Faculty of Pharmacy
Biochemistry-2

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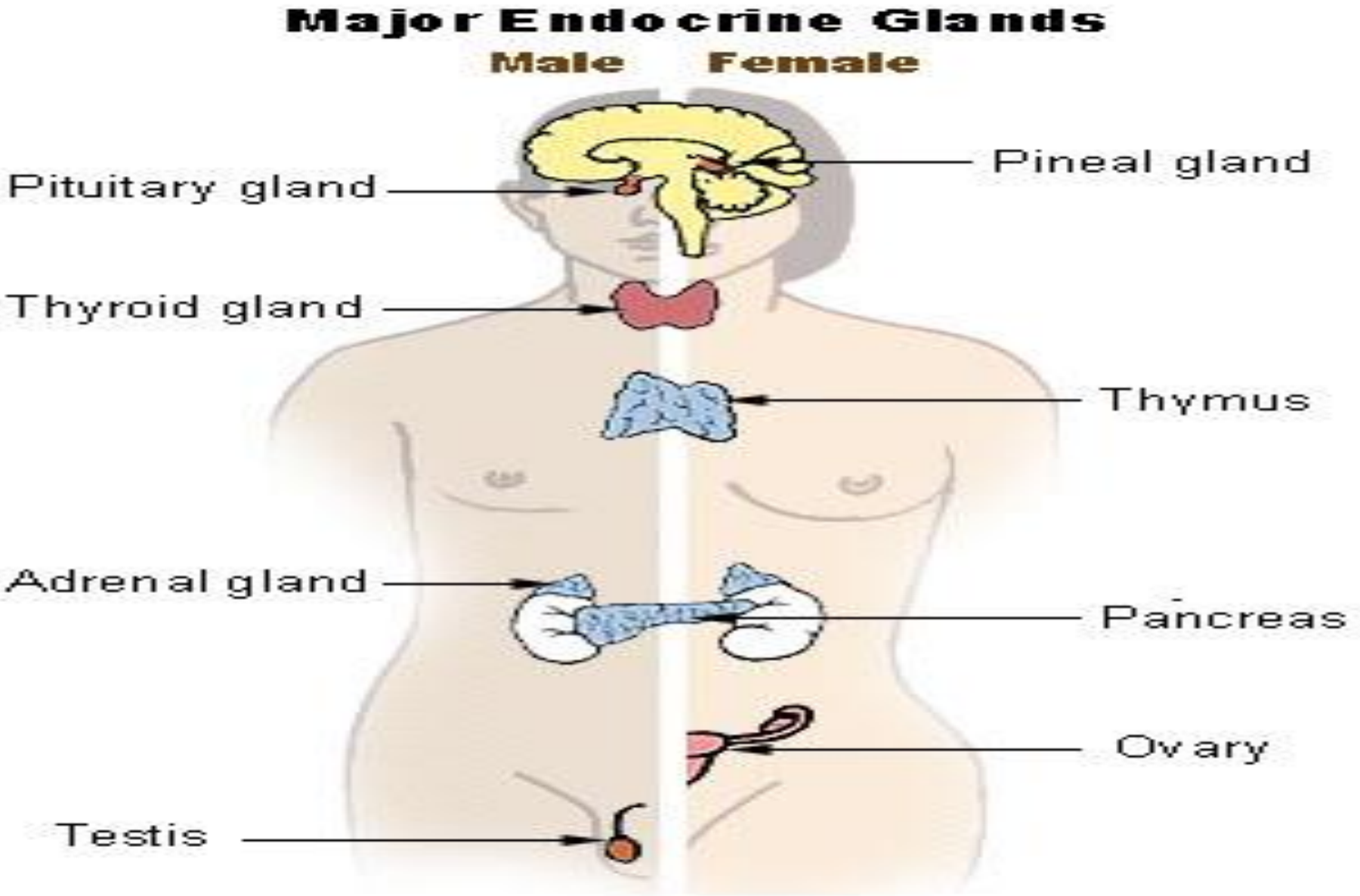
Lecturer of Biochemistry

Lecture 5

Cell Communications

- Necessary for integration of cell activities
- Mechanisms
  - **gap junctions**
    - pores in cell membrane along which signalling chemicals move from cell to cell
  - **neurotransmitters**
    - released from neurons to travel across gap to 2nd cell
  - **paracrine (local) hormones**
    - secreted into tissue fluids to effect nearby cells
  - **hormones (strict definition)**
    - chemical messengers that travel in the bloodstream

Endocrine System



Endocrine System

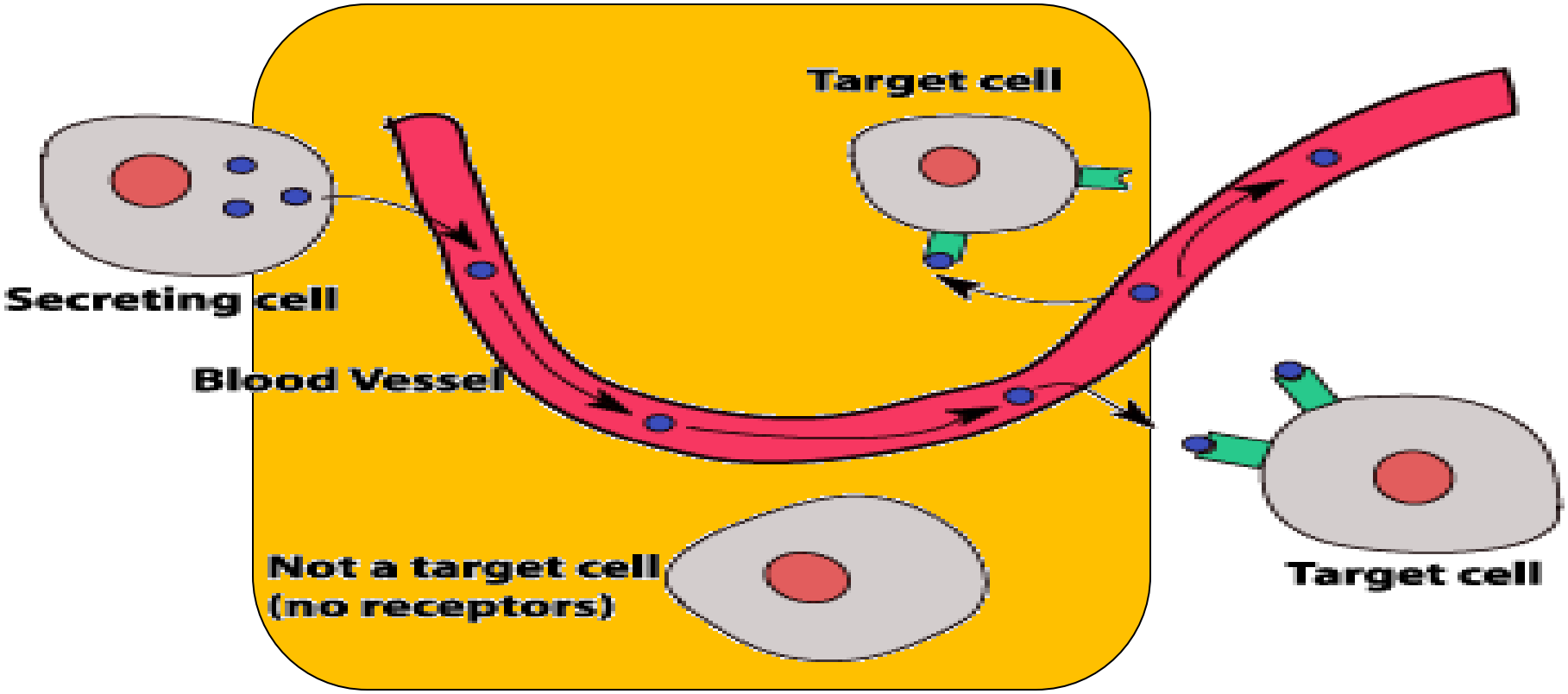
- The **endocrine system** includes the endocrine glands and their hormones
- The function of the endocrine system is to secrete **hormones** into the bloodstream.
- **Hormone**: A Chemical messenger which targets a specific group of cells, in order to cause that group of cells do some activity or stop doing an activity.

Endocrine System

- **Exocrine** glands release their secretions into ducts, or tubes
  - Liver→ Bile released into the gallbladder, then through a duct into the small intestine
  - Pancreas→ releases pancreatic juice into the small intestine via a duct
- **Endocrine** Glands are called ductless glands
  - Release hormones directly into the bloodstream
  - Blood transports hormones throughout the body
  - Each hormone acts on only a certain kind of tissue called its **target tissue**

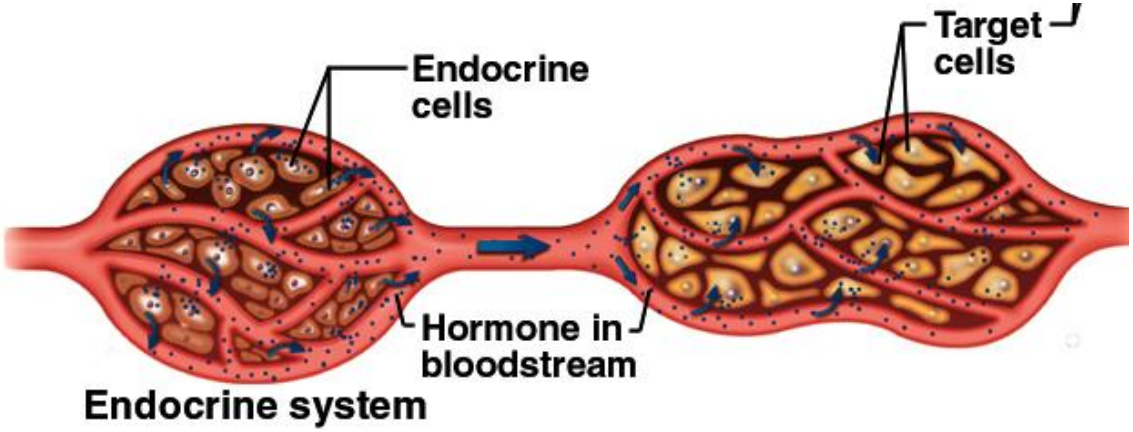
Endocrine System

- Each hormone acts on a certain kind of tissue called its **target tissue**



Components of Endocrine System

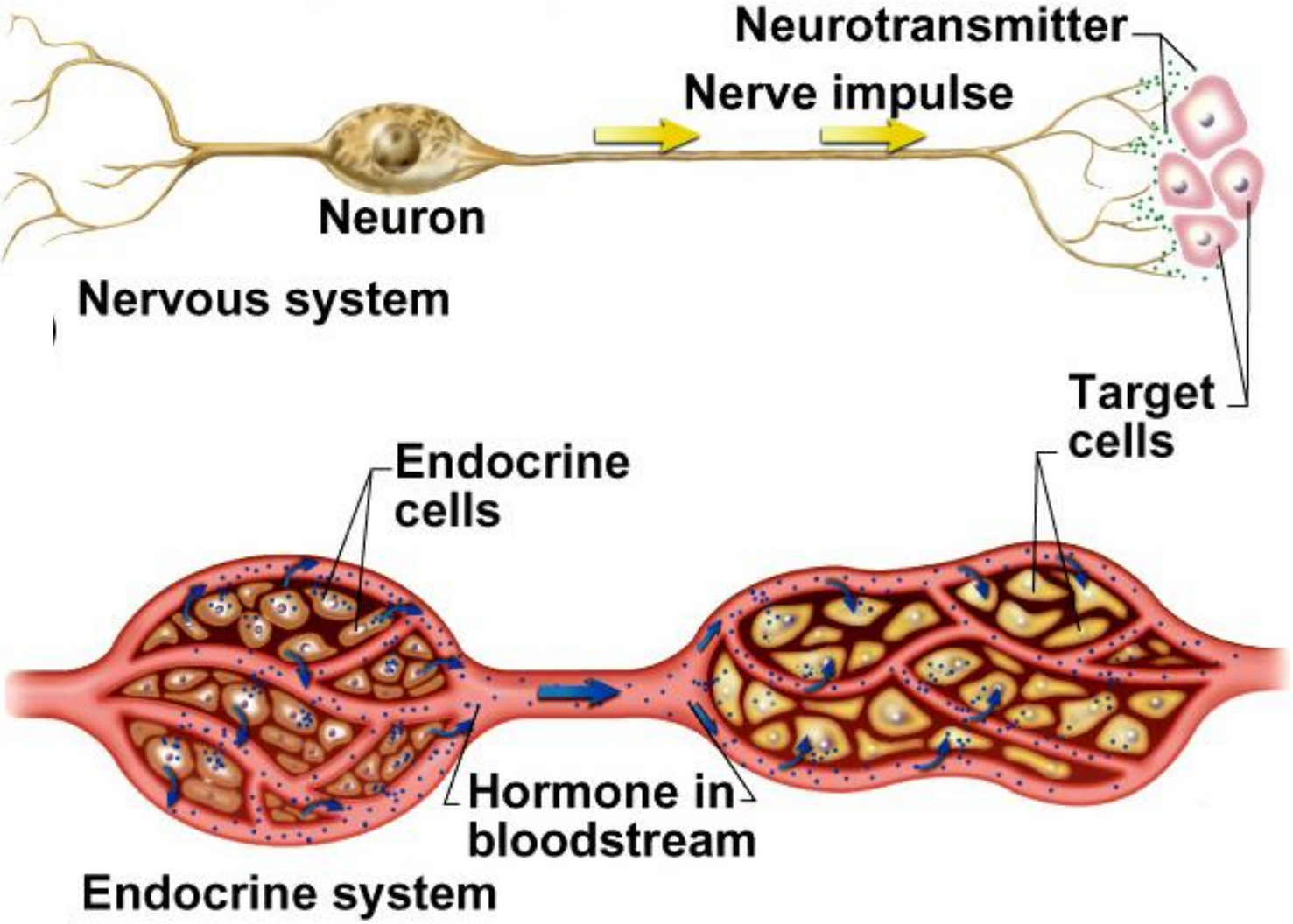
- Hormone
  - chemical messenger secreted into bloodstream, stimulates response in another tissue or organ
- Target cells
  - have receptors for hormone
- Endocrine glands
  - produce hormones



Differences in Nervous and Endocrine Systems

- **Means of communication**
  - nervous system has both electrical and chemical methods
  - endocrine system has only chemical methods
- **Speed of response**
  - nervous system reacts quickly (1 - 10 msec) and stops quickly
  - endocrine system reacts slowly (hormone release in seconds or days), effect may continue for weeks
- **Adaptation to long-term stimulation**
  - nervous system adapts quickly and response declines
  - endocrine system has more persistent responses
- **Area of effect**
  - nervous system effects are targeted and specific (one organ)
  - endocrine system may have general, widespread effects on many organs

Communication by the Nervous & Endocrine Systems

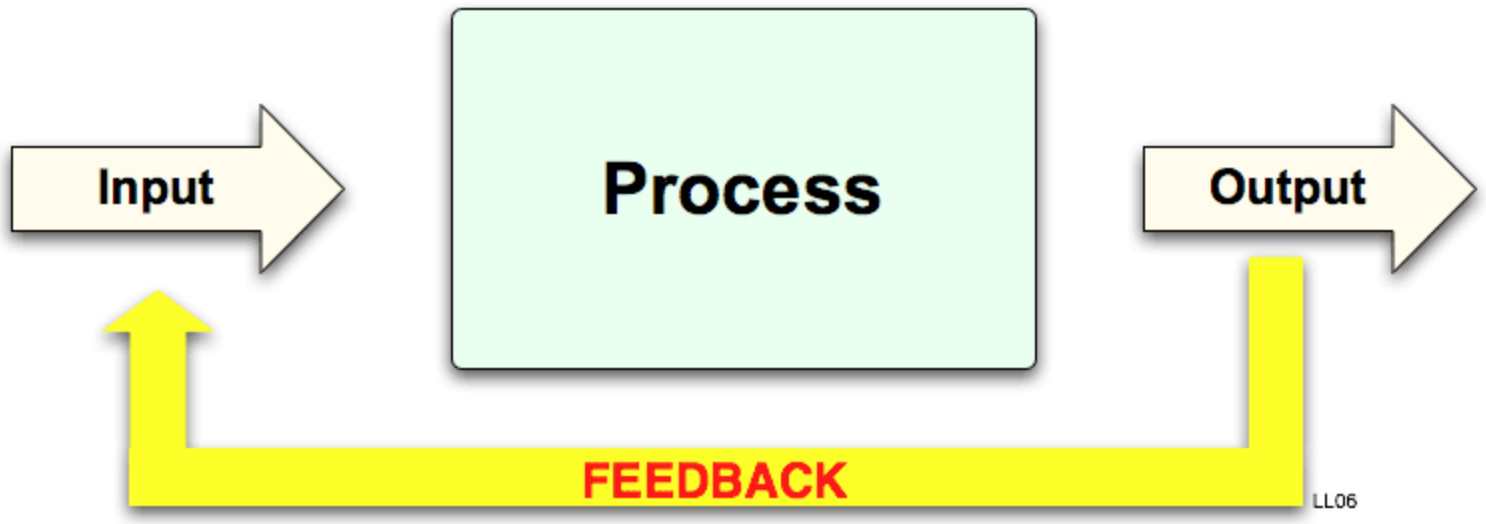


Endocrine System Control

- Regulated by feedback mechanisms

  Tow types of feedback mechanisms

  1. **positive** feedback
  2. **negative** feedback



Feedback Mechanisms

- **<u>Negative Feedback</u>** mechanisms:
  - Act like a thermostat in a home
  - As the temperature cools, the thermostat detects the change and triggers the stove to turn on and warm the house
  - Once the temperature reaches its thermostat setting, the stove turns off
    - Example: Body sugar increases after a meal, so the pancreas secretes **insulin**, which tells the body's cells to take in **glucose**. Once blood sugar levels reach normal, the pancreas stops making insulin.
    - Often used to maintain **homeostasis**

Negative Feedback

- **Homeostasis** is often maintained by two hormones who have antagonistic effects
  - Each hormone does the **opposite** of the other.
    - For example, if the blood pressure drops too low, the pituitary releases anti diuretic hormone (ADH), which causes the kidneys to reabsorb more water. If it the blood pressure increases too much, then the heart will release atrial natriuretic hormone (ANH), which will cause the kidneys to reabsorb less water.

Positive Feedback Mechanisms

- Positive Feedback mechanisms control events that can be out of control and do not require continuous adjustment
- Rarely used to maintain homeostasis
- Example of positive feedback found in childbirth
  - Oxytocin stimulates and enhances labor contractions
  - As labor continues, more oxytocin is produced
  - Intensifies contractions until the baby is outside birth canal
  - Oxytocin production stops and labor contractions stop

Hormones

- Hormones = chemical substances synthesized from amino acids & cholesterol that act on body tissues & organs and affect cell activity.

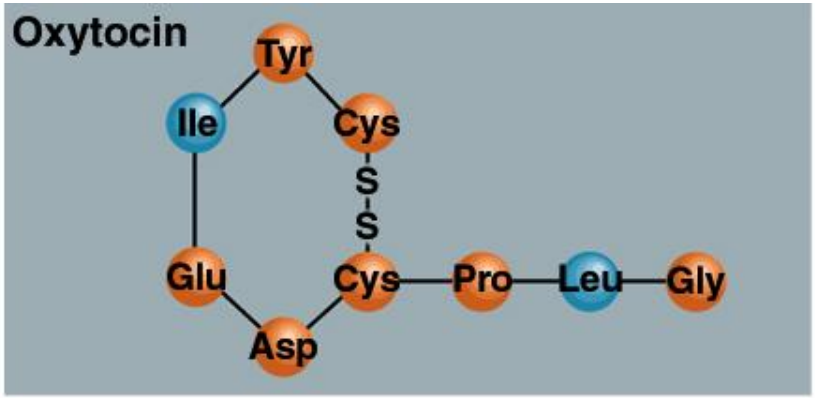
2 categories:

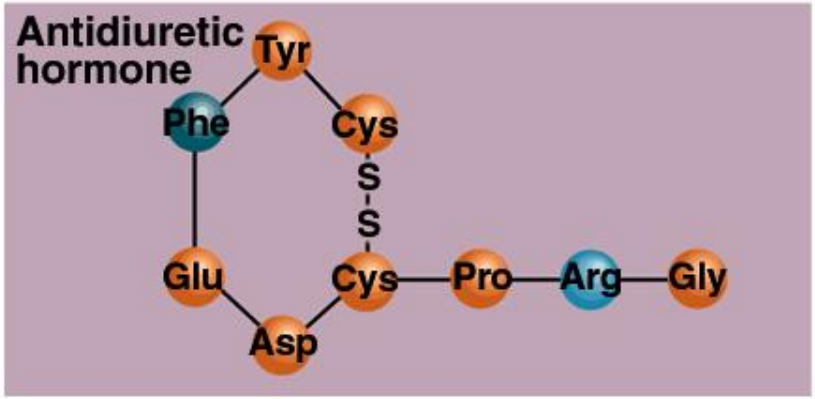
- Proteins or Monoamines

- Steroids – hormones from the adrenal glands & gonads are steroids.

Hormone Chemistry

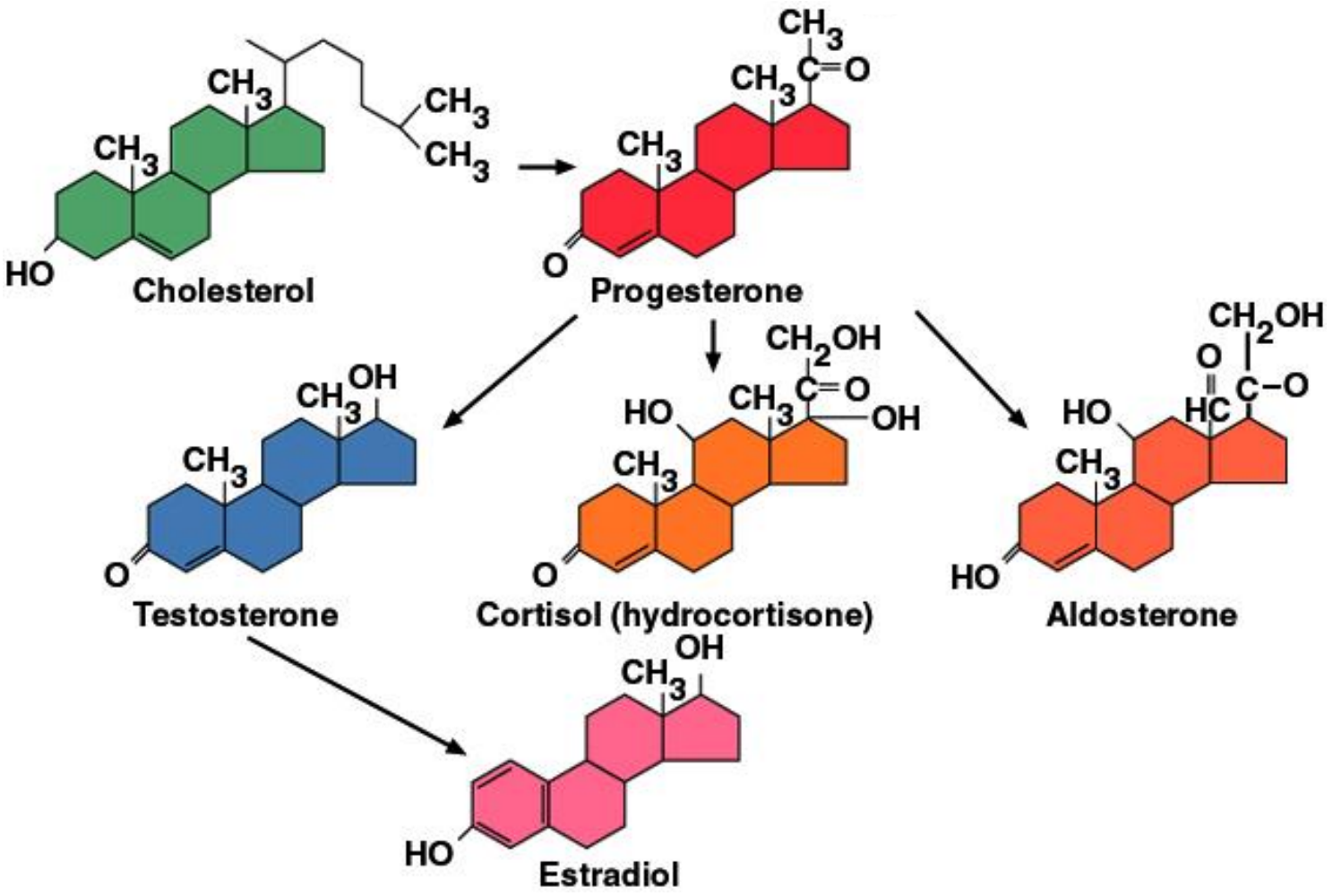
- Steroids
  - derived from cholesterol
    - sex steroids, corticosteroids
- Peptides and glycoproteins
  - Oxytocin, antidiuretic hormone; all releasing and inhibiting hormones of hypothalamus; most of anterior pituitary hormones





- Monoamines (biogenic amines)
  - derived from amino acids
    - catecholamines (norepinephrine, epinephrine, dopamine) and thyroid hormones

Hormone Synthesis: Steroid Hormones



- Synthesized from cholesterol – differs in functional groups attached to 4-ringed steroid backbone

Hormone Synthesis: Monoamines

- All are synthesized from tyrosine
  - except melatonin which is synthesized from tryptophan
- Thyroid hormone is unusual
  - composed of 2 tyrosine molecules
  - requires a mineral, iodine

Hormone Transport

- Monoamines and peptides are hydrophilic so mix easily with blood plasma
- Steroids and thyroid hormone are hydrophobic and must bind to transport proteins for transport
  - **bound hormone** - hormone attached to transport protein,
  - only **unbound hormone** can leave capillary to reach target cell (half-life a few minutes)
- Transport proteins in blood plasma
  - albumin, thyretin and TGB (thyroxine binding globulin) bind to thyroid hormone
  - steroid hormones bind to globulins
  - aldosterone has no transport protein, 20 min. half-life

What is a hormone receptor?

Hormone Receptors are cellular proteins that bind with high affinity to hormones & are altered in shape & function by binding; they exist in limited numbers.

Binding to hormone is non covalent & reversible.

Hormone Receptors

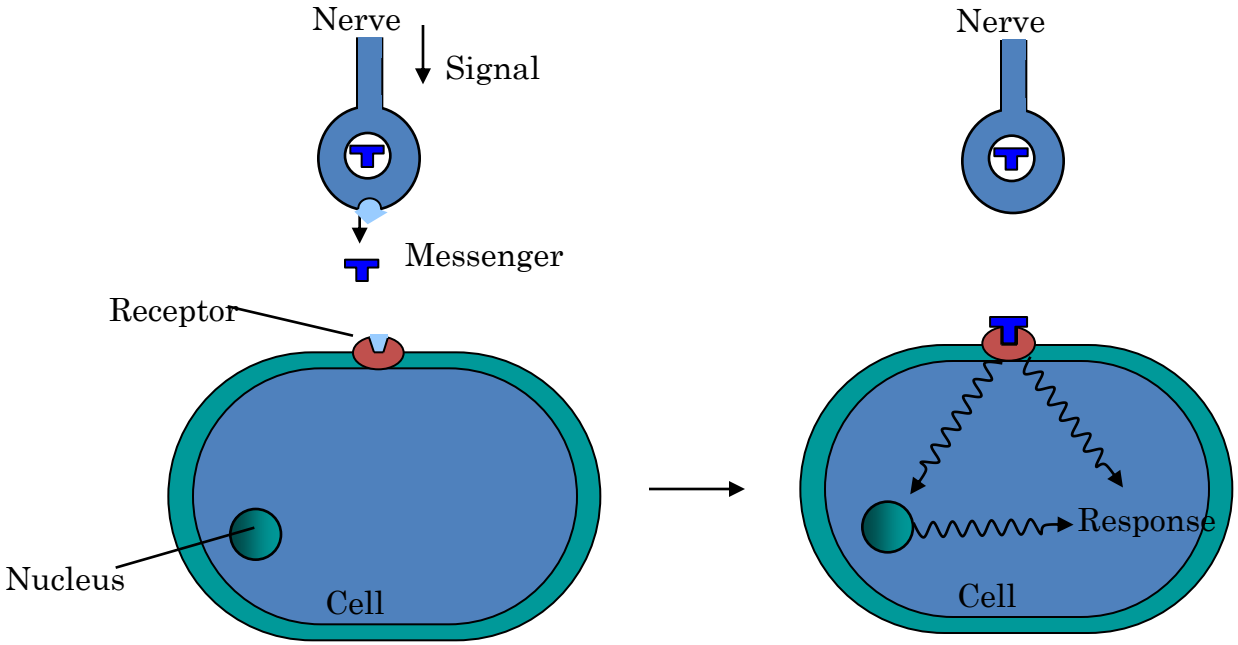
- Located on plasma membrane, mitochondria and other organelles, or in nucleus
- Usually thousands for given hormone
  - turn metabolic pathways on or off when hormone binds

Receptors Structure and Function

The role of the receptor

- Globular proteins
- Located mostly in the cell membrane
- Receive messages from chemical messengers coming from other cells
- Transmit a message into the cell leading to a cellular effect
- Different receptors specific for different chemical messengers
- Each cell has a range of receptors in the cell membrane making it responsive to different chemical messengers

The Role of the receptor



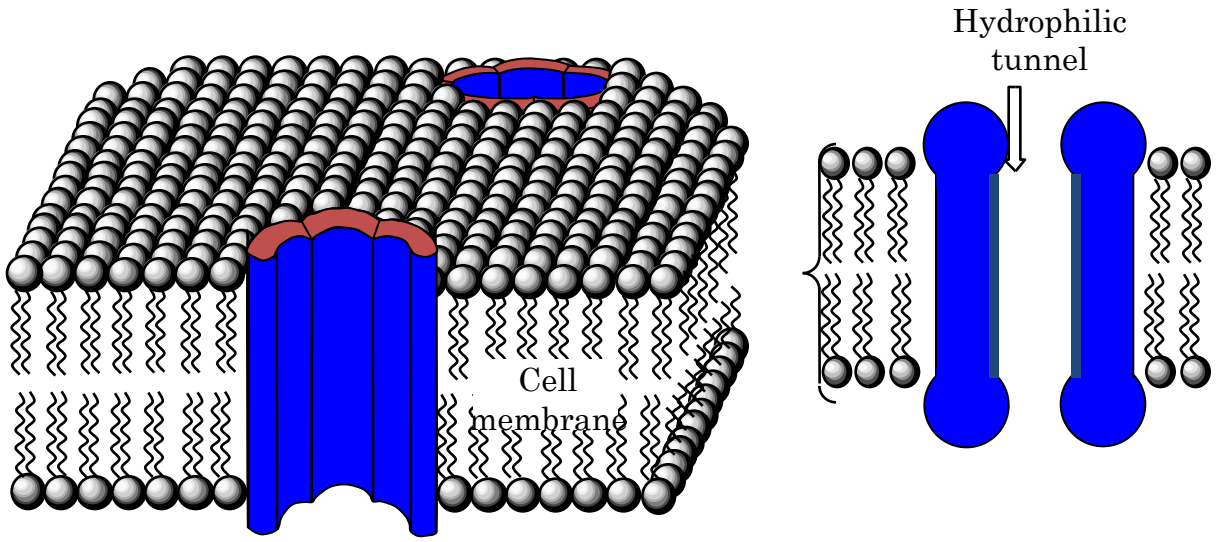
Main Types of Receptors

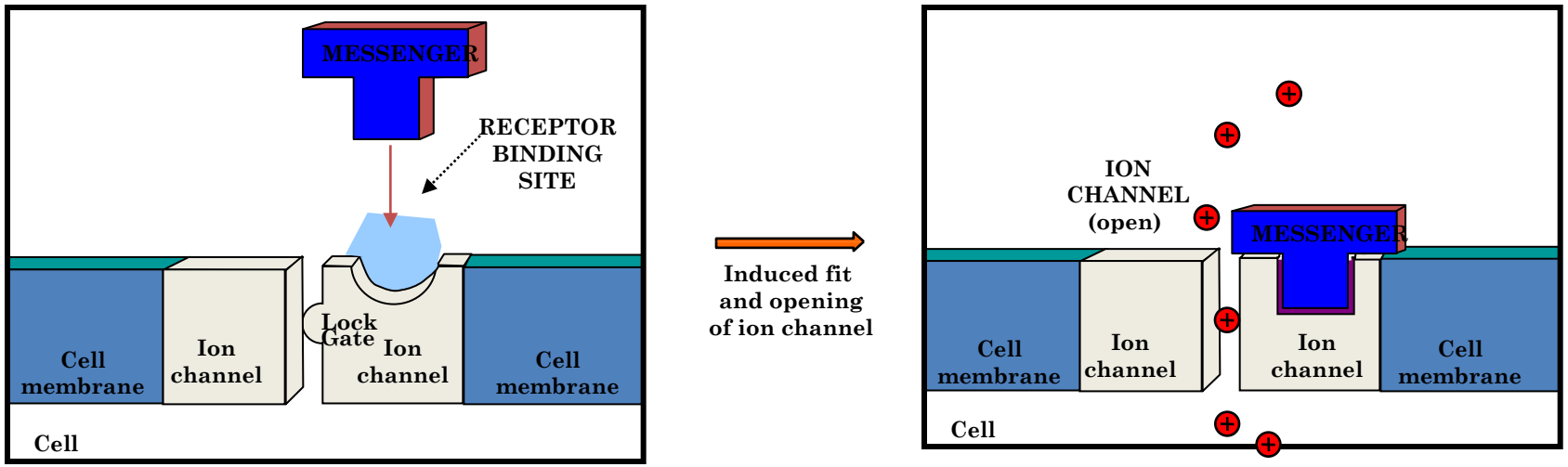
- ION CHANNEL RECEPTORS
- G-PROTEIN-COUPLED RECEPTORS
- KINASE-LINKED RECEPTORS
- INTRACELLULAR RECEPTORS

Ion Channel Receptors

- Receptor protein is part of an ion channel protein complex
- Receptor binds a messenger leading to an induced fit
- Ion channel is opened or closed
- Ion channels are specific for specific ions (Na^+, Ca^{2+}, Cl^-, K^+)
- Ions flow across cell membrane
- Polarises or depolarises membranes
- Activates or deactivates enzyme catalysed reactions within cell

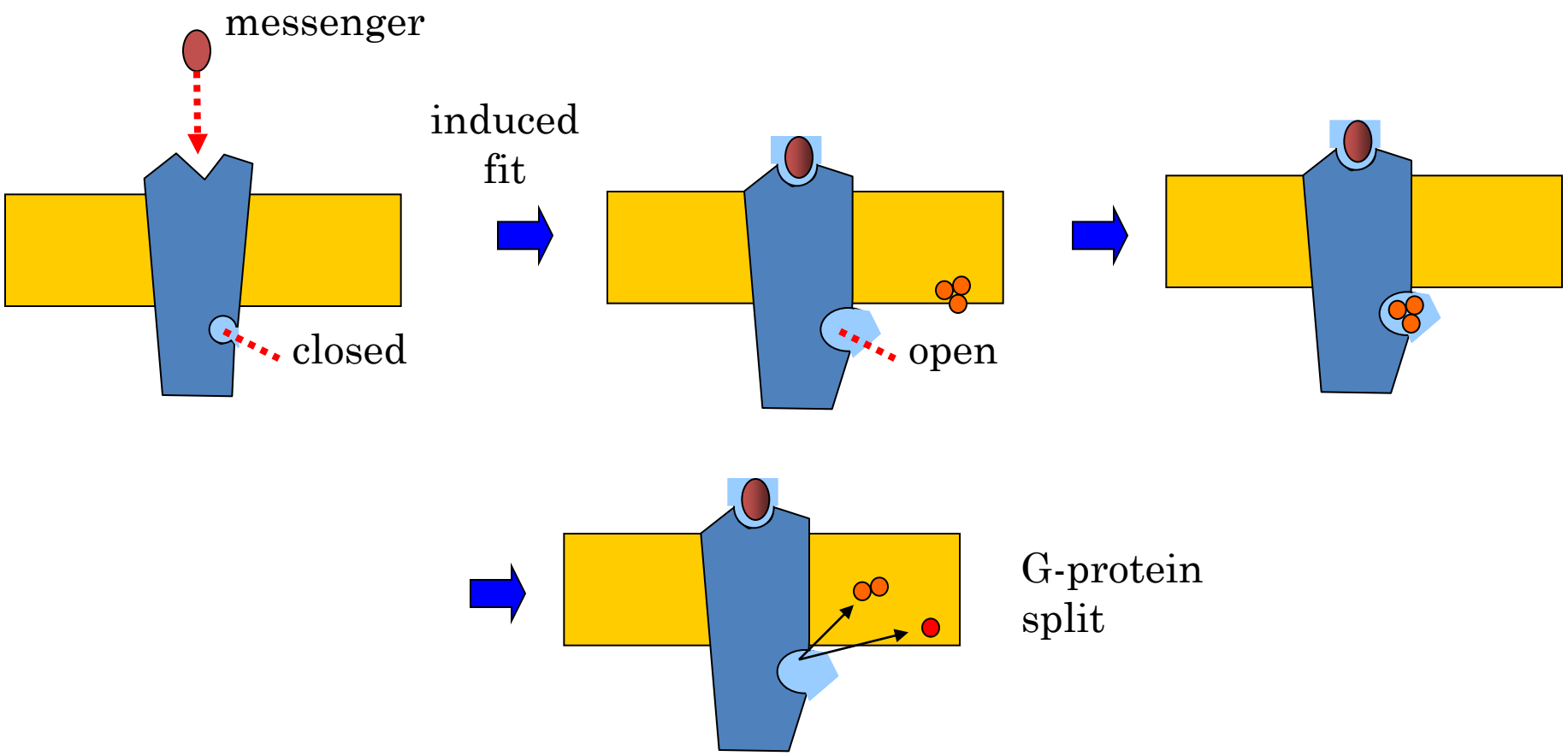
Ion Channel Receptors





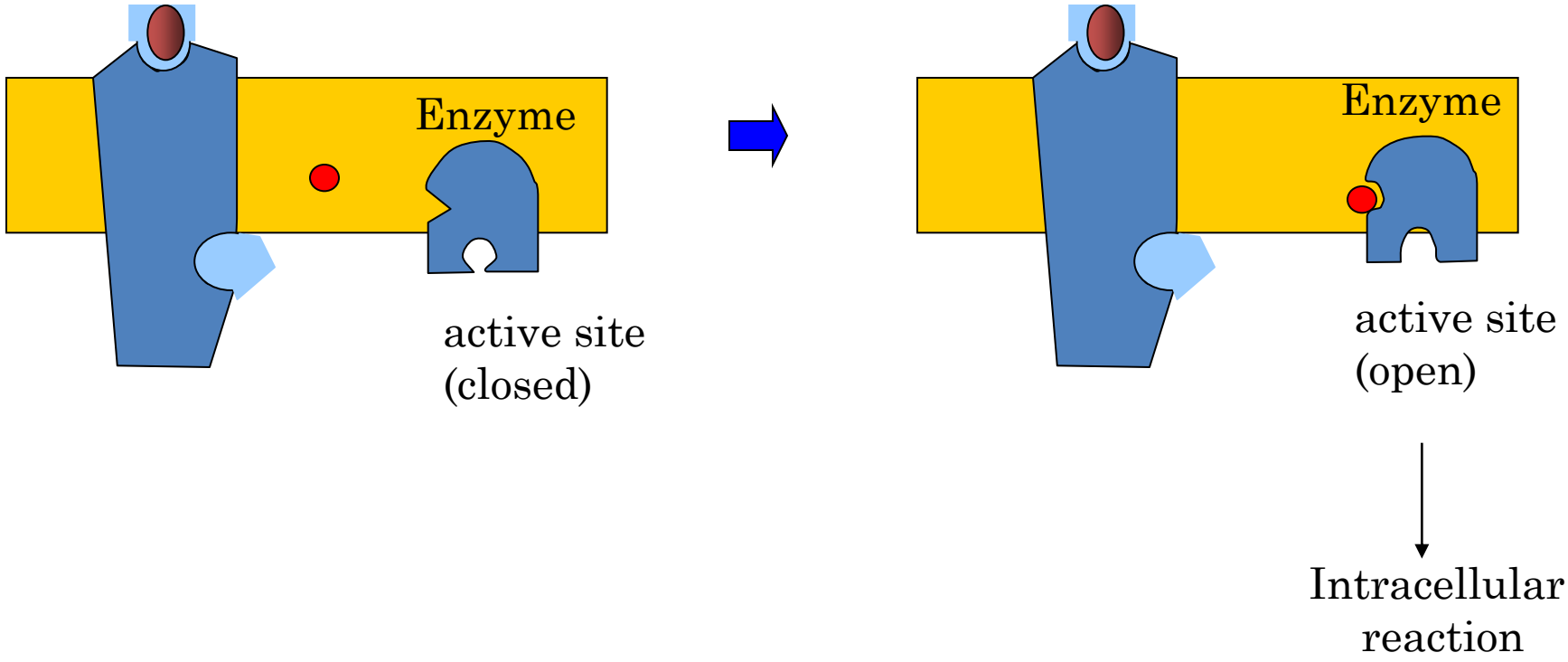
G-PROTEIN-COUPLED RECEPTORS

- Receptor binds a messenger leading to an induced fit
- Opens a binding site for a signal protein (G-protein)
- G-protein binds, is destabilised then split



G-PROTEIN-COUPLED RECEPTORS

- **G-protein subunit activates membrane bound enzyme**
- **Binds to allosteric binding site**
- **Induced fit results in opening of active site**
- **Intracellular reaction catalysed**

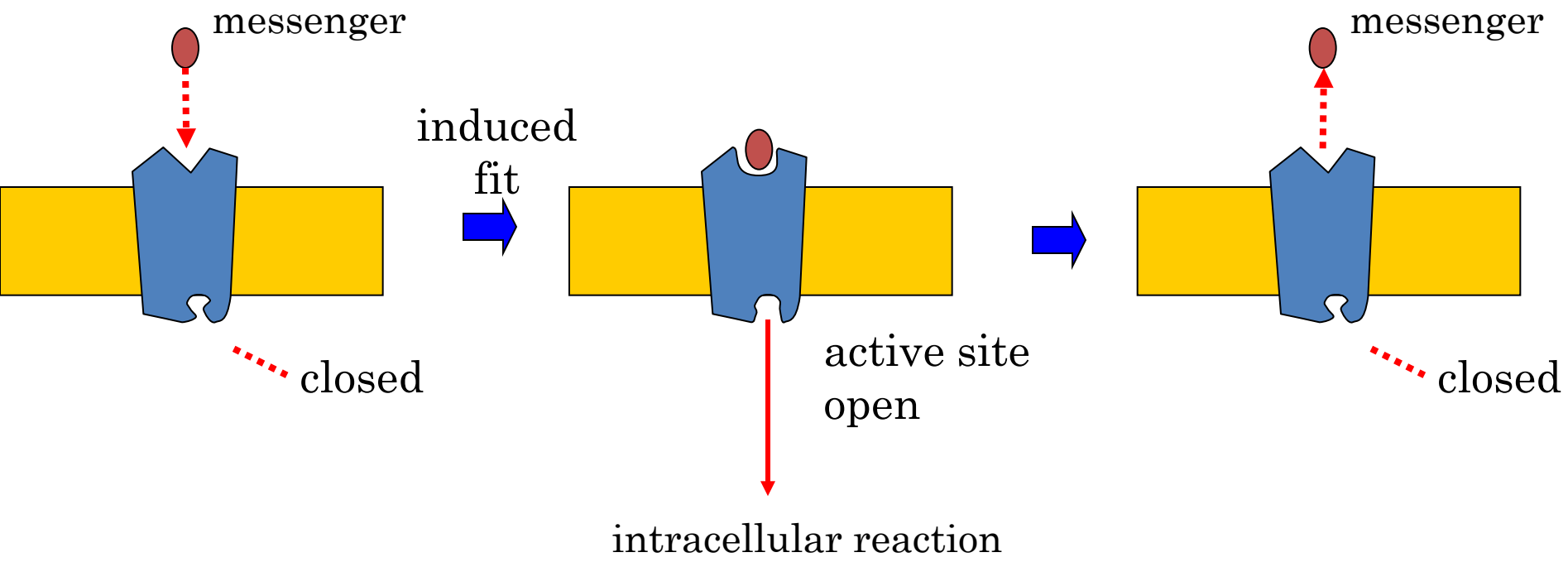


Tyrosine kinase - linked receptors

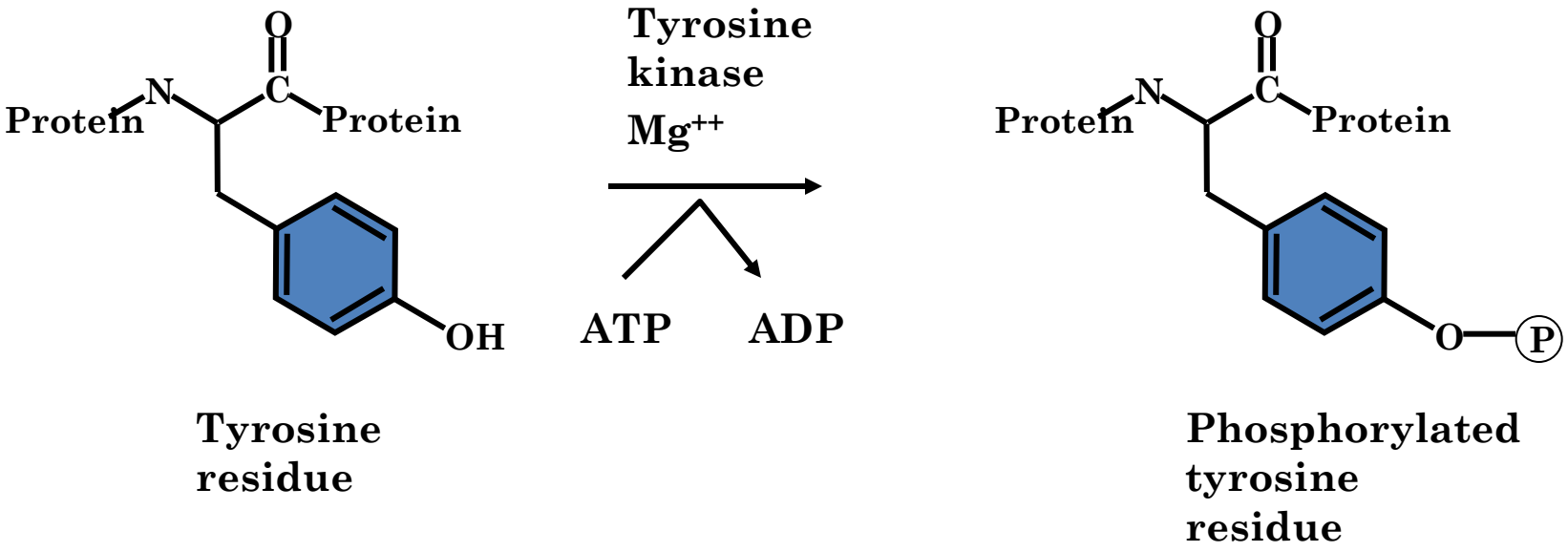
- Bifunctional receptor / enzyme
- Activated by hormones
- Overexpression can result in cancer

Tyrosine kinase-linked receptors

- Protein serves dual role - receptor plus enzyme
- Receptor binds messenger leading to an induced fit
- Protein changes shape and opens active site
- Reaction catalysed within cell



Reaction catalysed by tyrosine kinase

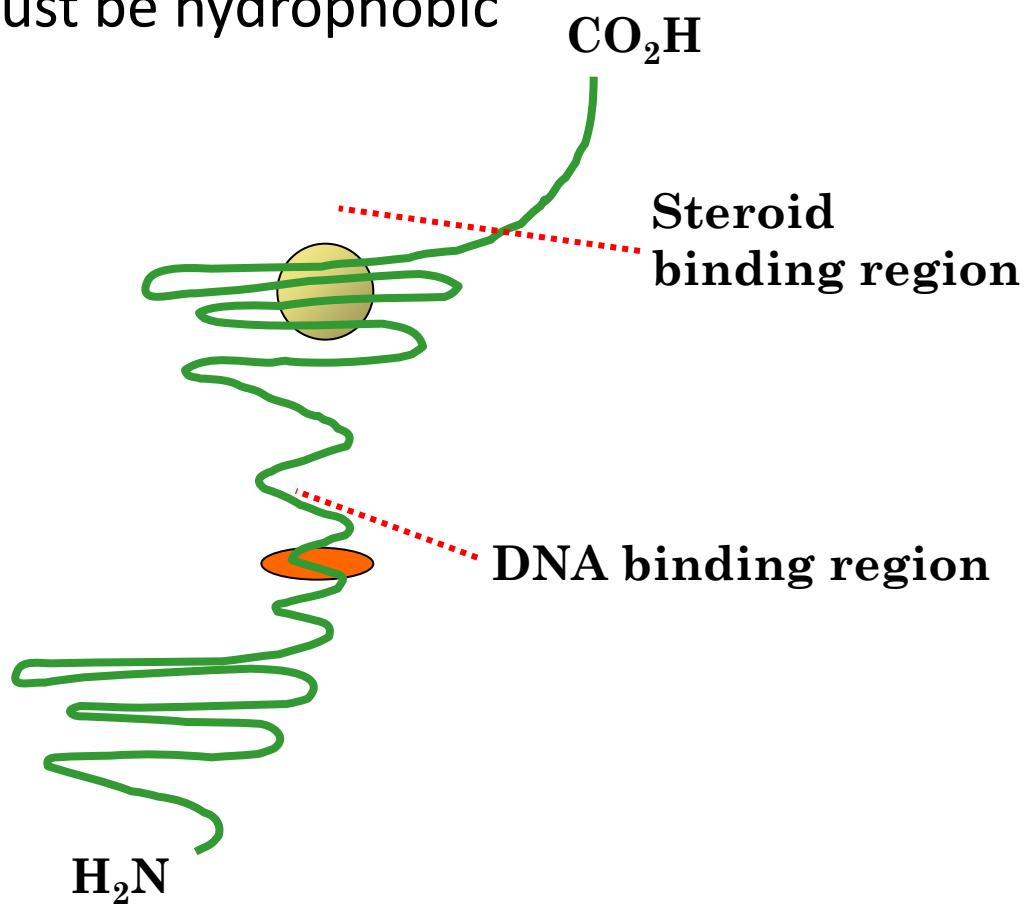


Tyrosine residue

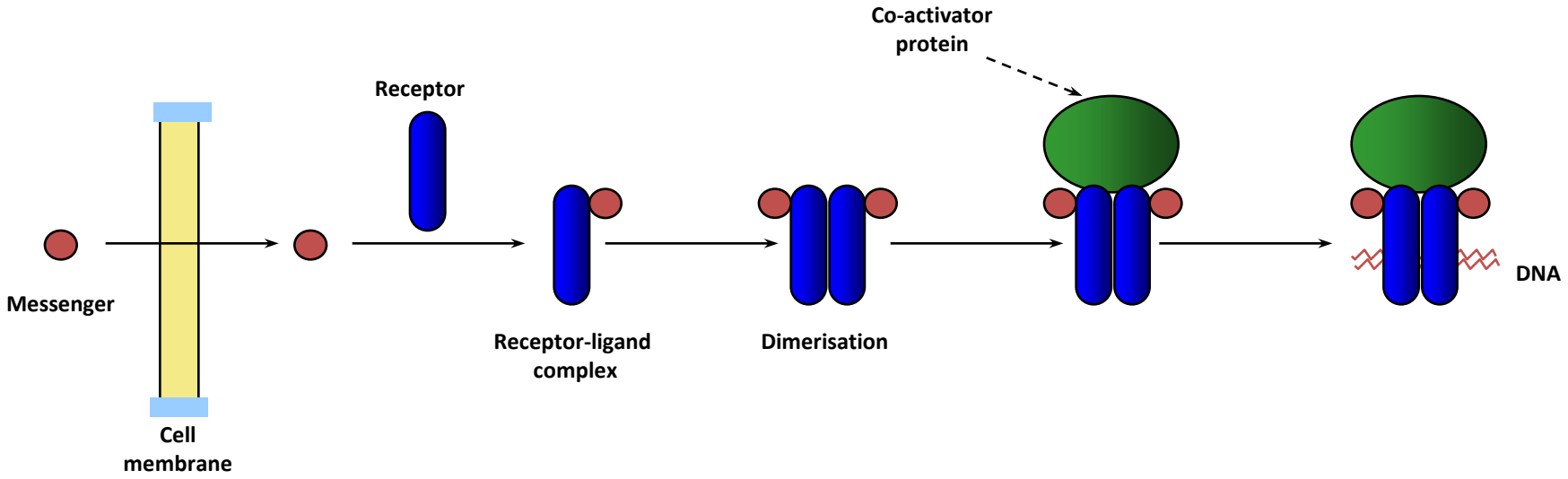
Phosphorylated tyrosine residue

Intracellular receptors

- Chemical messengers must cross cell membrane
- Chemical messengers must be hydrophobic
- Example-steroids and steroid receptors



Intracellular receptor Mechanism

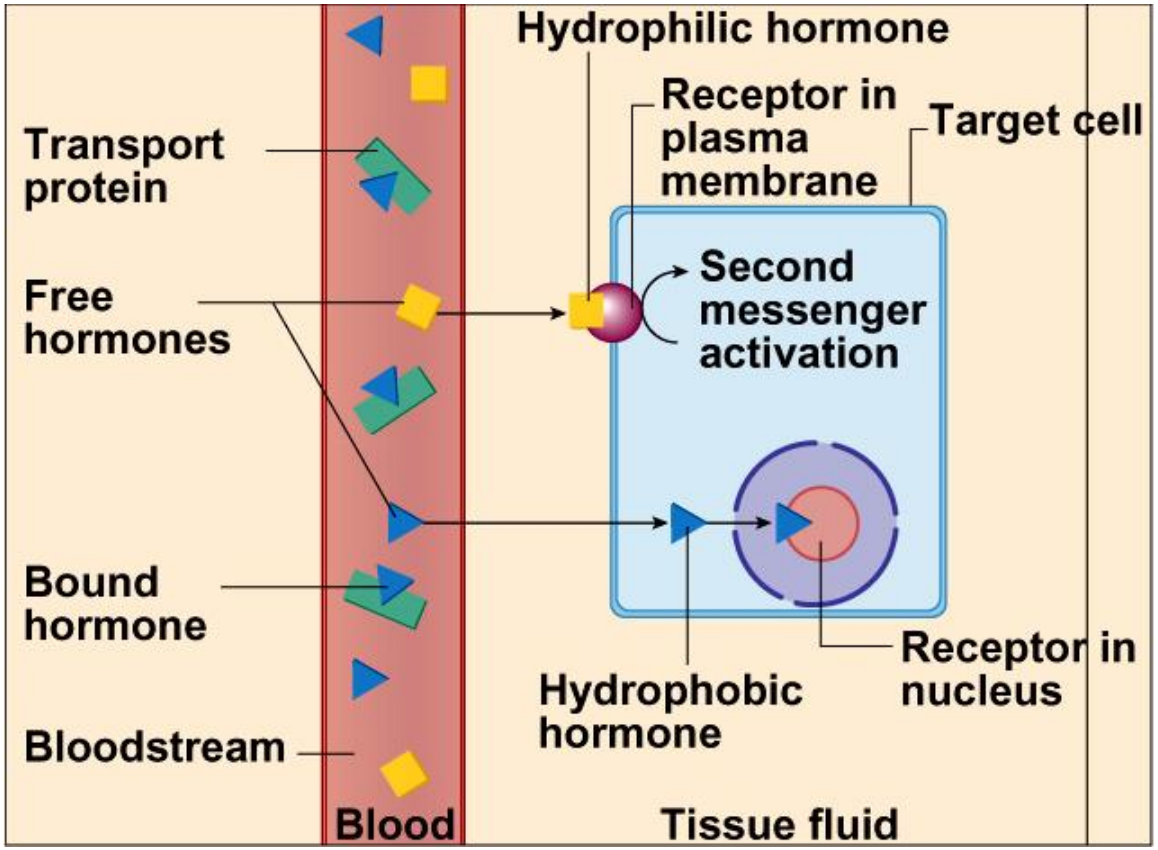


1. Messenger crosses membrane
2. Binds to receptor
3. Receptor dimerisation
4. Binds co-activator protein
5. Complex binds to DNA
6. Transcription switched on or off
7. Protein synthesis activated or inhibited

What are effectors?

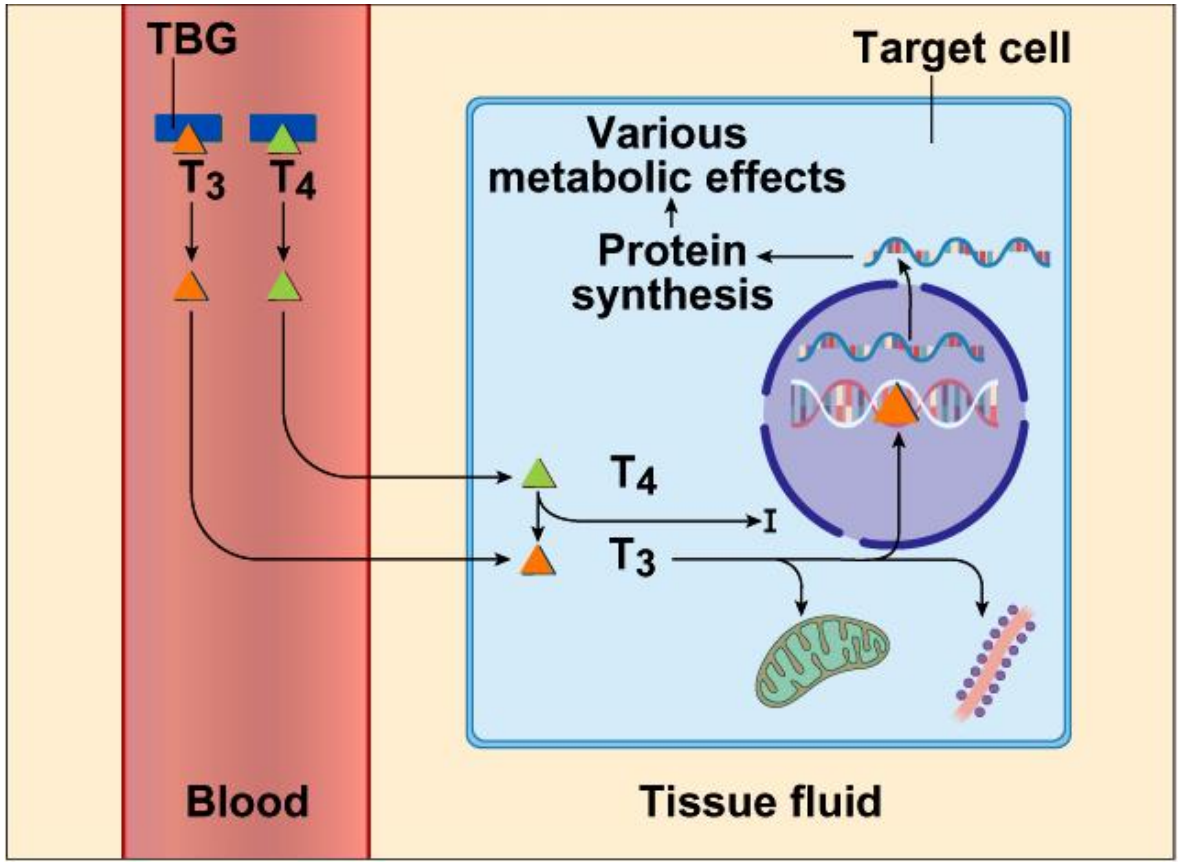
- Effectors are the enzymes & other proteins that convert the hormonal signal into biochemical changes that generate the cellular response to hormone binding.

Hormone Mode of Action



- Hydrophobic hormones (steroids and thyroid hormone) penetrate plasma membrane – enter nucleus
- Hydrophilic hormones (monoamines and peptides) can not pass through membrane so must bind to cell-surface receptors

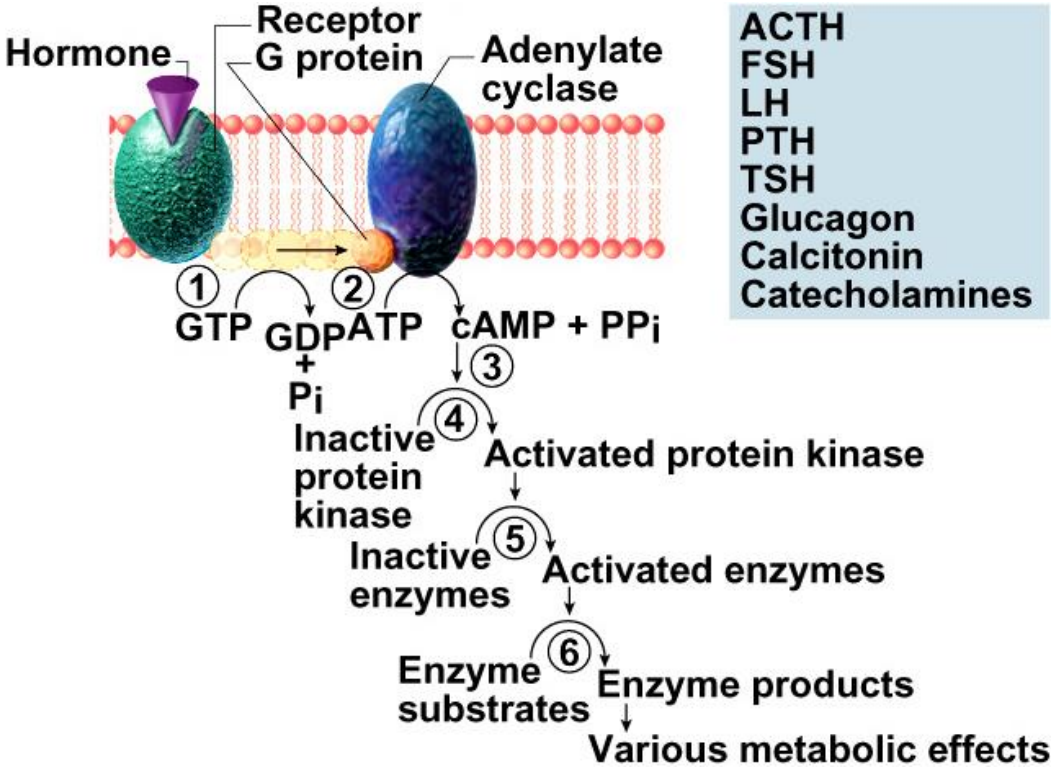
Thyroid Hormone Effects



- TH binds to receptors on mitochondria (↑rate of aerobic respiration), on ribosomes and chromatin (↑ protein synthesis)

Hydrophilic Hormones: Mode of Action

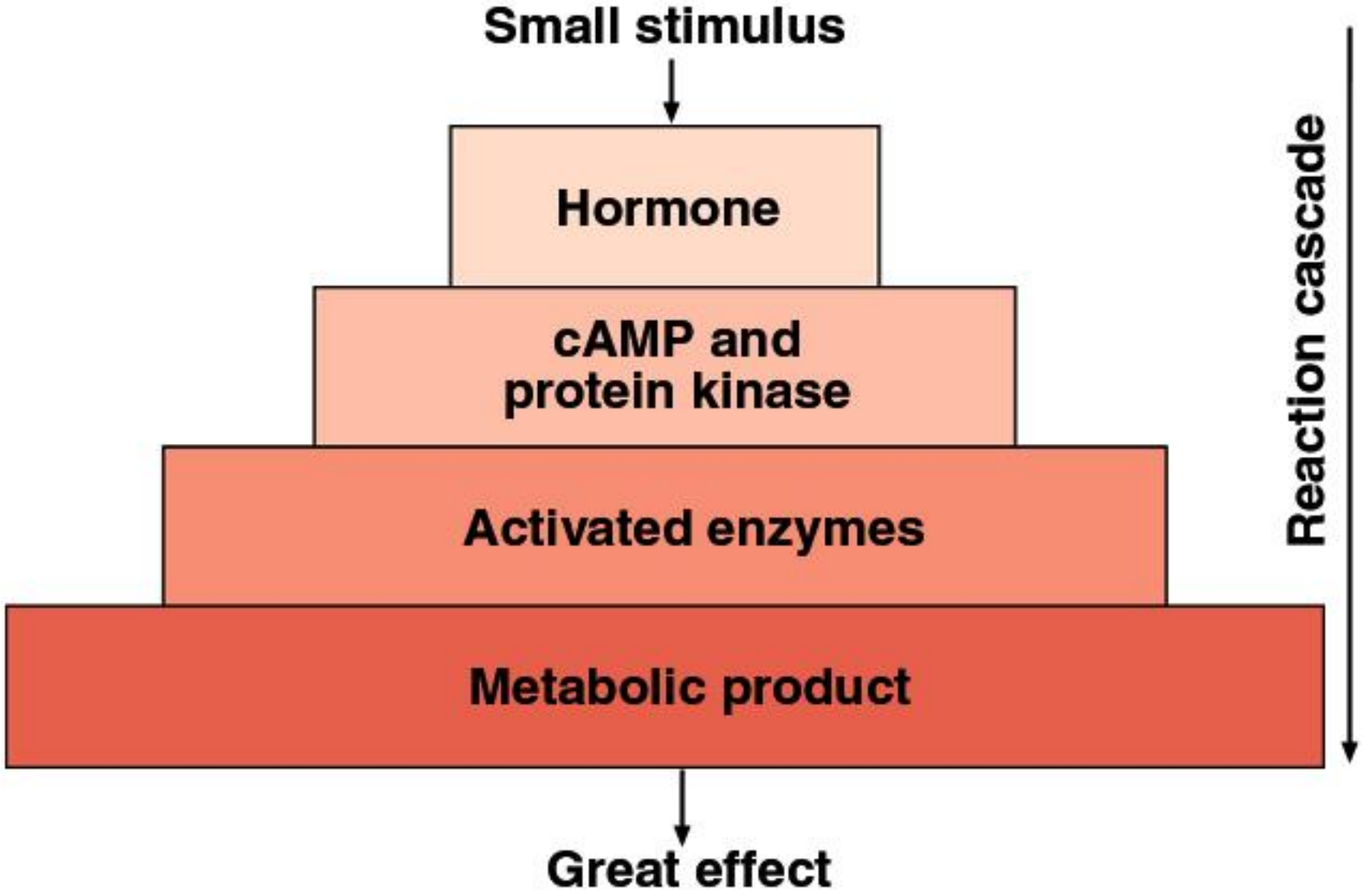
cAMP as Second Messenger



1) Hormone binding activates G protein
2) Activates adenylate cyclase
3) Produces cAMP
4) Activates kinases
5) Activates enzymes
6) Metabolic reactions: synthesis, secretion, change membrane potentials

Peptides and catecholamines bind to receptors in cell membrane

Enzyme Amplification



Hormone Clearance

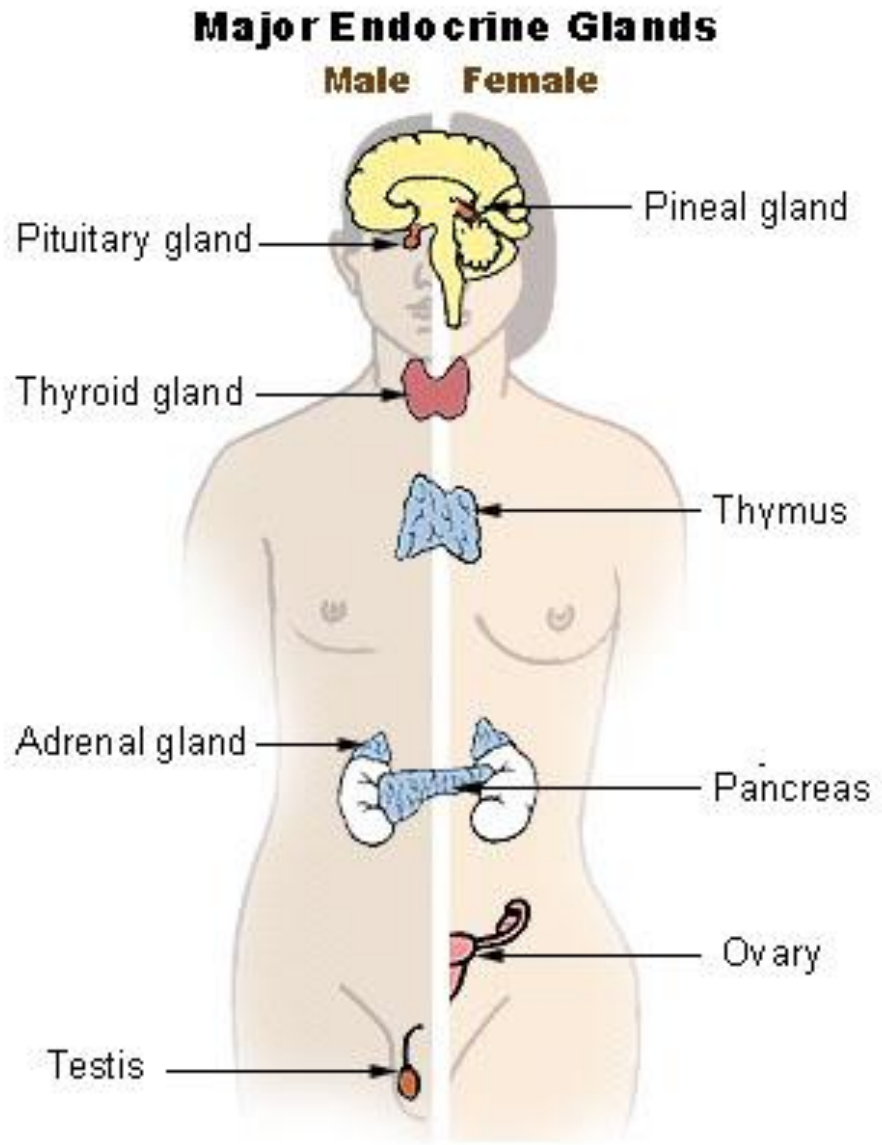
- Hormone signals must be turned off
- Take up and degraded by liver and kidney
- Excreted in bile or urine

Hormone Interactions

- Most cells sensitive to more than one hormone and exhibit interactive effects
- Synergistic effects
- Permissive effects
  - one hormone enhances response to a second hormone
- Antagonistic effects

Human Endocrine Glands

- **Pituitary**
- **Thyroid**
- Parathyroid
- **Adrenal**
- Pancreas (Islets of Langerhans)
- Testes and Ovaries



Pineal Gland

- Produces serotonin by day,
- converts it to melatonin at night
  - depression, sleepiness

Pineal gland

Thymus

- Secretes hormones that regulate development and later activation of T-lymphocytes
  - thymopoietin and thymosins