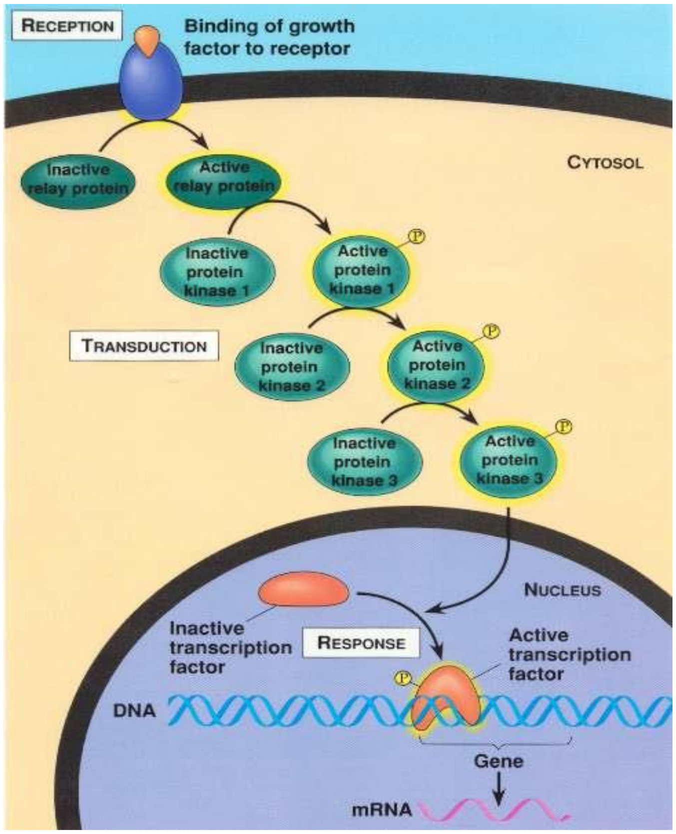
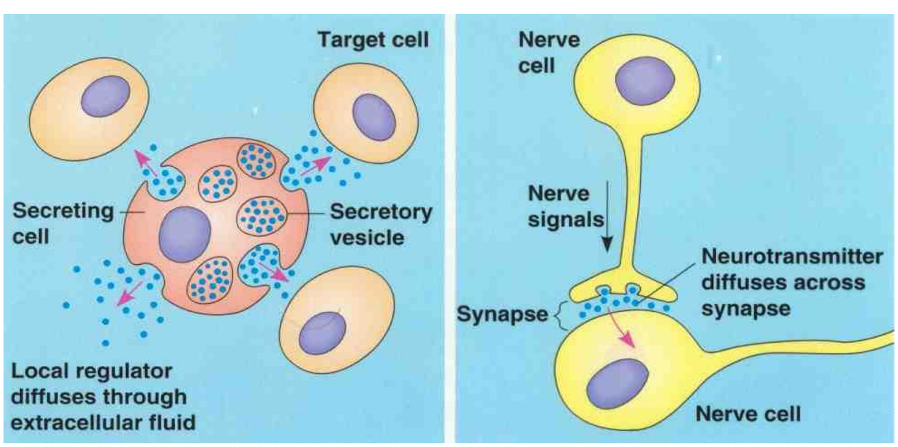
Ch. 11 Cellular Communication Notes

Signal Transduction Pathways



- Chemical messages which elicit a response in cells server as a form of communication between cells
- Found in all cells
- Extremely conserved (similar) in widely different organisms (such as humans and yeast) leads one to believe that this evolved very early in the history of life

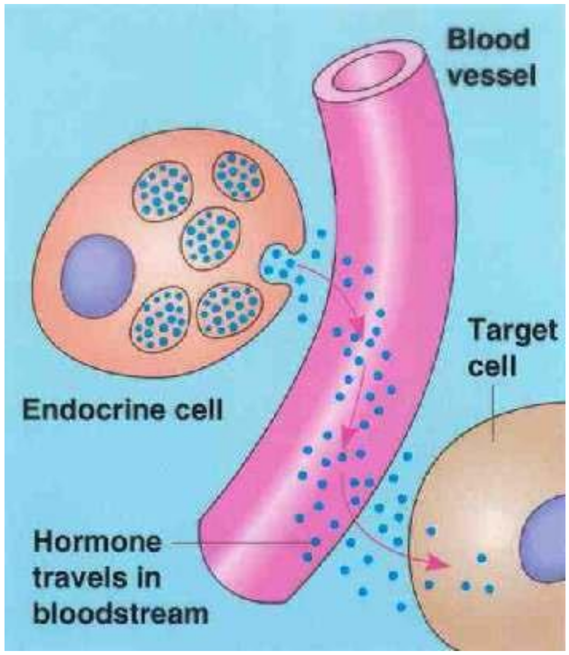
Local Communication in Animal Cells



- Used by cells to communicate to their immediate neighbors
- One cell secretes a signal molecule into the extracellular fluid which is picked up by the target cells

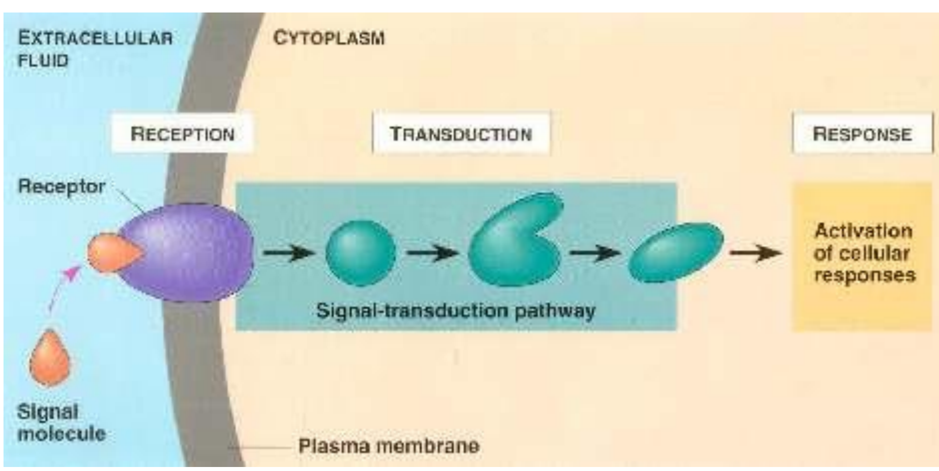
- One example of this is at the synapse of two neurons

Hormonal Signaling in Plants and Animals



- Used by cells to communicate to other cells a great distance away (but still in the same organism)
- One cell secrets a signal molecule (hormone) into the blood system (if an animal) or into the extracellular fluid (if a plant)
- The signal molecules travels throughout the body, most likely contacting nearly all cells in the organism
- Only the target cells, however, will have the receptors necessary to elicit the response

The Three Stages of Cell Signaling - Reception, Transduction, Response

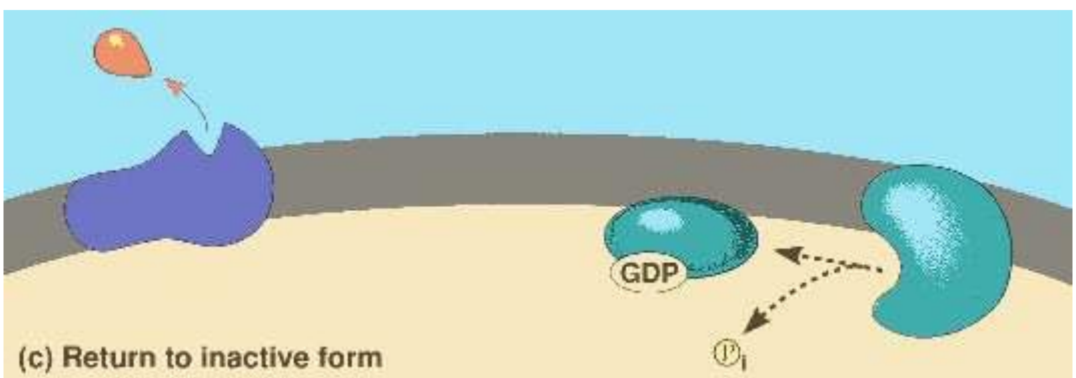


- Reception
  - A chemical message binds to a protein on the cell surface
- Transduction
  - The binding of the signal molecule alters the receptor protein in some way.

- The signal usually starts a cascade of reactions known as a signal transduction pathway
- Response
    - The transduction pathway finally triggers a response
    - The responses can vary from turning on a gene, activating an enzyme, rearranging the cytoskeleton
    - There is usually an amplification of the signal (one hormone can elicit the response of over 10^8 molecules

G-Protein-Linked Receptor Sequences

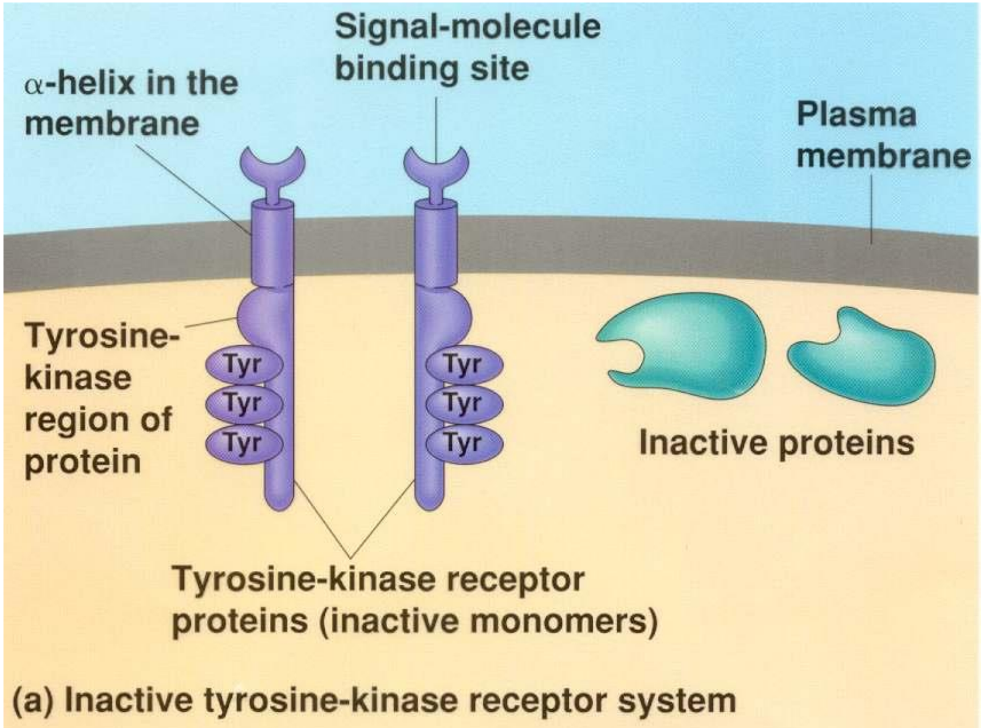
- G-protein-linked receptor is bound to the plasma membrane.
    - All G-protein-linked receptors have similar structure regardless of the organism in which they are found
    - Seven alpha-helices integrate the G-protein-linked receptor to the membrane
    - Signal-binding site on outside of cell
    - G-protein-interacting site on inside of cell
- When signal molecules binds to G-protein-linked receptor, the receptor is activated
- Altered G-protein-linked receptor activates a nearby G-protein
    - G-protein - molecule in signal transduction sequence which has a bound GDP (guanine diphosphate, a relative of ADP and ATP)
- The activation occurs when a GTP displaces the GDP bound to the the G-protein.
- The activated G-protein then binds to another protein, usually an enzyme, and alters *its* activity
- This activation is usually temporary as the activated G-protein soon hydrolyzes the terminal phosphate on the bound GTP, forming GDP, thereby deactivating the G-protein



- The deactivated G-protein is available for reactivation if the G-protein-linked receptor becomes activated again
- All three molecules, the G-protein-linked receptor, the G-protein, and the target enzyme, remain bound to the plasma membrane
- G-protein signal transduction sequences are extremely common in animal systems
    - embryonic development
    - human vision and smell
    - over 60% of all medications used today exert their effects by influencing G-protein pathways

Tyrosine-Kinase Receptors - Another Example of a Signal Transduction Pathway

- Tyrosine-Kinase Receptors often have a structure similar to the diagram below:



- Part of the receptor on the cytoplasmic side serves as an enzyme which catalyzes the transfer of phosphate groups from ATP to the amino acid Tyrosine on a substrate protein
- <u>The activation of a Tyrosine-Kinase Receptor occurs as follows:</u>
    - Two signal molecule binds to two nearby Tyrosine-Kinase Receptors, causing them to aggregate, forming a dimer
    - The formation of a dimer activated the Tyrosine-Kinase portion of each polypeptide
    - The activated Tyrosine-Kinases phosphorylate the Tyrosine residues on the protein
- The activated receptor protein is now recognized by specific relay proteins
- They bind to the phosphorylated tyrosines, which cause a conformation change.
- The activated relay protein can then trigger a cellular response
    - One activated Tyrosine-Kinase dimer can activate over ten different relay proteins, each which triggers a different response
    - The ability of one ligand binding event to elicit so many response pathways is a key difference between these receptors and G-protein-linked receptors (that, and the absence of G- proteins of course...)
    - Abnormal Tyrosine-Kinases that aggregate without the binding of a ligand have been linked with some forms of cancer

<u>Signal Transduction Pathways</u> are often complex, having many, many intermediates participating in the cascade.