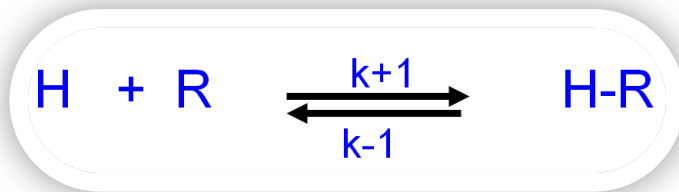


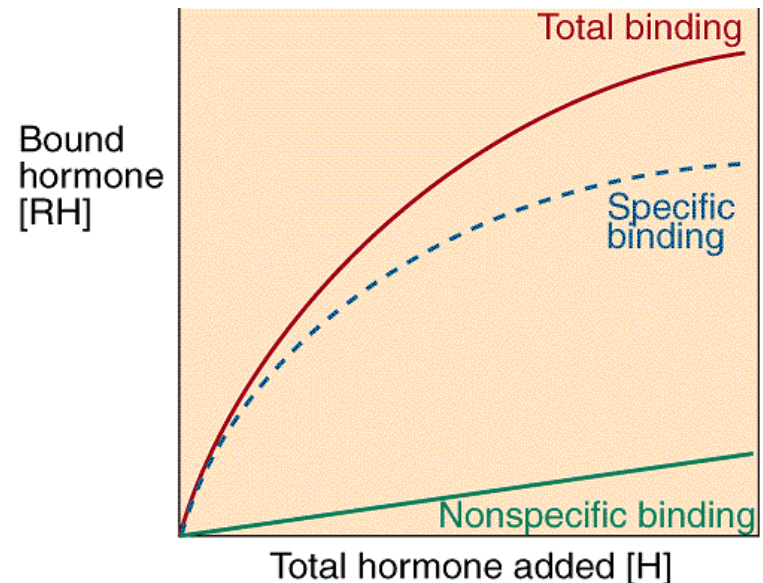


Accordingly; Hormone-Receptor Interactions

- Should be specific, however displaceable by agonist or antagonist
- Should be saturable
- Should occur within the concentration range provided



- Association constant K_a
- **Dissociation constant K_d**
- $K_d = \{[\text{H}] \times [\text{R}]\} / [\text{H-R}]$

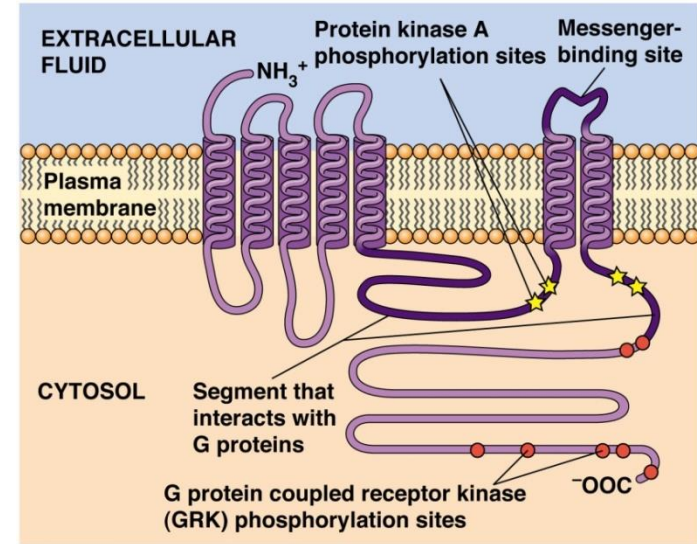


- **(20X)** dissociation constant is enough to saturate the receptor
- K_d values for many hormones range from 10^{-9} to 10^{-11} M



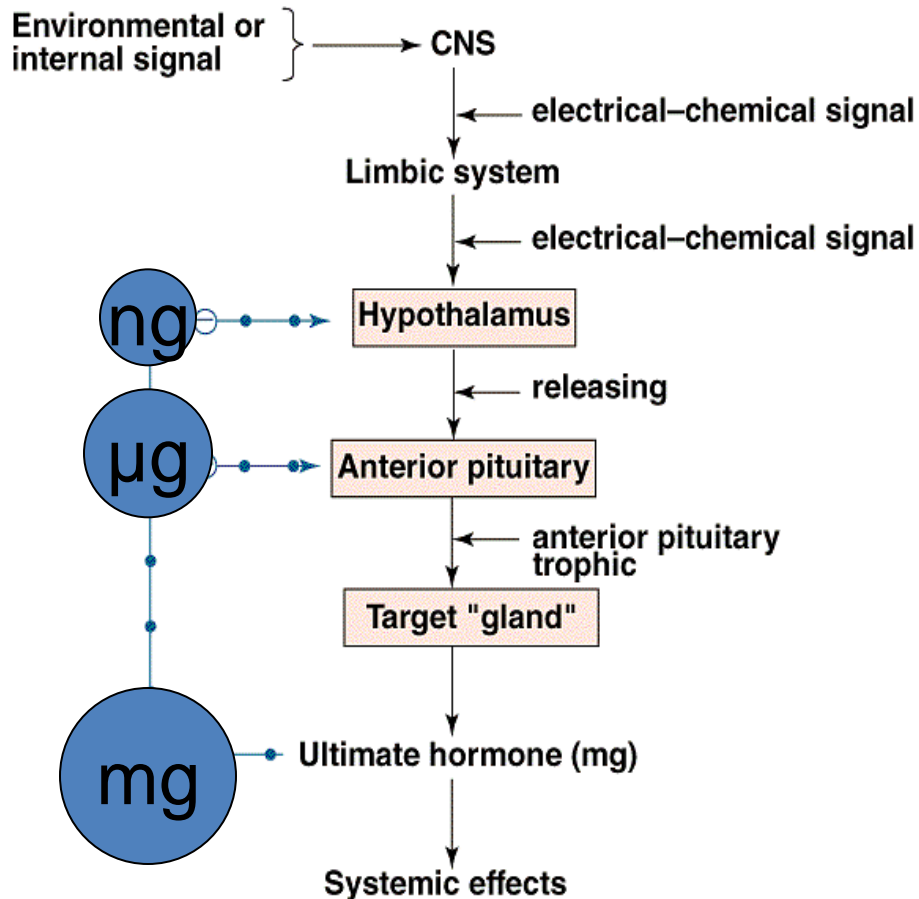
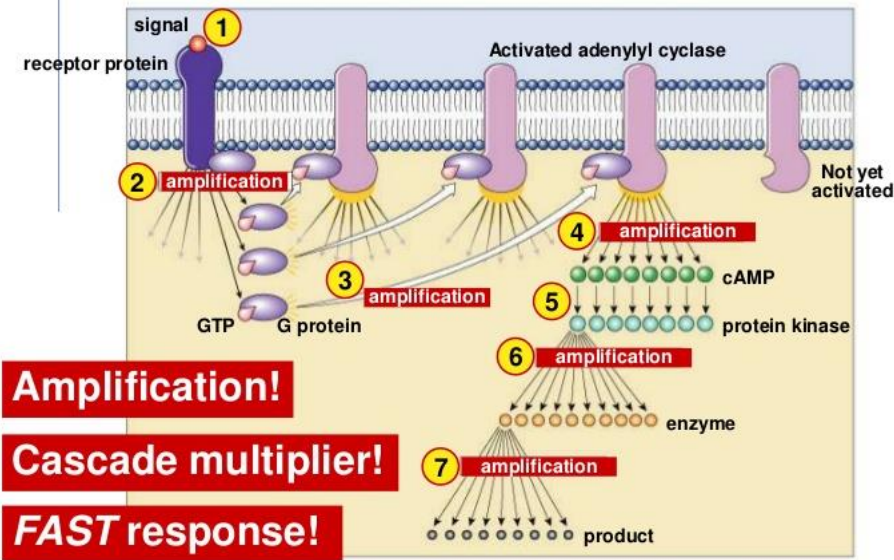
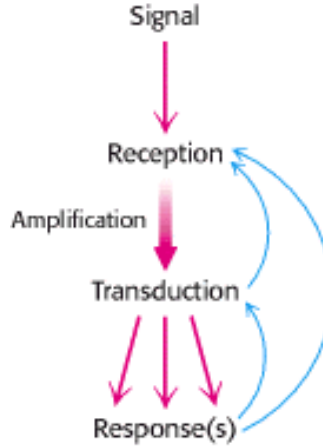
Receptor Domains

- At least two functional domains:
 - **Recognition &**
 - **Coupling** or signal transduction domain
- **Coupling occurs in two general ways:**
 - **Indirect:** changing the activity of an **enzyme** (Polypeptide & catecholamines, plasma membrane)
 - **Direct** (steroids, retinoids, and thyroid hormones, **intracellular**)
- Steroid, thyroid, and retinoid hormone receptors:
 - Hormone binding site ; DNA binding site; co-regulator proteins binding site, cellular trafficking proteins binding site
- Receptor–effector coupling— provides the first step in amplification





Signal Amplification

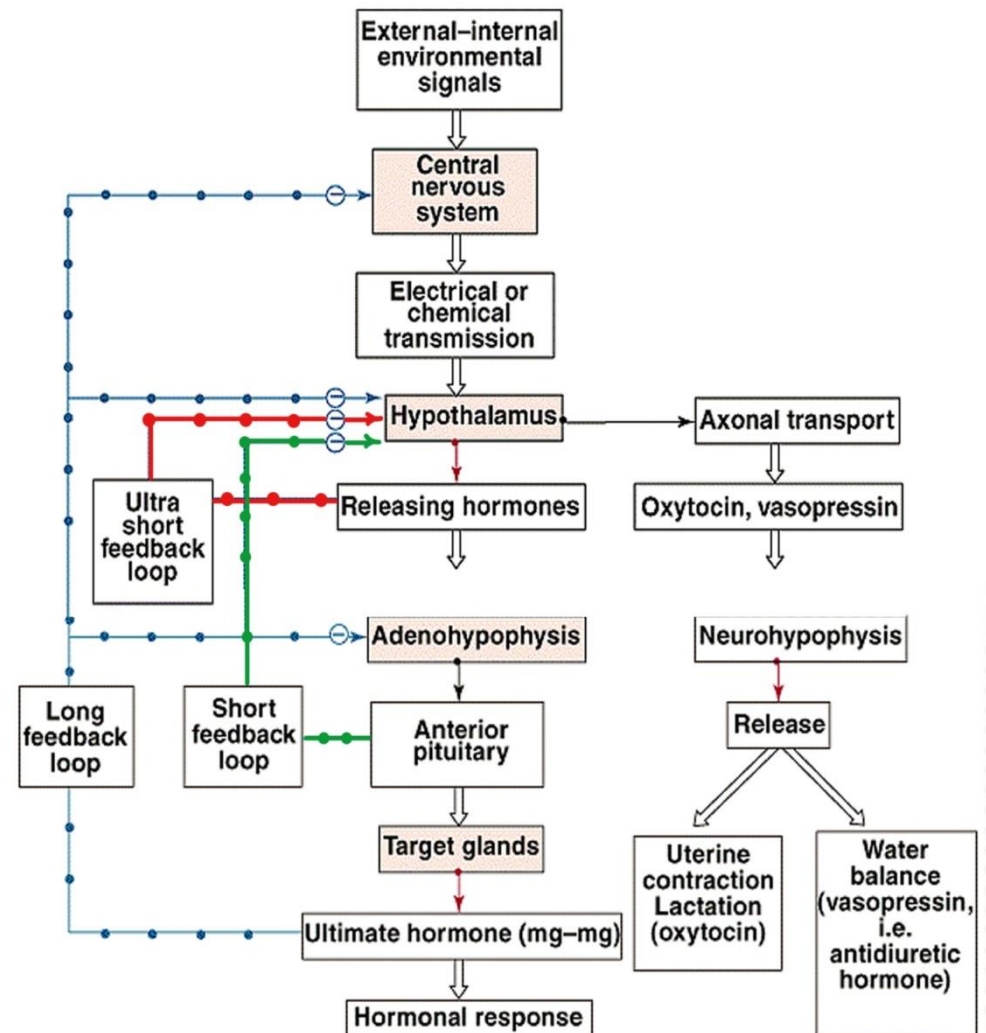
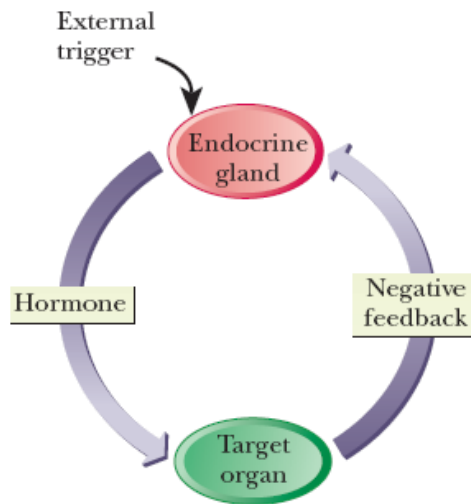


| (a) Signaling pathway | (b) Number of molecules activated |
|---|-----------------------------------|
| RECEPTION Binding of epinephrine to G protein-linked receptor | 1 molecule |
| TRANSDUCTION Inactive G protein → Active G protein | 10^2 molecules |
| Inactive adenylyl cyclase → Active adenylyl cyclase | 10^2 molecules |
| ATP → Cyclic AMP | 10^4 molecules |
| Inactive protein kinase A → Active protein kinase A | 10^4 molecules |
| Inactive phosphorylase kinase → Active phosphorylase kinase | 10^5 molecules |
| Inactive glycogen phosphorylase → Active glycogen phosphorylase | 10^6 molecules |
| RESPONSE Glycogen → Glucose-1-phosphate | 10^8 molecules |



How the release is controlled?

- Feedback inhibition at many levels, **why?**
 - Ultrashort loop
 - Short loop
 - Long loop





Classification of Hormones

Chemical Structure

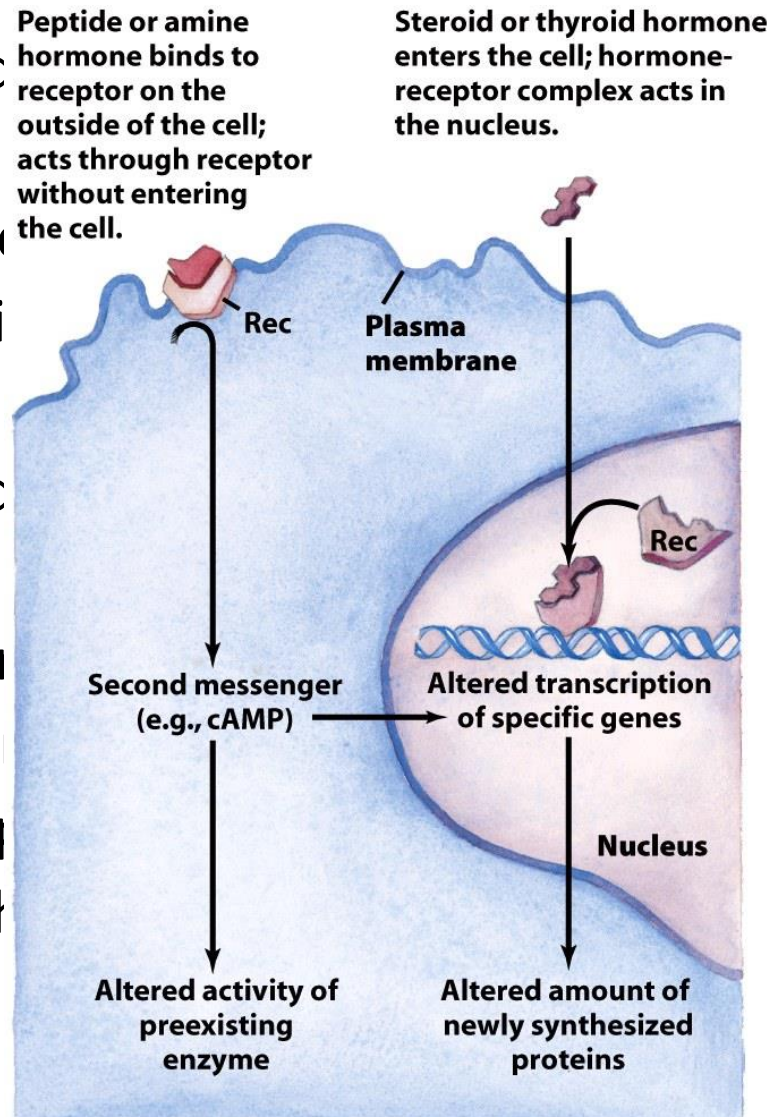
- Chemical composition; solubility; location of receptors; nature of the signal used to mediate hormonal action
- ✓ **Polypeptides:** Pituitary hormones; Hypothalamic releasing hormones; Insulin, Growth factors...
- ✓ **Amino acid derivatives:** Adrenalin, Thyroid hormones
- ✓ **Steroids**



Classification of Hormones

Mechanism of Action

- Hormones that bind to receptors on the outside of the cell:
 - Steroids
 - Thyroid hormones
 - Calcitriol, retinoids
- Hormones that bind to intracellular receptors:
 - cAMP (β adrenergic)
 - cGMP (atrial natriuretic)
 - Calcium or phospholipids
 - Kinase or phosphatase



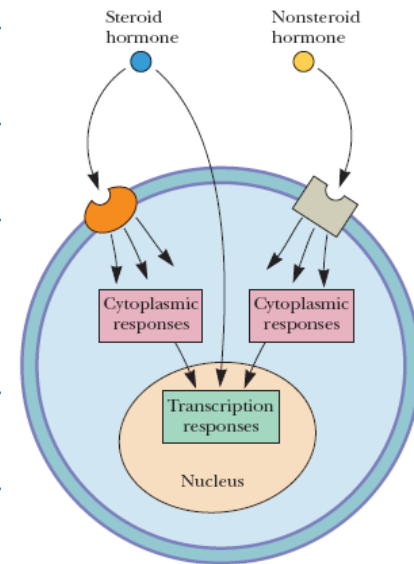
Transport protein

1)



General Features of Hormone Classes

| | Group I | Group II |
|--------------------|---|--|
| Types | Steroids, iodothyronines, calcitriol, retinoids | Polypeptides, proteins, glycoproteins, catecholamines |
| Action | Slow | Fast |
| Solubility | Lipophilic | Hydrophilic |
| Transport proteins | Yes | No |
| Plasma $t_{1/2}$ | Long (hrs - days) | Short (minutes) |
| Receptor | Intracellular | Plasma membrane |
| Mediator | Receptor-hormone complex | cAMP, cGMP, Ca^{2+} , kinase cascades, metabolites of phosphoinositols |

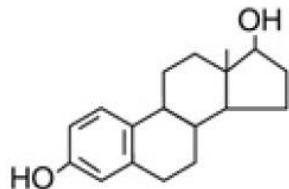




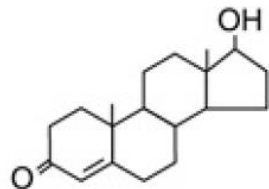
Structure of Hormones

- Lipid – soluble hormones:

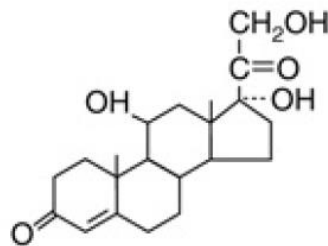
A. Cholesterol derivatives



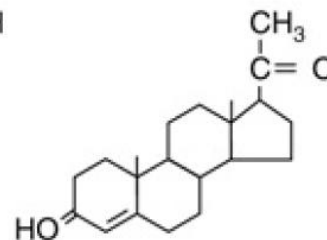
17β-Estradiol



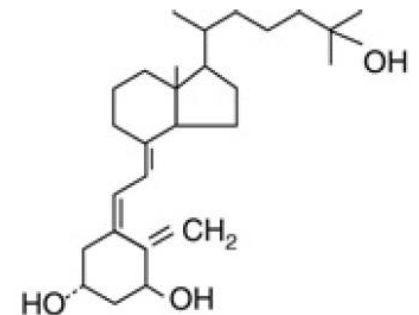
Testosterone



Cortisol



Progesterone



1,25(OH)₂-D₃