

Lecture 10 Cell communication Part one

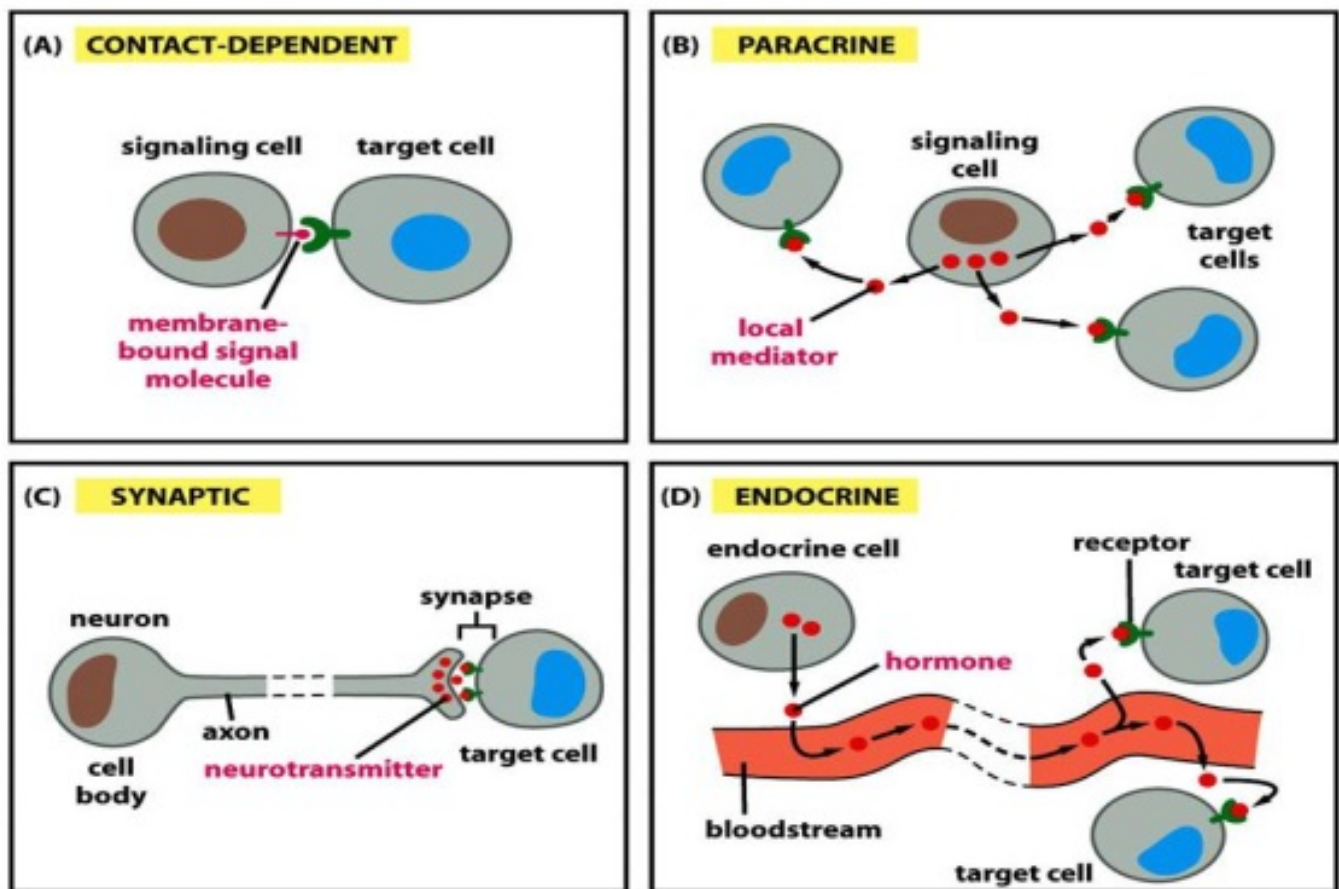
Quorum sensing in bacteria(群体感应现象) A Nice video to introduce [anglerfish](#)

##1. Overview of cell communication

- CELL-SURFACE receptors
- INTRACELLULAR receptors

What is the difference between ligand and receptor?

Here are Cell-Cell contact, Synaptic (fast), Paracrine(旁分泌)/autocrine 自分泌 (local environment) , endocrine 内分泌 (long distance)



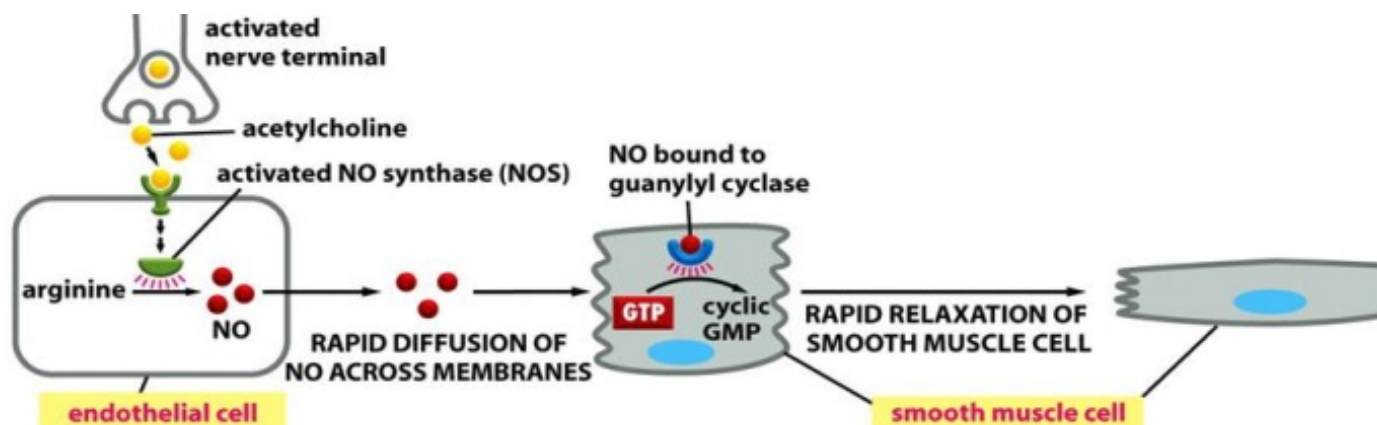
Effects in signaling can be fast and slow. Protein synthesis is slow, but protein behavior is fast. The same signals trigger different effects, which include same signal in different receptors, same signal and receptor but different effector, same signal but vary concentration(morphogen).

Cell is programmed to respond to specific combinations of signals. If deprived of appropriate survival signals, a cell will undergo a form of cell suicide known as apoptosis.

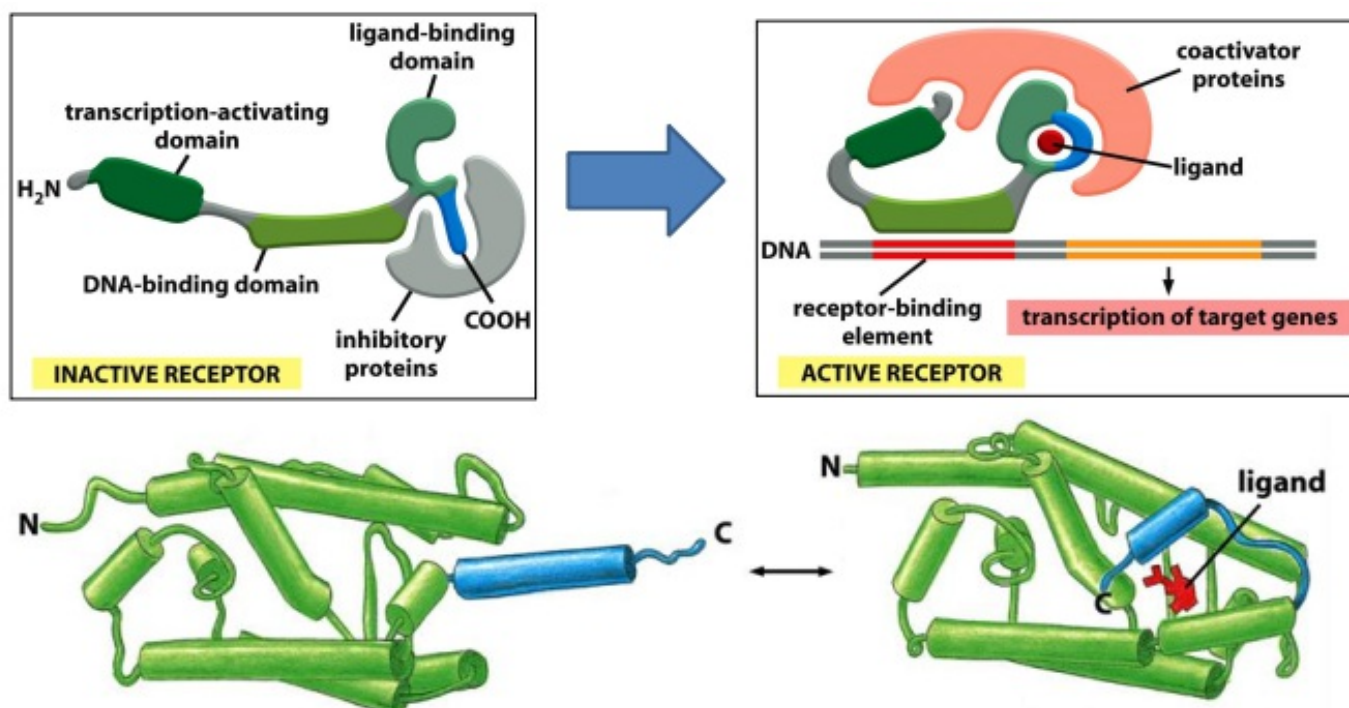
To ensure quicker response, many proteins in signaling have short half lives, which have faster turn over rate react.

2. Intracellular receptors

Signaling of NO in smooth muscle can relaxate blood vessel. NO's half life is 5-10 sec, which convert salt by water and O₂. So nitroglycerin is used to treat angina pectoris 心绞痛, which increase cGMP to dilate of blood vessel. And Viagra (Sildenafil) can inhibit cGMP degradation.



Signaling via nuclear receptor. Here are steroid hormones, Thyroid hormone, Retinoids 维生素A。Nuclear receptors work either as homodimer or heterodimer. Serve both as ligand receptor and gene transcription factor. Hormone receptors can trigger both primary and secondary responses.

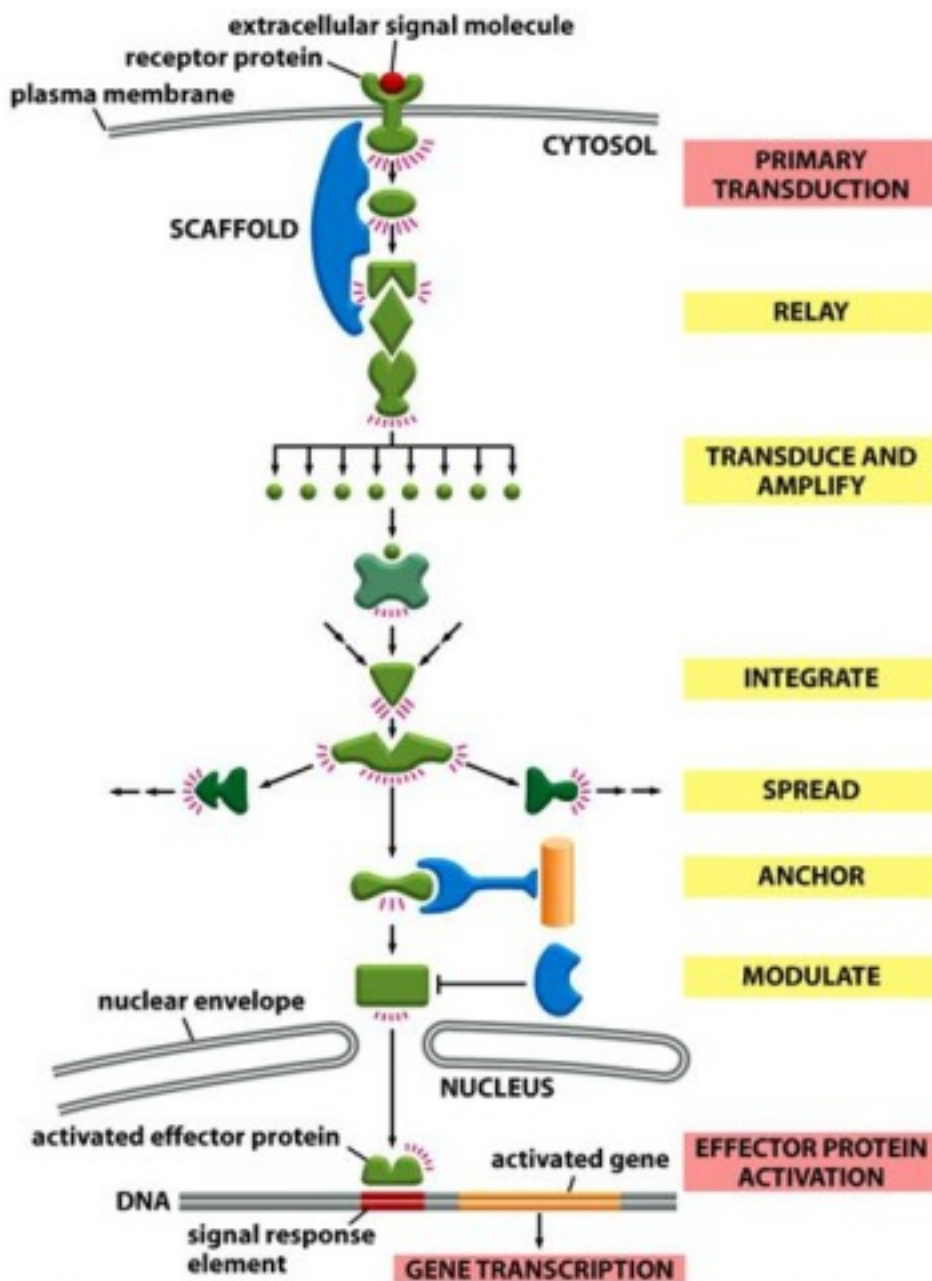


3. General principles of cell surface signaling

These are three major classes of cell surface receptors, ion-channel-coupled receptors, G-Protein-Coupled Receptor, Enzyme-Coupled Receptor.

The first messenger is extracellular signals. And the second messenger is small molecules generated in larger number after receptor activation. They are either hydrophilic or lipid diffusing, which work on effector proteins and relay signals. Such as, cAMP, cGMP, Ca^{2+} , diacylglycerol(DAG 甘油二酯), Inositol triphosphate(IP3 肌醇三磷酸)。

Intracellular signaling proteins can: **relay** signals to the next component, act as a **scaffold** to bring two signaling proteins more quickly and efficiently, **transform** the signal into a different form, **Amplify** the signal it receives---signal cascade 瀑布, **Integrate** signals from two or more pathways, Spread signals from one pathway to another--**crosstalk**, **Anchor** signaling proteins to a specific structure. **Modulate** the activity of signaling proteins.



Protein phosphorylation, GTP-binding, cAMP or Ca^{2+} binding, Ubiquitination are important types of switch to regulate protein activity.

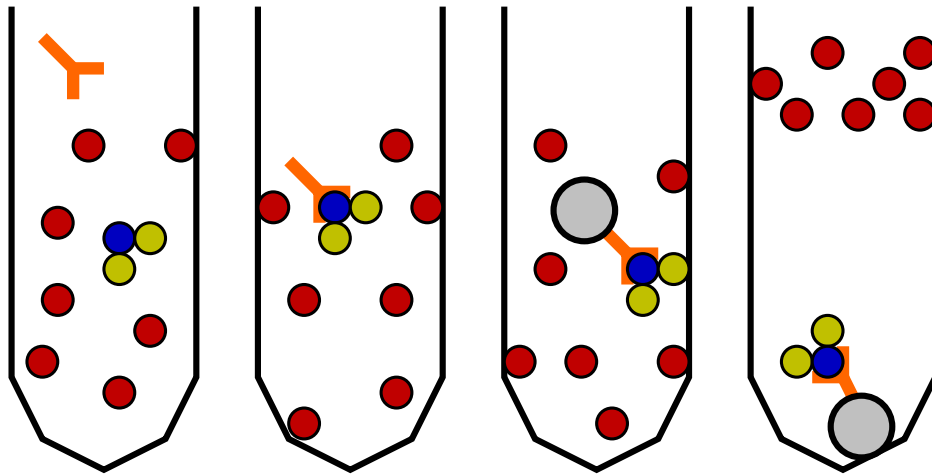
Protein phosphorylation is one major way of post-translational modification to regulate protein activity. Here are two categories: Serine/Threonine kinase and Tyrosine kinase. Protein kinases are major therapeutic targets in human diseases. Signaling protein itself is a kinase which can phosphorylate and activate downstream effectors--- Phosphorylation cascade.

GTP-binding proteins(G-proteins)

To achieve high speed and specificity in signaling.

- Preformed signaling complex on a scaffold protein.
- Assembly of signaling complex on an activated receptor.
- Assembly of signaling complex on phosphoinositide docking sites.

4. Several methods to study cell signaling



1. Researcher adds antibody.
2. Antibody binds target.
3. Protein A beads bind antibody.
4. Centrifugation sediments beads.

Protein co-immunoprecipitation

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5. Positive and negative feedback in signaling and signaling kinetics
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