

Cells communicate by a variety of chemical signals

Communication via **CELL-TO-CELL CONTACT** - here the signaling is direct:

1. **Gap junctions & plasmodesma...**
results in cytoplasmic continuity favoring cellular interactions
2. **Cell surface contacts...**
receptor protein specificity (**same with yeast cells**)

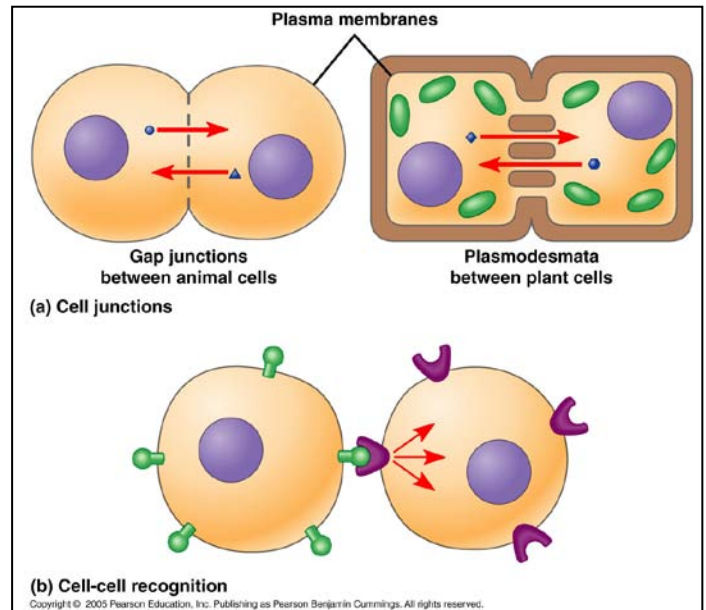
Cell-to-cell contact is critical for multi-cellular organisms.

- cell membranes contain **specific protein-receptors**, which bind & transmit **extra-cellular signal molecules** converting signals into specific cellular responses.

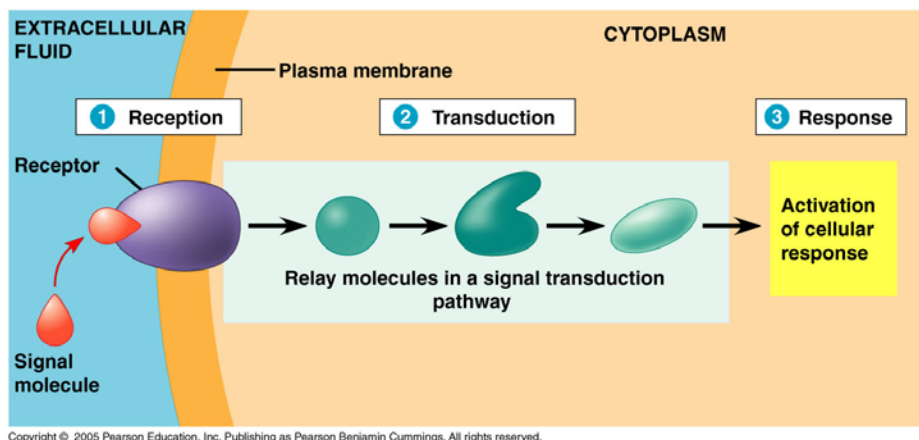
UNIVERSAL PRINCIPLES

Cells may use many different **signal molecules**, but only **a few mechanisms** have survived throughout evolution.

An analogy: auto industry → cars basically have same parts (engines, fenders, lights) but the variety of different patterns is boundless.



SIGNAL TRANSDUCTION is most common method of **CELL COMMUNICATION**, here an exogenous **molecule** is **received** by a cell, & converted (**transduced**) into a **response** by the receiving cell.

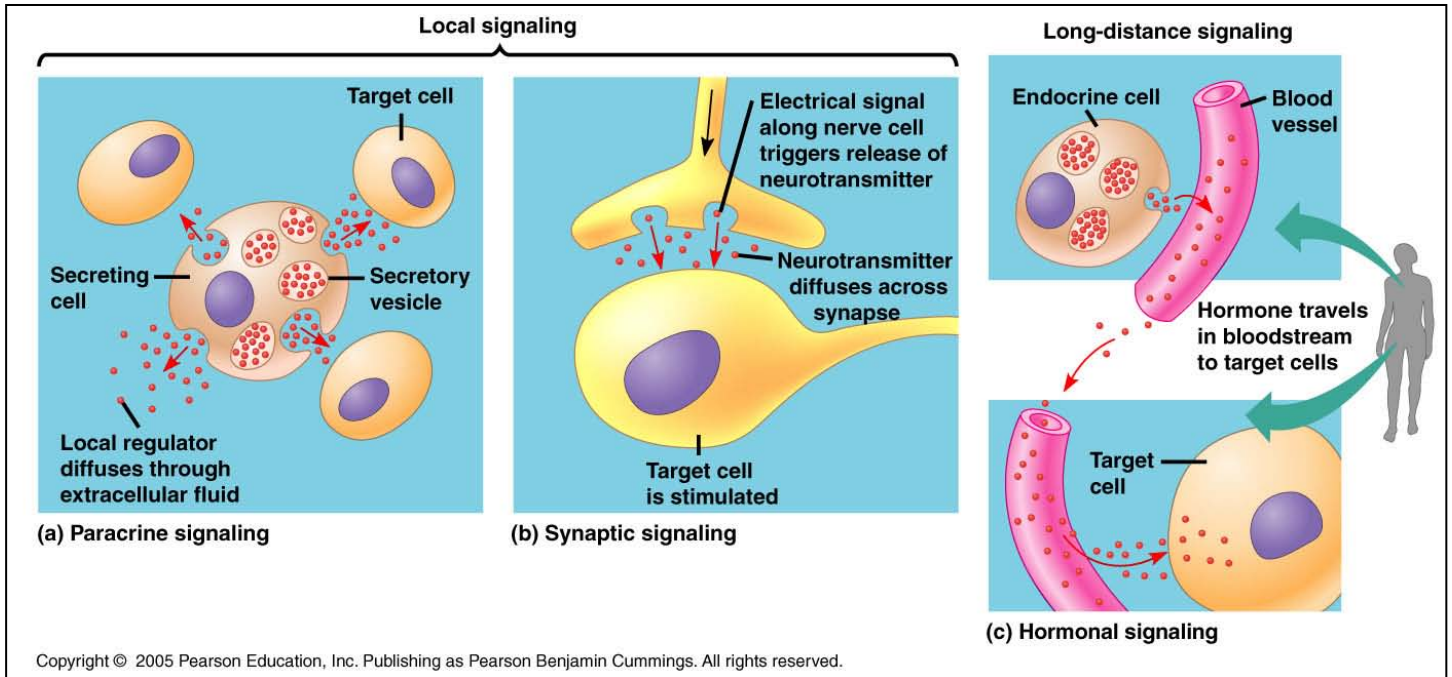


The pattern is remarkably **similar in all cells**; probably evolved very early, even before first multi-cellular cells (maybe in single cell prokaryote); and has been **highly conserved** in today's ancestral cells.

SIGNALING CAN BE LOCAL OR DISTANT

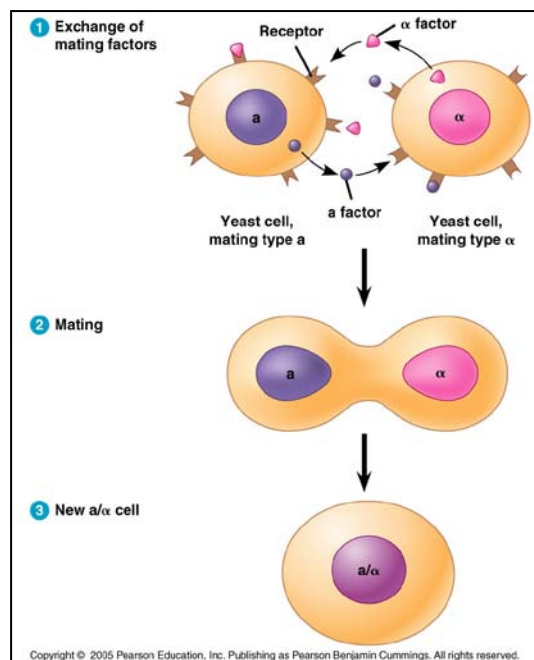
PARACRINE SIGNALING (local)

- Local regulator chemical messengers are targeted to specific receptors
- Often includes: **growth factor proteins** that promote cell division & growth and **neurotransmitters** that move across synapses to other neurons



ENDOCRINE SIGNALING (distant) ↗

- Specialized cells release molecules (often **hormones**) into blood vessels of circulatory system, hormones move to distant target cells... elicit response



Single Cells COMMUNICATION... CELL to CELL SIGNALING SYSTEMS

mating in yeast cells*

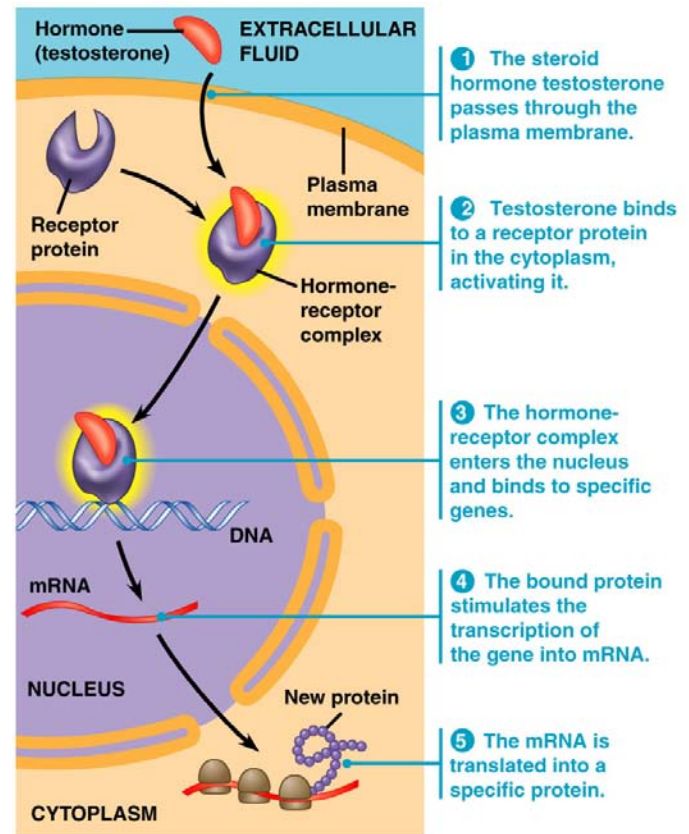
- sex-1 ["a"-cell : releases a-factor (peptide of 12 aa's) - binds to sex-2 receptors]
- sex-2 ["α"-cell : releases α-factor - binds to sex-1 receptors]
- result = fusion of 2 cells (mating) producing diploid cell.

Communication via CELL SIGNALING (aka SIGNAL TRANSDUCTION PATHWAY)

The 3 Stages of Cell Signaling Process...

RECEPTION, TRANSDUCTION, and RESPONSE

1. **Reception...** is not unlike **recognition** of enzyme for its substrate [ES complex]
 - akin to the **lock-&-key hypothesis** of enzyme-substrate recognition (**K_m** & **V_{max}**)
 - **ligand** molecules (usually water soluble) are **recognized by only one receptor protein** bound within a cell membrane
2. **Transduction...** leads to a **conformation change** in receptor
 - shape change results in receptor interacting with other intra-cellular molecules
 - may result in multiple, conformational/structural changes in other cellular proteins
 - **inactive enzymes** → **active enzymes**, & so on, etc...
3. **Response...** usually a **cellular activity**, as **enzyme catalysis**, or the rearrangement of cytoskeleton (movement), or specific gene activity.



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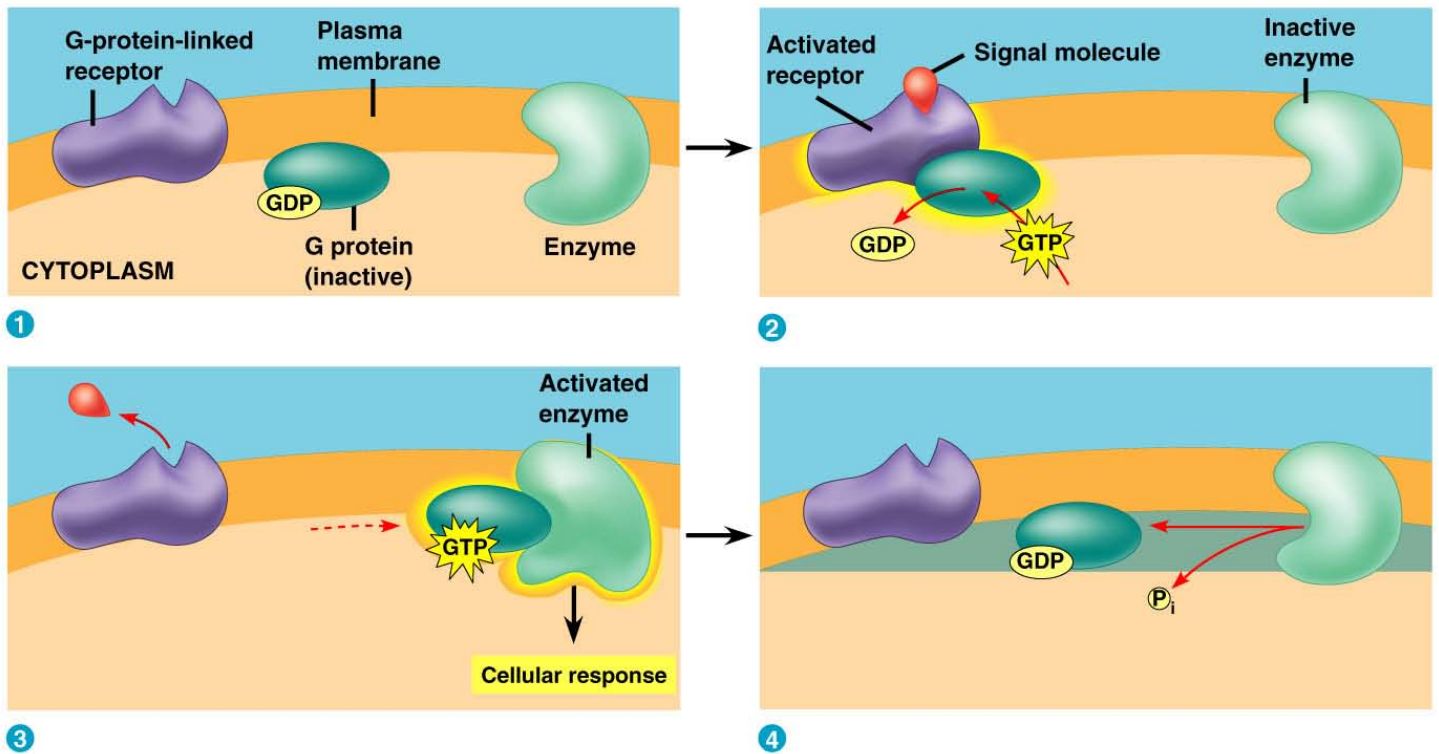
Example of a Receptor Protein & Signal Transduction System

1. **G-Protein Receptors...** receptor proteins that bind **GTP/GDP** & convert between **active** & **inactive** forms
 - **G-protein receptor structure...** has 7 transmembrane - helices & has site for receptor molecule and **G-protein** to bind
 - a **signal molecule** binds to a receptor → conformation change → an inactive **G-(GDP)-protein** now binds **GTP** (replacing **GDP**)... and active **G-(GTP)-protein** stimulates other inactive enzymes.
 - **G-Protein** has its **GTP** hydrolyzed → inactivates **G-protein**
cholera and botulin **toxins...** bind to **G-protein** keeping it active --> diarrhea.

A specific example of G-protein cellular responses:

Fight of Flight Response...

net result... 1 signal molecule gives multiple-enhanced response.



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The **specificity of cell signaling** is varied among cells and leads to a multiplicity of **RESPONSE MECHANISMS**

Other examples of signal transduction mechanisms:

1. Gene activation by a growth factor
2. Steroid hormone reception & myosin protein synthesis
3. Ligand gated ion channel signaling
4. IP₃-DAG and Ca signaling

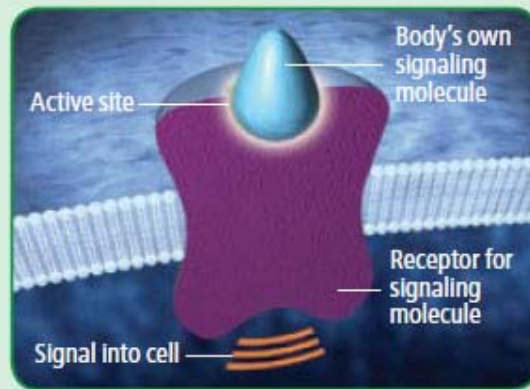
all of these signaling mechanism model themselves after the basic **signal transduction mechanism**. example.

5. Cell Communication, Drug Action, & Drug Allosterism (next page)

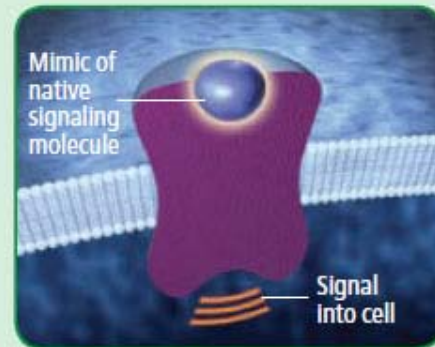
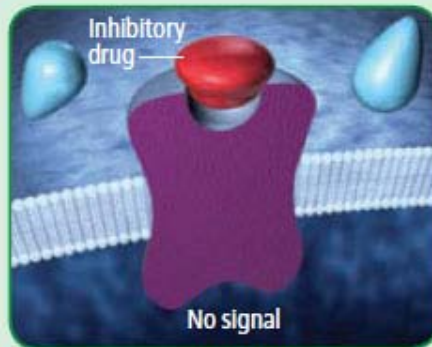
5. Cell Communication, Drug Action, & Drug Allosterism

When one of the body's own molecules, such as a neurotransmitter, attaches to the so-called active site of its receptor on a cell (*right*)—something like a key fitting into a lock—the receptor sets off an intracellular signaling cascade that ultimately causes the cell to change its activity. Many drugs inhibit or enhance such signaling.

NORMAL CELLULAR ACTIVITY

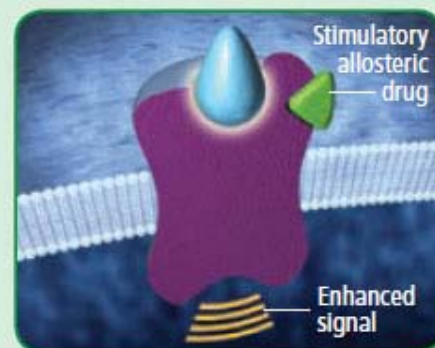
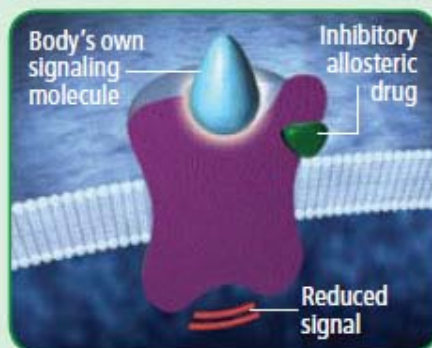


HOW CLASSIC DRUGS ACT



Typical pharmaceuticals bind to the active site in place of the native substance and either block the endogenous molecule's signaling (*left*) or mimic its effects (*right*).

HOW ALLOSTERIC DRUGS ACT



Allosteric drugs do not go to the active site. Instead they bind to other areas, altering the receptor's shape in a way that decreases (*left*) or increases (*right*) the receptor's response to the native substance. Allosteric agents might, for instance, cause the active site to grasp a neurotransmitter less or more effectively than usual.