Mechanisms of Hormone Action

Receptors

- **Cell surface receptors:** peptide Hormones,
  Neurotransmitters
- **Nuclear receptors:** steroids, thyroid hormones, vitamin D.
- **Scatchard Plot:**

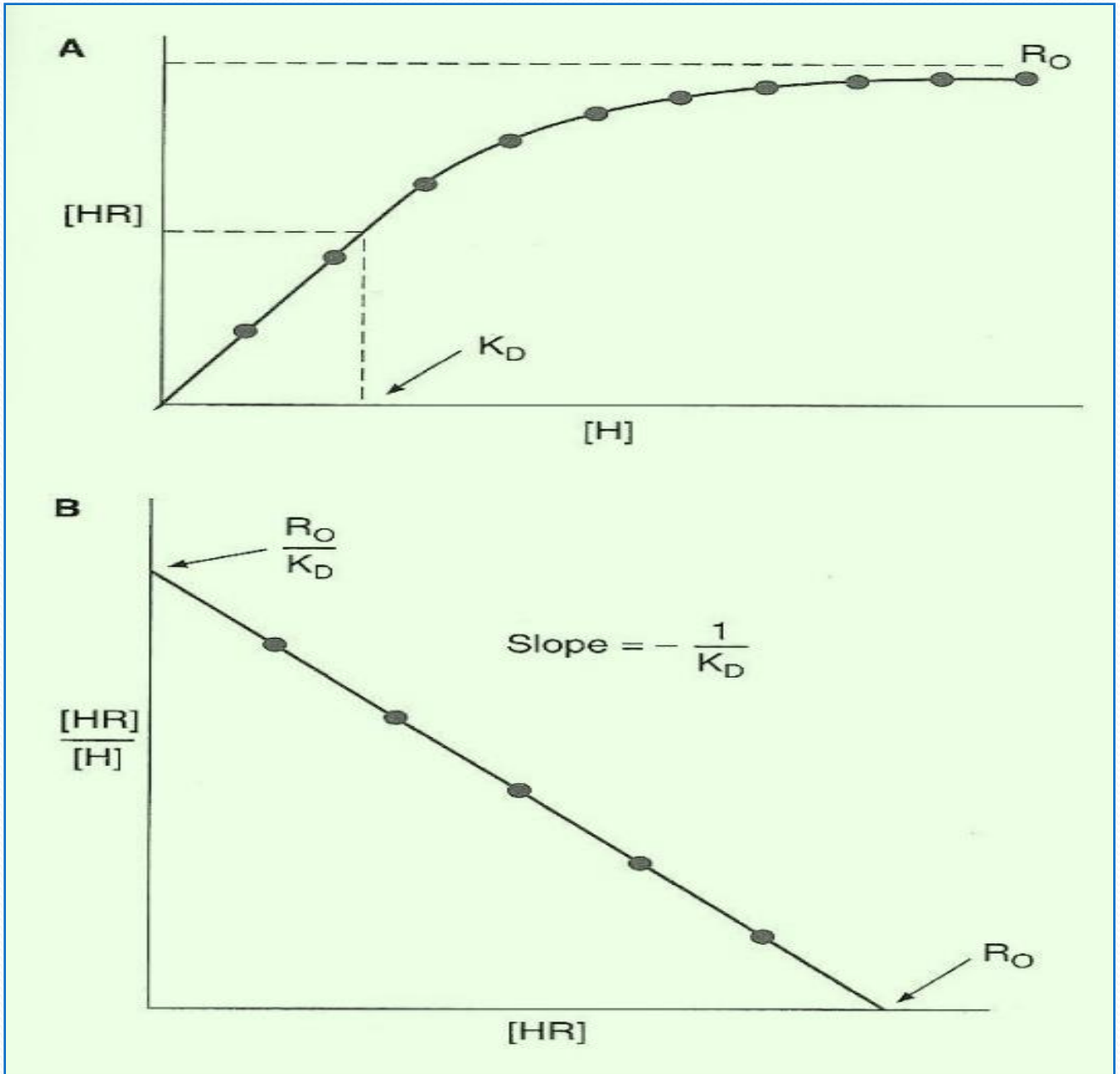
  KD, receptor conc.

  Spare receptors.

Effectors

- **Ion transport**
- **Gene expression**
- **Enzymes**

Scatchard Analysis



Neurotransmitter - Peptide Hormone receptor Families

Serpentine or "Seven- transmembrane- domain" receptor

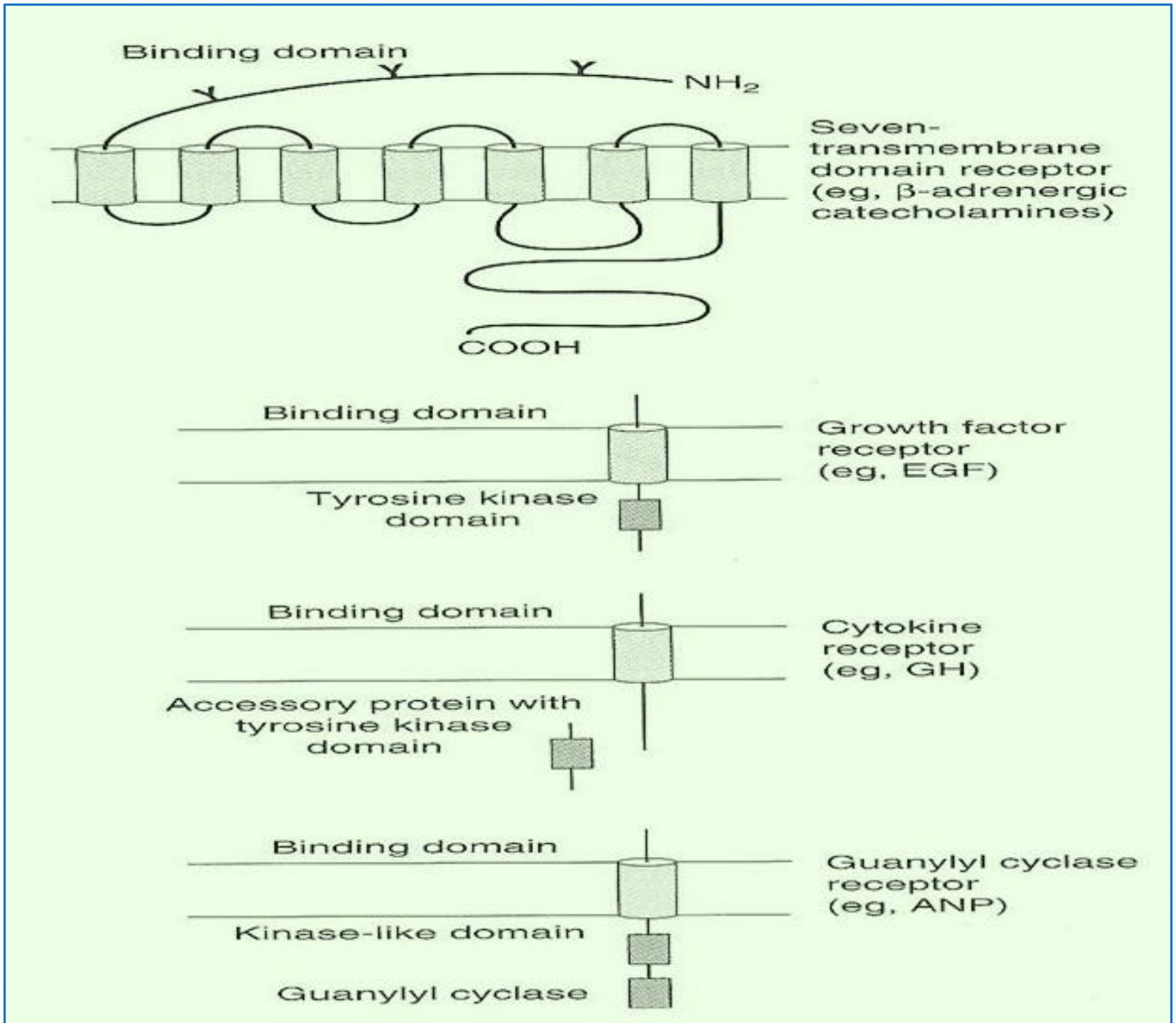
- ***G-protein transducer***

  β-adrenergic- PTH – LH – TSH – TRH- ACTH

Single – transmembrane domain receptors

- ***Intrinsic tyrosine kinase "growth factor receptors": insulin – IGF – EGF.***
- ***Cytokine receptors "soluble transducer": GH, PRL***
- ***Guanylyl cyclase receptors: Natriuretic peptides.***

Membrane-Associated Hormone Receptors



G protein Transducers

G proteins

- ***α subunit (Effector activation)***
- ***Gs, Gi (adenylate cyclase)***
- ***Gq/11 (phospholipase C)***

G protein subunits

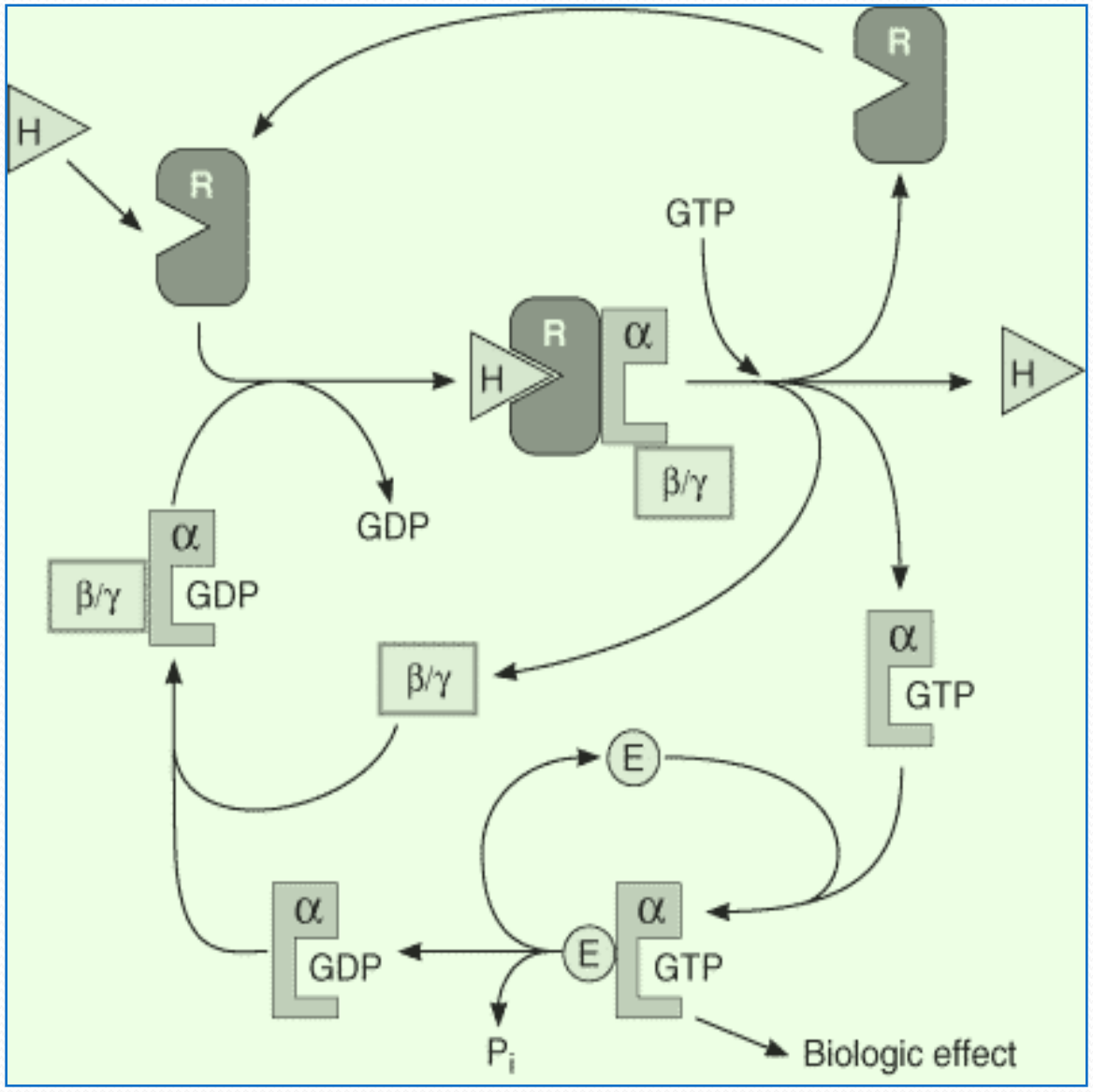
G Protein Subunit	Associated Receptors	Effector
α_s	β-Adrenergic TSH Glucagon	Adenylyl cyclase Ca^{2+} channels K^+ channels
α_i	α_2-Adrenergic Muscarinic (type II)	Adenylyl cyclase Ca^{2+} channels K^+ channels
α_q	α_1-Adrenergic	PLCβ
β/α		Adenylyl cyclase (+ or –) PLC Supports βARK-mediated receptor phosphorylation and desensitization

G protein Transducers (1)

G protein Activation

- ***Inactive G protein (GDP bound to α subunit)***
- ***GDP release, GTP binding, βγ dissociation.***
- ***α – subuint (GTPase activity)***

G Protein-Mediated Signal Transduction

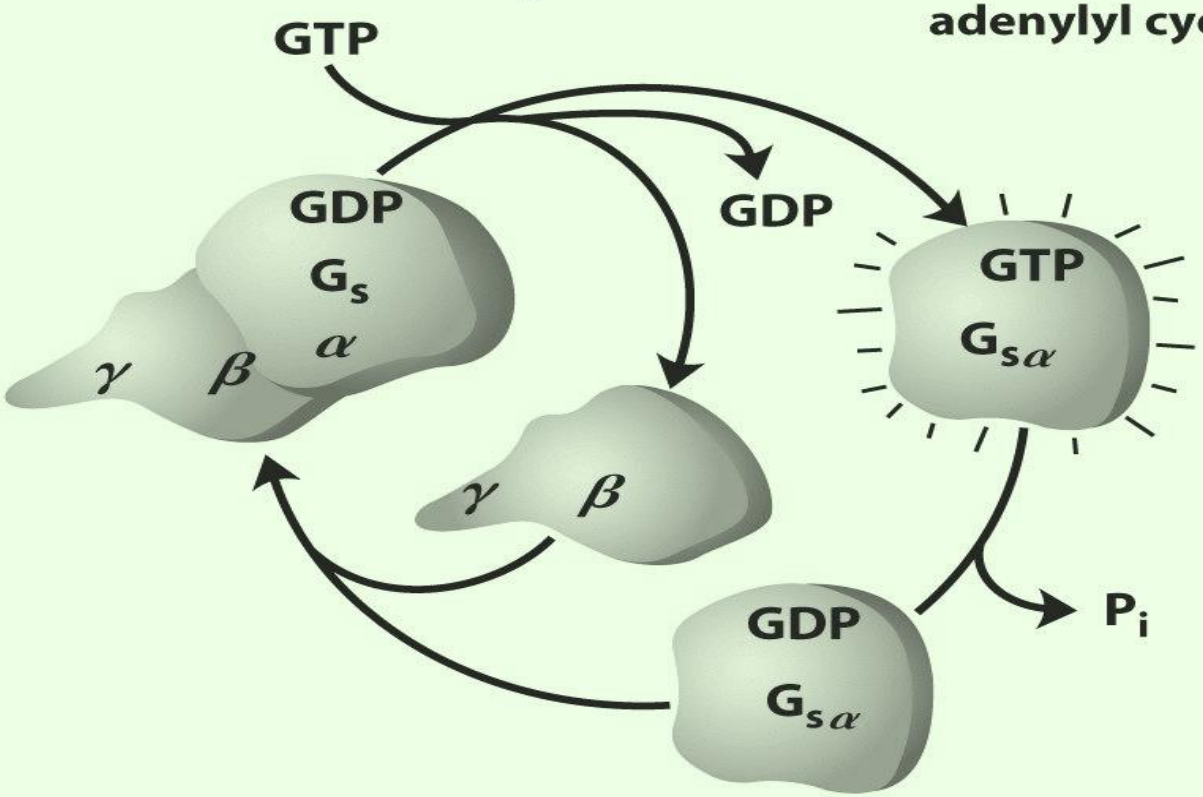


The G protein cycle

① G_s with GDP bound is turned off; it cannot activate adenylyl cyclase.

② Contact of G_s with hormone-receptor complex causes displacement of bound GDP by GTP.

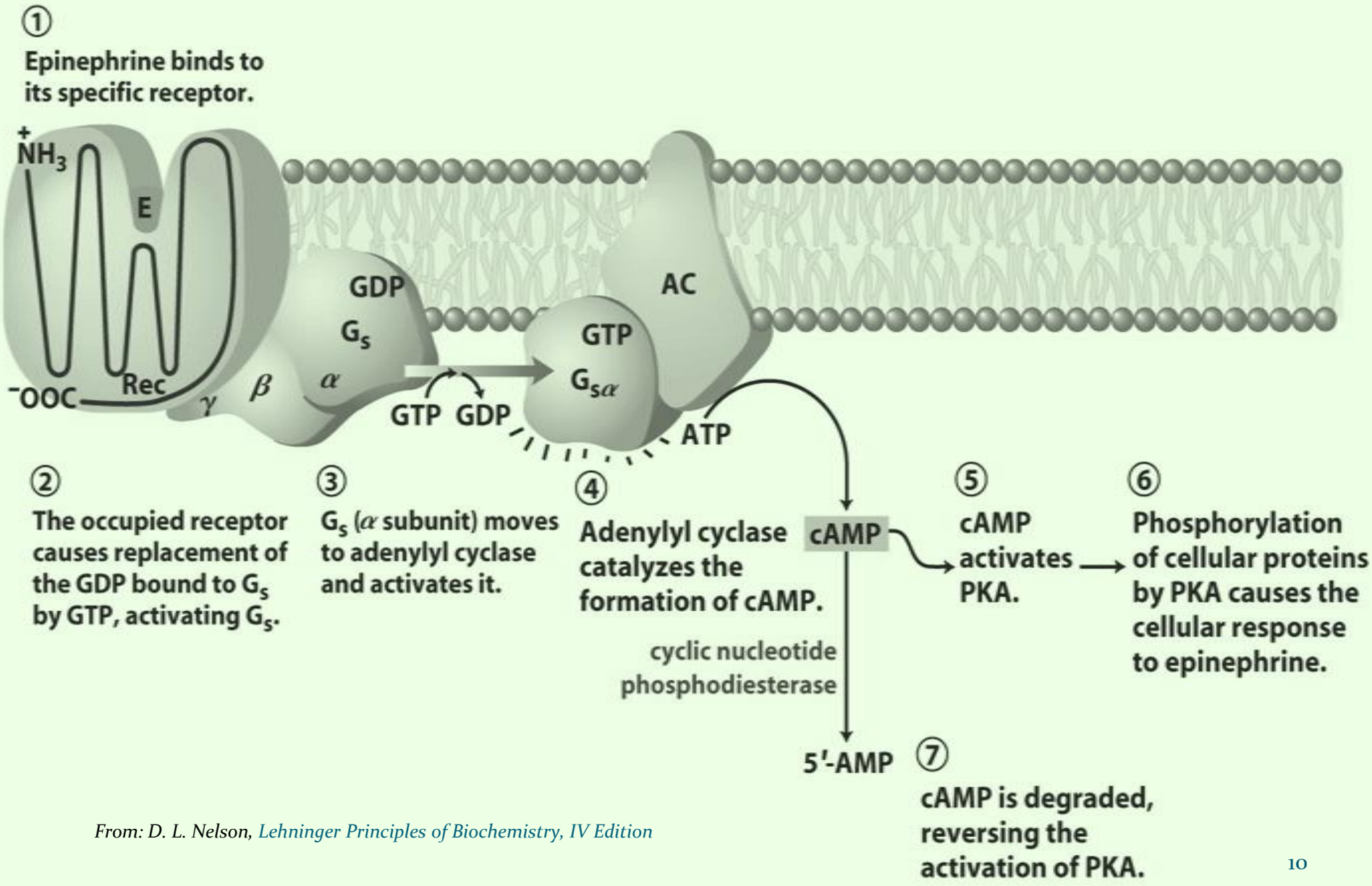
③ G_s with GTP bound dissociates into α and $\beta\gamma$ subunits. $G_{s\alpha}$-GTP is turned on; it can activate adenylyl cyclase.



④ GTP bound to $G_{s\alpha}$ is hydrolyzed by the protein's intrinsic GTPase; $G_{s\alpha}$ thereby turns itself off. The inactive α subunit reassociates with the $\beta\gamma$ subunit.

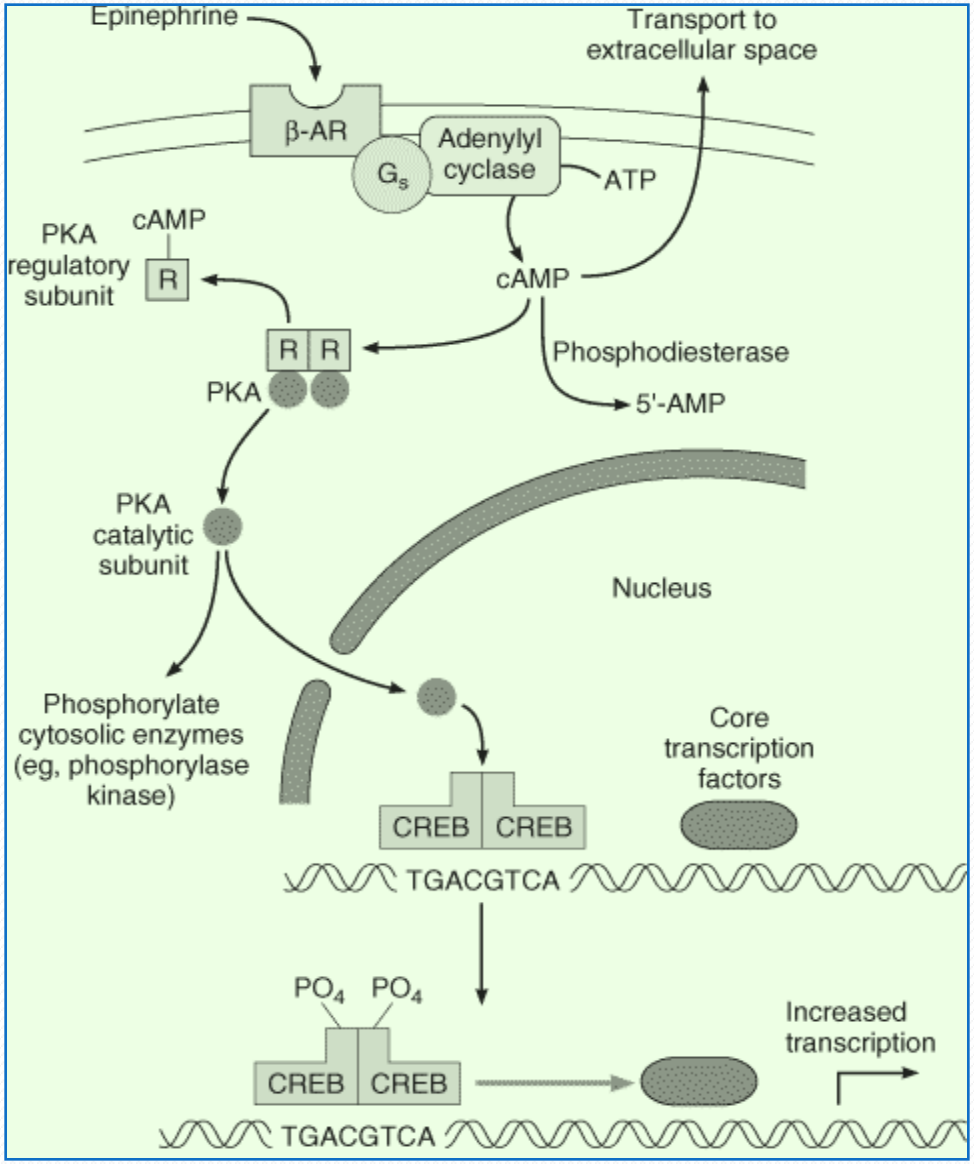
From: D. L. Nelson, *Lehninger Principles of Biochemistry, IV Edition*

An example of G protein Coupled Receptor…



From: D. L. Nelson, Lehninger Principles of Biochemistry, IV Edition

β-Adrenergic receptor signaling



Activation of PKA by cAMP