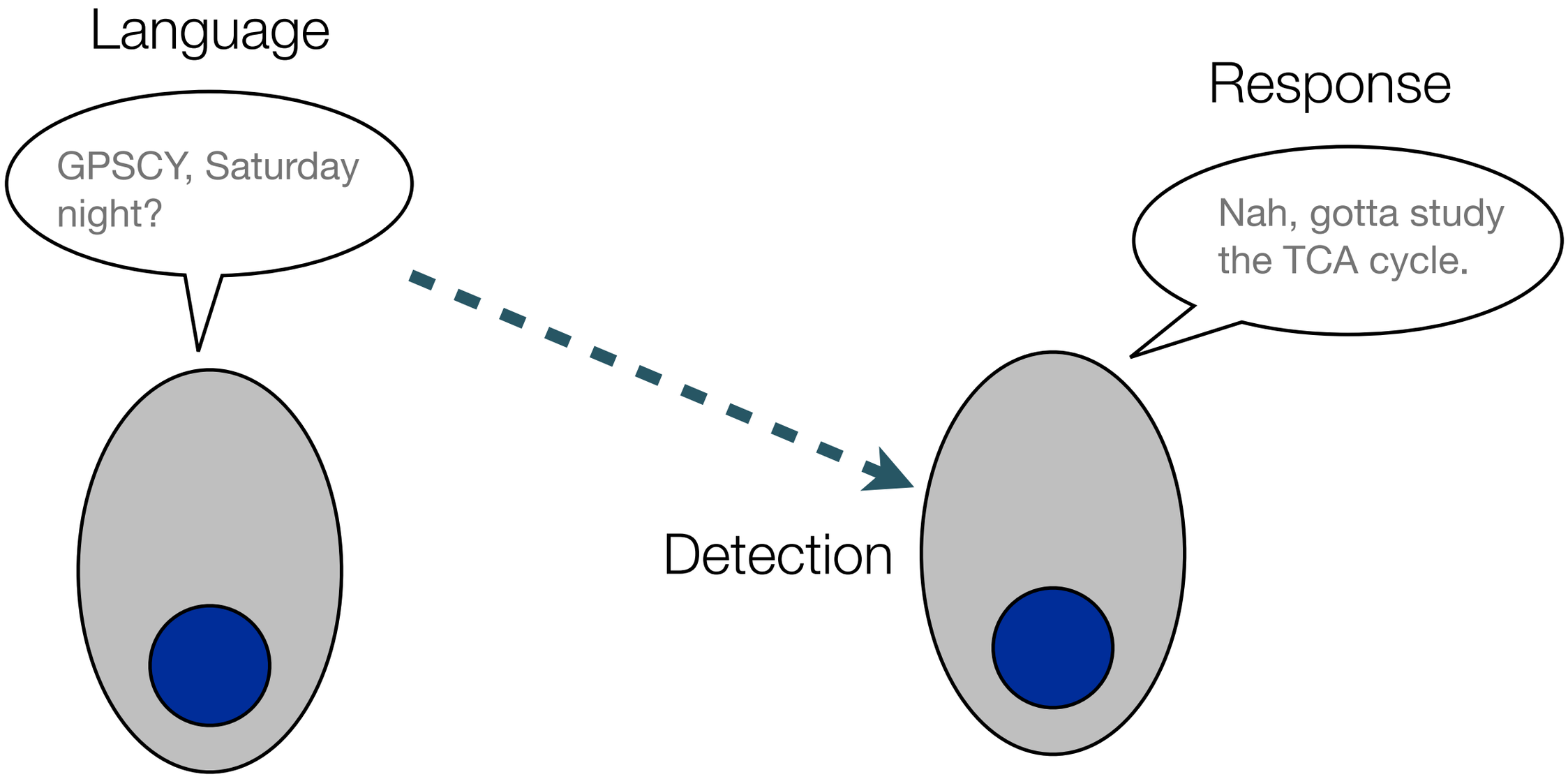
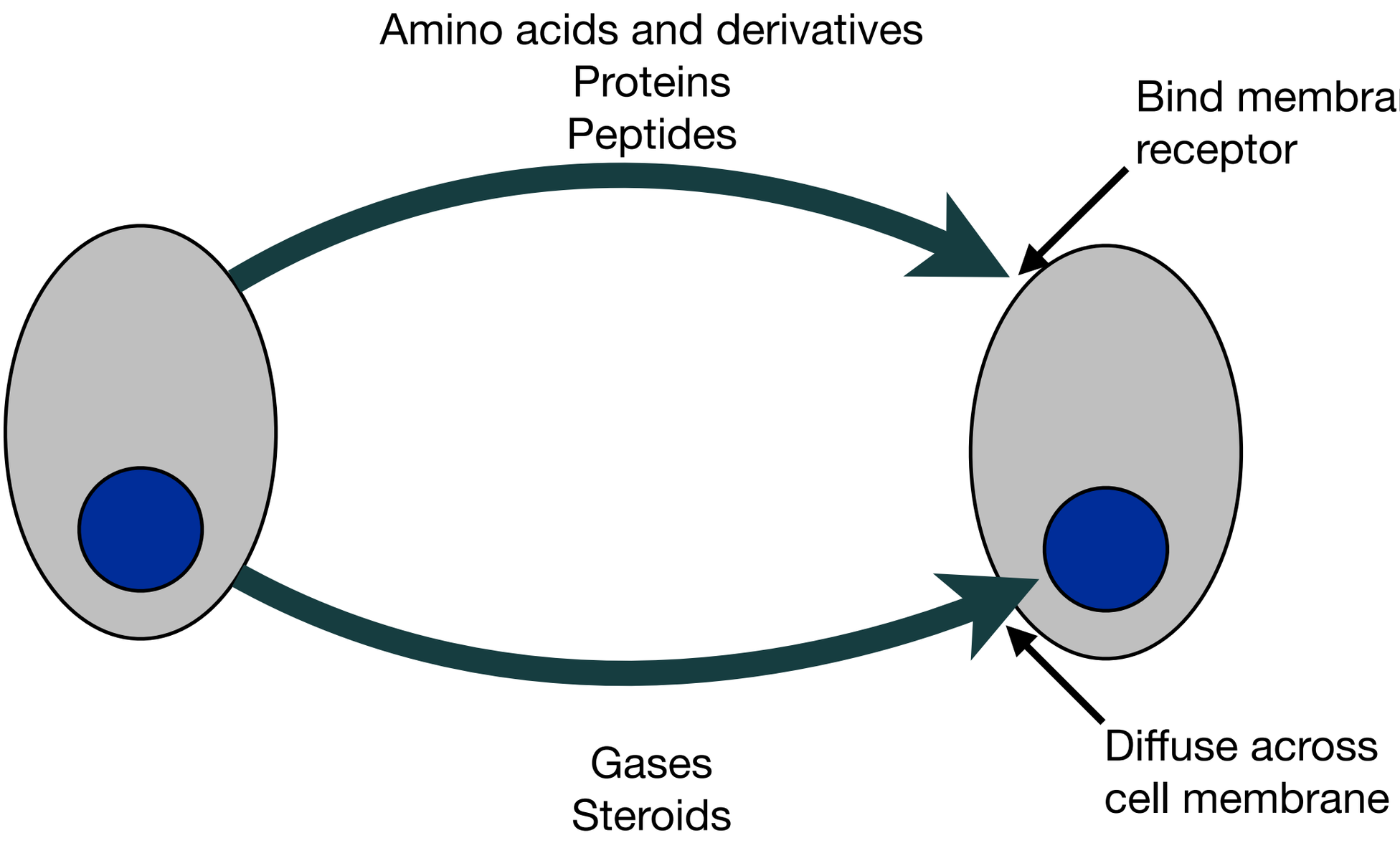
What we'll talk about...

- General principles of signaling
- Signaling through steroids and ion channels
- Signal transduction pathways
- Signaling through G-protein coupled receptors
- Signaling through tyrosine kinase receptors

Cells communicate by and respond to messages.

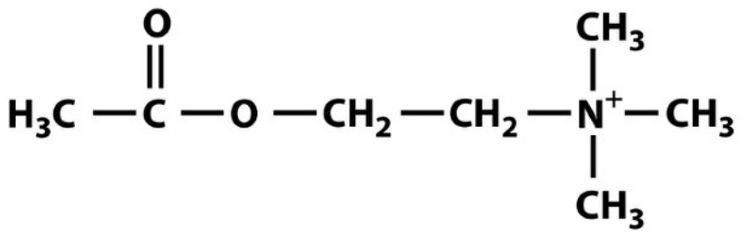


Small molecules are the language of cell communication.



The same signaling molecule can evoke different responses.

Acetylcholine



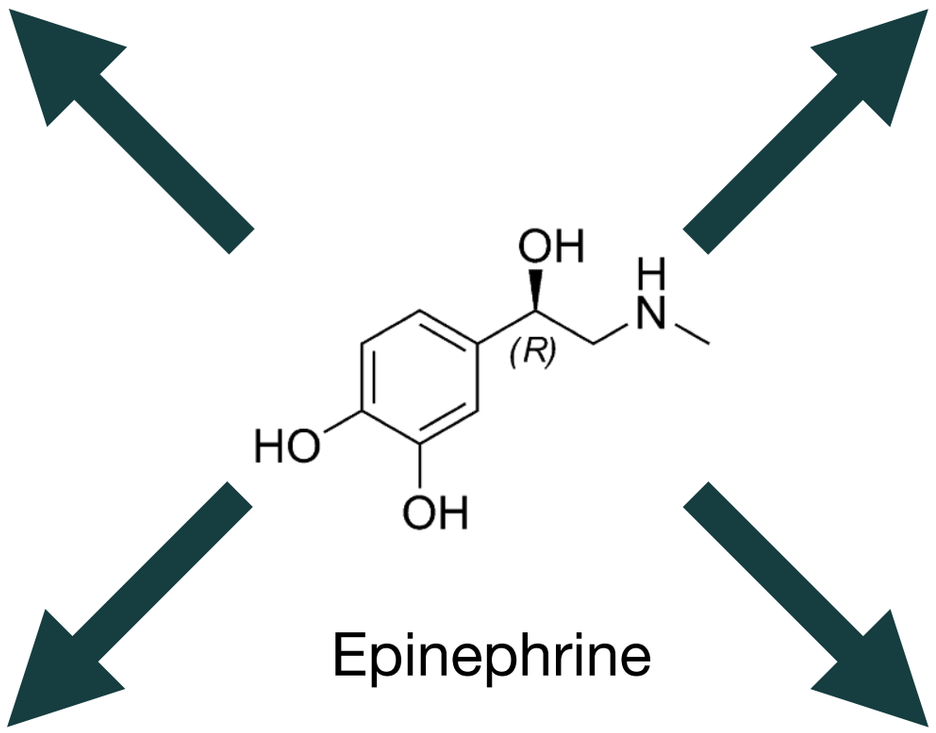
Skeletal muscle:
stimulate contraction

Cardiac muscle:
reduce contraction

One molecule can elicit multiple cellular changes to produce an integrated response.

Muscle: dilate blood vessels

Heart: increase contraction

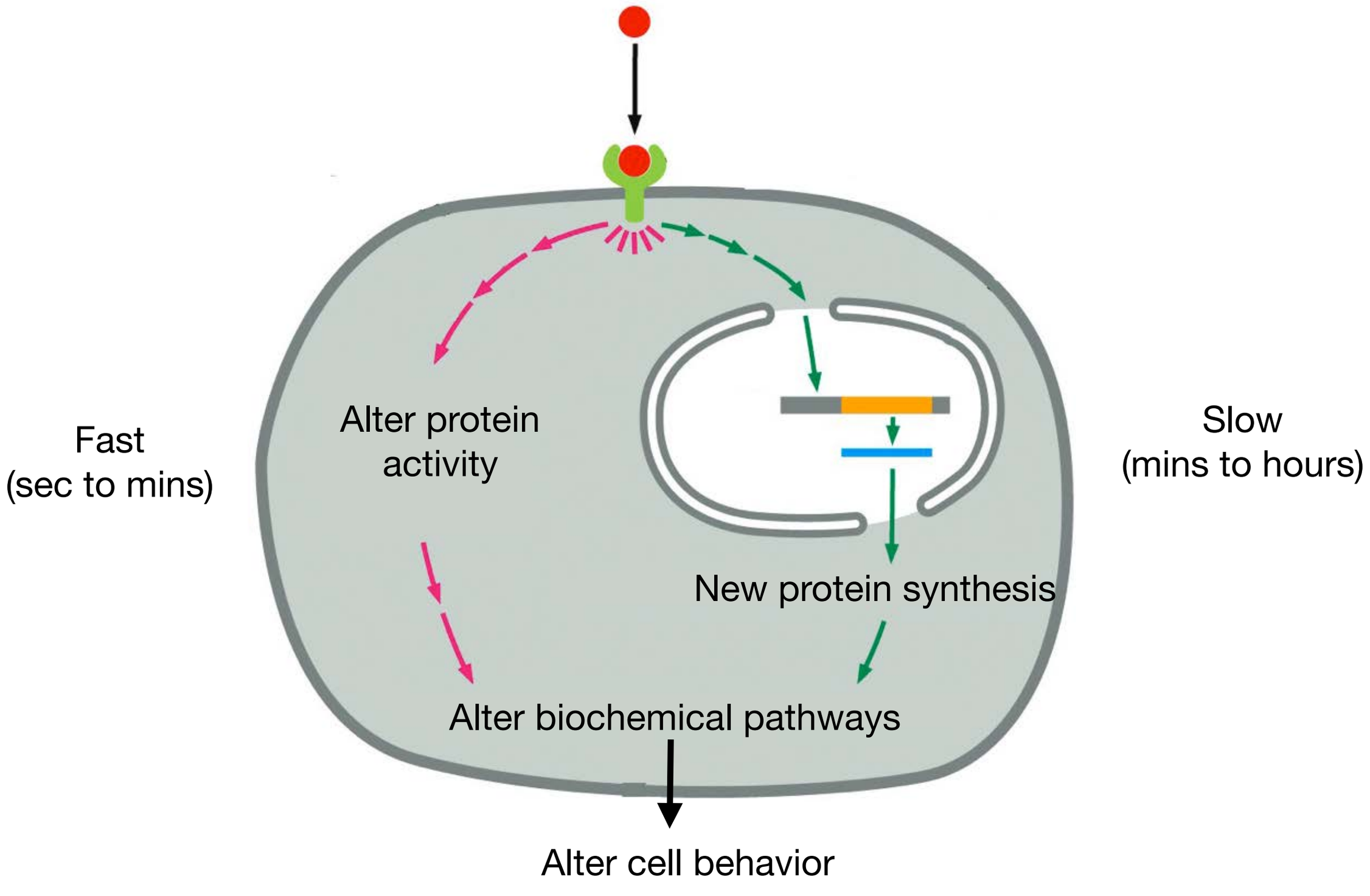


Epinephrine

Skin: constrict blood vessels

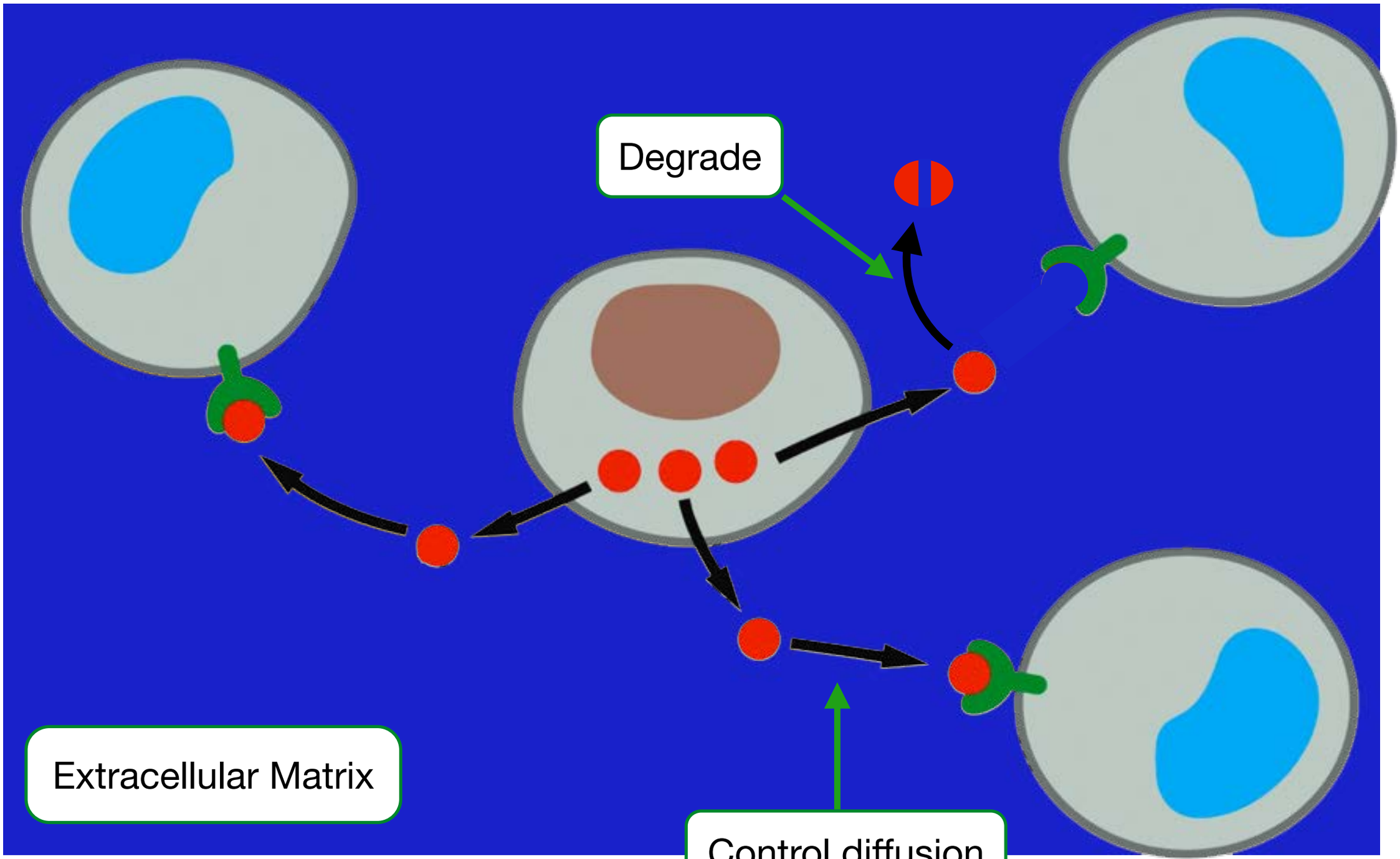
Liver: activate glycolysis

Cells generate fast and transient or slow and long-term responses to signaling molecules.

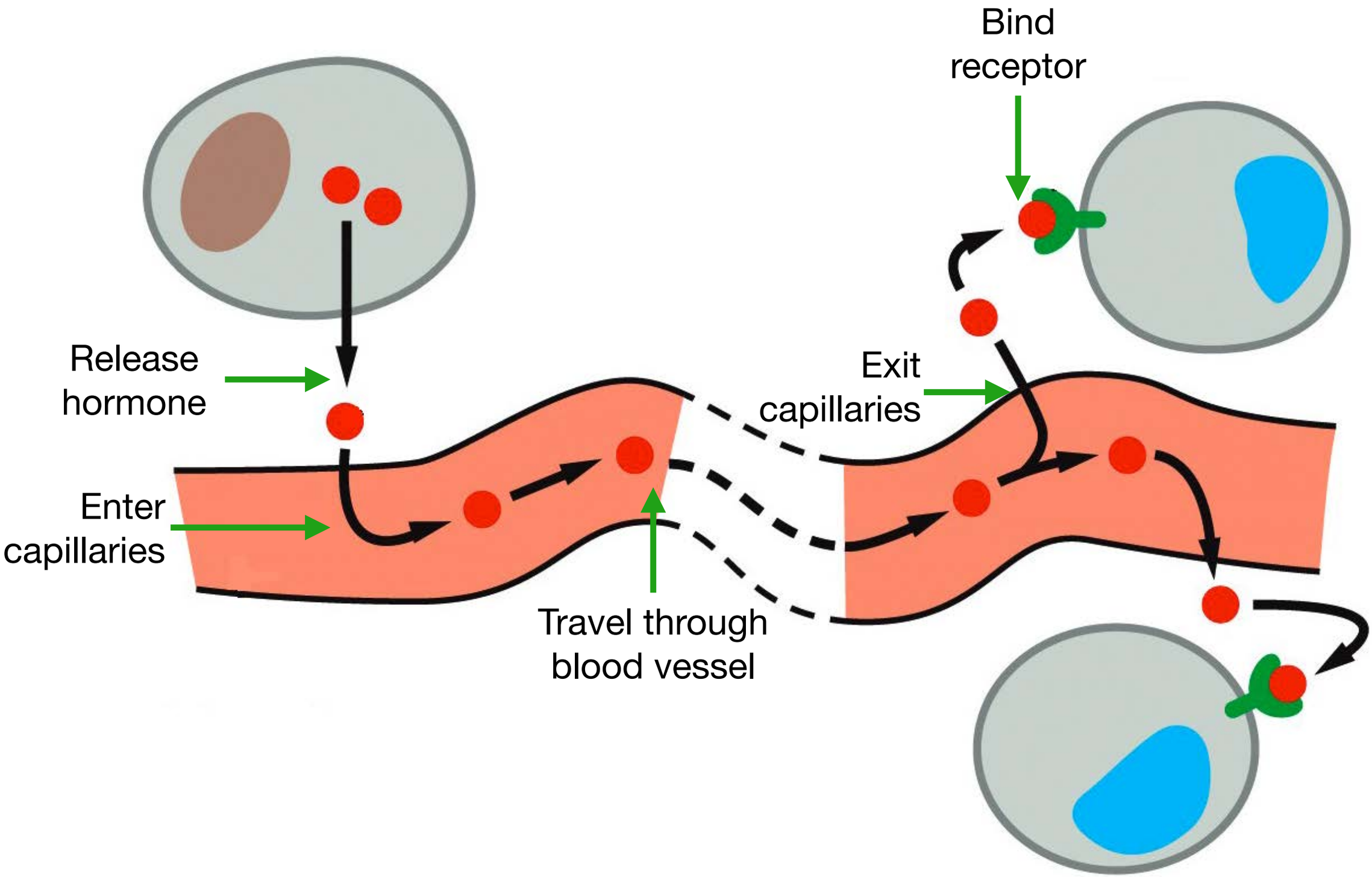


Types of Cell Communication

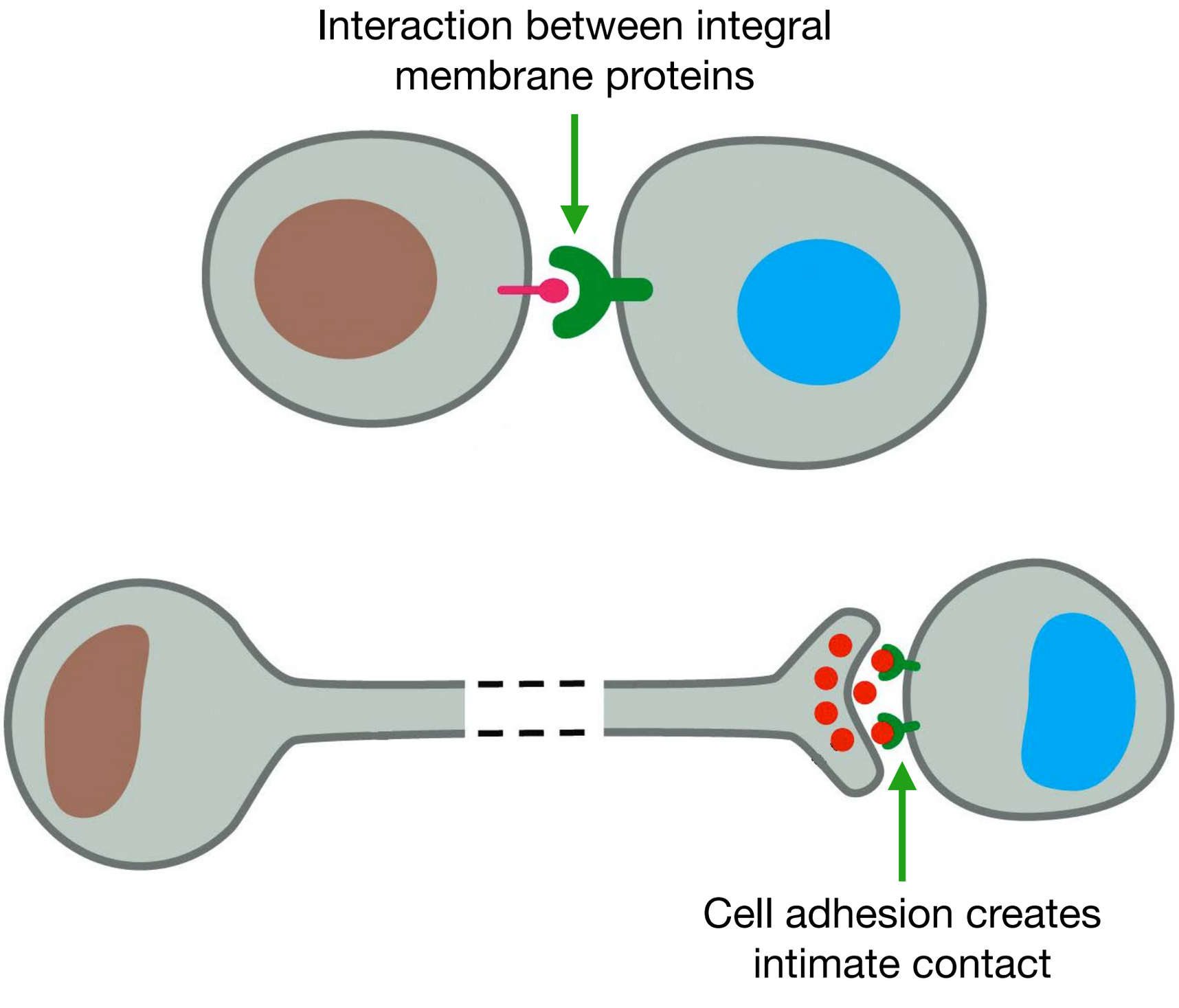
Paracrine signaling involves communication between neighboring cells.



Endocrine signaling involves communication between cells in different regions of the body.

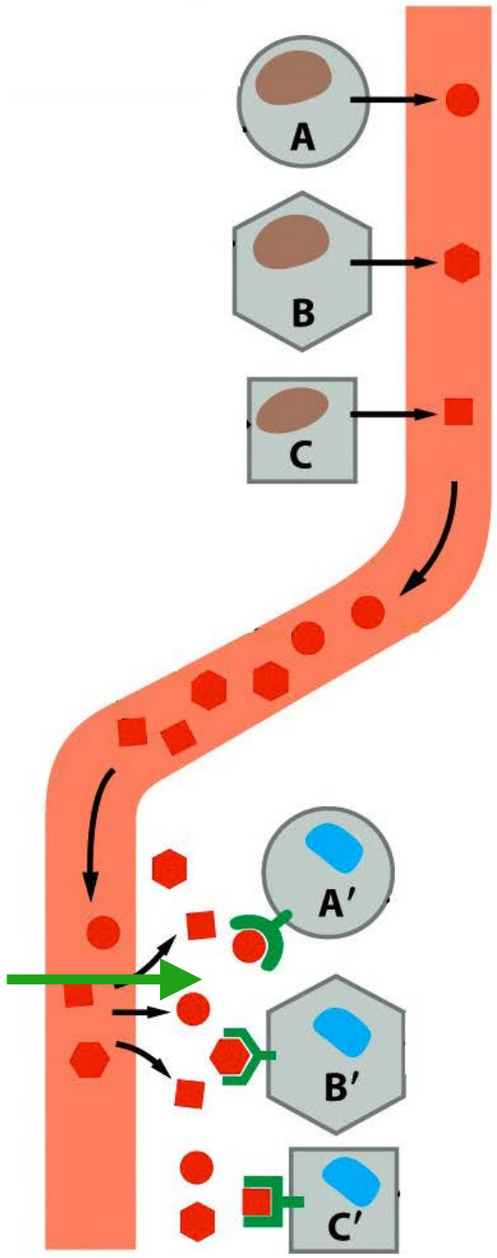


Cells can communicate through direct or close contacts.

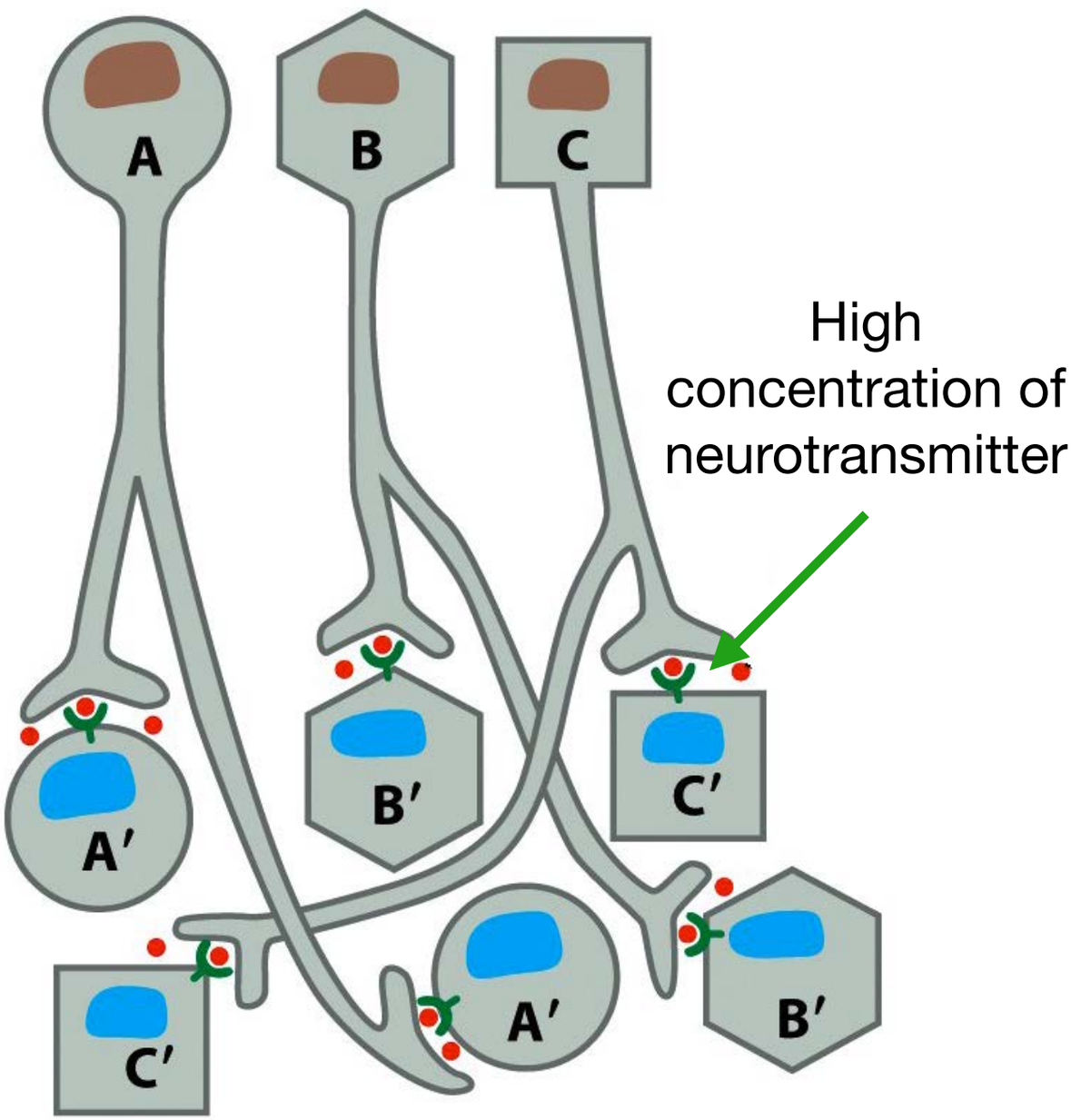


Endocrine and cell-contact signaling require ligand-receptor binding of different strengths.

High affinity interaction



Low affinity interaction



Examples of Signaling Pathways

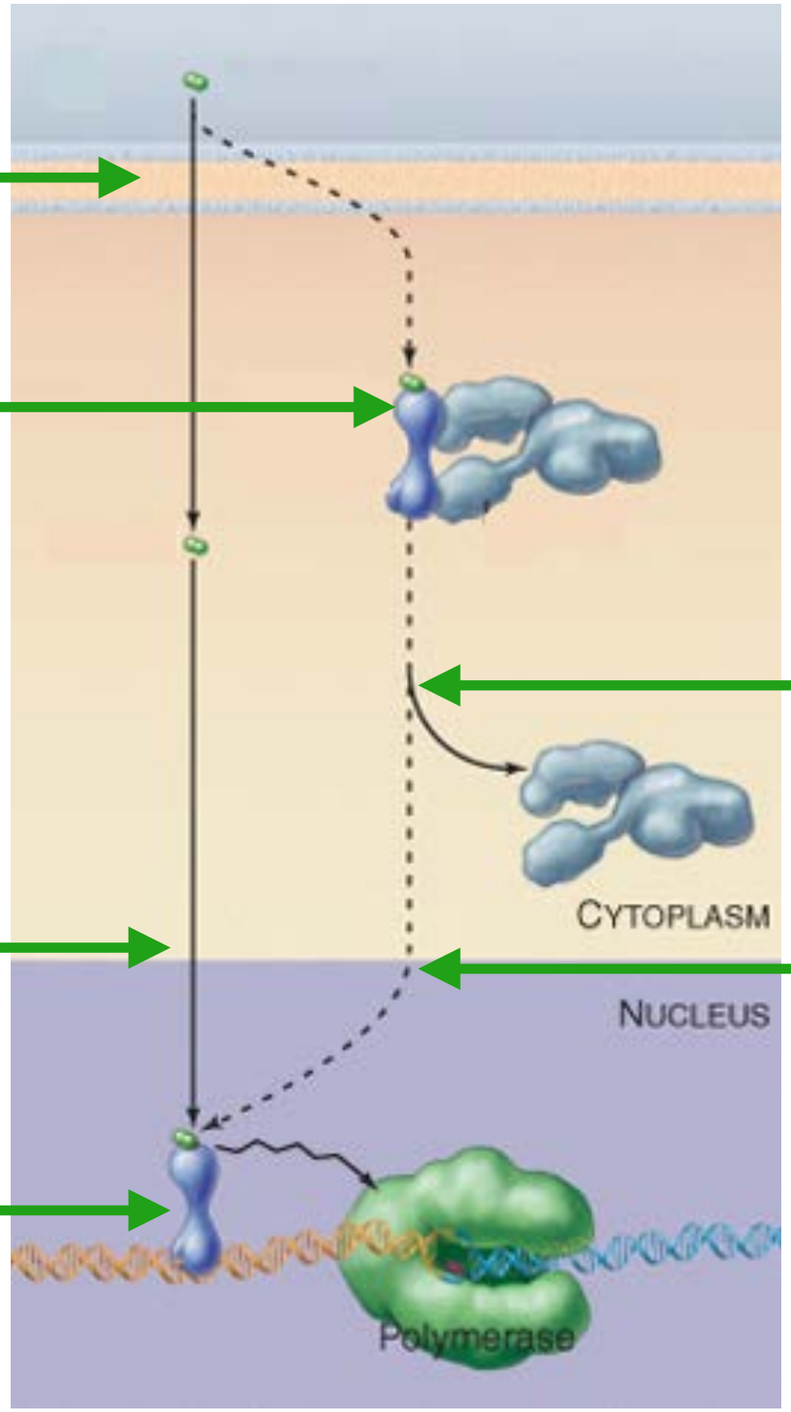
Steroids and small hydrophobic molecules diffuse across plasma membrane.

Steroid diffuse across cell membrane

Binds receptor or…

…diffuses into nucleus to bind receptor

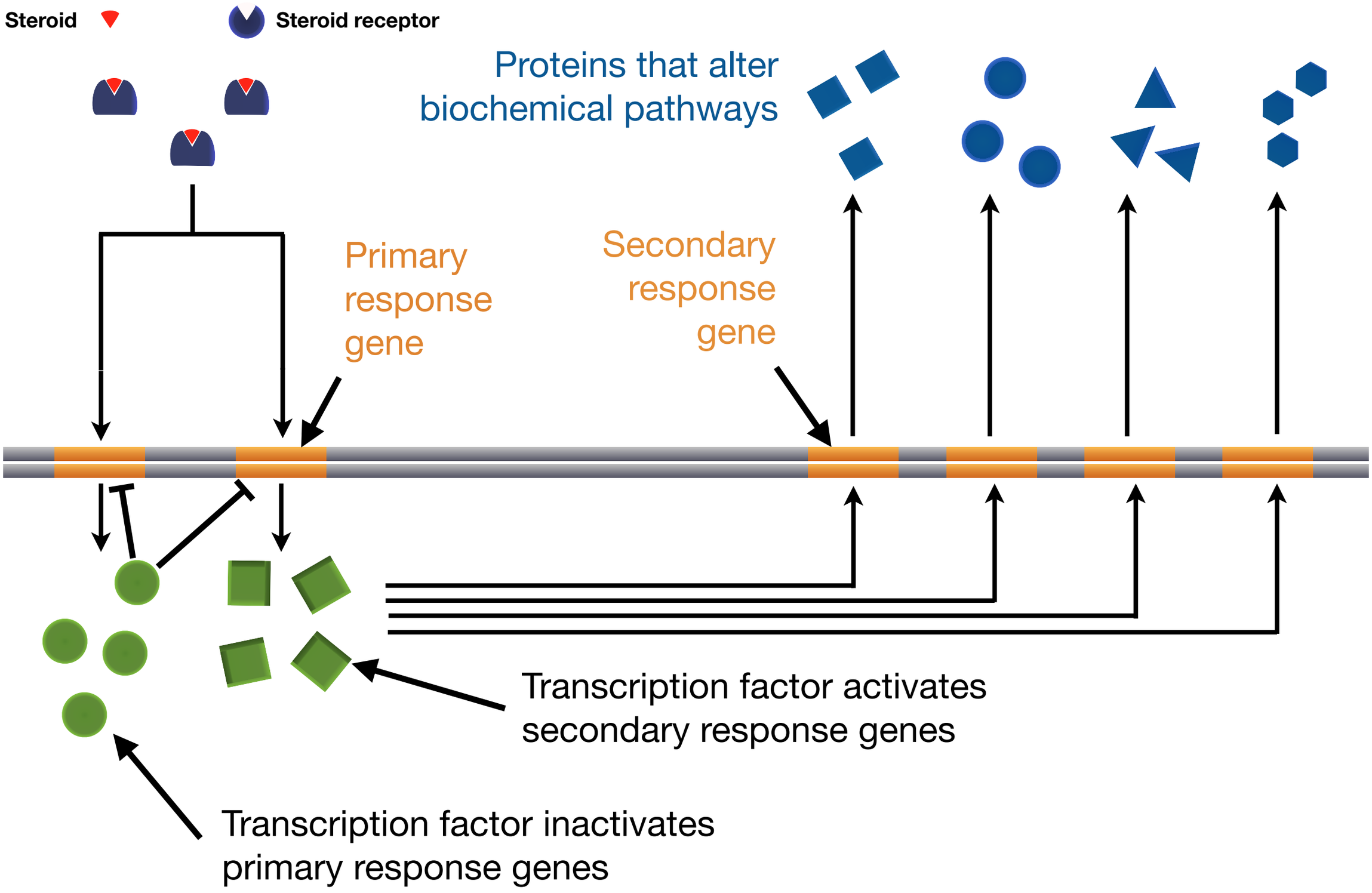
Receptor activates transcription



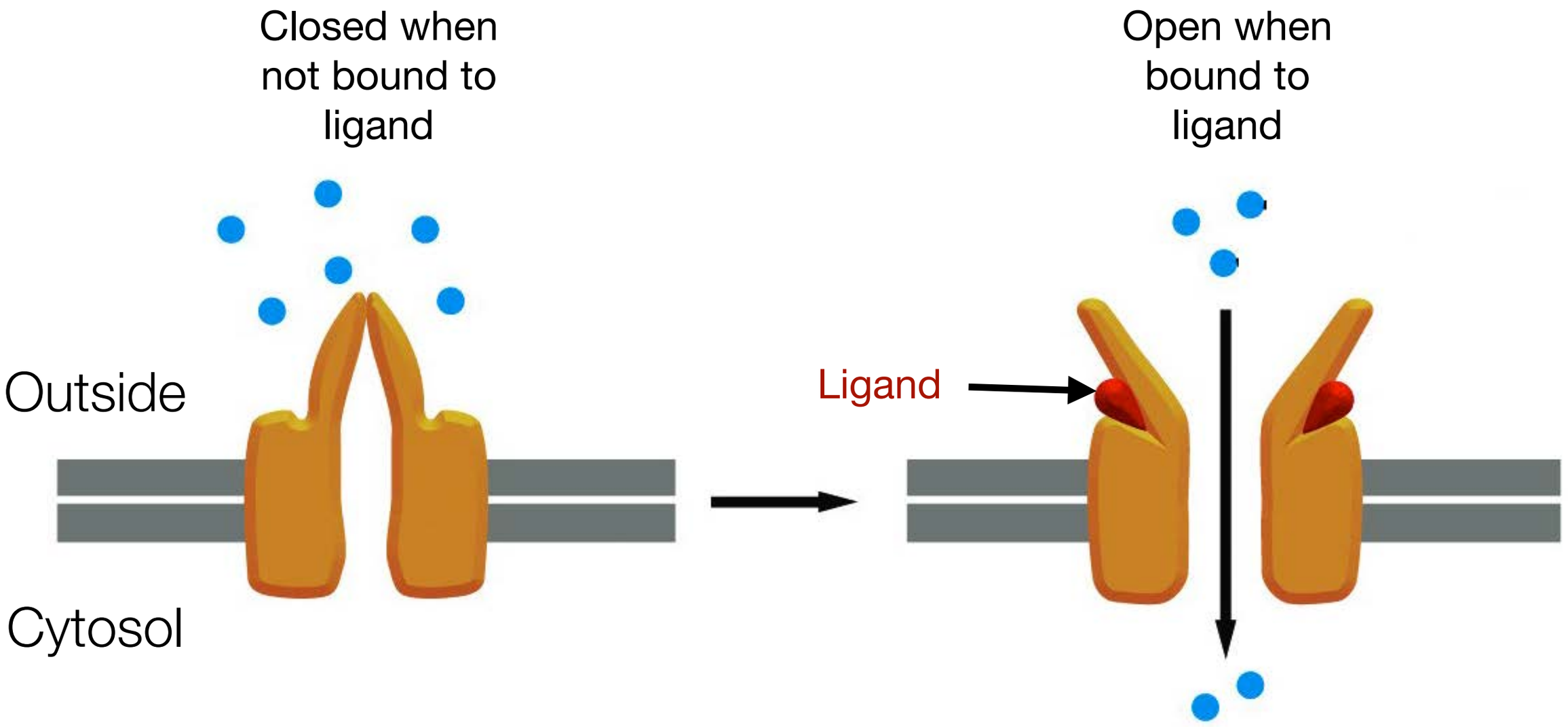
Receptor releases chaperone

Receptor enters nucleus

Steroids trigger expression of primary and secondary response genes.

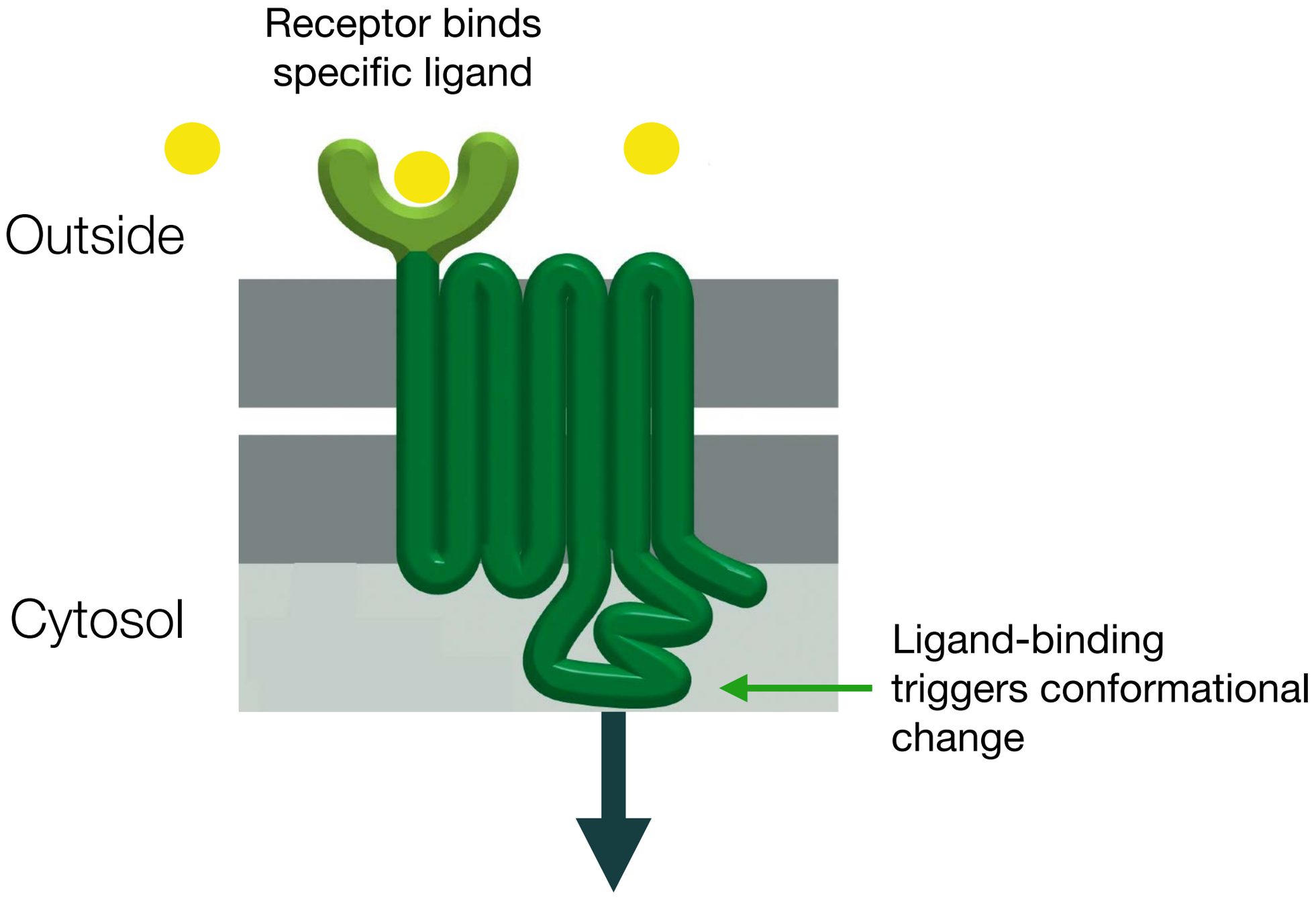


Ligand-gated ion channels open upon binding ligand.

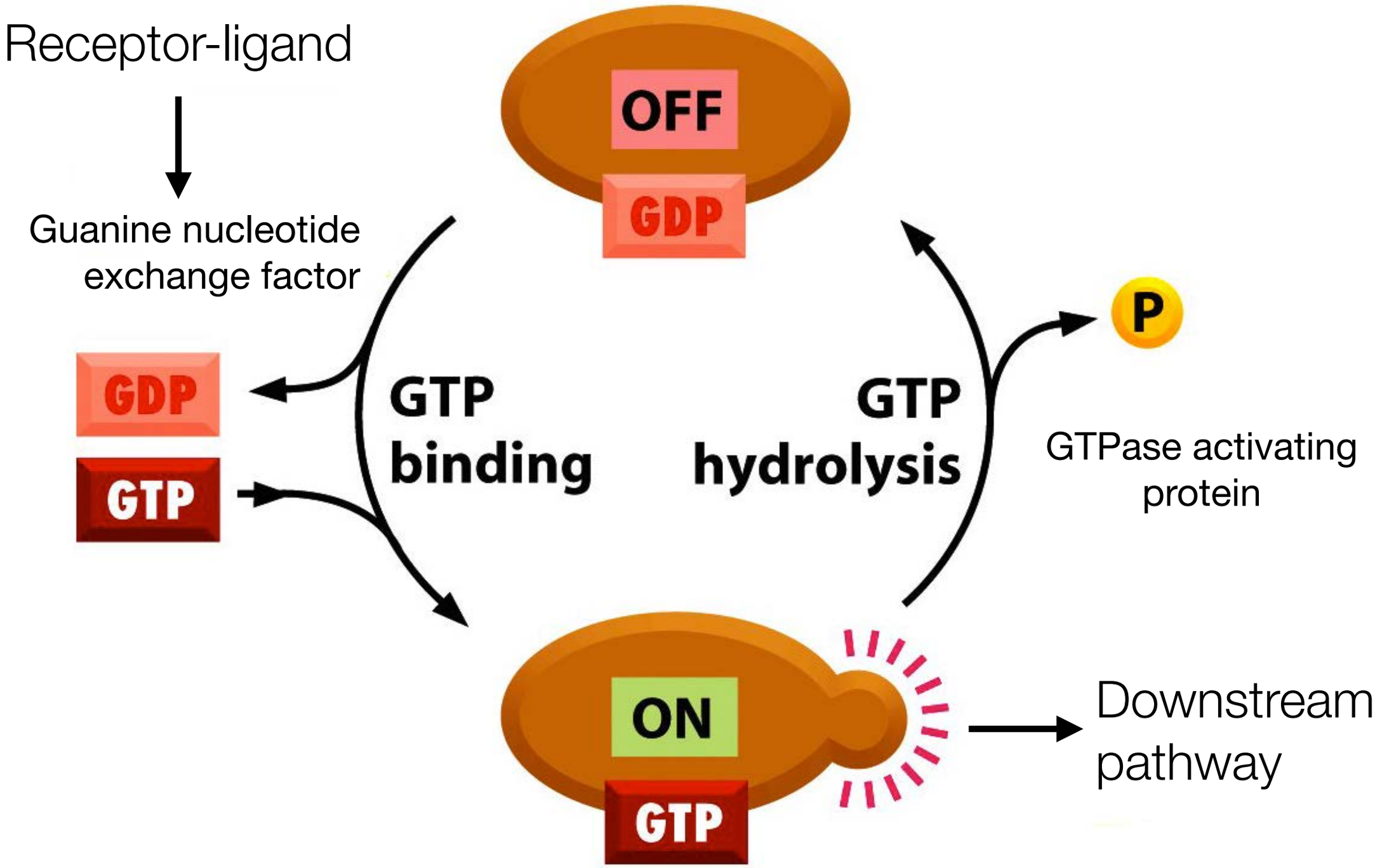


Signal Transduction Pathways

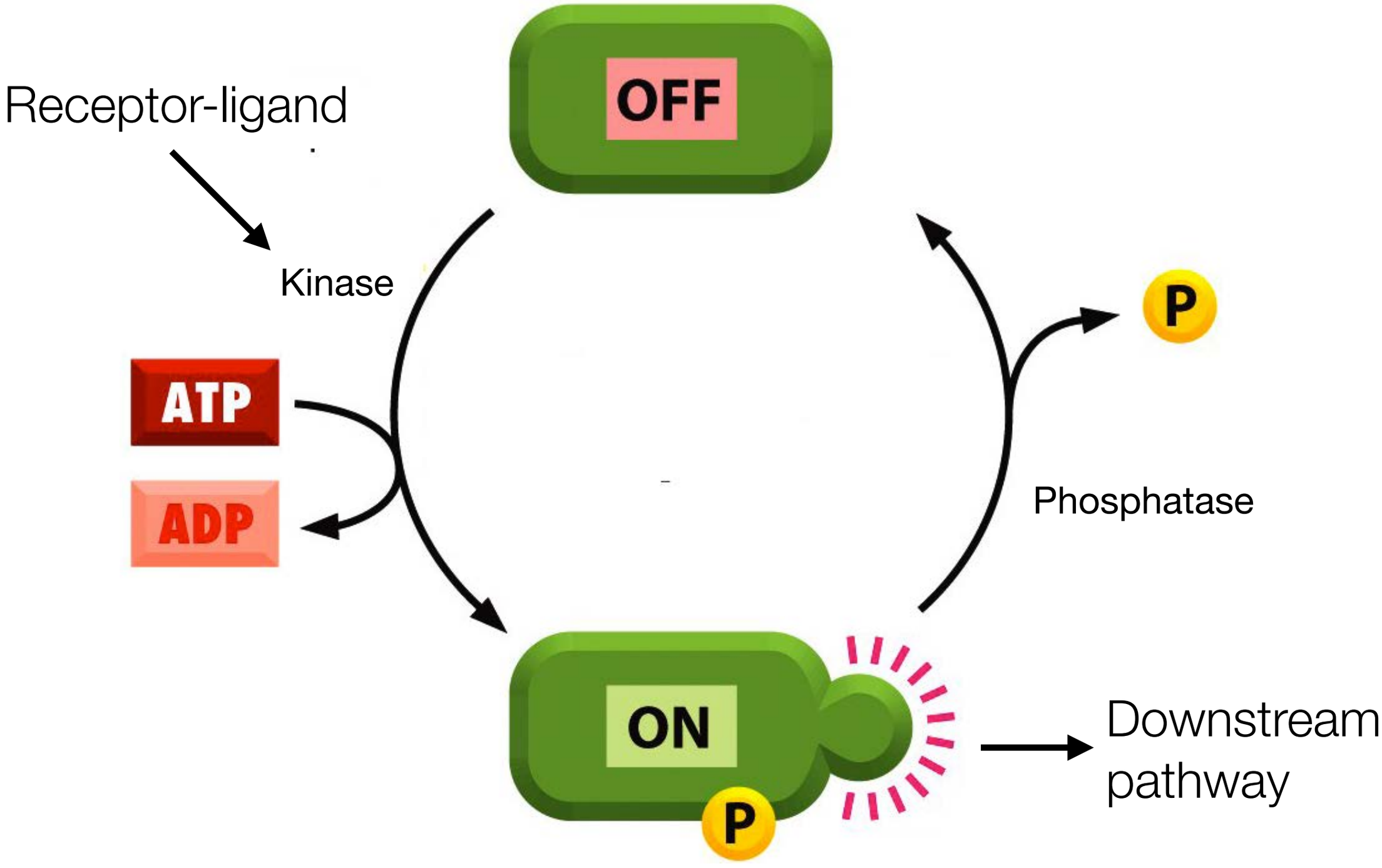
Receptors bind specific signaling molecules and activate cellular events.



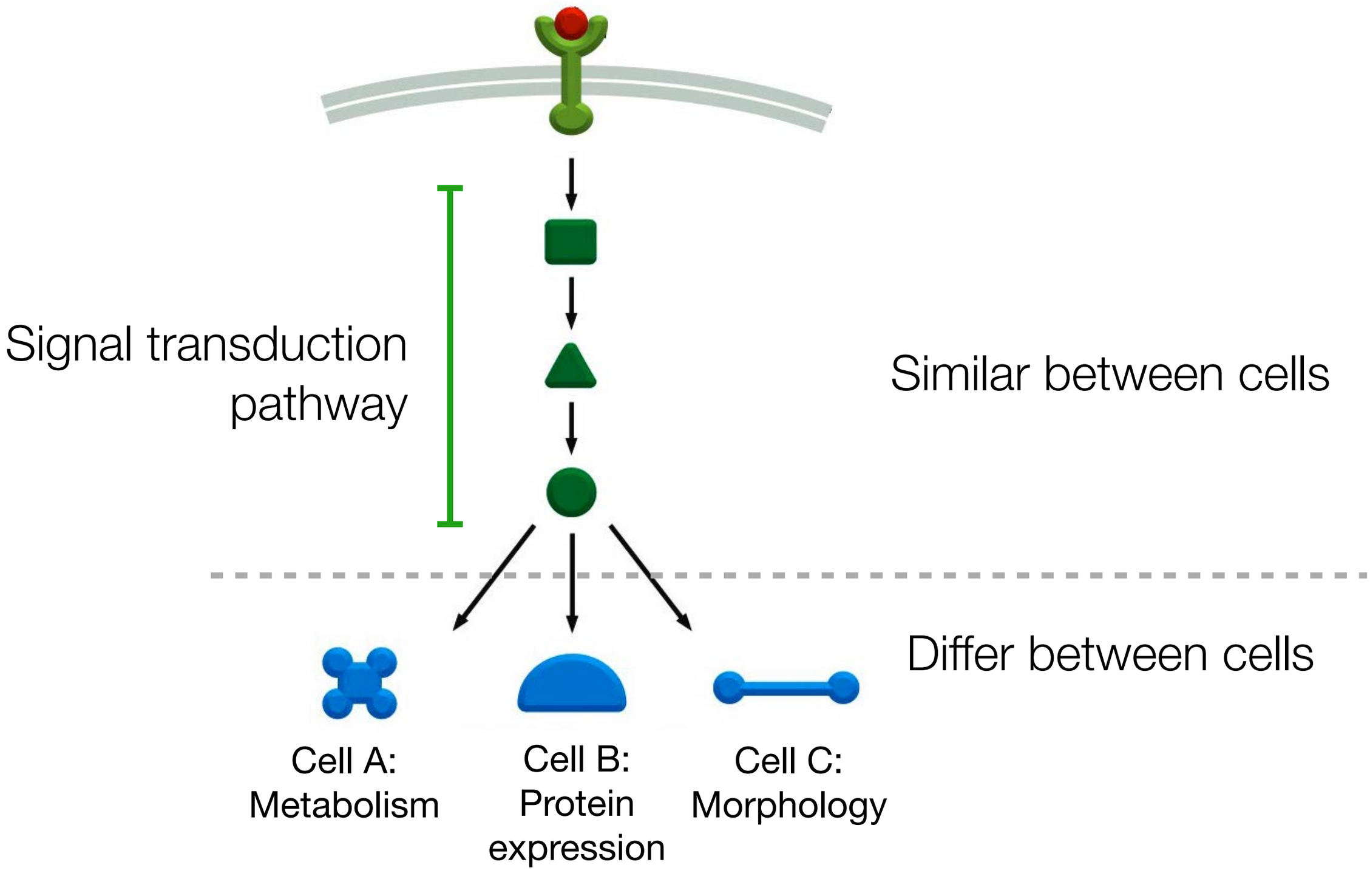
GTP-binding proteins function as switches to indicate receptor activation.



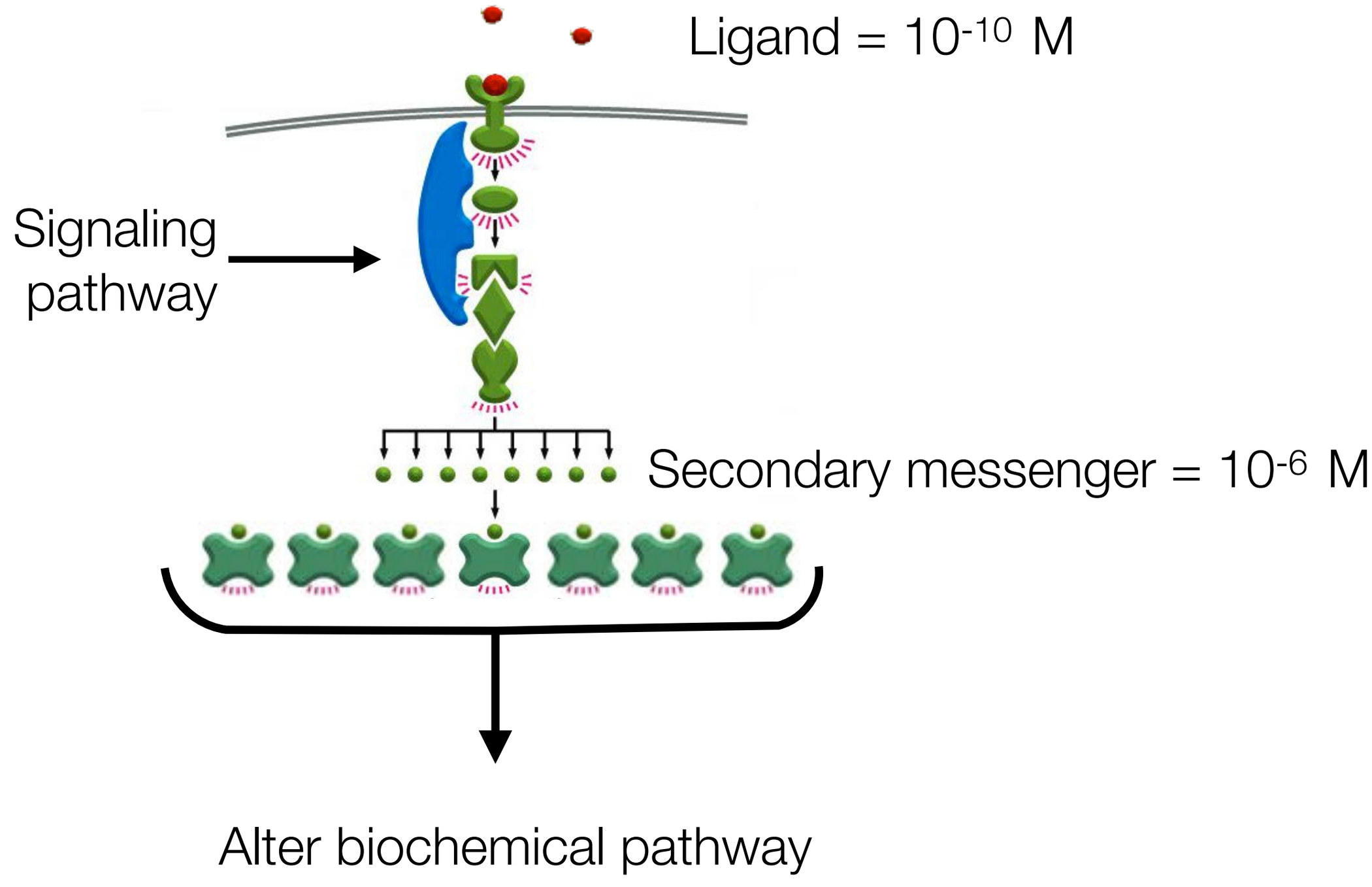
Kinases modulate activity of proteins during signaling reactions.



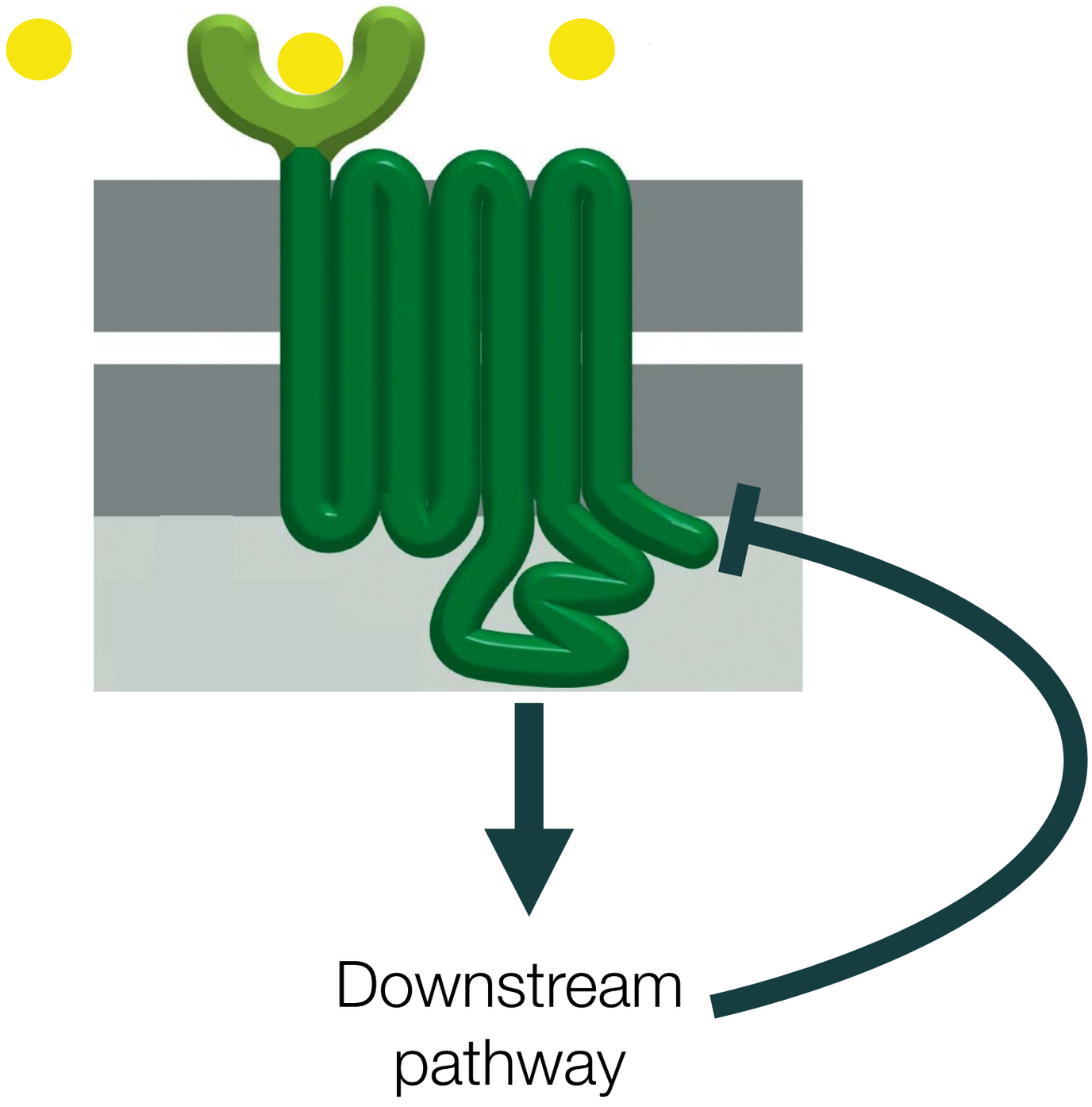
Several proteins relay binding state of receptor to cell machinery.



Secondary messengers amplify concentration of signaling molecules by producing

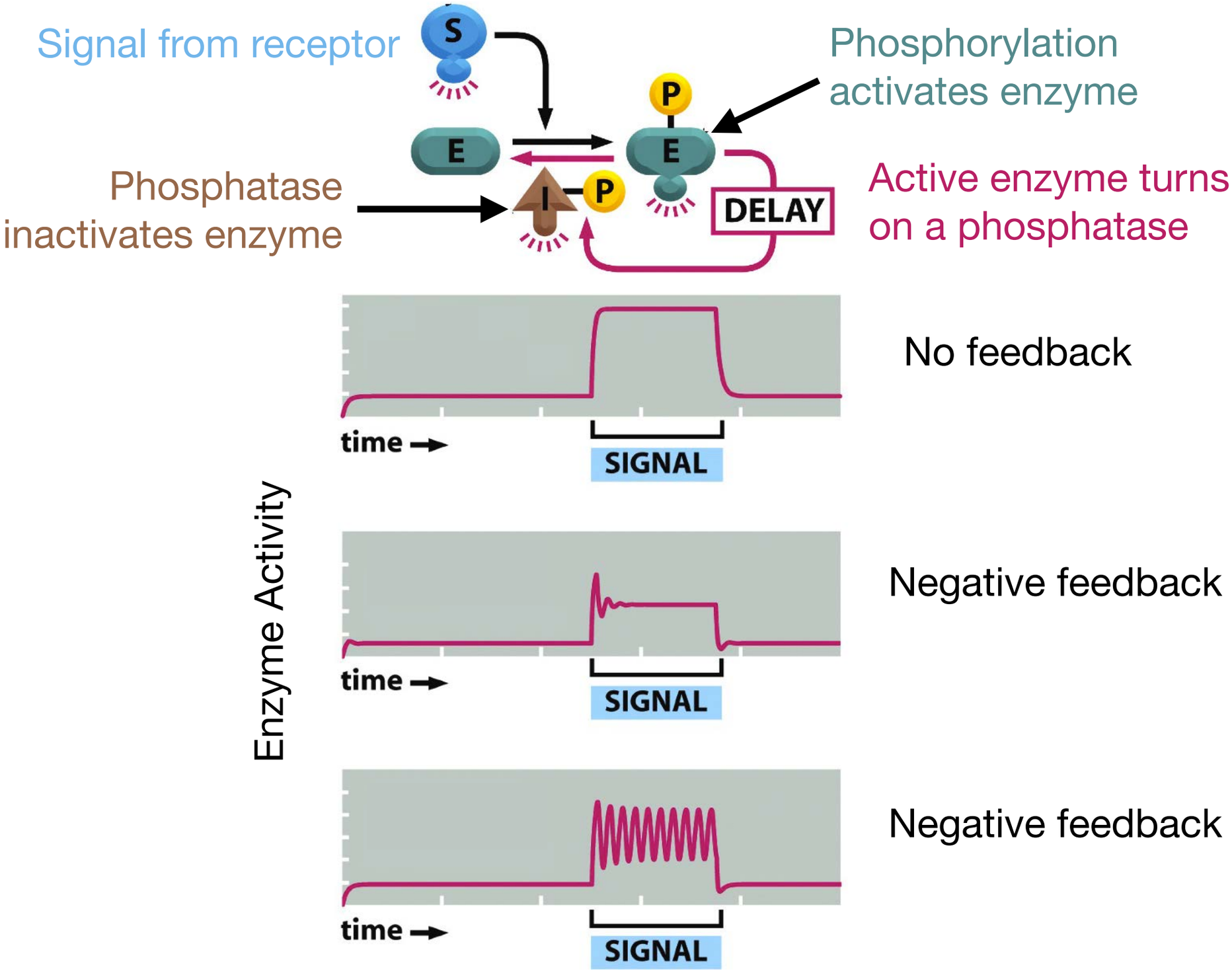


Cells attenuate signaling reactions to limit amount and time of cellular response.

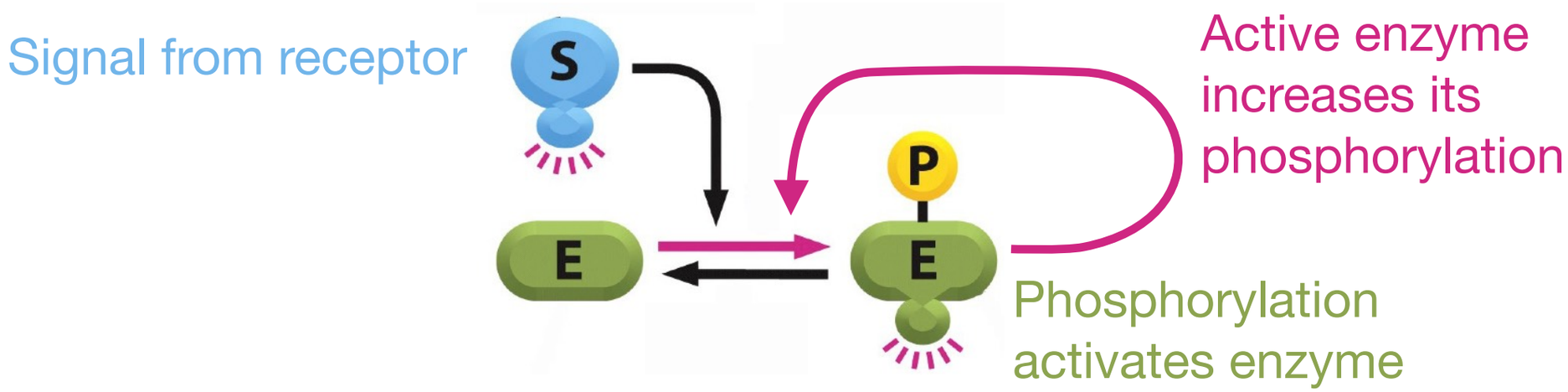


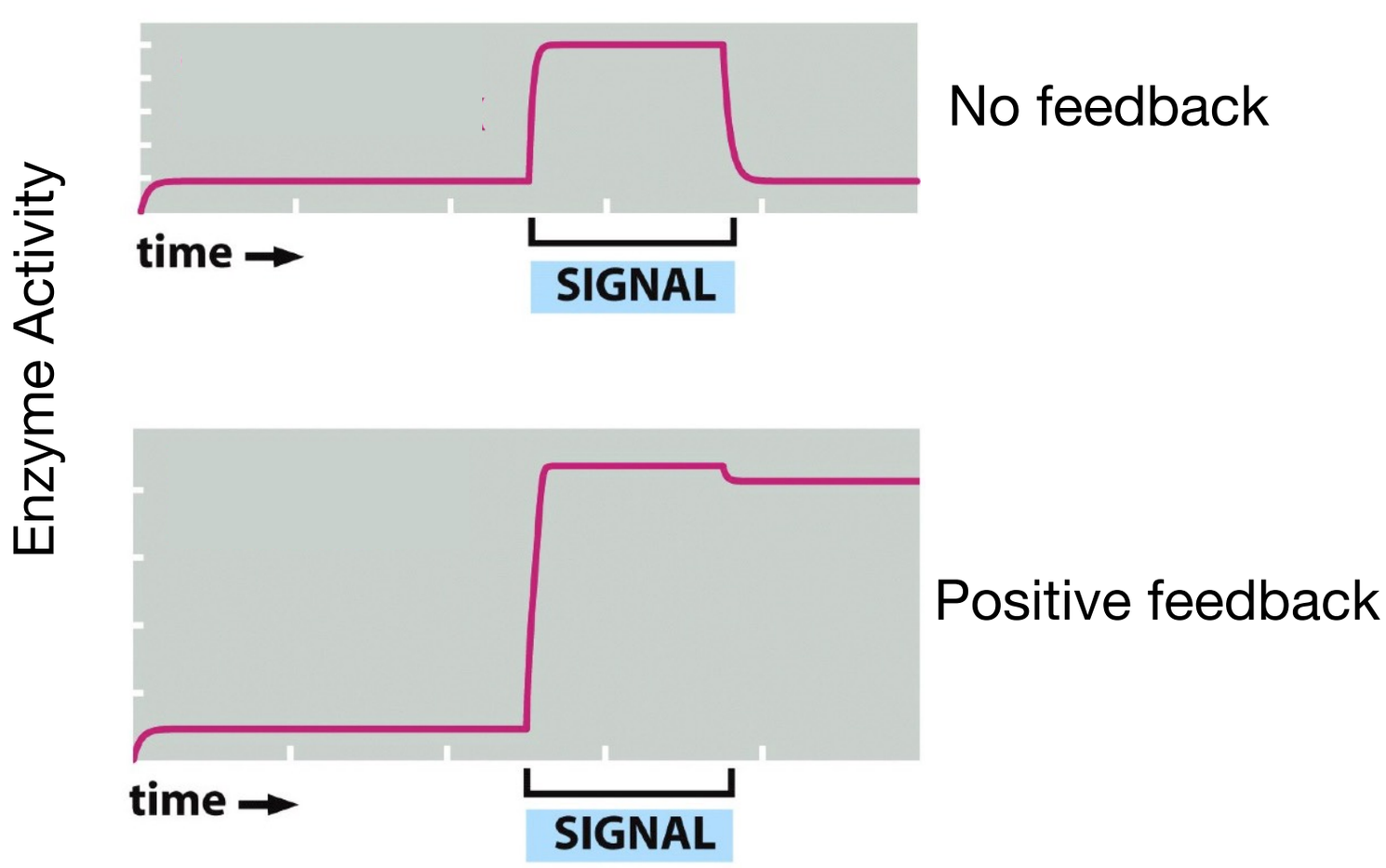
Feedback

Negative feedback attenuated signals but also produces patterns of responses.



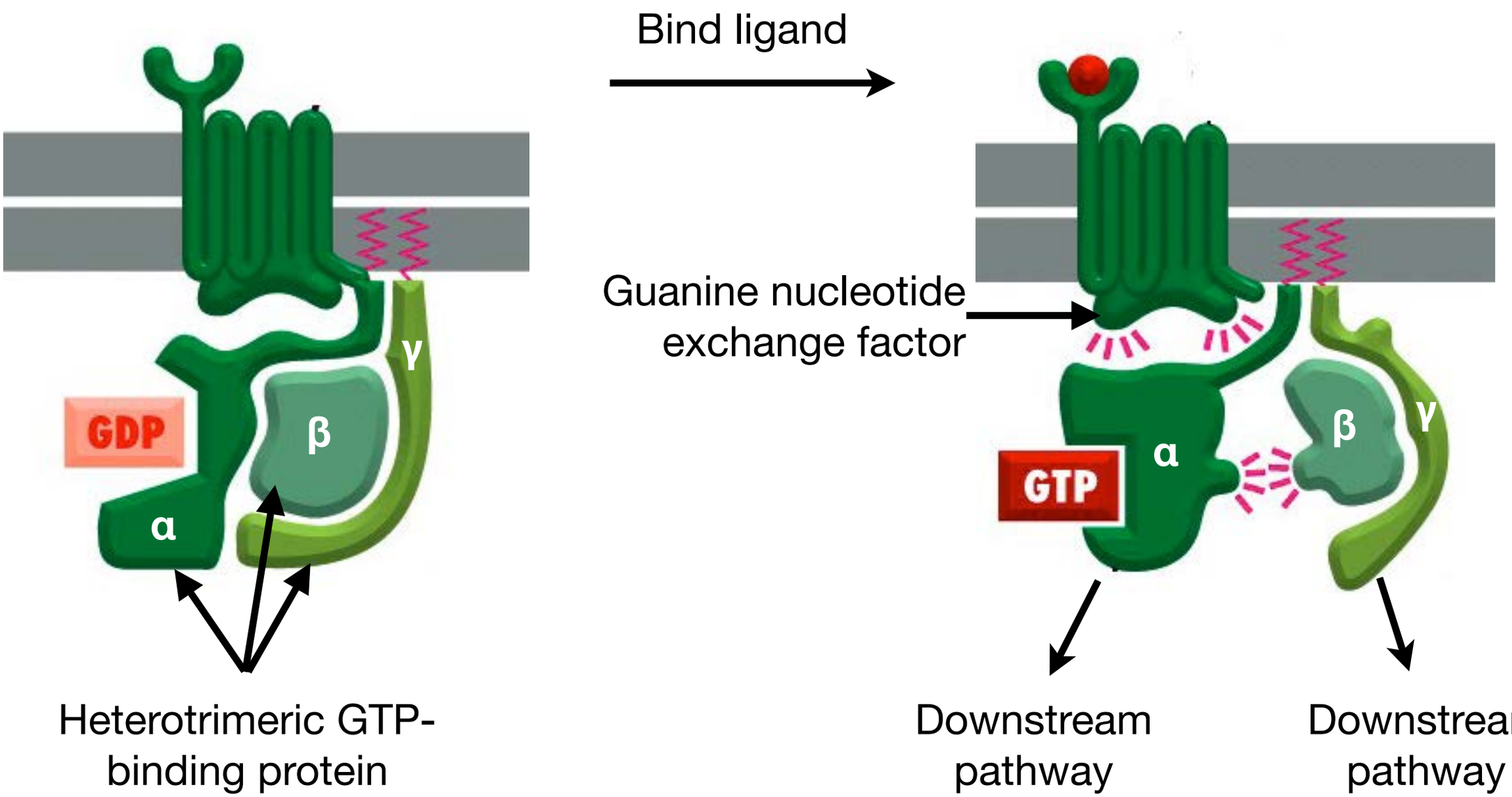
Feedback loops regulate the strength and frequency of signals.



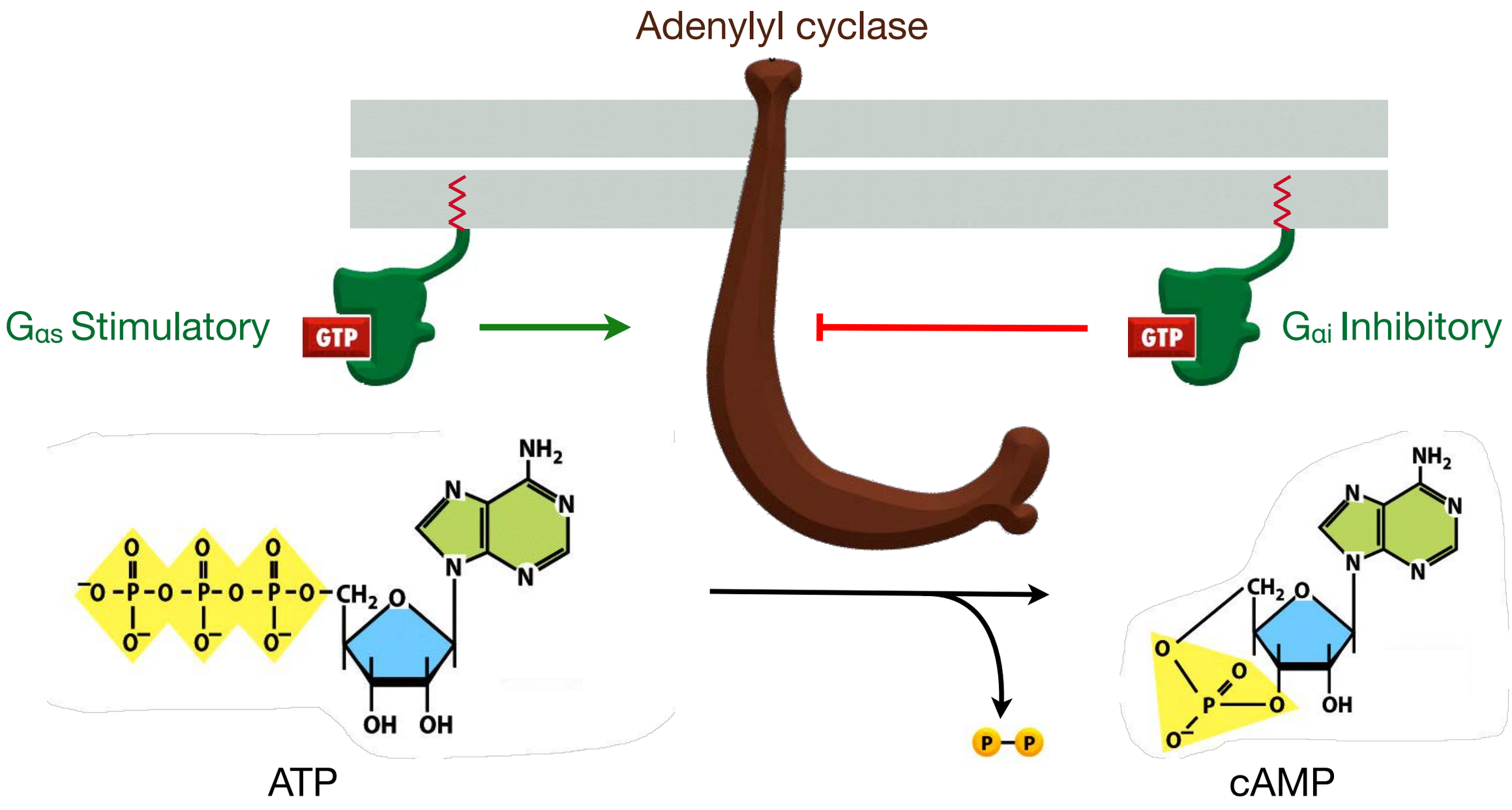


Types of Signal Transduction Pathways

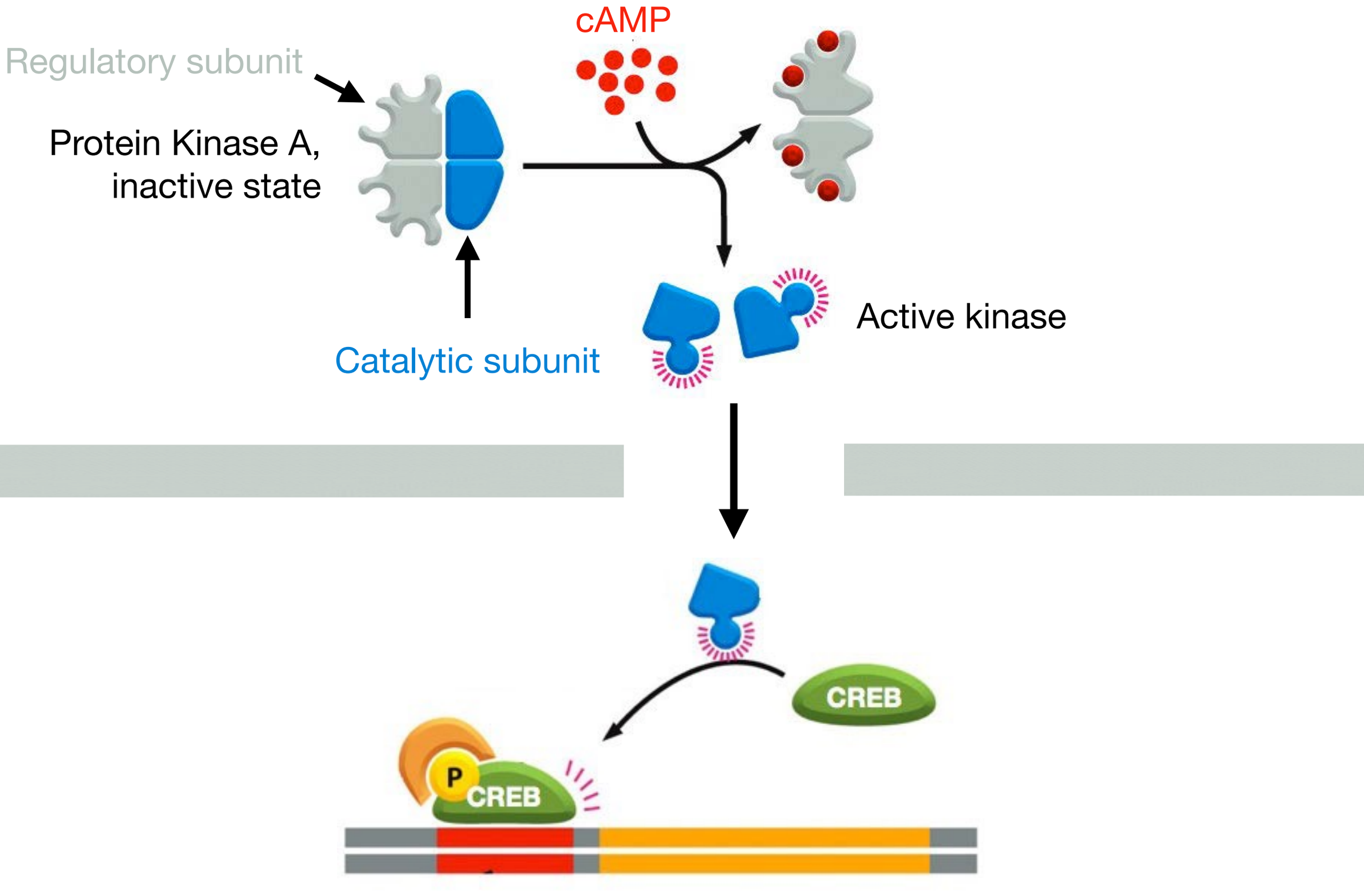
G-protein coupled receptors transmit signals through heterotrimeric GTP-binding proteins.



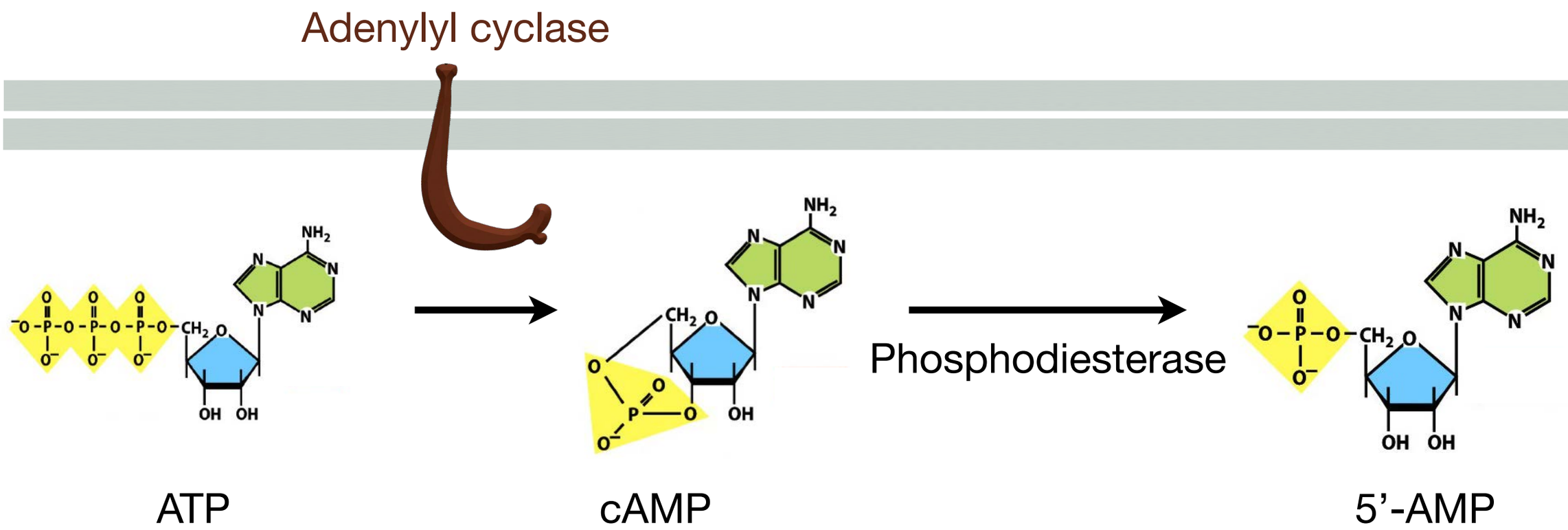
$G_{\alpha s}$ subunits activate adenylyl cyclase which convert ATP to cAMP.



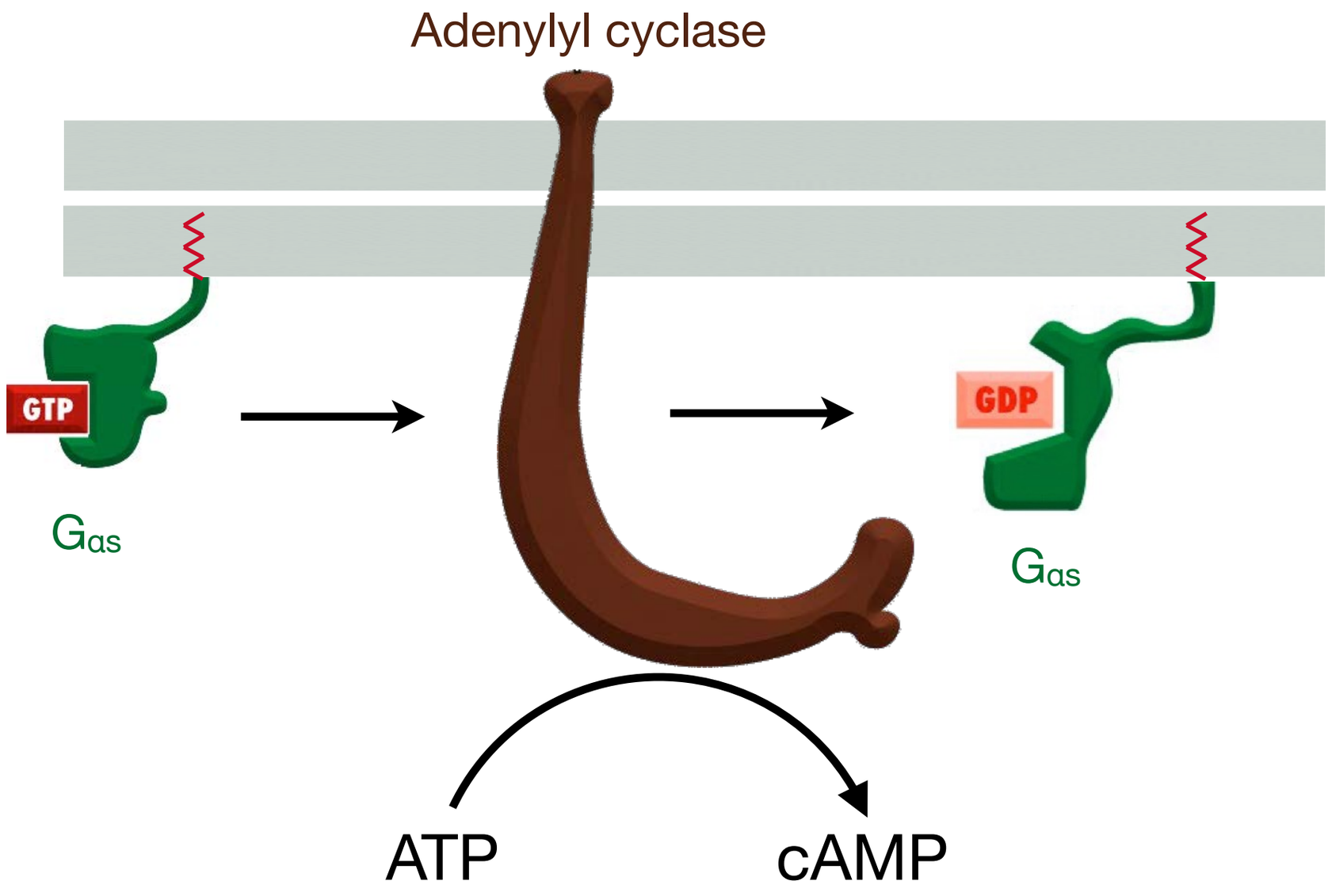
cAMP activates protein kinase A that has several downstream targets.



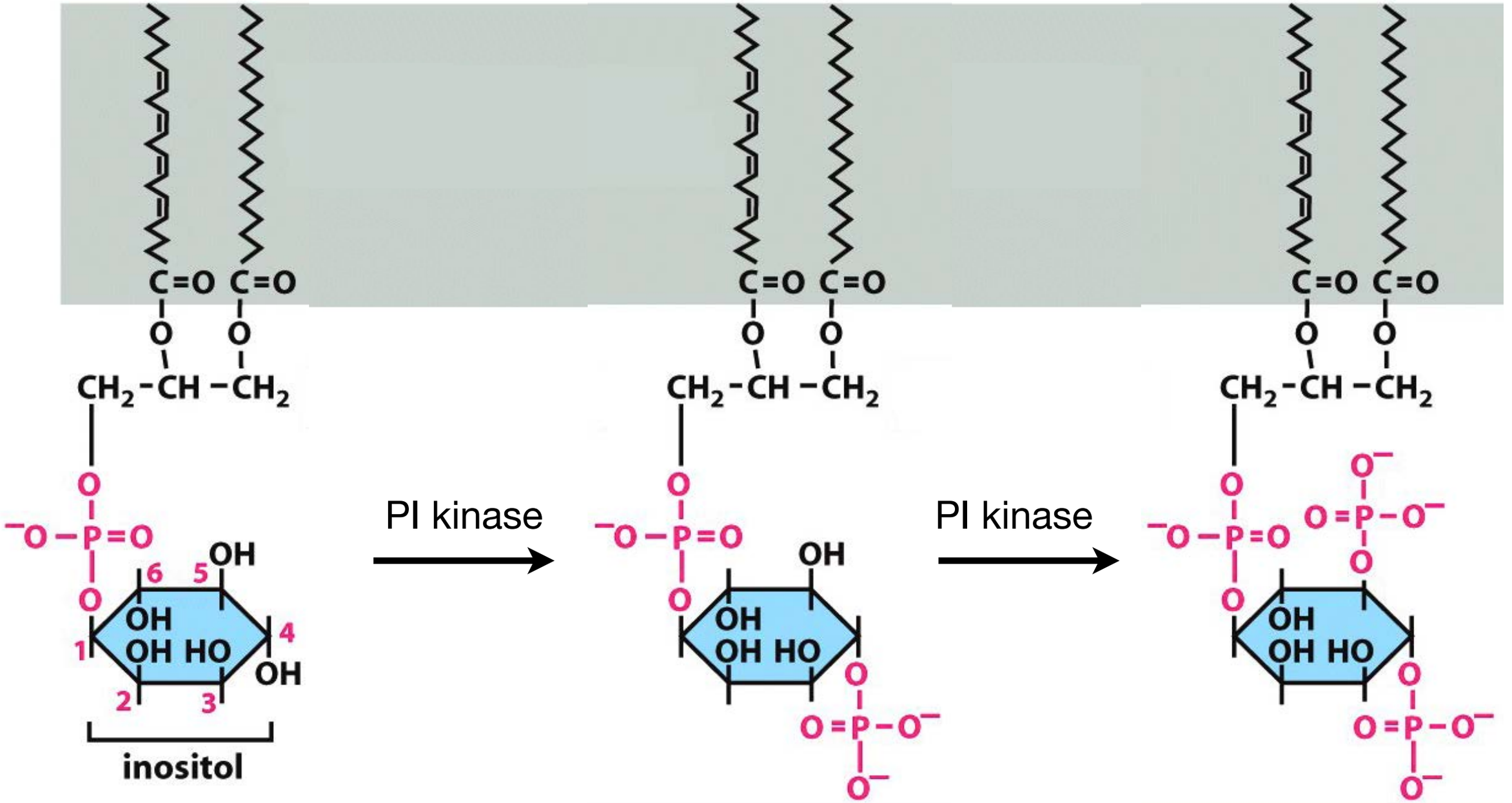
Phosphodiesterase reduces cAMP levels to limit signaling reactions.



Adenylyl cyclase functions as GTPase-activating protein for G alpha subunits.

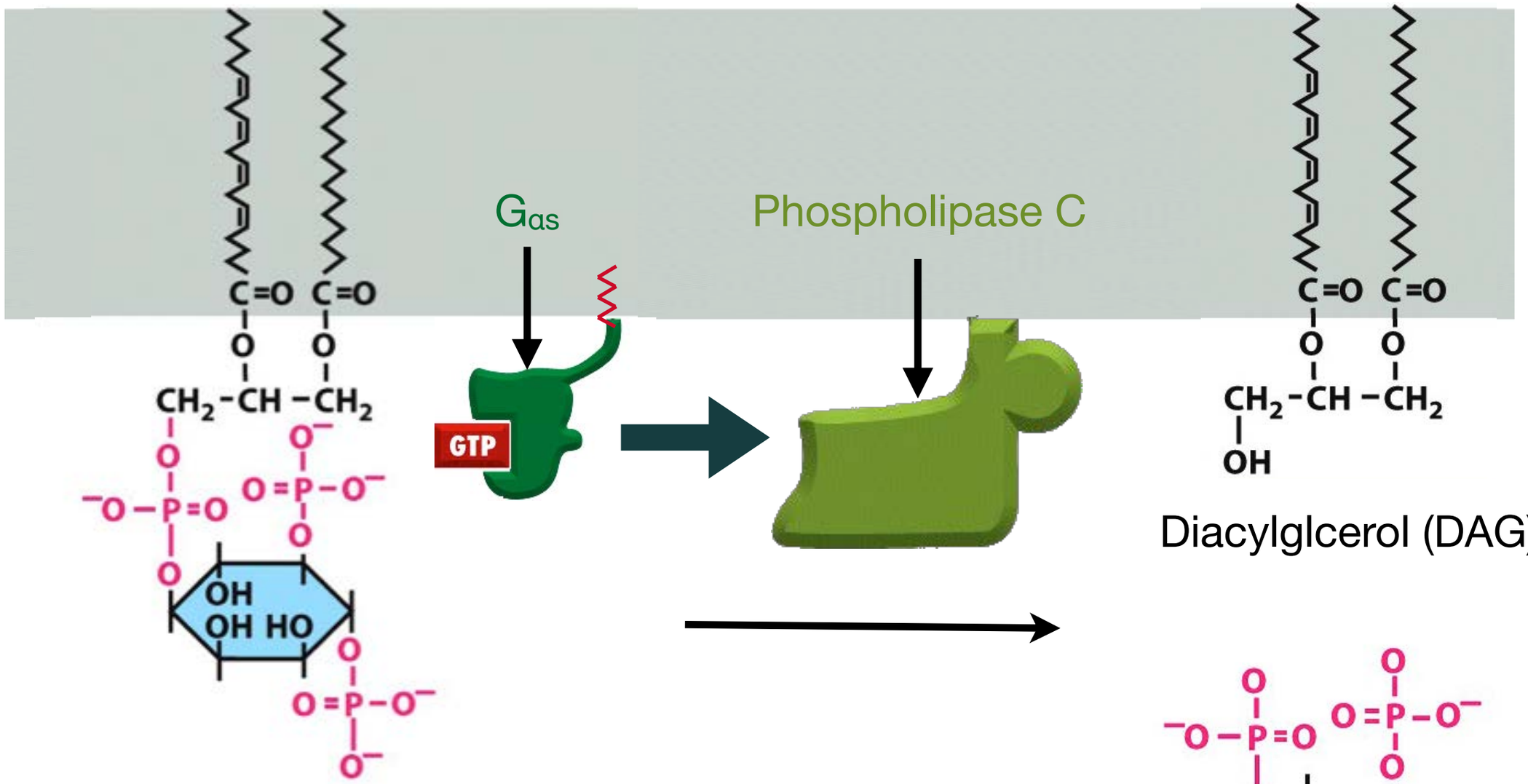


Phosphatidylinositols are secondary messengers for G-protein coupled receptor pathways.



Phophatidylinositol (PI) PI 4-phosphate [PI(4)P] PI 4,5-phosphate [PI(4,5)P2]

$G_{\alpha s}$ activates phospholipases to generate two new signaling molecules.

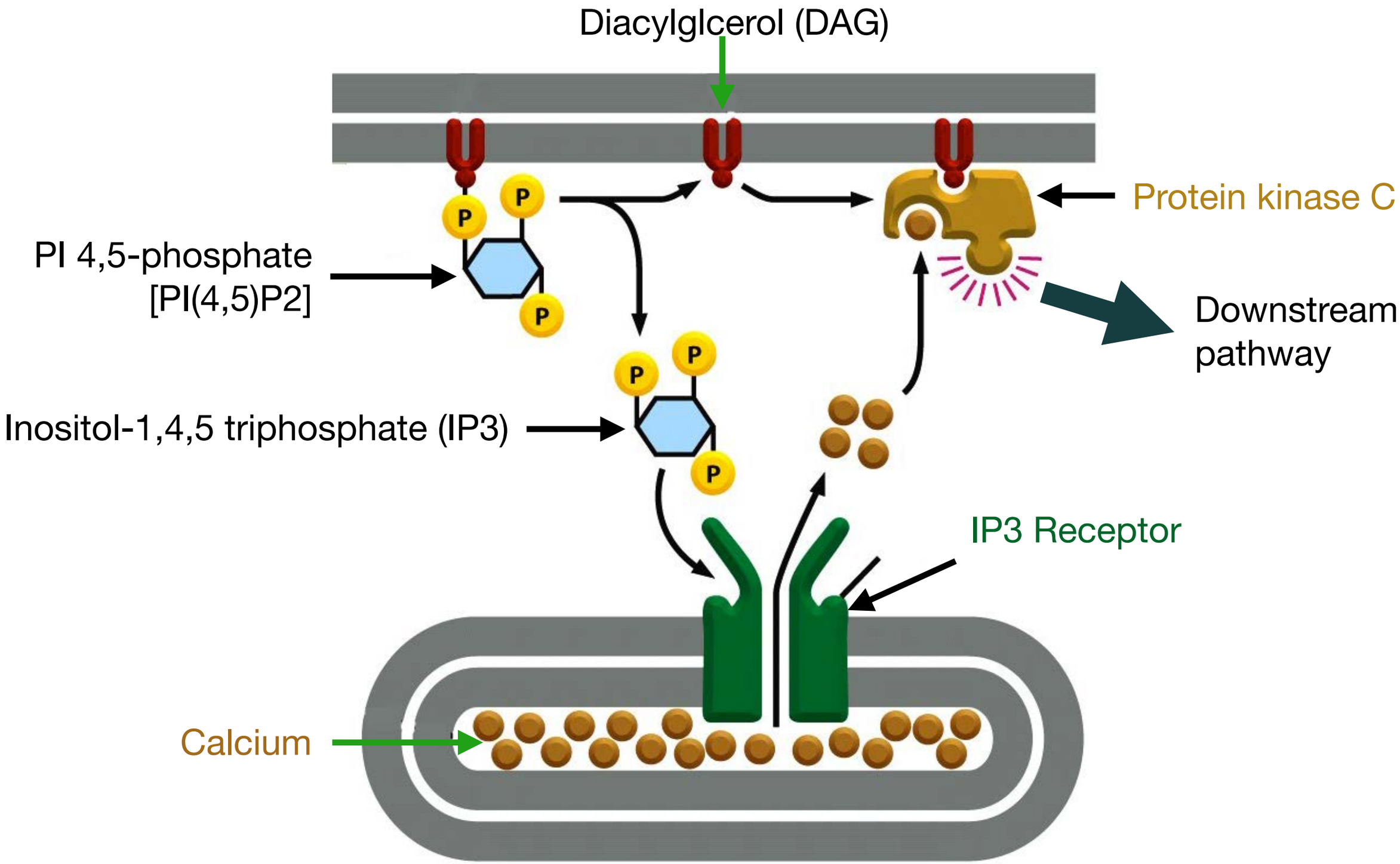


PI 4,5-phosphate [PI(4,5)P2]

Diacylglcerol (DAG)

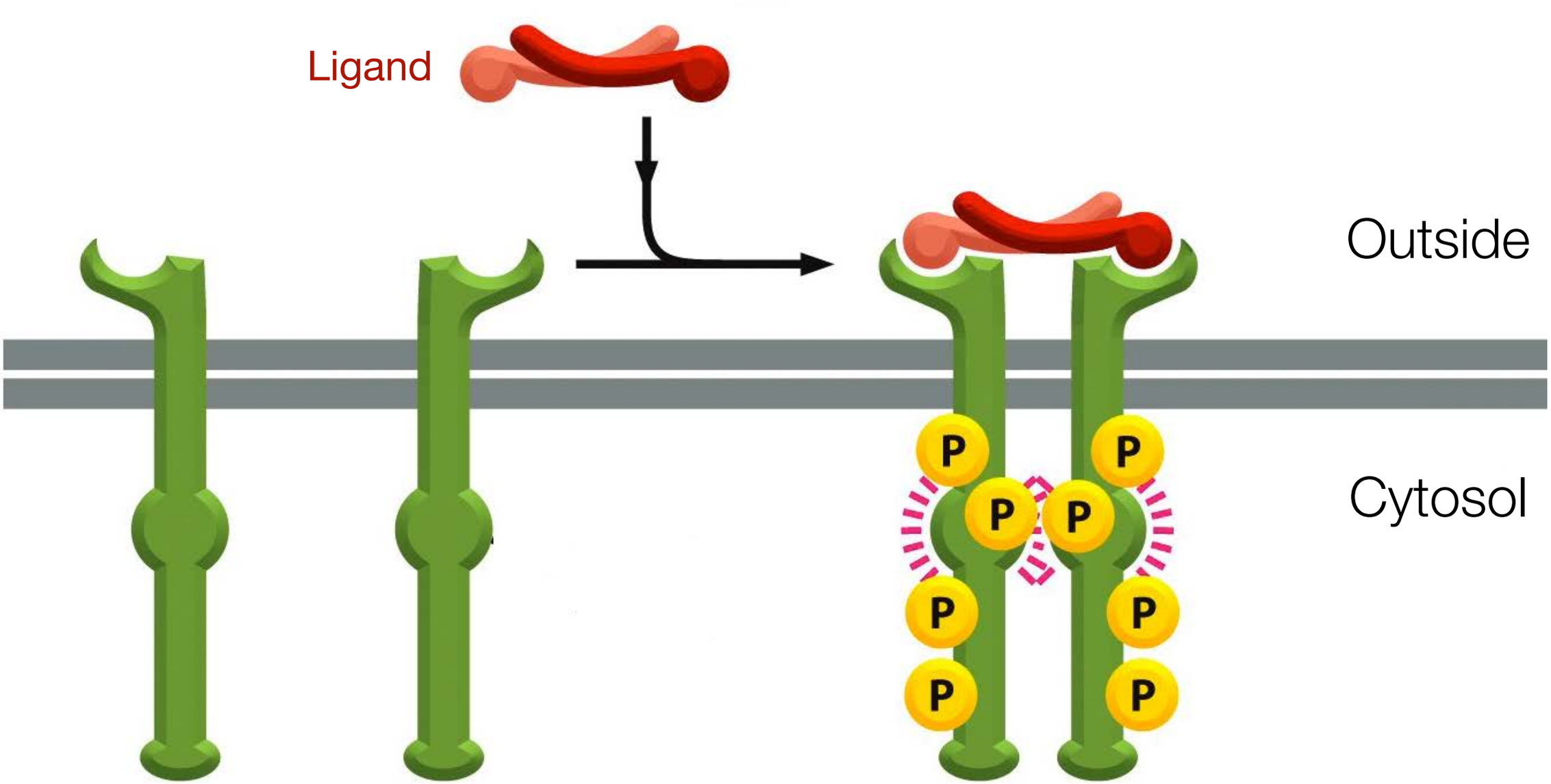
Inositol-1,4,5 triphosphate (IP3)

IP_3 opens calcium channels in ER and DAG activates protein kinase C.

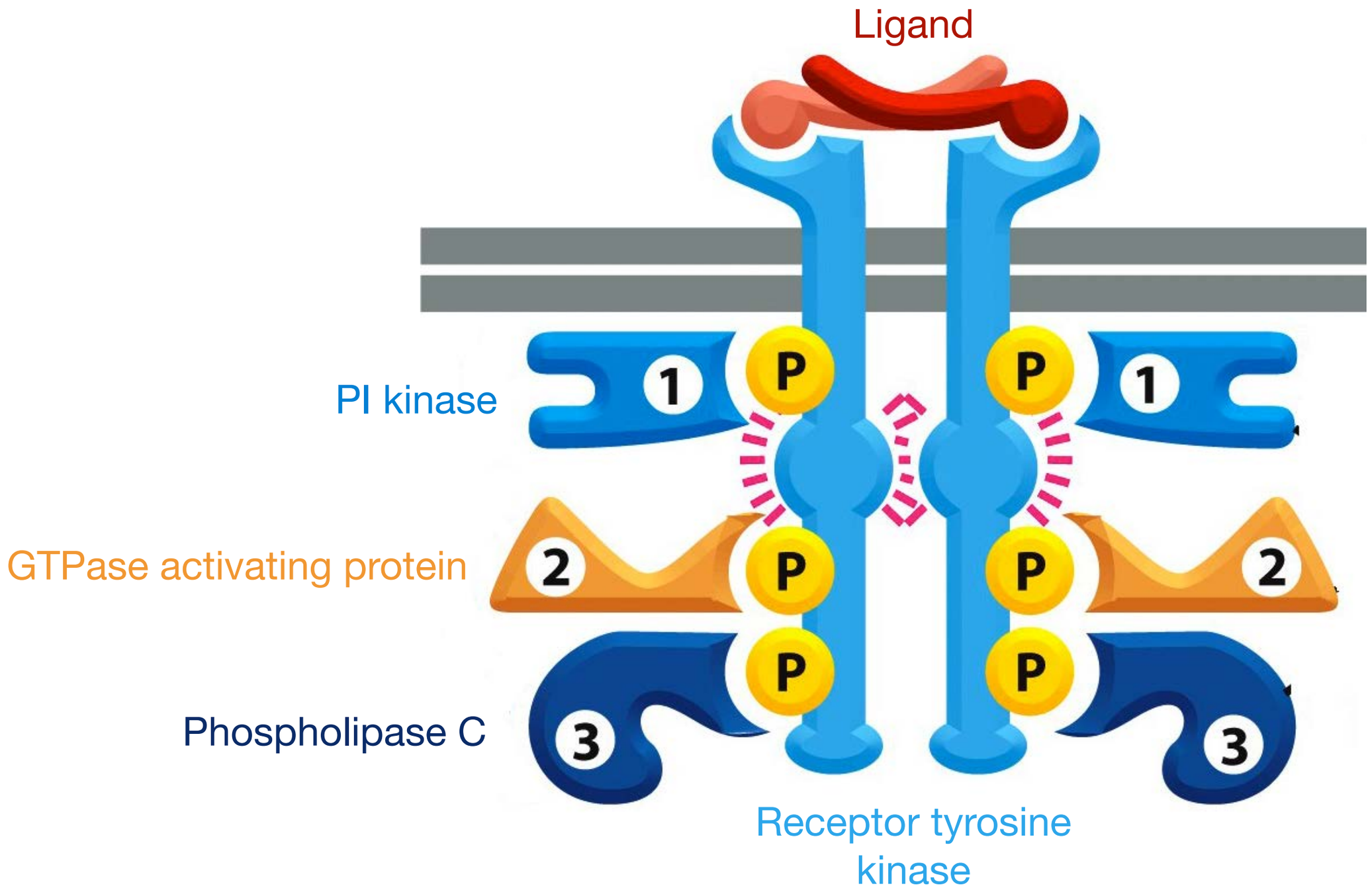


Receptor Tyrosine Kinases

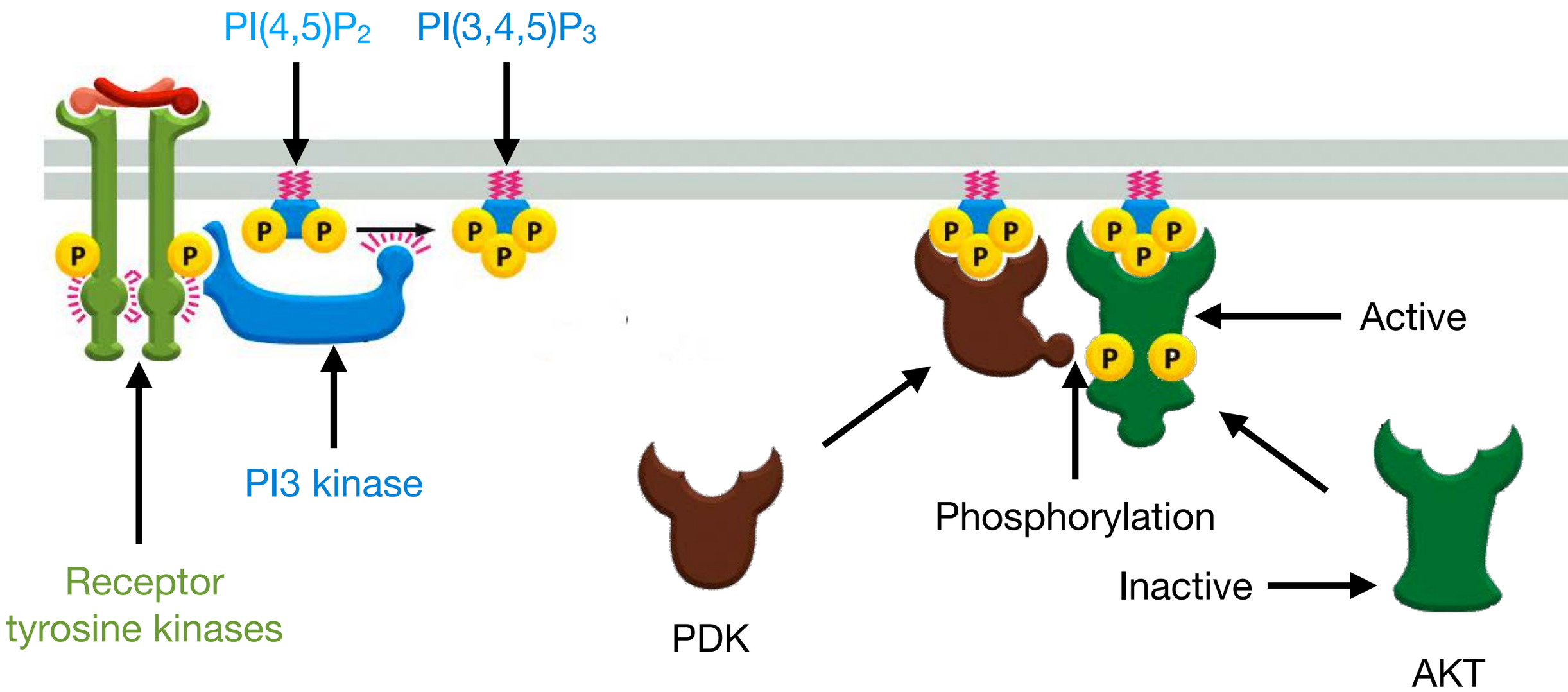
Ligand facilities dimerization of receptor tyrosine kinases faciliating cross-phosphorylation.



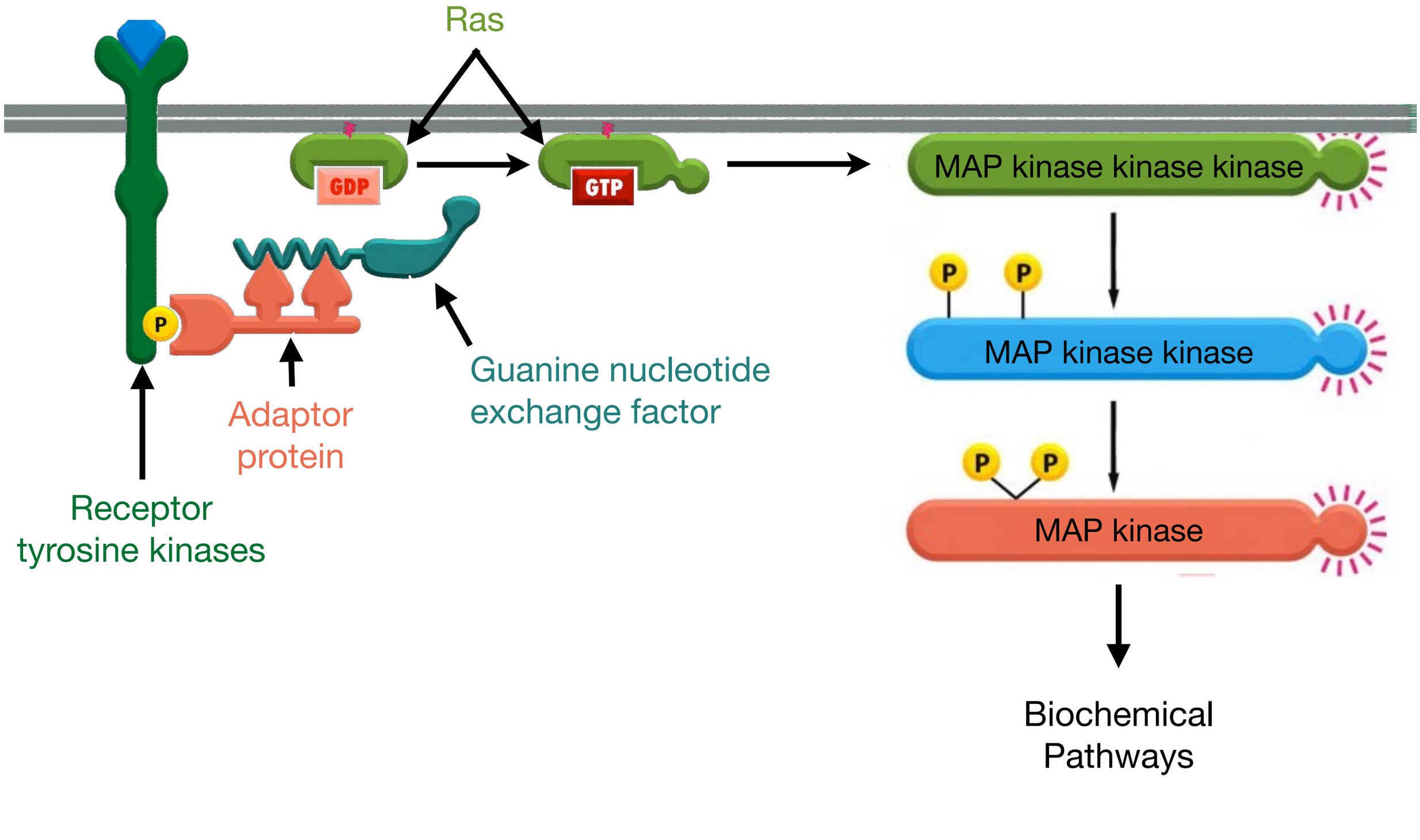
Phosphorylated cytoplasmic domains recruit downstream signaling proteins.



Phosphatidylinositols recruit signaling proteins to the cell membrane which facilitates their activation.

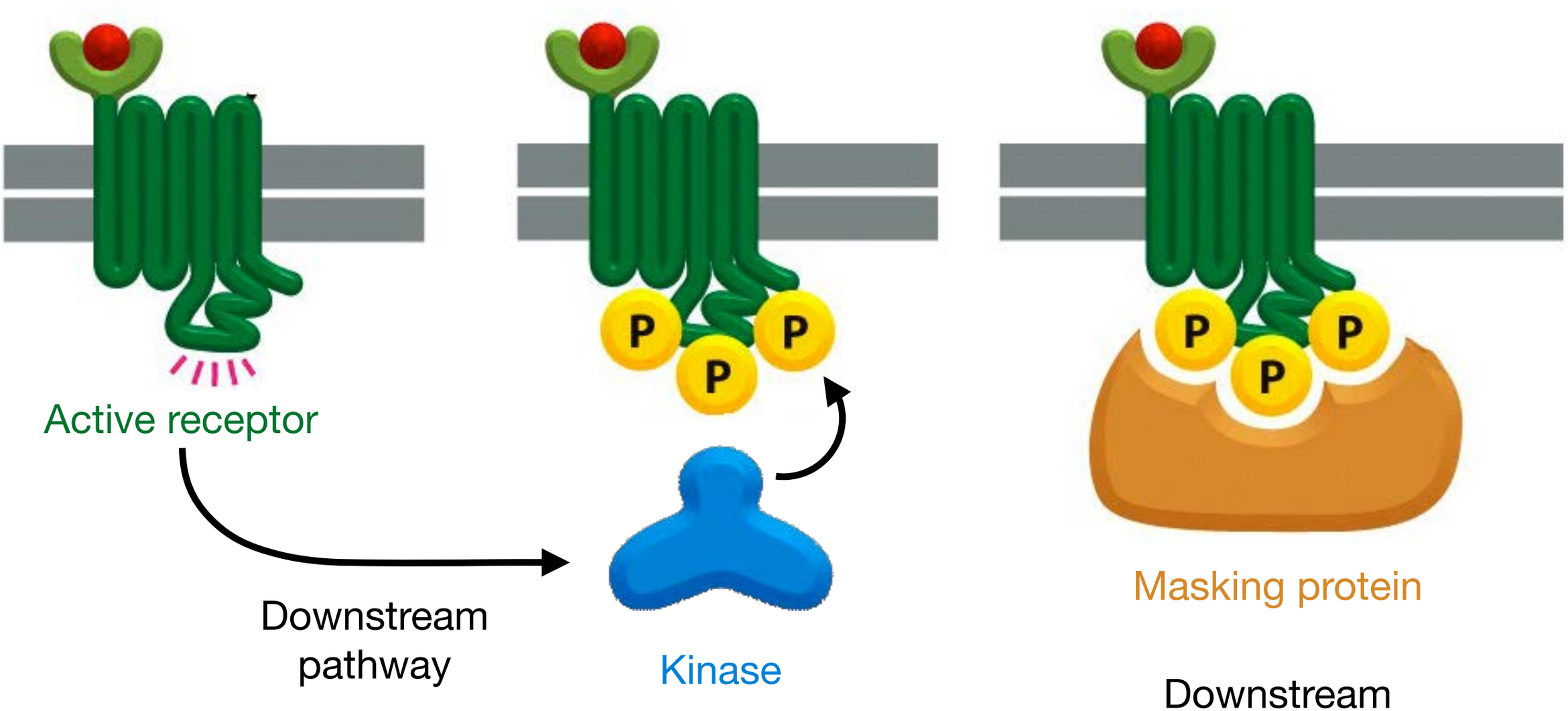


Receptor tyrosine kinases recruit proteins to activate Ras which activates a MAP kinase cascade.

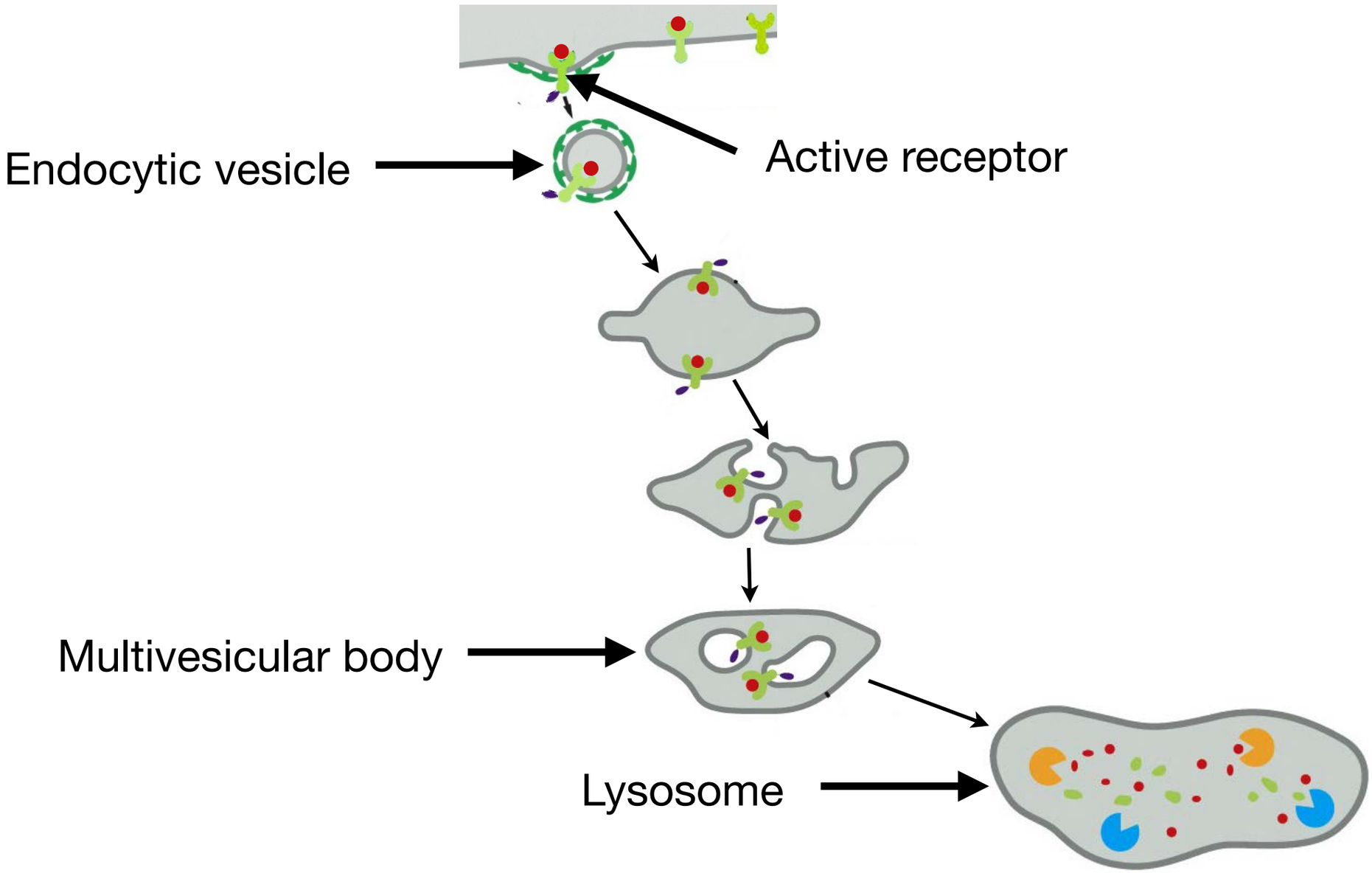


Inactivating Receptors

Masking proteins limit the ability receptors to activate downstream components.

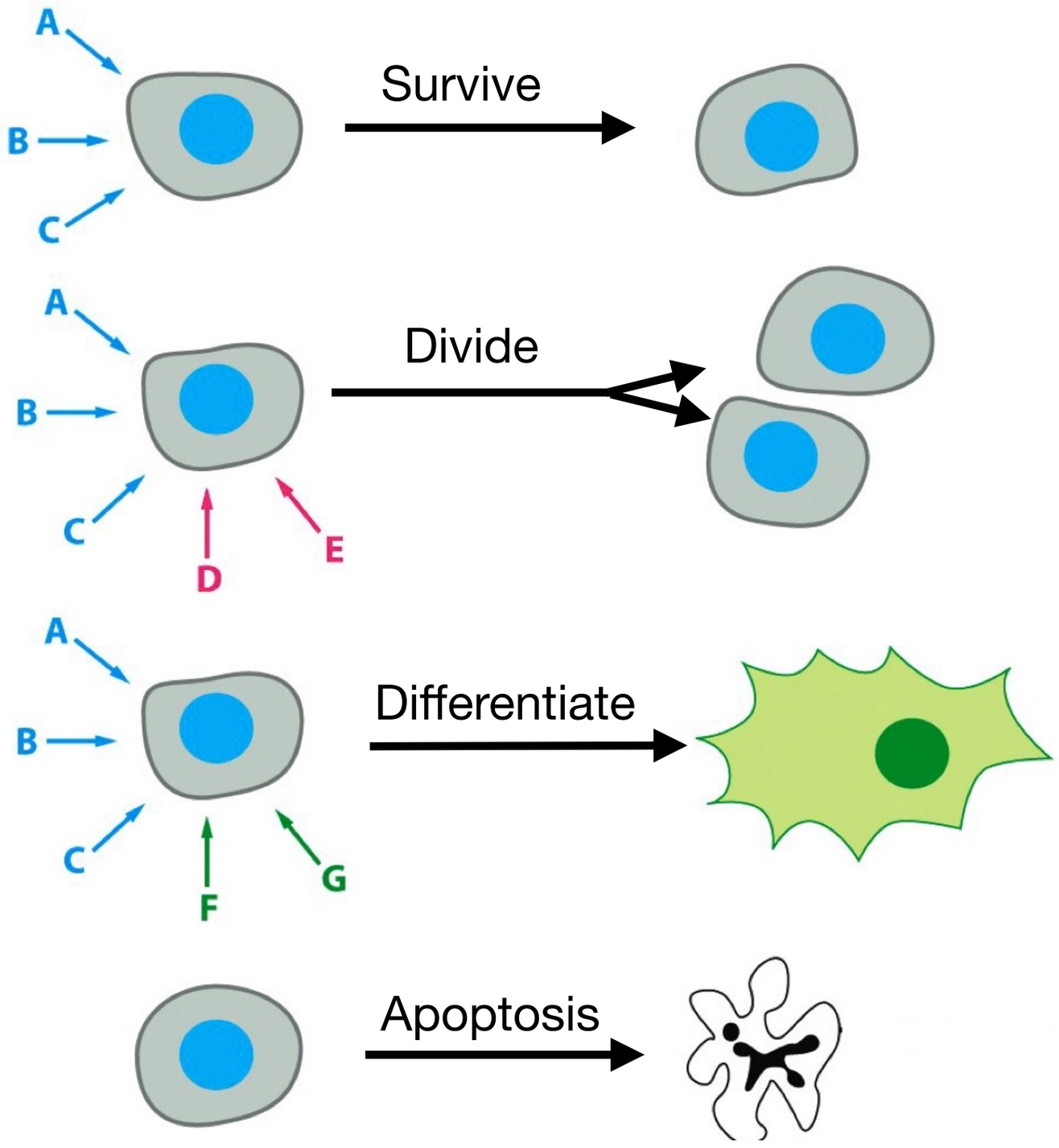


Multivesicular bodies process receptors for degradation in lysosomes.

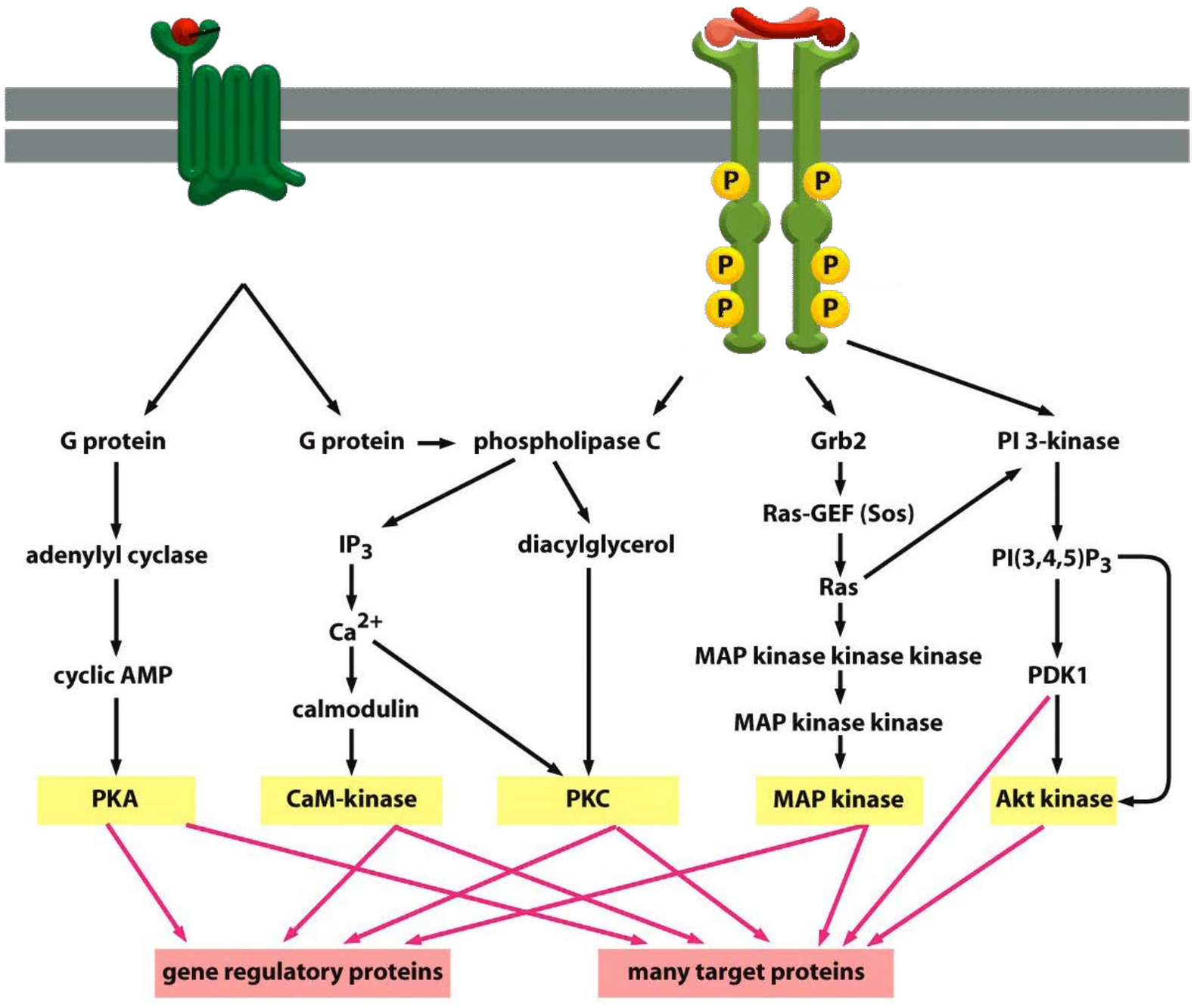


Integrated signaling pathways

Generating a cellular response requires combinations of signaling molecules.



Crosstalk between signaling proteins generates nuanced responses.



Take home points...

- Signal transduction starts with receptors binding ligand at the cell membrane.
- Heterotrimeric G-proteins activate adenylate cyclase and phospholipase C to trigger increase in cytosolic calcium.
- Receptor tyrosine kinases recruit proteins to cell membrane and often trigger MAP-kinase pathways.
- Cells utilize several mechanisms to turn off signals.
- Cells integrate signaling pathways stimulated by different ligand.