

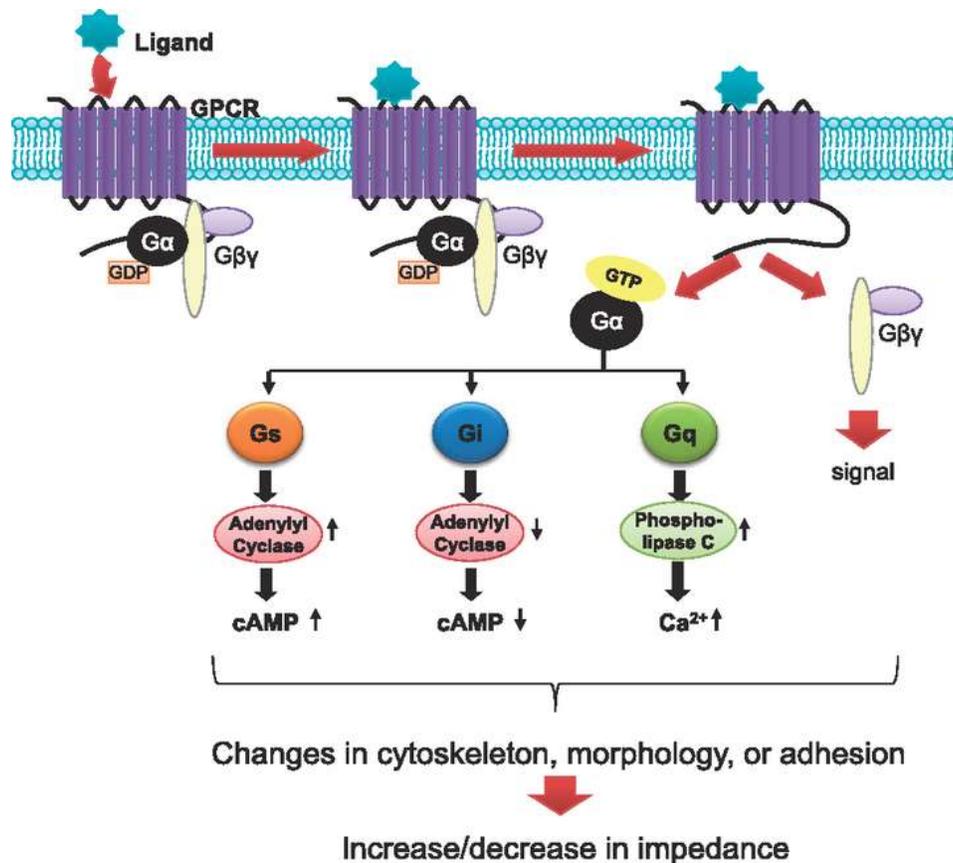
# Crack CSIR-NET 2021

(Study Notes on  
G Protein-Coupled  
Receptor (GPCR))

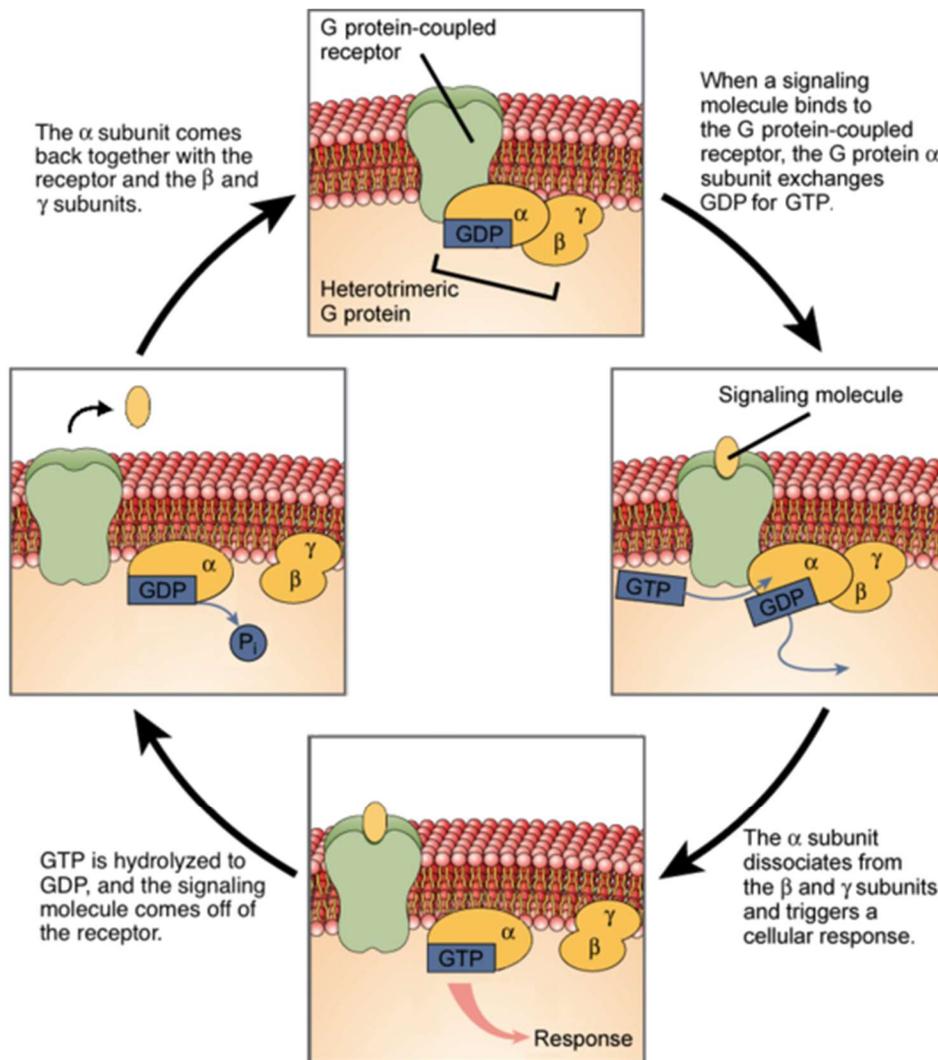


## G Protein-Coupled Receptor (GPCR)

- **G-protein-coupled receptors** (GPCRs) are the largest and most diverse group of membrane receptors in eukaryotes.
- GPCRs consist of a single polypeptide that is folded into a globular shape and embedded in a cell's plasma membrane.
- Seven segments of this molecule span the entire width of the membrane explaining why GPCRs are sometimes called **seven-transmembrane receptors** and the intervening portions loop both inside and outside the cell.
- When an external signalling molecule binds to a GPCR, it causes a conformational change in the GPCR. This change then triggers the interaction between the GPCR and a nearby G protein.
- **G proteins** are specialized proteins with the ability to bind the nucleotides guanosine triphosphate (GTP) and guanosine diphosphate (GDP).
- However, the G proteins that associate with GPCRs are **heterotrimeric**, meaning they have three different subunits: an alpha subunit, a beta subunit, and a gamma subunit.



- A G protein alpha subunit binds either GTP or GDP depending on whether the protein is active (GTP) or inactive (GDP).
- In the absence of a signal, GDP attaches to the alpha subunit, and the entire G protein-GDP complex binds to a nearby GPCR.
- This arrangement persists until a signalling molecule joins with the GPCR.
- At this point, a change in the conformation of the GPCR activates the G protein, and GTP physically replaces the GDP bound to the alpha subunit
- As a result, the G protein subunits dissociate into two parts: the GTP-bound alpha subunit and a beta-gamma dimer.
- Both parts remain anchored to the plasma membrane, but they are no longer bound to the GPCR, so they can now diffuse laterally to interact with other membrane proteins.



- G proteins remain active as long as their alpha subunits are joined with GTP.
- However, when this GTP is hydrolyzed back to GDP, the subunits once again assume the form of an inactive heterotrimer, and the entire G protein associated with the now-inactive GPCR.

- Specific targets for activated G proteins include various enzymes that produce second messengers.
- One common target of activated G proteins is adenylyl cyclase, a membrane-associated enzyme that, when activated by the GTP-bound alpha subunit, catalyzes the synthesis of the second messenger cAMP from molecules of ATP.
- In humans, cAMP is involved in responses to sensory input, hormones, and nerve transmission, among others.

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