**Cell Signaling**

In order to respond to changes in their immediate environment, cells must be able to receive and process signals that originate outside their borders. Individual cells often receive many signals simultaneously, and they then integrate the information they receive into a unified action plan. But cells aren't just targets. They also send out messages to other cells both near and far.

## What Kind of Signals Do Cells Receive?

Most cell signals are chemical in nature. For example, prokaryotic organisms have sensors that detect nutrients and help them navigate toward food sources. In multicellular organisms, growth factors, hormones, neurotransmitters, and extracellular matrix components are some of the many types of chemical signals cells use. These substances can exert their effects locally, or they might travel over long distances. For instance, **neurotransmitters** are a class of short-range signaling molecules that travel across the tiny spaces between adjacent neurons or between neurons and muscle cells. Other signaling molecules must move much farther to reach their targets. One example is follicle-stimulating hormone, which travels from the mammalian brain to the ovary, where it triggers egg release.

How Do Cells Recognize Signals? Some cells also respond to mechanical stimuli. For example, sensory cells in the skin respond to the pressure of touch, whereas similar cells in the ear react to the movement of sound waves. In addition, specialized cells in the human vascular system detect changes in blood pressure — information that the body uses to maintain a consistent cardiac load.

Cells have proteins called **receptors** that bind to signaling molecules and initiate a physiological response. Different receptors are specific for different molecules. Dopamine receptors bind dopamine, insulin receptors bind insulin, nerve growth factor receptors bind nerve growth factor, and so on. In fact, there are hundreds of receptor types found in cells, and varying cell types have different populations of receptors. Receptors can also respond directly to light or pressure, which makes cells sensitive to events in the atmosphere.

Receptors are generally transmembrane proteins, which bind to signaling molecules outside the cell and subsequently transmit the signal through a sequence of molecular switches to internal signaling pathways. Membrane receptors fall into three major classes: G-protein-coupled receptors, ion channel receptors, and enzyme-linked receptors. The names of these receptor classes refer to the mechanism by which the receptors transform external signals into internal ones — via protein action, ion channel opening, or enzyme activation, respectively. Because membrane receptors interact with both extracellular signals and molecules within the cell, they permit signaling molecules to affect cell function without actually entering the cell. This is important because most signaling molecules are either too big or too charged to cross a cell's plasma membrane (Figure 1).

Not all receptors exist on the exterior of the cell. Some exist deep inside the cell, or even in the nucleus. These receptors typically bind to molecules that can pass through the plasma membrane, such as gases like nitrous oxide and steroid hormones like estrogen.



## How Do Cells Respond to Signals?

Once a receptor protein receives a signal, it undergoes a conformational change, which in turn launches a series of biochemical reactions within the cell. These intracellular signaling pathways, also called **signal transduction cascades**, typically amplify the message, producing multiple intracellular signals for every one receptor that is bound.

Activation of receptors can trigger the synthesis of small molecules called **second messengers**, which initiate and coordinate intracellular signaling pathways. For example, **cyclic AMP** (cAMP) is a common second messenger involved in signal transduction cascades. (In fact, it was the first second messenger ever discovered.) cAMP is synthesized from ATP by the enzyme **adenylyl cyclase**, which resides in the cell membrane. The activation of adenylyl cyclase can result in the manufacture of hundreds or even thousands of cAMP molecules. These cAMP molecules activate the enzyme **protein kinase A** (PKA), which then **phosphorylates** multiple protein substrates by attaching phosphate groups to them. Each step in the cascade further amplifies the initial signal, and the phosphorylation reactions mediate both short- and long-term responses in the cell (Figure 2). How does cAMP stop signaling? It is degraded by the enzyme phosphodiesterase.

Other examples of second messengers include **diacylglycerol** (DAG) and **inositol 1,4,5-triphosphate** (IP3), which are both produced by the enzyme **phospholipase**, also a membrane protein. IP3 causes the release of Ca2+ — yet another second messenger — from intracellular stores. Together, DAG and Ca2+ activate another enzyme called **protein kinase C** (PKC).



## How Do Signals Affect Cell Function?

Protein kinases such as PKA and PKC catalyze the transfer of phosphate groups from ATP molecules to protein molecules. Within proteins, the amino acids serine, threonine, and tyrosine are especially common sites for phosphorylation. These phosphorylation reactions control the activity of many enzymes involved in intracellular signaling pathways. Specifically, the addition of phosphate groups causes a conformational change in the enzymes, which can either activate or inhibit the enzyme activity. Then, when appropriate, protein phosphatases remove the phosphate groups from the enzymes, thereby reversing the effect on enzymatic activity.

Phosphorylation allows for intricate control of protein function. Phosphate groups can be added to multiple sites in a single protein, and a single protein may in turn be the substrate for multiple kinases and phosphatases.

At any one time, a cell is receiving and responding to numerous signals, and multiple signal transduction pathways are operating in its cytoplasm. Many points of intersection exist among these pathways. For instance, a single second messenger or protein kinase might play a role in more than one pathway. Through this network of signaling pathways, the cell is constantly integrating all the information it receives from its external environment.

## Conclusion

Cells typically receive signals in chemical form via various signaling molecules. When a signaling molecule joins with an appropriate receptor on a cell surface, this binding triggers a chain of events that not only carries the signal to the cell interior, but amplifies it as well. Cells can also send signaling molecules to other cells. Some of these chemical signals — including neurotransmitters — travel only a short distance, but others must go much farther to reach their targets.

**Cell signaling**

**Cell signalling** is part of a [complex system](http://en.wikipedia.org/wiki/Complex_system) of communication that governs basic cellular activities and coordinates cell actions. The ability of cells to perceive and correctly respond to their microenvironment is the basis of development, tissue repair, and [immunity](http://en.wikipedia.org/wiki/Immunity_%28medical%29) as well as normal tissue [homeostasis](http://en.wikipedia.org/wiki/Homeostasis). Errors in cellular information processing are responsible for diseases such as [cancer](http://en.wikipedia.org/wiki/Cancer), [autoimmunity](http://en.wikipedia.org/wiki/Autoimmunity), and [diabetes](http://en.wikipedia.org/wiki/Diabetes). By understanding cell signaling, diseases may be treated effectively and, theoretically, artificial tissues may be created.

Traditional work in biology has focused on studying individual parts of cell signaling pathways. [Systems biology](http://en.wikipedia.org/wiki/Systems_biology) research helps us to understand the underlying structure of cell signaling networks and how changes in these networks may affect the transmission and flow of information. Such networks are [complex systems](http://en.wikipedia.org/wiki/Complex_systems) in their organization and may exhibit a number of [emergent properties](http://en.wikipedia.org/wiki/Emergent_properties) including [bistability](http://en.wikipedia.org/wiki/Bistability) and ultrasensitivity. Analysis of cell signaling networks requires a combination of experimental and theoretical approaches including the development and analysis of [simulations](http://en.wikipedia.org/wiki/Simulations) and [modeling](http://en.wikipedia.org/wiki/Scientific_modelling).[[*citation needed*](http://en.wikipedia.org/wiki/Wikipedia%3ACitation_needed)] Long-range [allostery](http://en.wikipedia.org/wiki/Allostery) is often a significant component of cell signaling events

## Unicellular and multicellular organism cell signaling

Cell signaling has been most extensively studied in the context of human diseases and signaling between [cells](http://en.wikipedia.org/wiki/Cell_%28biology%29) of a single organism. However, cell signaling may also occur between the cells of two different organisms. In many mammals, early [embryo](http://en.wikipedia.org/wiki/Embryo) cells exchange signals with cells of the [uterus](http://en.wikipedia.org/wiki/Uterus).[[2]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Mohamed2005-2) In the human [gastrointestinal tract](http://en.wikipedia.org/wiki/Gastrointestinal_tract), [bacteria](http://en.wikipedia.org/wiki/Bacteria) exchange signals with each other and with human [epithelial](http://en.wikipedia.org/wiki/Epithelium) and [immune system](http://en.wikipedia.org/wiki/Immune_system) cells.[[3]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Clarke2005-3) For the yeast [*Saccharomyces cerevisiae*](http://en.wikipedia.org/wiki/Saccharomyces_cerevisiae) during [mating](http://en.wikipedia.org/wiki/Mating_of_yeast), some cells send a [peptide](http://en.wikipedia.org/wiki/Peptide) signal (mating factor [*pheromones*](http://en.wikipedia.org/wiki/Pheromones)) into their environment. The mating factor peptide may bind to a cell surface [receptor](http://en.wikipedia.org/wiki/Receptor_%28biochemistry%29) on other yeast cells and induce them to prepare for mating

Signaling within, between, and among cells is subdivided into the following classifications:

* [*Intracrine*](http://en.wikipedia.org/wiki/Intracrine) signals are produced by the target cell that stay within the target cell.
* [*Autocrine*](http://en.wikipedia.org/wiki/Autocrine_signalling) signals are produced by the target cell, are secreted, and effect the target cell itself via receptors. Sometimes autocrine cells can target cells close by if they are the same type of cell as the emitting cell. An example of this are [immune cells](http://en.wikipedia.org/wiki/Immune_cell).
* [*Juxtacrine*](http://en.wikipedia.org/wiki/Juxtacrine_signalling) signals target adjacent (touching) cells. These signals are transmitted along cell membranes via protein or lipid components integral to the membrane and are capable of affecting either the emitting cell or cells immediately adjacent.
* [*Paracrine*](http://en.wikipedia.org/wiki/Paracrine_signalling) signals target cells in the vicinity of the emitting cell. [Neurotransmitters](http://en.wikipedia.org/wiki/Neurotransmitters) represent an example.
* [*Endocrine*](http://en.wikipedia.org/wiki/Endocrine_system) signals target distant cells. Endocrine cells produce hormones that travel through the [blood](http://en.wikipedia.org/wiki/Circulatory_system) to reach all parts of the body.
* Cells communicate with each other via direct contact ([juxtacrine signaling](http://en.wikipedia.org/wiki/Juxtacrine_signaling%22%20%5Co%20%22Juxtacrine%20signaling)), over short distances ([paracrine signaling](http://en.wikipedia.org/wiki/Paracrine_signaling%22%20%5Co%20%22Paracrine%20signaling)), or over large distances and/or scales ([endocrine signaling](http://en.wikipedia.org/wiki/Endocrine_system)).
* Some cell–cell communication requires direct [cell–cell contact](http://en.wikipedia.org/wiki/Cell%E2%80%93cell_interaction). Some cells can form [gap junctions](http://en.wikipedia.org/wiki/Gap_junction) that connect their [cytoplasm](http://en.wikipedia.org/wiki/Cytoplasm) to the cytoplasm of adjacent cells. In [cardiac muscle](http://en.wikipedia.org/wiki/Cardiac_muscle), gap junctions between adjacent cells allows for [action potential](http://en.wikipedia.org/wiki/Action_potential) propagation from the [cardiac pacemaker](http://en.wikipedia.org/wiki/Cardiac_pacemaker) region of the heart to spread and coordinately cause contraction of the heart.
* The [notch signaling](http://en.wikipedia.org/wiki/Notch_signaling) mechanism is an example of [juxtacrine signaling](http://en.wikipedia.org/wiki/Juxtacrine_signalling) (also known as contact-dependent signaling) in which two adjacent cells must make physical contact in order to communicate. This requirement for direct contact allows for very precise control of cell [differentiation](http://en.wikipedia.org/wiki/Differentiation_%28cellular%29) during embryonic development. In the worm [*Caenorhabditis elegans*](http://en.wikipedia.org/wiki/Caenorhabditis_elegans), two cells of the developing [gonad](http://en.wikipedia.org/wiki/Gonad) each have an equal chance of terminally differentiating or becoming a uterine precursor cell that continues to divide. The choice of which cell continues to divide is controlled by competition of cell surface signals. One cell will happen to produce more of a cell surface protein that activates the Notch [receptor](http://en.wikipedia.org/wiki/Cell_signaling#Receptors_for_cell_signals) on the adjacent cell. This activates a [feedback loop](http://en.wikipedia.org/wiki/Feedback_loop) or system that reduces Notch expression in the cell that will differentiate and that increases Notch on the surface of the cell that continues as a [stem cell](http://en.wikipedia.org/wiki/Stem_cell).[[5]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Greenwald1998-5)
* Many cell signals are carried by molecules that are released by one cell and move to make contact with another cell. [*Endocrine*](http://en.wikipedia.org/wiki/Endocrine_system) signals are called [hormones](http://en.wikipedia.org/wiki/Hormone). Hormones are produced by endocrine cells and they travel through the [blood](http://en.wikipedia.org/wiki/Circulatory_system) to reach all parts of the body. Specificity of signaling can be controlled if only some cells can respond to a particular hormone. [*Paracrine*](http://en.wikipedia.org/wiki/Paracrine_signalling) signals such as [retinoic acid](http://en.wikipedia.org/wiki/Retinoic_acid) target only cells in the vicinity of the emitting cell.[[6]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Duester-6) [Neurotransmitters](http://en.wikipedia.org/wiki/Neurotransmitter) represent another example of a paracrine signal. Some signaling molecules can function as both a hormone and a neurotransmitter. For example, [epinephrine](http://en.wikipedia.org/wiki/Epinephrine) and [norepinephrine](http://en.wikipedia.org/wiki/Norepinephrine) can function as hormones when released from the [adrenal gland](http://en.wikipedia.org/wiki/Adrenal_gland) and are transported to the heart by way of the blood stream. Norepinephrine can also be produced by [neurons](http://en.wikipedia.org/wiki/Neuron) to function as a neurotransmitter within the brain.[[7]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Cartford2004-7) [Estrogen](http://en.wikipedia.org/wiki/Estrogen) can be released by the [ovary](http://en.wikipedia.org/wiki/Ovary) and function as a hormone or act locally via paracrine or [autocrine](http://en.wikipedia.org/wiki/Autocrine) signaling.[[8]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Jesmin2004-8) Active species of oxygen and [nitric oxide](http://en.wikipedia.org/wiki/Nitric_oxide) can also act as cellular messengers. This process is dubbed [redox signaling](http://en.wikipedia.org/wiki/Redox_signaling).

## Cell signaling in multicellular organisms

In a multicellular organism, signaling between cells occurs either through release into the [extracellular space](http://en.wikipedia.org/wiki/Extracellular_space), divided in [paracrine](http://en.wikipedia.org/wiki/Paracrine) signaling (over short distances) and [endocrine](http://en.wikipedia.org/wiki/Endocrine) signaling (over long distances), or by direct contact, known as [juxtacrine signaling](http://en.wikipedia.org/wiki/Juxtacrine_signaling).[[9]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-9) [Autocrine](http://en.wikipedia.org/wiki/Autocrine) signaling is a special case of paracrine signaling where the secreting cell has the ability to respond to the secreted signaling molecule.[[10]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-bruce-10) [Synaptic](http://en.wikipedia.org/wiki/Synapse) signaling is a special case of paracrine signaling (for [chemical synapses](http://en.wikipedia.org/wiki/Chemical_synapse)) or juxtacrine signaling (for [electrical synapses](http://en.wikipedia.org/wiki/Electrical_synapse)) between [neurons](http://en.wikipedia.org/wiki/Neuron) and target cells. Signaling molecules interact with a target cell as a [ligand](http://en.wikipedia.org/wiki/Ligand) to [cell surface receptors](http://en.wikipedia.org/wiki/Cell_surface_receptor), and/or by entering into the cell through its [membrane](http://en.wikipedia.org/wiki/Cell_membrane) or [endocytosis](http://en.wikipedia.org/wiki/Endocytosis) for [intracrine](http://en.wikipedia.org/wiki/Intracrine) signaling. This generally results in the activation of [second messengers](http://en.wikipedia.org/wiki/Second_messenger), leading to various physiological effects.

A particular molecule is generally used in diverse modes of signaling, and therefore a classification by mode of signaling is not possible. At least three important classes of signaling molecules are widely recognized, although non-exhaustive and with imprecise boundaries, as such membership is non-exclusive and depends on the context:

* [Hormones](http://en.wikipedia.org/wiki/Hormone) are the major signaling molecules of the [endocrine system](http://en.wikipedia.org/wiki/Endocrine_system), though they often regulate each other's secretion via local signaling (e.g. [islet of Langerhans](http://en.wikipedia.org/wiki/Islet_of_Langerhans) cells), and most are also expressed in tissues for local purposes (e.g. [angiotensin](http://en.wikipedia.org/wiki/Angiotensin)) or failing that, [structurally related](http://en.wikipedia.org/wiki/Protein_family) molecules are (e.g. [PTHrP](http://en.wikipedia.org/wiki/PTHrP)).
* [Neurotransmitters](http://en.wikipedia.org/wiki/Neurotransmitter) are signaling molecules of the [nervous system](http://en.wikipedia.org/wiki/Nervous_system), also including [neuropeptides](http://en.wikipedia.org/wiki/Neuropeptide) and [neuromodulators](http://en.wikipedia.org/wiki/Neuromodulator). Neurotransmitters like the [catecholamines](http://en.wikipedia.org/wiki/Catecholamine) are also secreted by the endocrine system into the systemic circulation.
* [Cytokines](http://en.wikipedia.org/wiki/Cytokine) are signaling molecules of the [immune system](http://en.wikipedia.org/wiki/Immune_system), with a primary paracrine or juxtacrine role, though they can during significant immune responses have a strong presence in the circulation, with systemic effect (altering [iron metabolism](http://en.wikipedia.org/wiki/Iron_metabolism) or [body temperature](http://en.wikipedia.org/wiki/Body_temperature)). [Growth factors](http://en.wikipedia.org/wiki/Growth_factor) can be considered as cytokines or a different class.

Signaling molecules can belong to several chemical classes: [lipids](http://en.wikipedia.org/wiki/Lipid), [phospholipids](http://en.wikipedia.org/wiki/Phospholipid), [amino acids](http://en.wikipedia.org/wiki/Amino_acid), [monoamines](http://en.wikipedia.org/wiki/Monoamine), [proteins](http://en.wikipedia.org/wiki/Protein), [glycoproteins](http://en.wikipedia.org/wiki/Glycoprotein), or [gases](http://en.wikipedia.org/wiki/Gas). Signaling molecules binding surface receptors are generally large and [hydrophilic](http://en.wikipedia.org/wiki/Hydrophilic) (e.g. [TRH](http://en.wikipedia.org/wiki/TRH), [Vasopressin](http://en.wikipedia.org/wiki/Vasopressin), [Acetylcholine](http://en.wikipedia.org/wiki/Acetylcholine)), while those entering the cell are generally small and [hydrophobic](http://en.wikipedia.org/wiki/Hydrophobic) (e.g. [glucocorticoids](http://en.wikipedia.org/wiki/Glucocorticoid), [thyroid hormones](http://en.wikipedia.org/wiki/Thyroid_hormone), [cholecalciferol](http://en.wikipedia.org/wiki/Cholecalciferol), [retinoic acid](http://en.wikipedia.org/wiki/Retinoic_acid)), but important exceptions to both are numerous, and a same molecule can act both via surface receptor or in an intracrine manner to different effects.[[10]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-bruce-10) In intracrine signaling, once inside the cell, a signaling molecule can bind to [intracellular receptors](http://en.wikipedia.org/wiki/Intracellular_receptor), other elements, or stimulate [enzyme](http://en.wikipedia.org/wiki/Enzyme) activity (e.g. gasses). The intracrine action of [peptide hormones](http://en.wikipedia.org/wiki/Peptide_hormone) remains a subject of debate.[[11]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid10523322-11)

[Hydrogen sulfide](http://en.wikipedia.org/wiki/Hydrogen_sulfide) is produced in small amounts by some cells of the human body and has a number of biological signaling functions. Only two other such gases are currently known to act as signaling molecules in the human body: [nitric oxide](http://en.wikipedia.org/wiki/Nitric_oxide) and [carbon monoxide](http://en.wikipedia.org/wiki/Carbon_monoxide)

## Receptors for cell motility and differentiation

Cells receive information from their neighbors through a class of proteins known as [receptors](http://en.wikipedia.org/wiki/Receptor_%28biochemistry%29). [Notch](http://en.wikipedia.org/wiki/Notch_signaling_pathway) is a cell surface protein that functions as a receptor. Animals have a small set of [genes](http://en.wikipedia.org/wiki/Gene) that code for signaling proteins that interact specifically with Notch receptors and stimulate a response in cells that express Notch on their surface. Molecules that activate (or, in some cases, inhibit) receptors can be classified as hormones, [neurotransmitters](http://en.wikipedia.org/wiki/Neurotransmitters), [cytokines](http://en.wikipedia.org/wiki/Cytokines), and [growth factors](http://en.wikipedia.org/wiki/Growth_factors), but all of these are called [receptor ligands](http://en.wikipedia.org/wiki/Ligand_%28biochemistry%29). The details of ligand-receptor interactions are fundamental to cell signaling.[*[citation needed](http://en.wikipedia.org/wiki/Wikipedia%3ACitation_needed%22%20%5Co%20%22Wikipedia%3ACitation%20needed)*]

As shown in Figure 2 (above, left), [notch](http://en.wikipedia.org/wiki/Notch_signaling_pathway) acts as a receptor for ligands that are expressed on adjacent cells. While some receptors are cell surface proteins, others are found inside cells. For example, [estrogen](http://en.wikipedia.org/wiki/Estrogen) is a [hydrophobic](http://en.wikipedia.org/wiki/Hydrophobic) molecule that can pass through the [lipid bilayer](http://en.wikipedia.org/wiki/Lipid_bilayer) of the [membranes](http://en.wikipedia.org/wiki/Cell_membrane). As part of the [endocrine system](http://en.wikipedia.org/wiki/Endocrine_system), intracellular [Estrogen receptors](http://en.wikipedia.org/wiki/Estrogen_receptor) from a variety of cell types can be activated by estrogen produced in the [ovaries](http://en.wikipedia.org/wiki/Ovary).

A number of transmembrane receptors[[13]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-13)[[14]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-14) for small molecules and peptide hormones[[15]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-15) as well as intracellular receptors for steroid hormones exist, giving cells the ability to respond to a great number of hormonal and pharmacological stimuli. In diseases, often, proteins that interact with receptors are aberrantly activated, resulting in constitutively activated downstream signals.[[16]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid19382224-16)

For several types of intercellular signaling molecules that are unable to permeate the hydrophobic cell membrane due to their hydrophilic nature, the target receptor is expressed on the membrane. When such signaling molecule activates its receptor, the signal is carried into the cell usually by means of a second messenger such as [cAMP](http://en.wikipedia.org/wiki/Cyclic_adenosine_monophosphate).[[17]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-17)[[18]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid18200529-18)

## Signaling pathways

In some cases, receptor activation caused by ligand binding to a receptor is directly coupled to the cell's response to the ligand. For example, the neurotransmitter [GABA](http://en.wikipedia.org/wiki/GABA) can activate a cell surface receptor that is part of an [ion channel](http://en.wikipedia.org/wiki/Ion_channel). GABA binding to a [GABA A receptor](http://en.wikipedia.org/wiki/GABA_A_receptor) on a neuron opens a [chloride](http://en.wikipedia.org/wiki/Chloride)-selective ion channel that is part of the receptor. GABA A receptor activation allows negatively-charged chloride ions to move into the neuron, which inhibits the ability of the neuron to produce [action potentials](http://en.wikipedia.org/wiki/Action_potential). However, for many cell surface receptors, ligand-receptor interactions are not directly linked to the cell's response. The activated receptor must first interact with other proteins inside the cell before the ultimate [physiological](http://en.wikipedia.org/wiki/Physiology) effect of the ligand on the cell's behavior is produced. Often, the behavior of a chain of several interacting cell proteins is altered following receptor activation. The entire set of cell changes induced by receptor activation is called a [signal transduction](http://en.wikipedia.org/wiki/Signal_transduction) mechanism or pathway.[[19]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-19)

In the case of Notch-mediated signaling, the signal transduction mechanism can be relatively simple. As shown in Figure 2 (above, left), activation of Notch can cause the Notch protein to be altered by a [protease](http://en.wikipedia.org/wiki/Protease). Part of the Notch protein is released from the cell surface membrane and takes part in [gene regulation](http://en.wikipedia.org/wiki/Gene_regulation). Cell signaling research involves studying the spatial and temporal dynamics of both receptors and the components of signaling pathways that are activated by receptors in various cell types.[*[citation needed](http://en.wikipedia.org/wiki/Wikipedia%3ACitation_needed%22%20%5Co%20%22Wikipedia%3ACitation%20needed)*]

A more complex signal transduction pathway is shown in Figure 3. This pathway involves changes of [protein-protein interactions](http://en.wikipedia.org/wiki/Protein-protein_interaction) inside the cell, induced by an external signal. Many growth factors bind to receptors at the cell surface and stimulate cells to progress through the [cell cycle](http://en.wikipedia.org/wiki/Cell_cycle) and [divide](http://en.wikipedia.org/wiki/Cell_division). Several of these receptors are [kinases](http://en.wikipedia.org/wiki/Kinase) that start to phosphorylate themselves and other proteins when binding to a ligand. This [phosphorylation](http://en.wikipedia.org/wiki/Phosphorylation) can generate a binding site for a different protein and thus induce [protein-protein interaction](http://en.wikipedia.org/wiki/Protein-protein_interaction). In Figure 3, the ligand (called [epidermal growth factor](http://en.wikipedia.org/wiki/Epidermal_growth_factor) (EGF)) binds to the receptor (called [EGFR](http://en.wikipedia.org/wiki/Epidermal_growth_factor_receptor)). This activates the receptor to phosphorylate itself. The phosphorylated receptor binds to an [adaptor protein](http://en.wikipedia.org/wiki/Adaptor_protein) (GRB2), which couples the signal to further downstream signaling processes. For example, one of the signal transduction pathways that are activated is called the mitogen-activated protein kinase ([MAPK](http://en.wikipedia.org/wiki/MAPK)) pathway. The signal transduction component labeled as "MAPK" in the pathway was originally called "ERK," so the pathway is called the [MAPK/ERK pathway](http://en.wikipedia.org/wiki/MAPK/ERK_pathway). The MAPK protein is an enzyme, a [protein kinase](http://en.wikipedia.org/wiki/Protein_kinase) that can attach [phosphate](http://en.wikipedia.org/wiki/Phosphate) to target proteins such as the [transcription factor](http://en.wikipedia.org/wiki/Transcription_factor) [MYC](http://en.wikipedia.org/wiki/C-myc) and, thus, alter gene transcription and, ultimately, cell cycle progression. Many cellular proteins are activated downstream of the growth factor receptors (such as EGFR) that initiate this signal transduction pathway.[*[citation needed](http://en.wikipedia.org/wiki/Wikipedia%3ACitation_needed%22%20%5Co%20%22Wikipedia%3ACitation%20needed)*]

Some signaling transduction pathways respond differently, depending on the amount of signaling received by the cell. For instance, the [hedgehog protein](http://en.wikipedia.org/wiki/Hedgehog_%28cell_signaling%29) activates different genes, depending on the amount of hedgehog protein present.[*[citation needed](http://en.wikipedia.org/wiki/Wikipedia%3ACitation_needed%22%20%5Co%20%22Wikipedia%3ACitation%20needed)*]



## Complex multi-component signal transduction pathways provide opportunities for feedback, signal amplification, and interactions inside one cell between multiple signals and signaling pathwaIntraspecies and interspecies signaling

Molecular signaling can occur between different organisms, whether [unicellular](http://en.wikipedia.org/wiki/Unicellular) or multicellular, the emitting organism produces the signaling molecule, secrete it into the environment, where it diffuses, and it is sensed or internalized by the receiving organism. In some cases of interspecies signaling, the emitting organism can actually be a [host](http://en.wikipedia.org/wiki/Host_%28biology%29) of the receiving organism, or vice-versa.

Intraspecies signaling occurs especially in [bacteria](http://en.wikipedia.org/wiki/Bacteria), [yeast](http://en.wikipedia.org/wiki/Yeast), [social insects](http://en.wikipedia.org/wiki/Social_insect), but also many [vertebrates](http://en.wikipedia.org/wiki/Vertebrate). The signaling molecules used by multicellular organisms are often called [pheromones](http://en.wikipedia.org/wiki/Pheromone), they can have such purposes as alerting against danger, indicating food supply, or assisting in reproduction.[[20]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-20) In unicellular organisms such as bacteria, signaling can be used to 'activate' peers from a [dormant state](http://en.wikipedia.org/wiki/Dormancy), enhance [virulence](http://en.wikipedia.org/wiki/Virulence), defend against [bacteriophages](http://en.wikipedia.org/wiki/Bacteriophage), etc.[[21]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid9671779-21) In [quorum sensing](http://en.wikipedia.org/wiki/Quorum_sensing), which is also found in social insects, the multiplicity of individual signals has the potentiality to create a positive feedback loop, generating coordinated response, in this context the signaling molecules are called [autoinducers](http://en.wikipedia.org/wiki/Autoinducer).[[22]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-miller-22)[[23]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid15908344-23)[[24]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid16497924-24) This phenomenon is similar to the autocrine co-stimulation of multicellular organisms, on the other hand [cellular differentiation](http://en.wikipedia.org/wiki/Cellular_differentiation) occurs in bacteria, with altered response to peer signals, demonstrating a similarity with paracrine signaling of multicellular organisms.[[25]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-25) This signaling mechanism may have been involved in [evolution](http://en.wikipedia.org/wiki/Evolution) from unicellular to multicellular organisms.[[22]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-miller-22)[[26]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid10343281-26) Bacteria also use contact-dependent signaling, notably to limit their growth.[[27]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid16109881-27)[[28]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid19246237-28)

Molecular signaling can also occur between individuals of different species, this has been particularly studied in bacteria.[[29]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid19251475-29)[[30]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-30)[[31]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid21227698-31) Different bacterial species can coordinate to colonize a host and participate in common quorum sensing.[[32]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid14739337-32) Therapeutic strategies to disrupt this phenomenon are being investigated.[[33]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid14597753-33)[[34]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Sperandio-34) Interactions mediated through signaling molecules are also thought to occur between the [gut flora](http://en.wikipedia.org/wiki/Gut_flora) and their host, as part of their [commensal](http://en.wikipedia.org/wiki/Commensal) or [symbiotic](http://en.wikipedia.org/wiki/Symbiotic) relationship.[[34]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-Sperandio-34)[[35]](http://en.wikipedia.org/wiki/Cell_signaling#cite_note-pmid11352068-35)

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