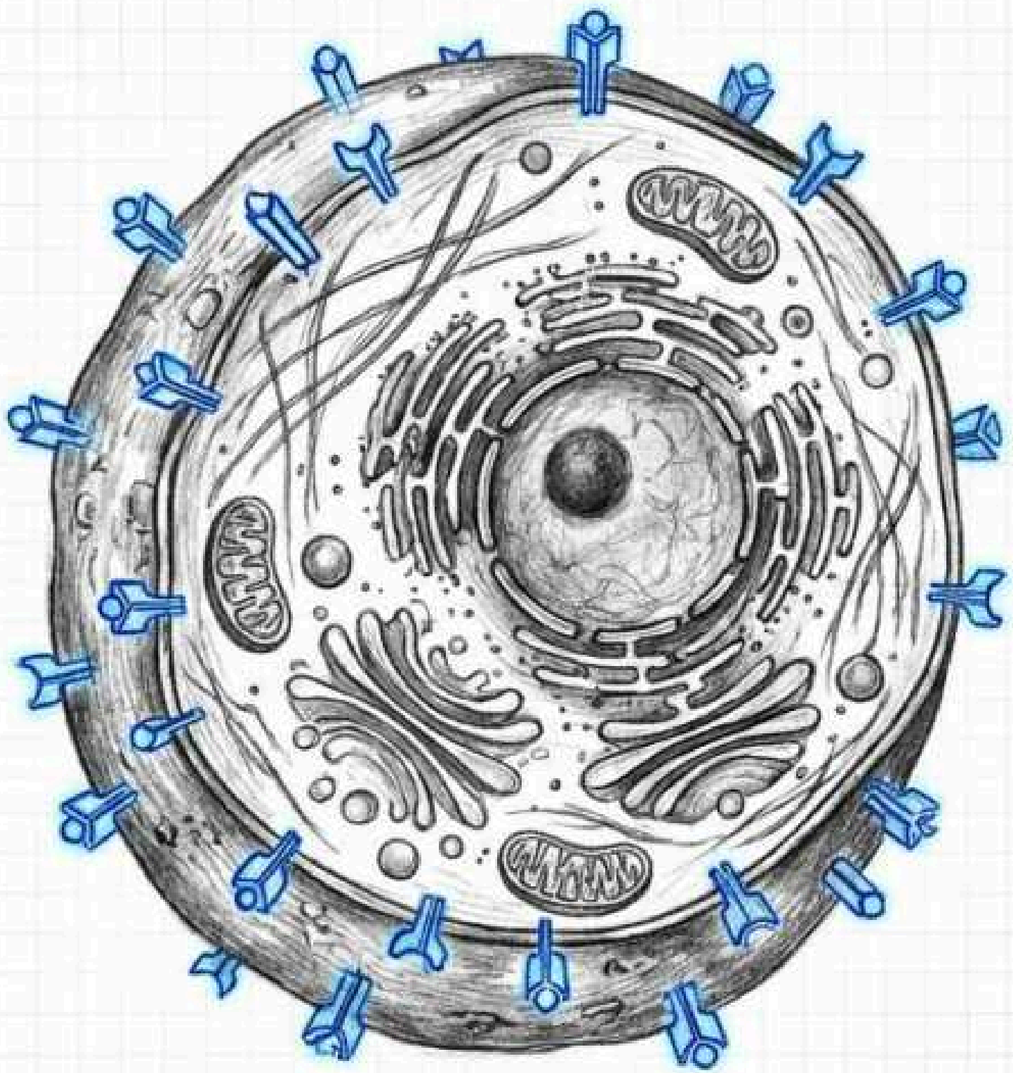
¶ 3.1

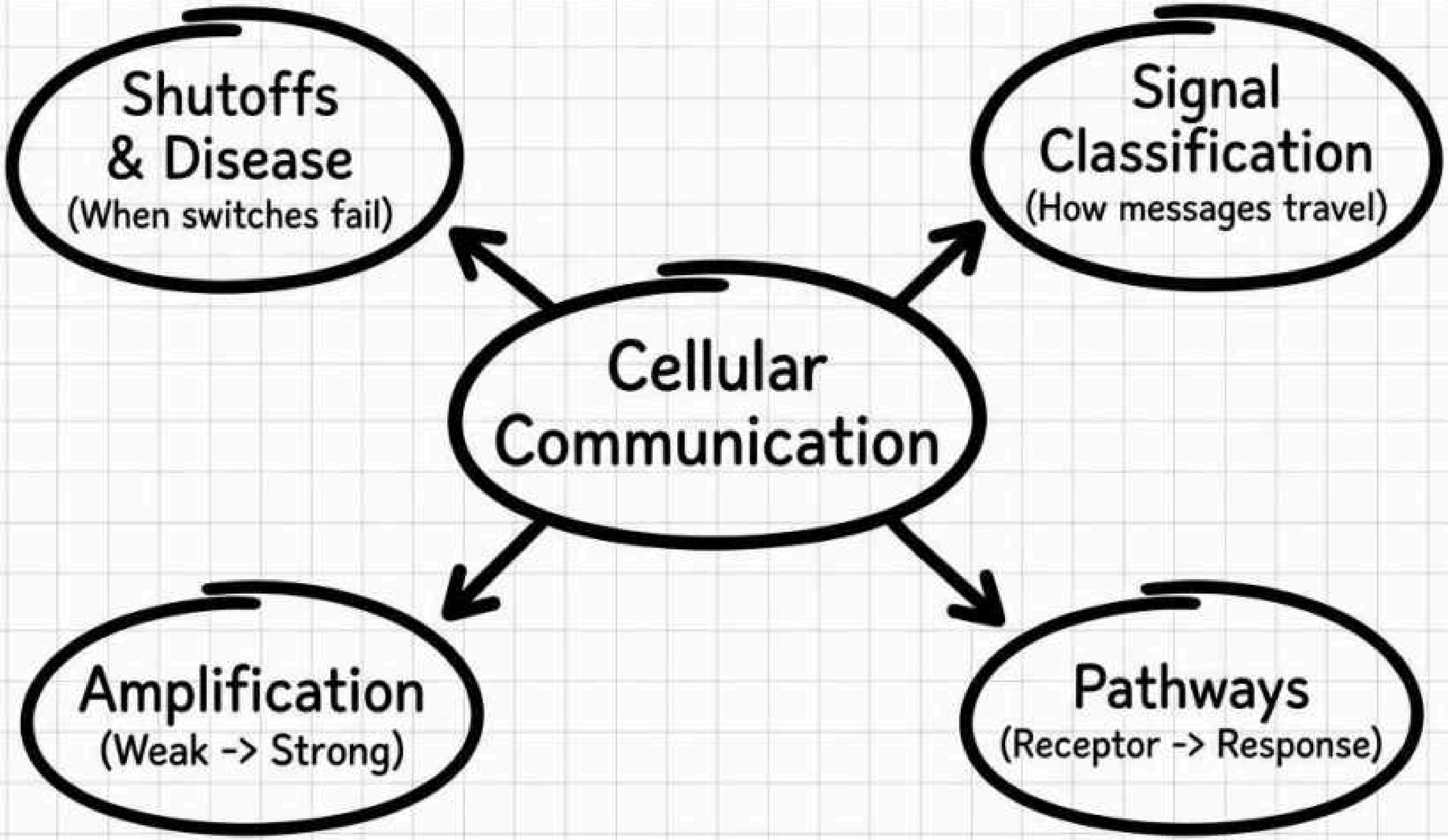


BIO 120 B: Lecture 3
Cell Signaling

Welcome to Lecture 3.

The Anatomy of a Message

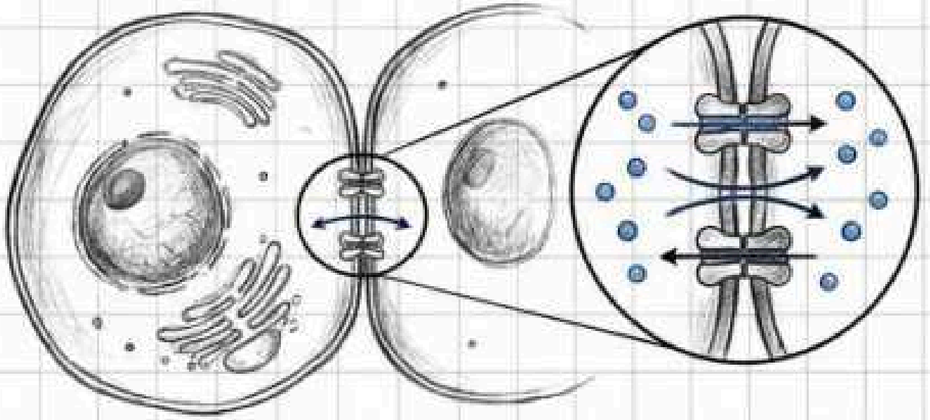
¶ 3.2



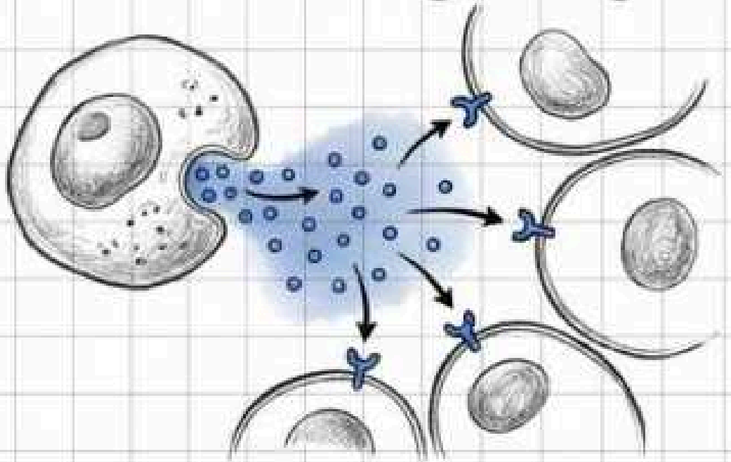
Four Modes of Signaling

¶ 3.3

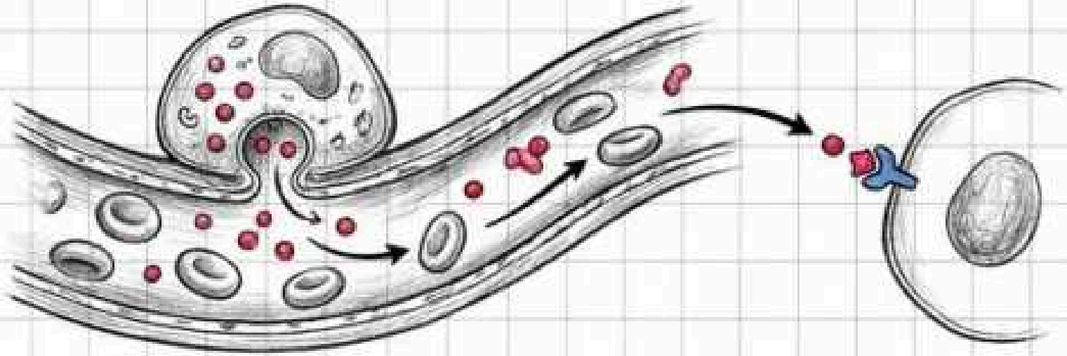
Direct Contact



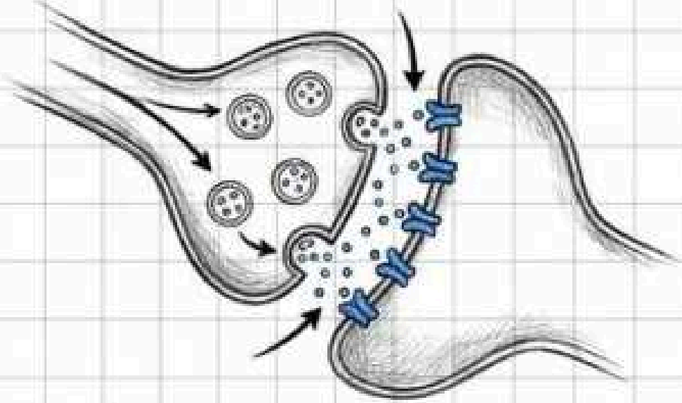
Paracrine Signaling



Endocrine Signaling



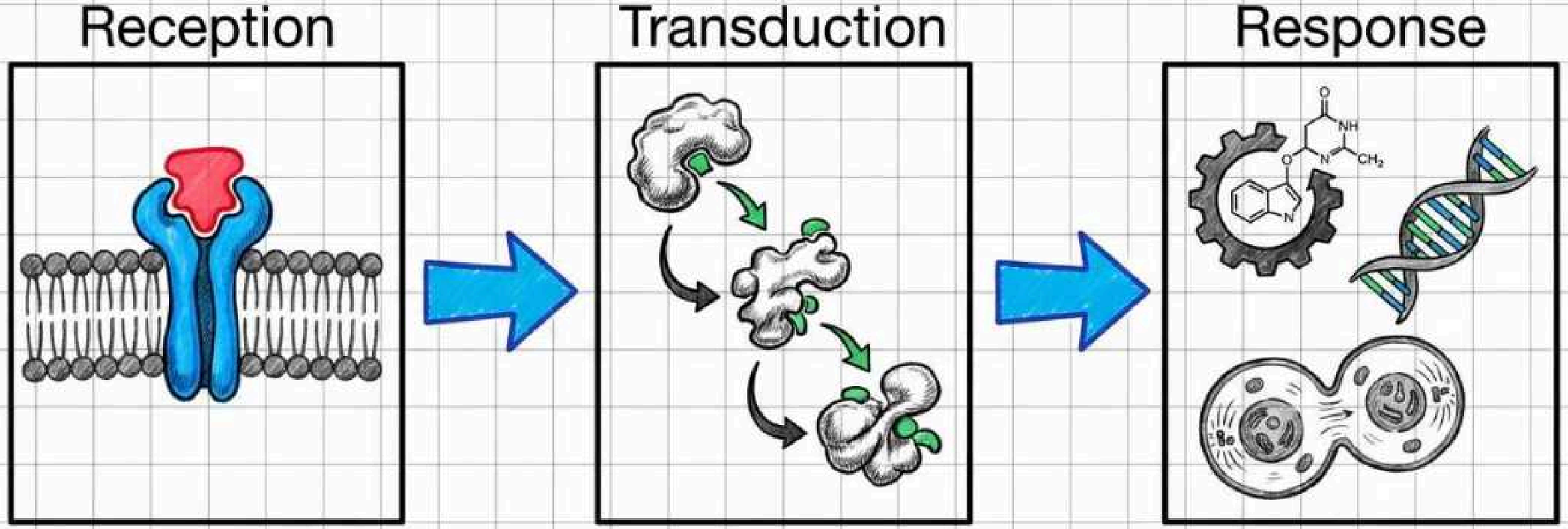
Synaptic Signaling



The chemistry is similar; the distance differs.

¶ 3.4

The Three Stages of a Signal

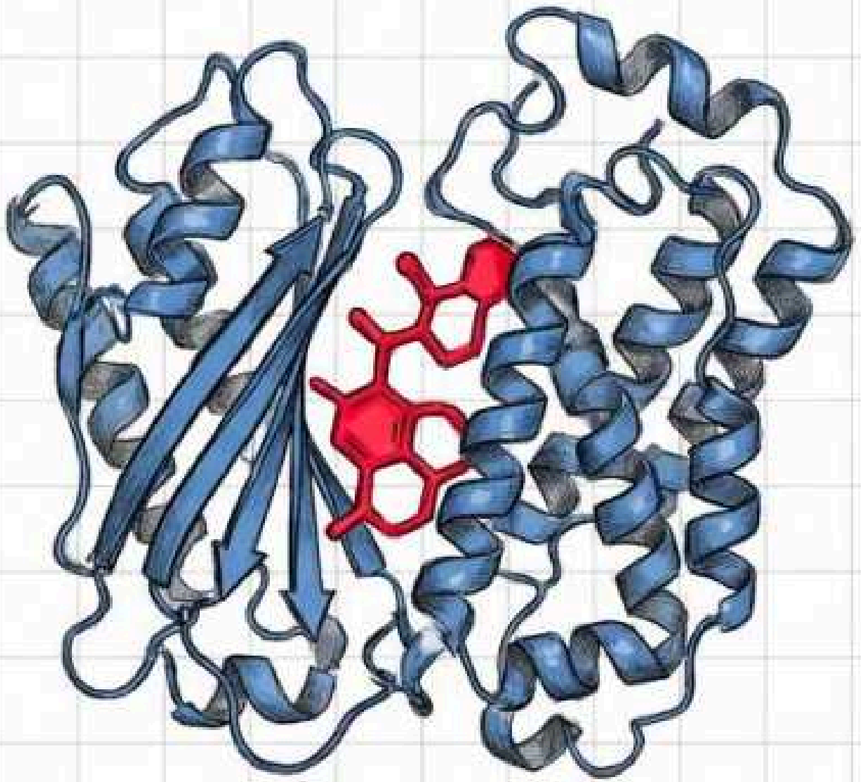


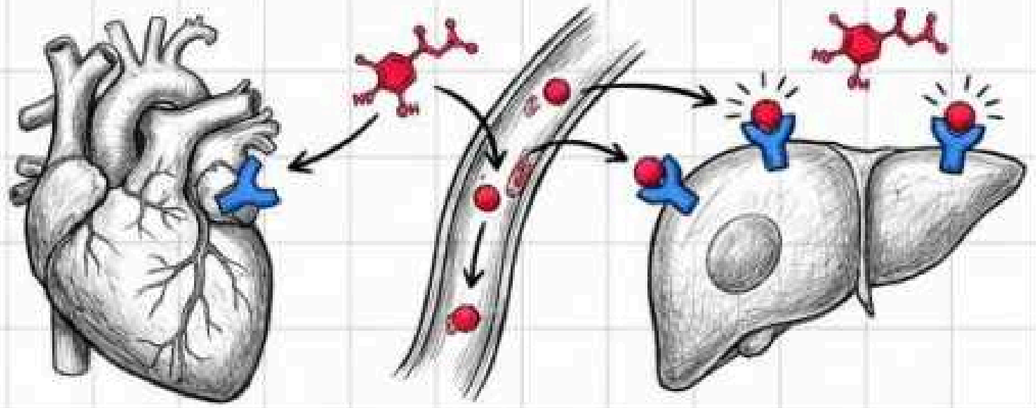
Crucial Rule: Every single stage can be regulated.

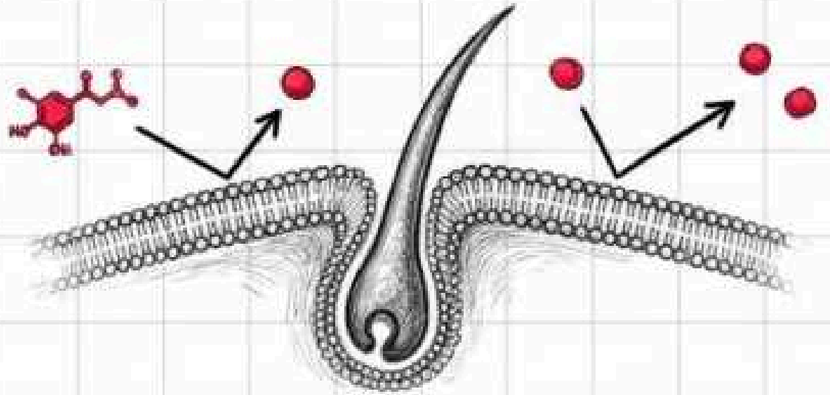
¶ 3.5

Receptor Specificity

Ligands fit receptors like a key in a lock.



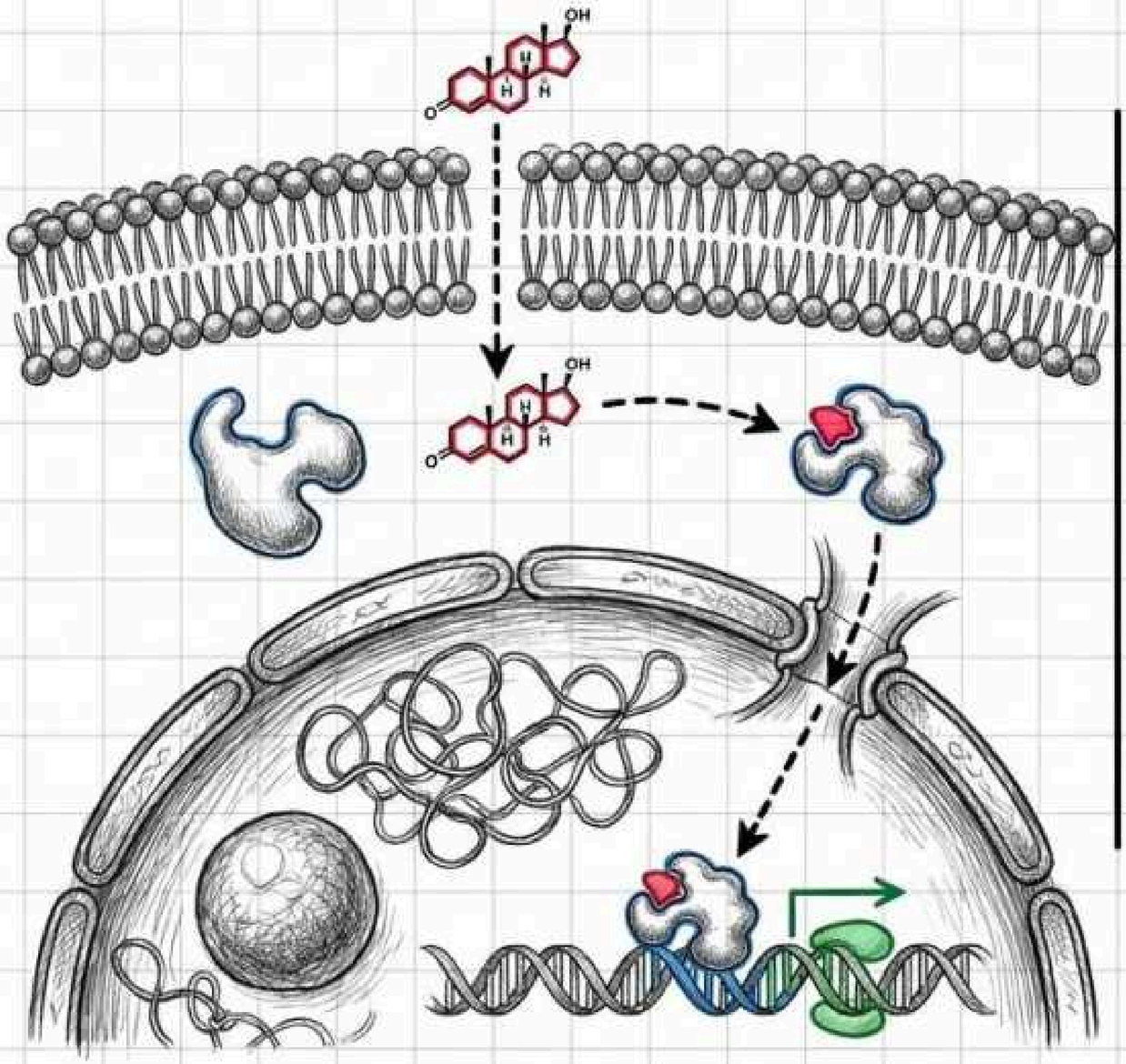




The hormone reaches everywhere, but only cells with matching receptors listen. (e.g., Adrenaline affects heart & liver, but not hair cells).

Intracellular Receptors

¶ 3.6



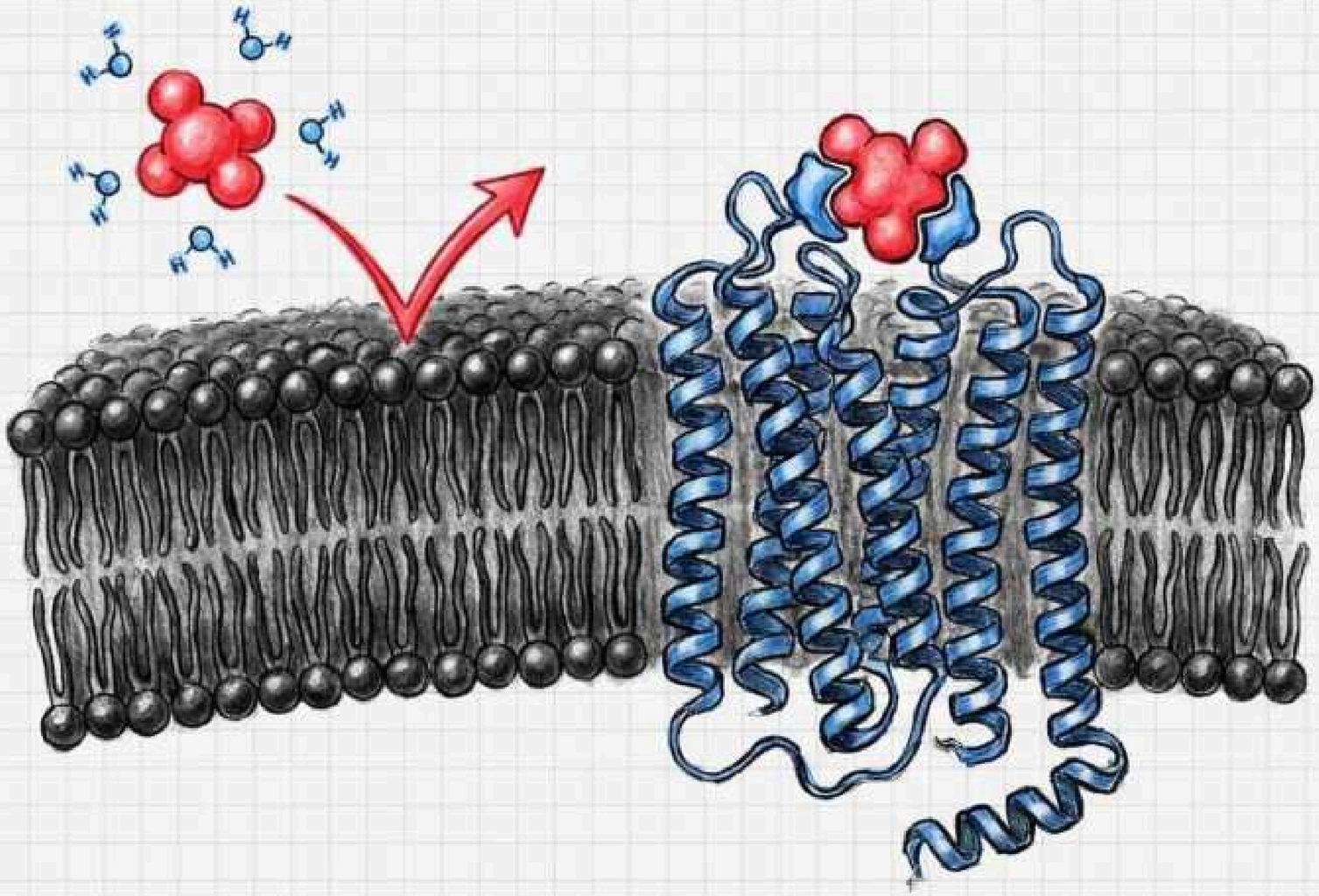
Key Traits:

- **Signal Type:** Small & Oily (e.g., Steroids) - easily crosses the membrane.
- **Speed:** Slow action (takes hours).
- **Result:** Lasting effects (switches genes on/off, changes the cell's entire program by making new proteins).

Cell-Surface Receptors

Focus: G Protein-Coupled Receptors (GPCRs)

¶ 3.7

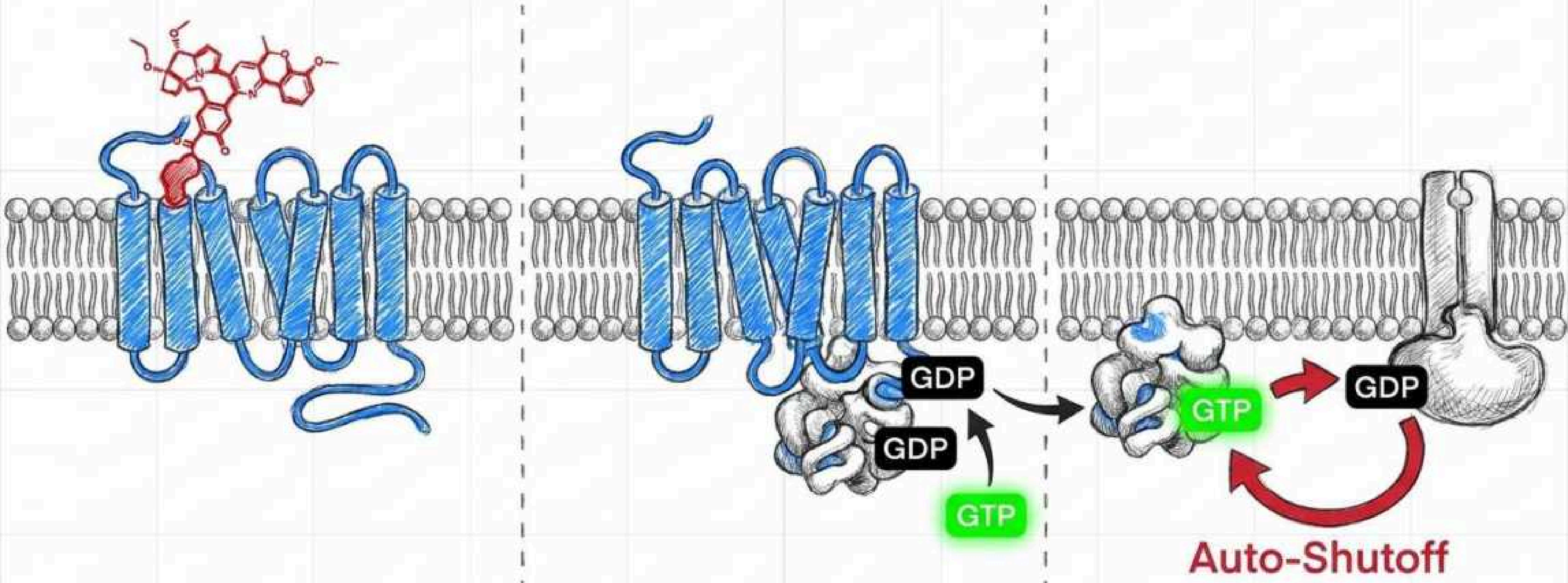


Most signals are water-soluble and cannot enter the cell.

- Largest Family: ~800 GPCRs in humans.
- Function: Detect light, smell, taste, and adrenaline.
- Medical Impact: ~33% of all approved drugs act on this single family.

The Mechanics of a GPCR

¶ 3.8



1. Binding

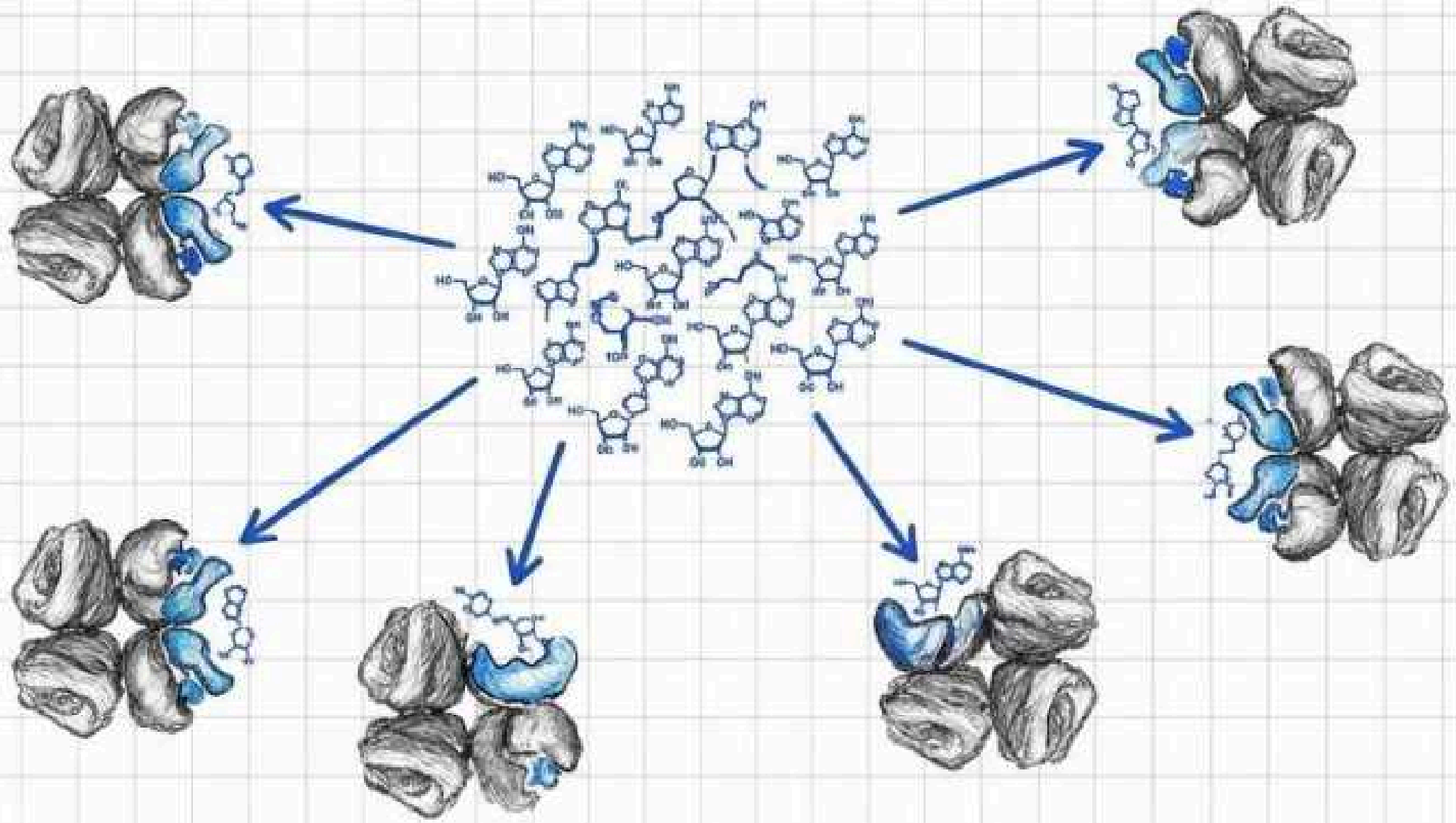
2. Shape Change

3. Relay & Reset

The Second Messenger: Cyclic AMP

¶ 3.9

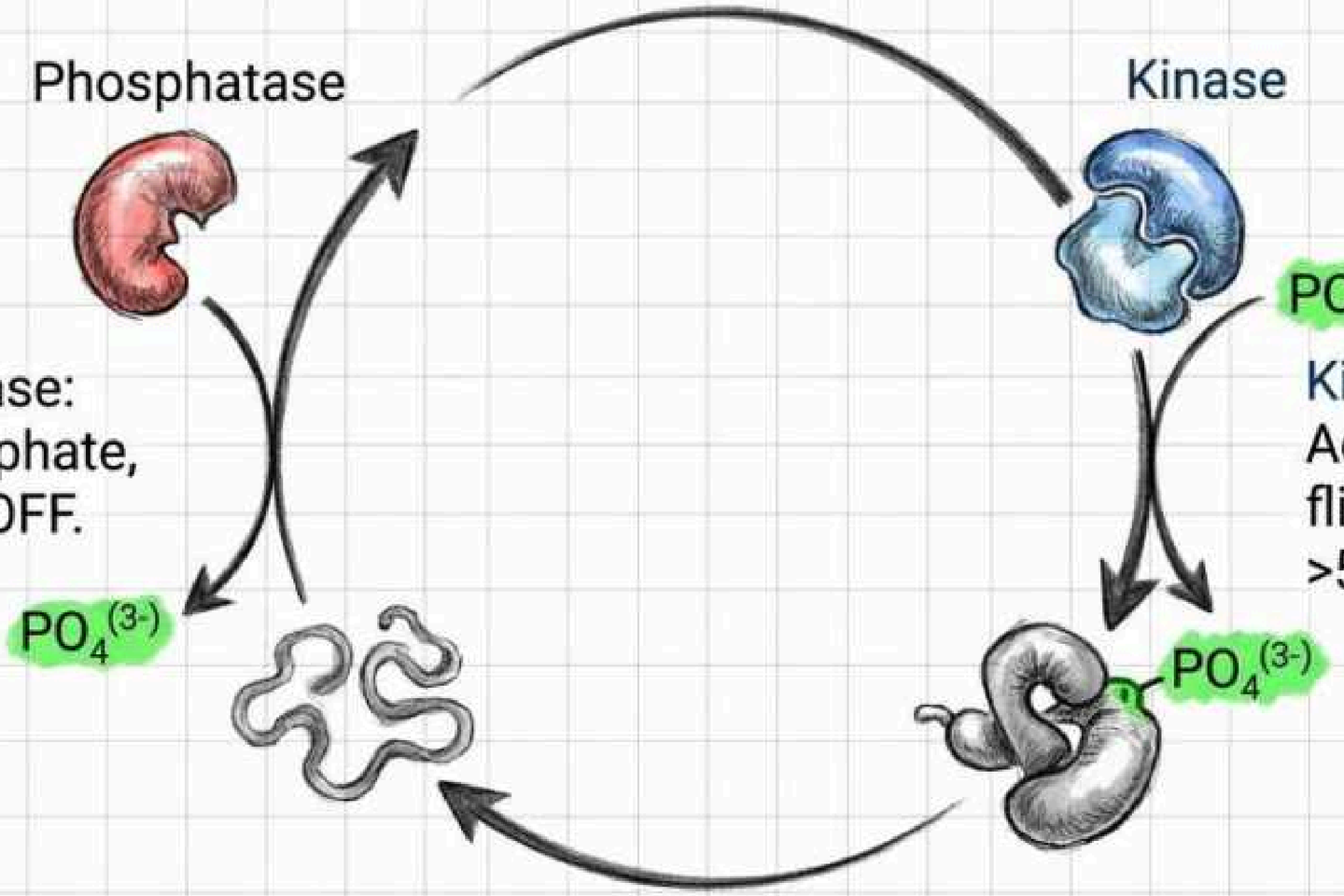
ATP —Adenylyl Cyclase→ cyclic AMP (cAMP)



cAMP spreads quickly through the cell → activates Protein Kinase A.

[Earl Sutherland won the 1971 Nobel Prize for discovering cAMP while studying how adrenaline triggers liver sugar release.]

The Main On-Off System



Phosphatase:
Removes phosphate,
flips switch OFF.

Kinase:
Adds phosphate,
flips switch ON.
>500 human kinases.

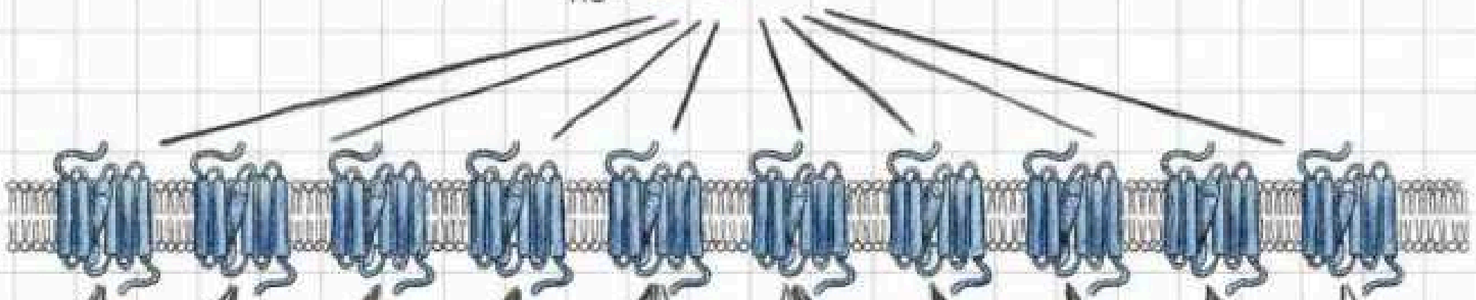
~33% of all proteins carry phosphate groups
at some point in their lifespan.

Cascades Amplify

¶ 3.11

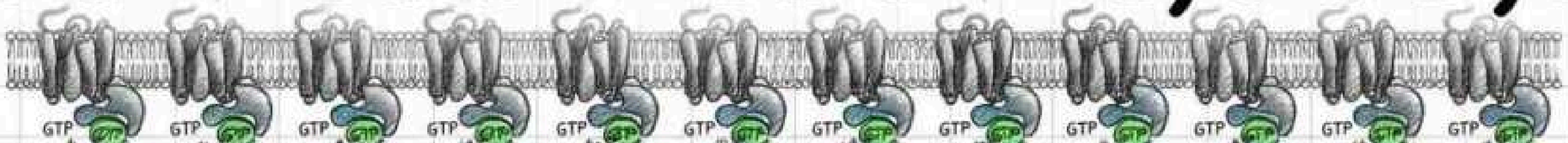


1 Hormone



2 Multiple Receptors

100 x 100 x 100 = 1,000,000



3 Many G Proteins

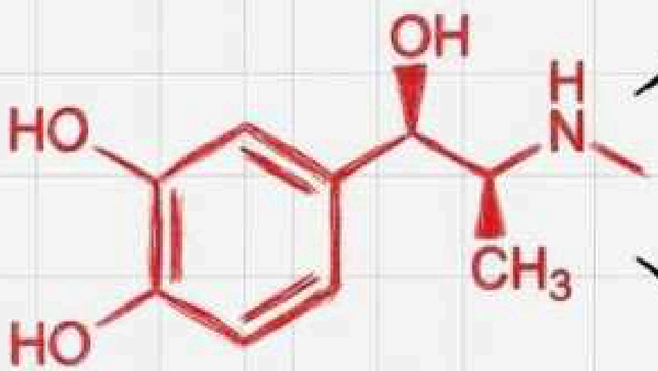


4 Millions of Messengers

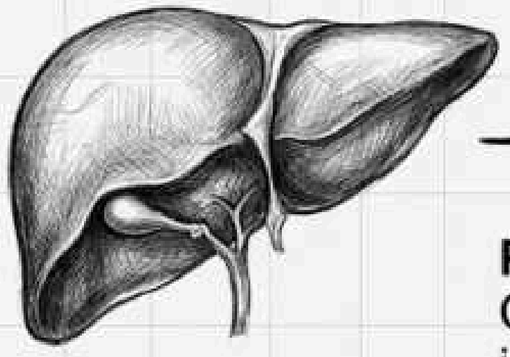
"A whisper becomes a shout."

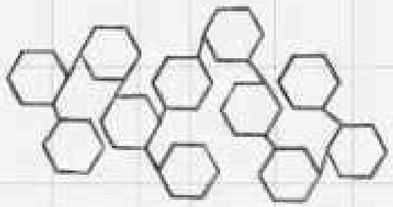
One Signal, Different Jobs: Adrenaline

¶ 3.12

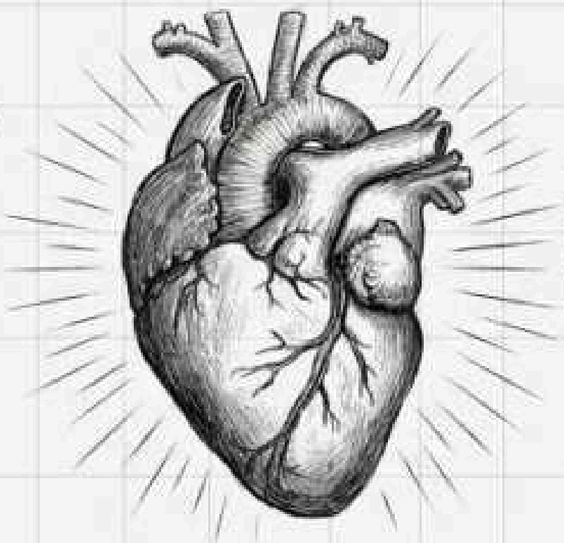


Adrenaline





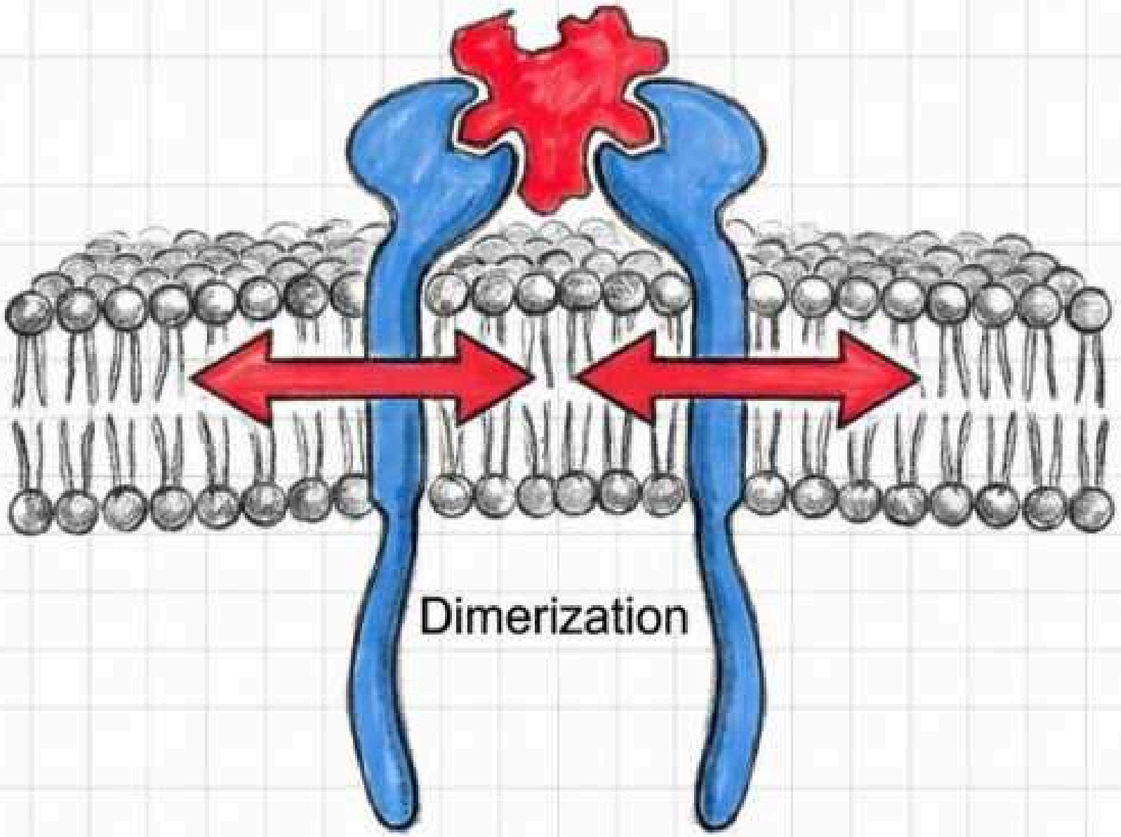
Path A (Liver cells):
Cascade breaks down glycogen into glucose. Result: Rapid muscle fuel before you have time to think.

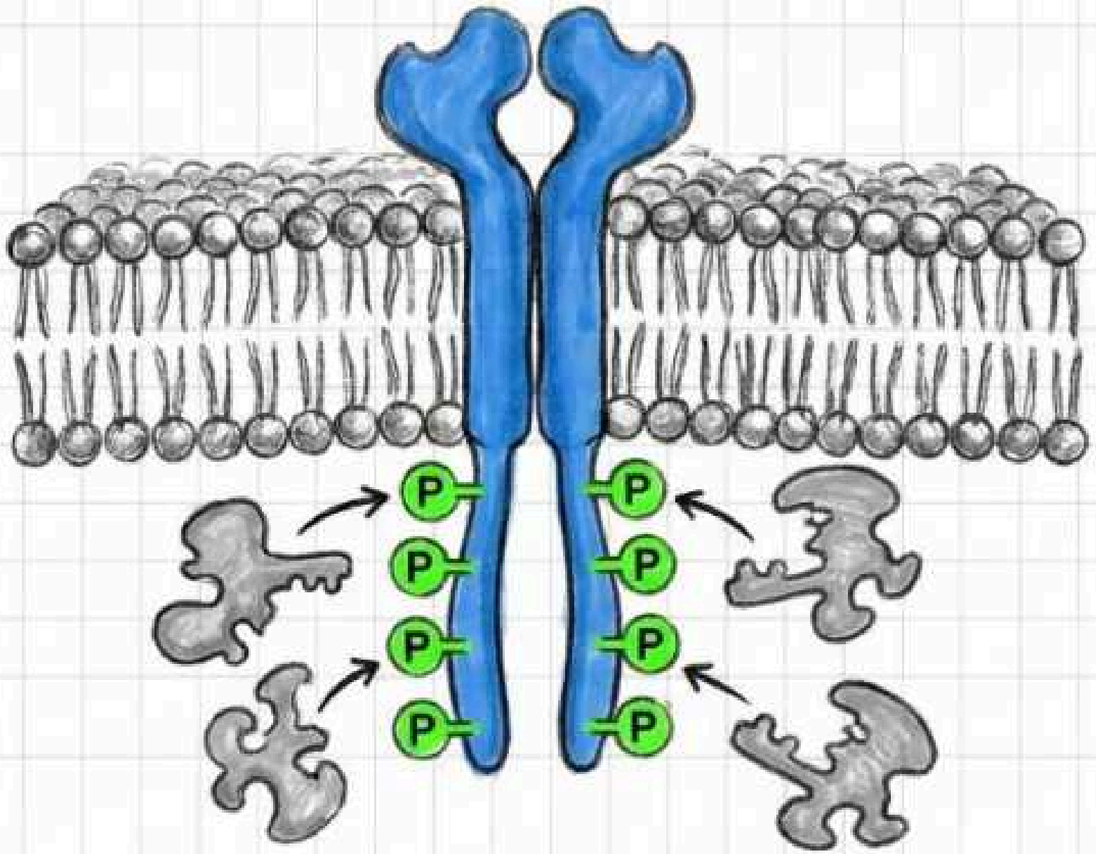


Path B (Heart cells):
Different receptor type.
Result: Speeds up heart rate.

Receptor Tyrosine Kinases (RTKs)

¶ 3.13



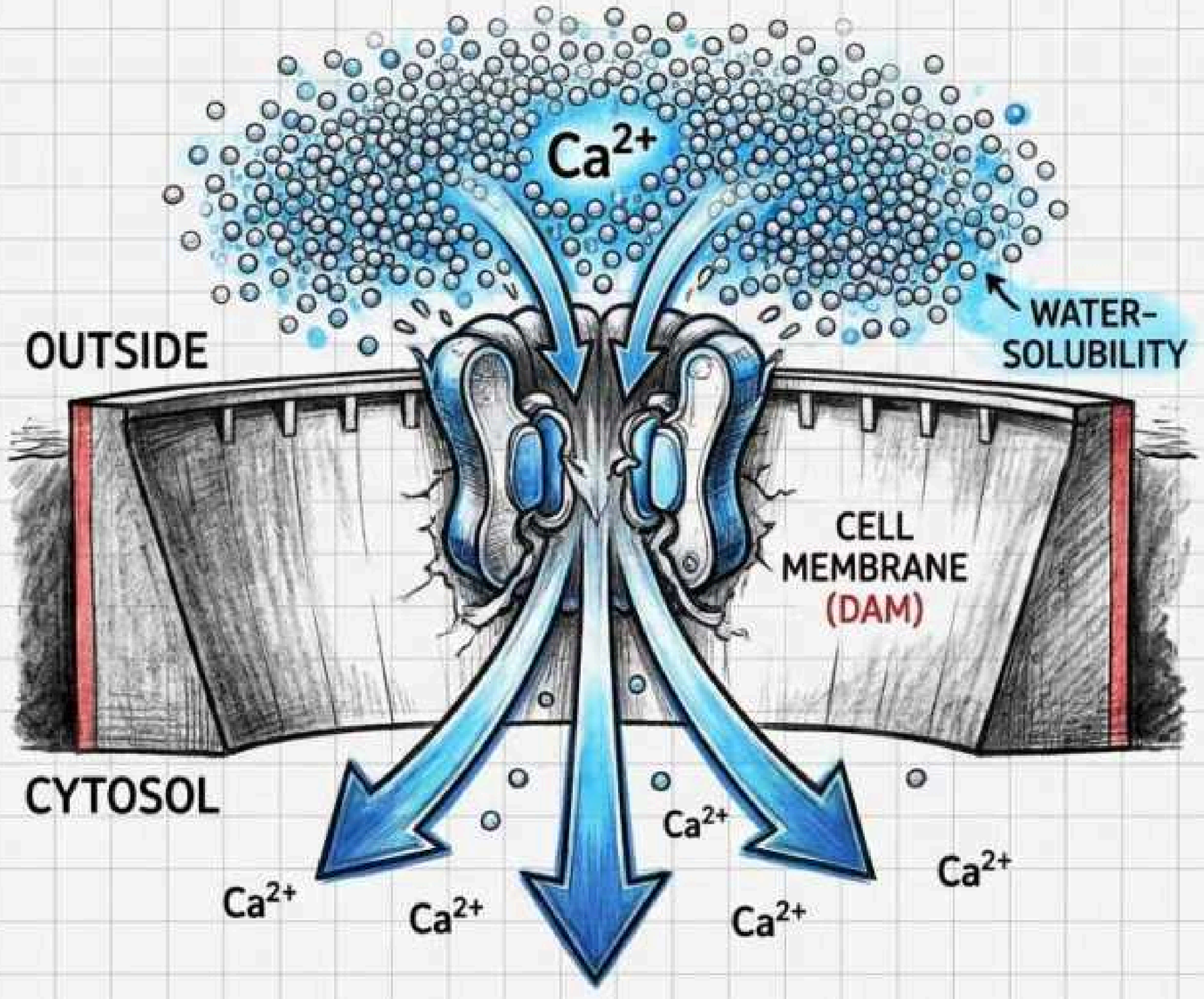


Mechanism: Ligands bind -> Receptors join together -> Cross-phosphorylation creates docking sites for relay proteins.

Examples: Insulin receptors, Growth factor receptors (often signaling toward the nucleus).

Calcium as a Messenger

¶ 3.14



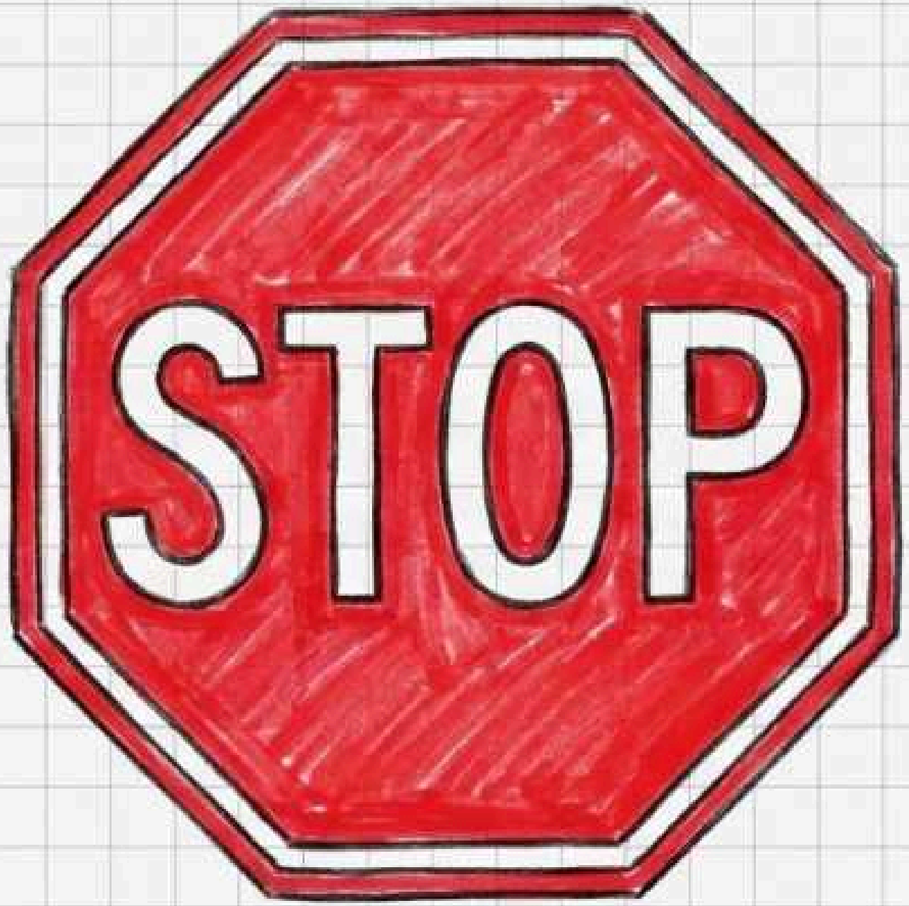
The Math:
Cytosol: 100 nM | Outside: 1-2 mM

The Physics:
Gradient = >10,000x difference.
Opening a channel creates a massive relative change instantly.

Results:
Muscle contraction, egg fertilization, neurotransmitter bursts.

Signals Must Stop

¶ 3.15



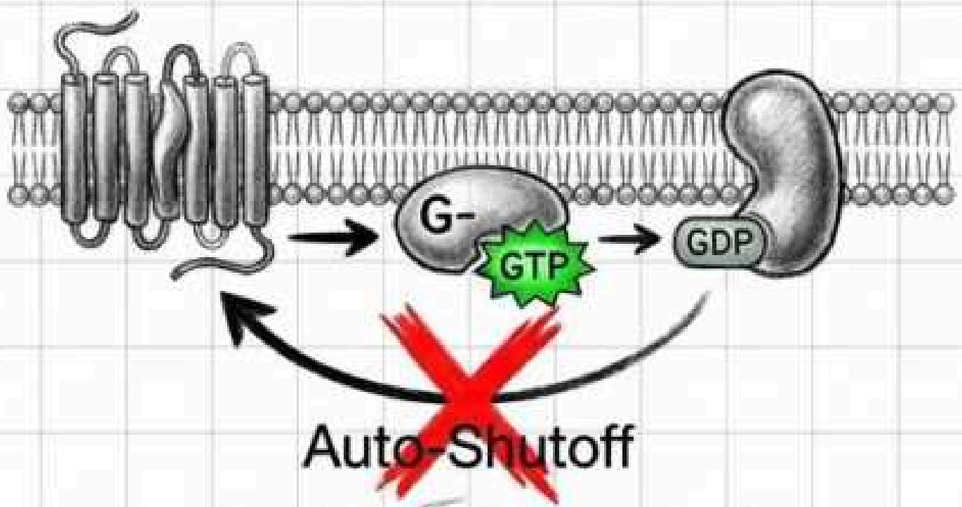
The Shutoff Checklist

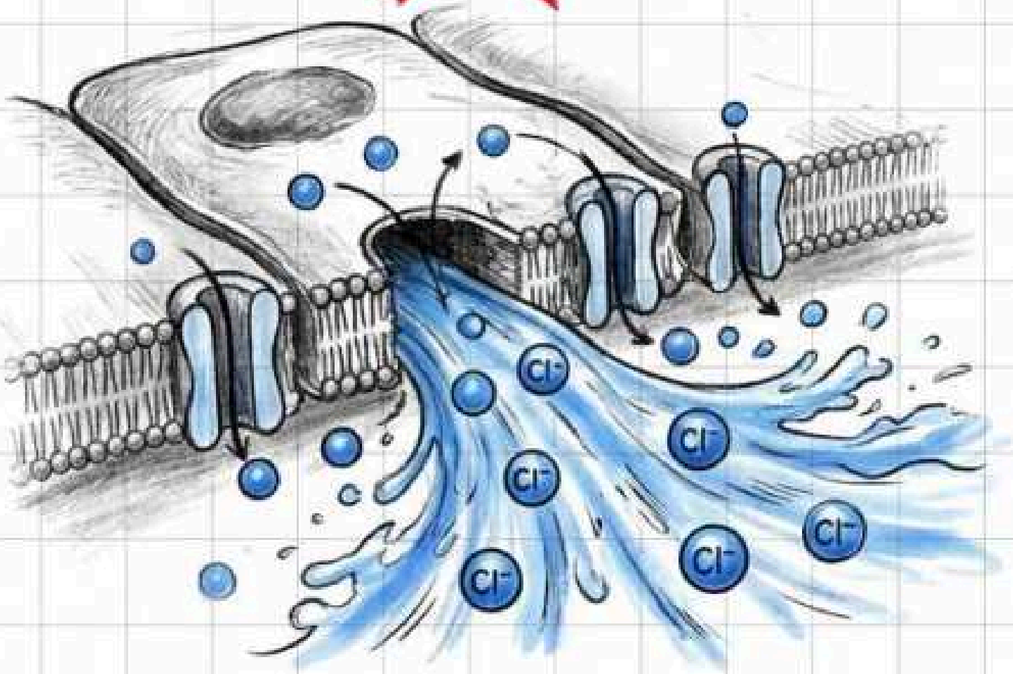
- ☒ Receptors removed from the surface.
- ☒ Ligands broken down.
- ☒ G proteins auto-deactivate (hydrolyze GTP).
- ☒ Phosphatases erase phosphate marks.
- ☑ **Phosphodiesterase** destroys cyclic AMP in seconds.

Good control requires both a start and a stop. Without shutoffs, a cell remains permanently stuck in its response.

When the Stop Fails: Cholera

¶ 3.16





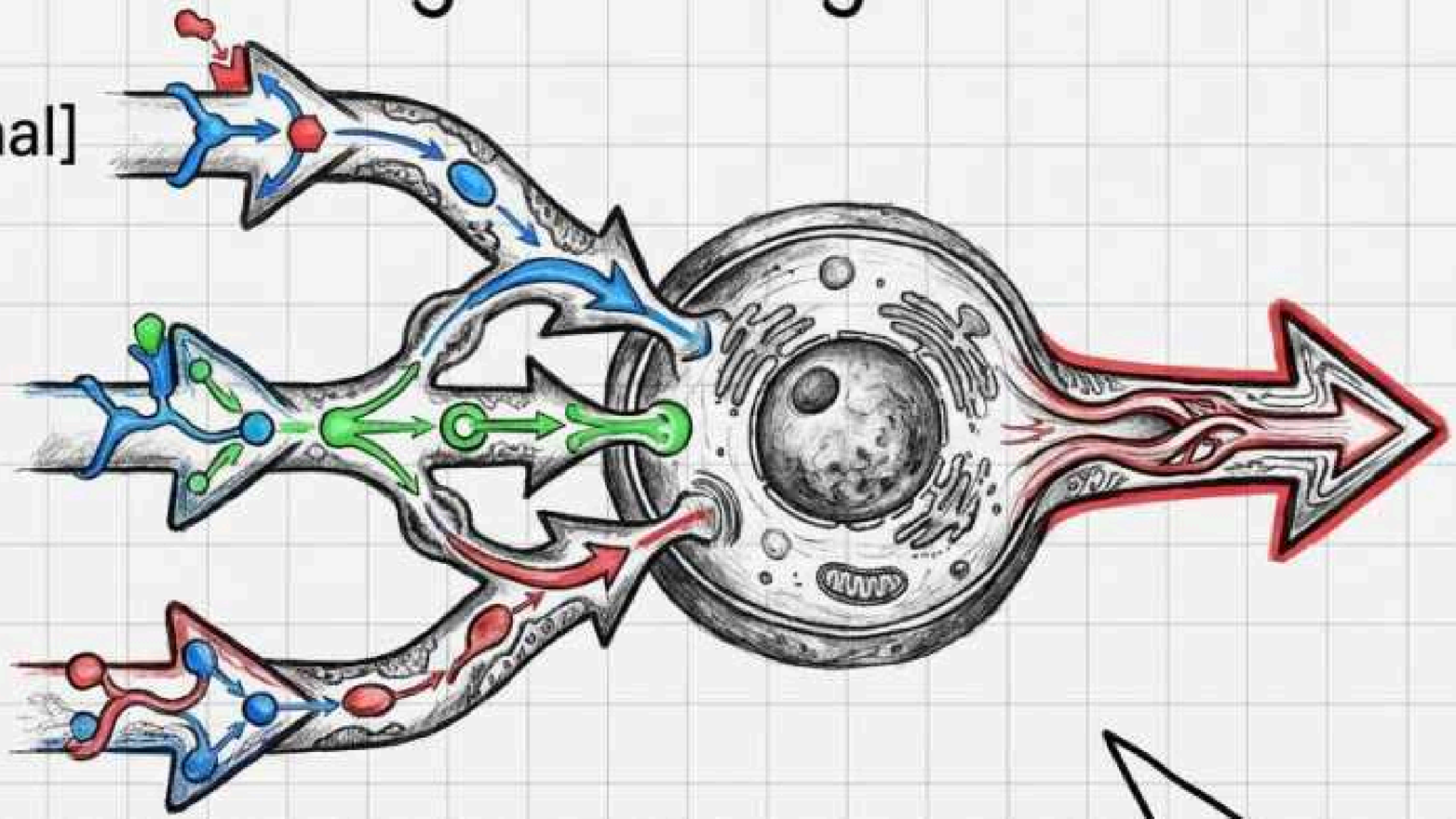
Mechanism: Cholera Toxin -> Modifies G protein -> Cannot hydrolyze GTP -> Protein stuck ON.

Cascade Failure: Adenylyl cyclase runs constantly -> massive cAMP build-up.

Clinical Result: Gut lining pours out chloride & water -> Fatal dehydration within hours.

Signal Integration

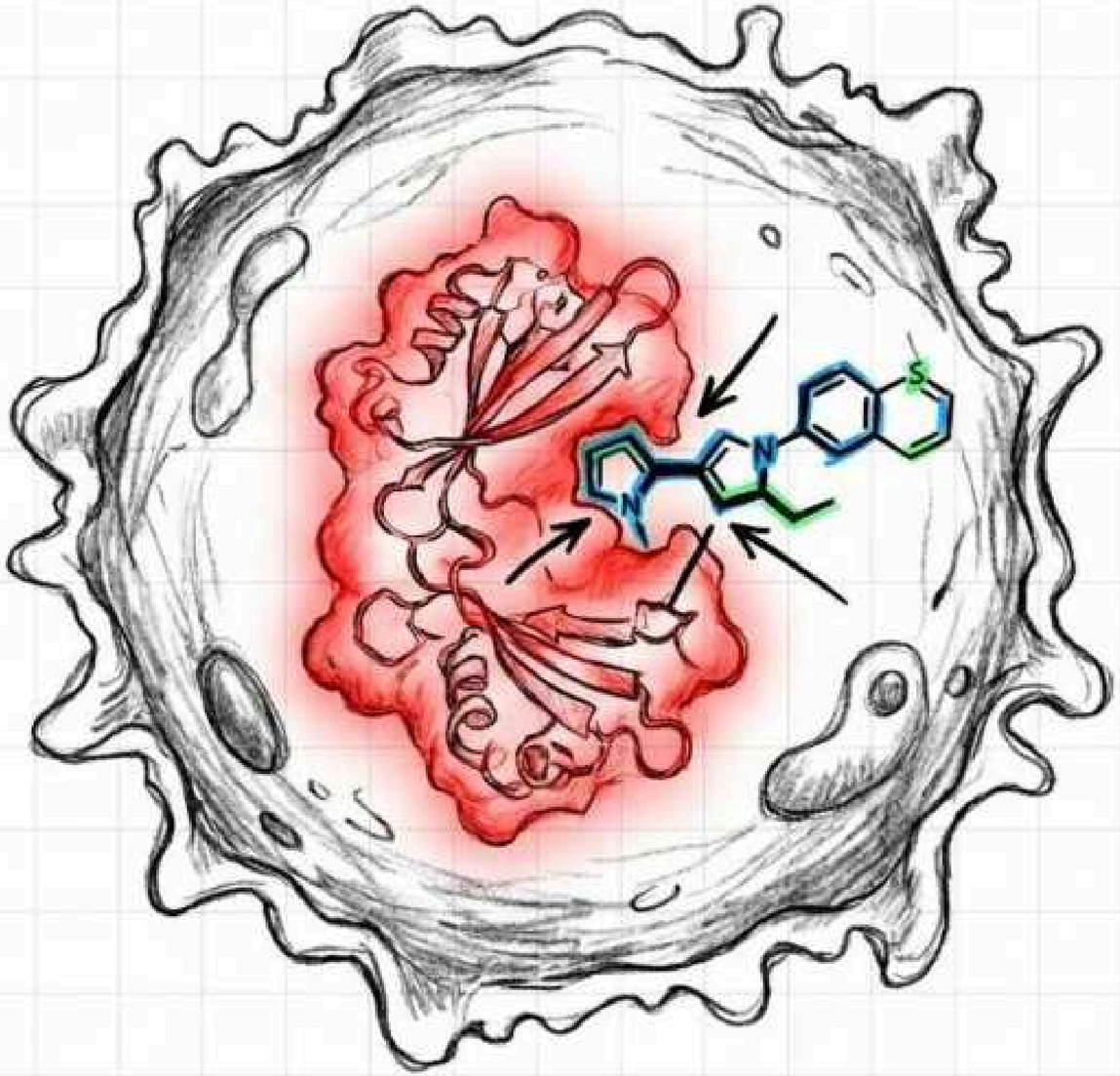
¶ 3.17



Core Principle: Pathways branch, merge, and cross-talk. Cells receive dozens of signals at once. Decisions come from the pattern of signals, not from any single one.

Signaling Errors & Cancer

¶ 3.18



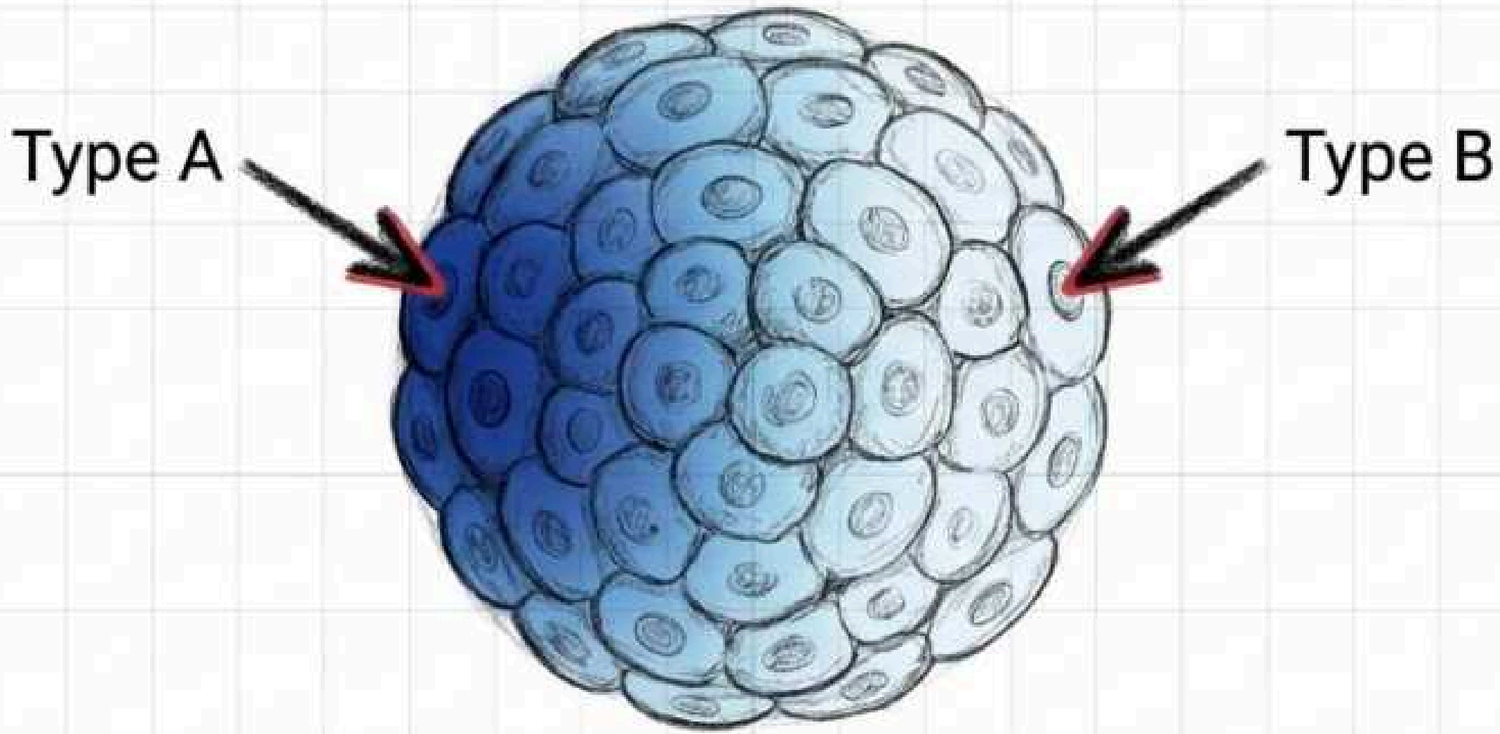
The Problem:
A receptor permanently ON or a kinase stuck ACTIVE tells a cell to divide when it should not.

The Solution:
Kinase Inhibitors.

Medical Breakthrough:
Imatinib (approved 2001). Blocks the stuck-on kinase driving one type of leukemia, transforming the disease.

Shaping Development

¶ 3.19



Concept: Gradients of signaling molecules paint patterns across embryos.
Distance = Destiny: A cell near the signal source becomes one type; a cell farther away becomes another.
Evolutionary Insight: Evolution reuses a small signaling toolkit again and again across different tissues and times.

Lecture Question

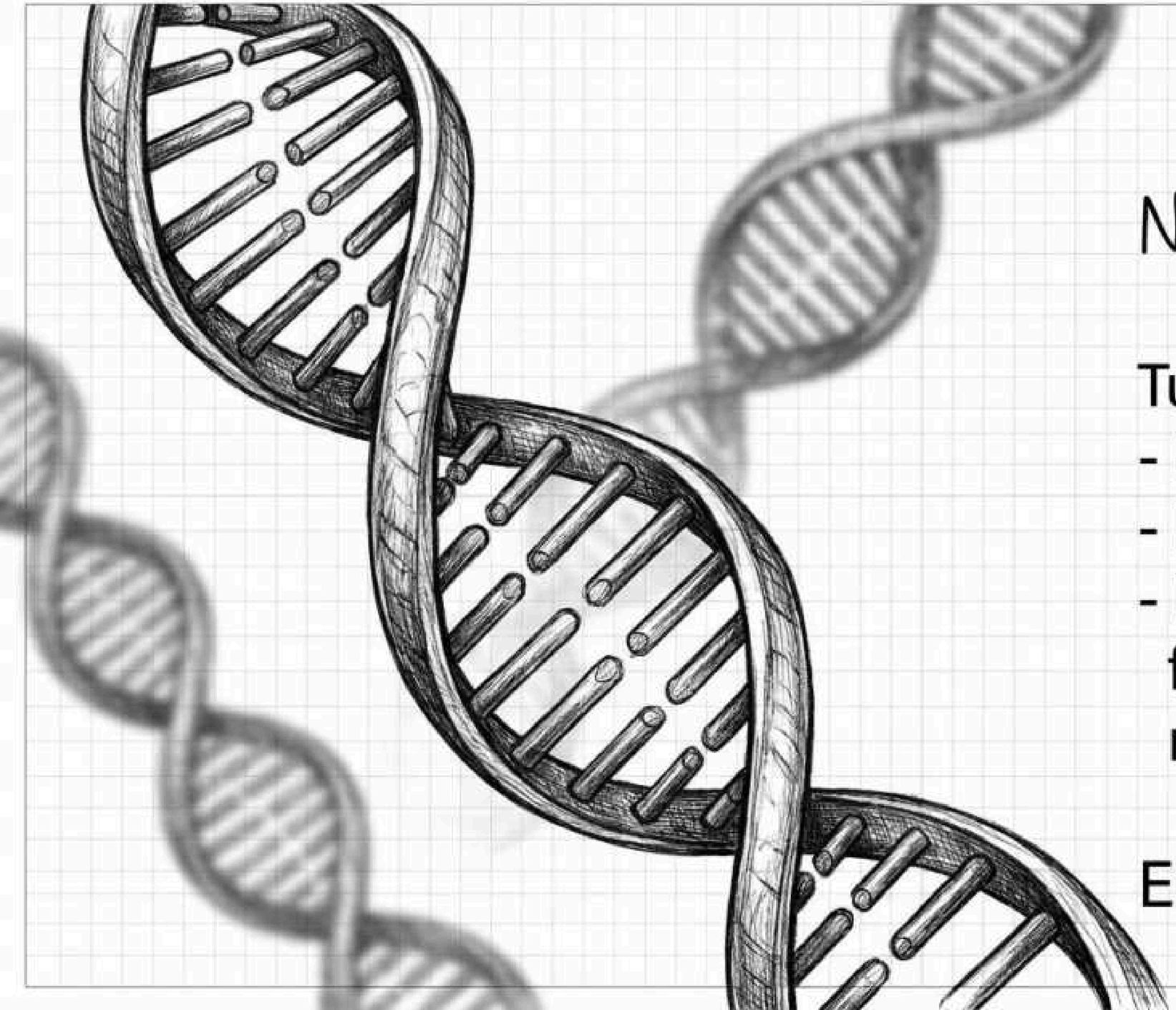
¶ 3.20

1. A drug blocks the enzyme phosphodiesterase. Predict what will happen to cyclic AMP levels after adrenaline arrives. What does this mean for the cell's response?

2. Suggest why a drug that blocks a shutoff might be medically useful. What could go wrong?



¶ 3.21



Next Time: Lecture 4

Turning to DNA itself.
- How it is copied.
- How errors are repaired.
- How 2 meters of DNA fit inside a single microscopic nucleus.

End of Lecture 3.