Bio Molecular Systems
Pacific Northwest National Laboratory
Operated by Battelle for the U.S. Department of Energy

Washington State University Tri-Cities

Cell Information

How do cells talk to each other and what do they say?

Lecture 6

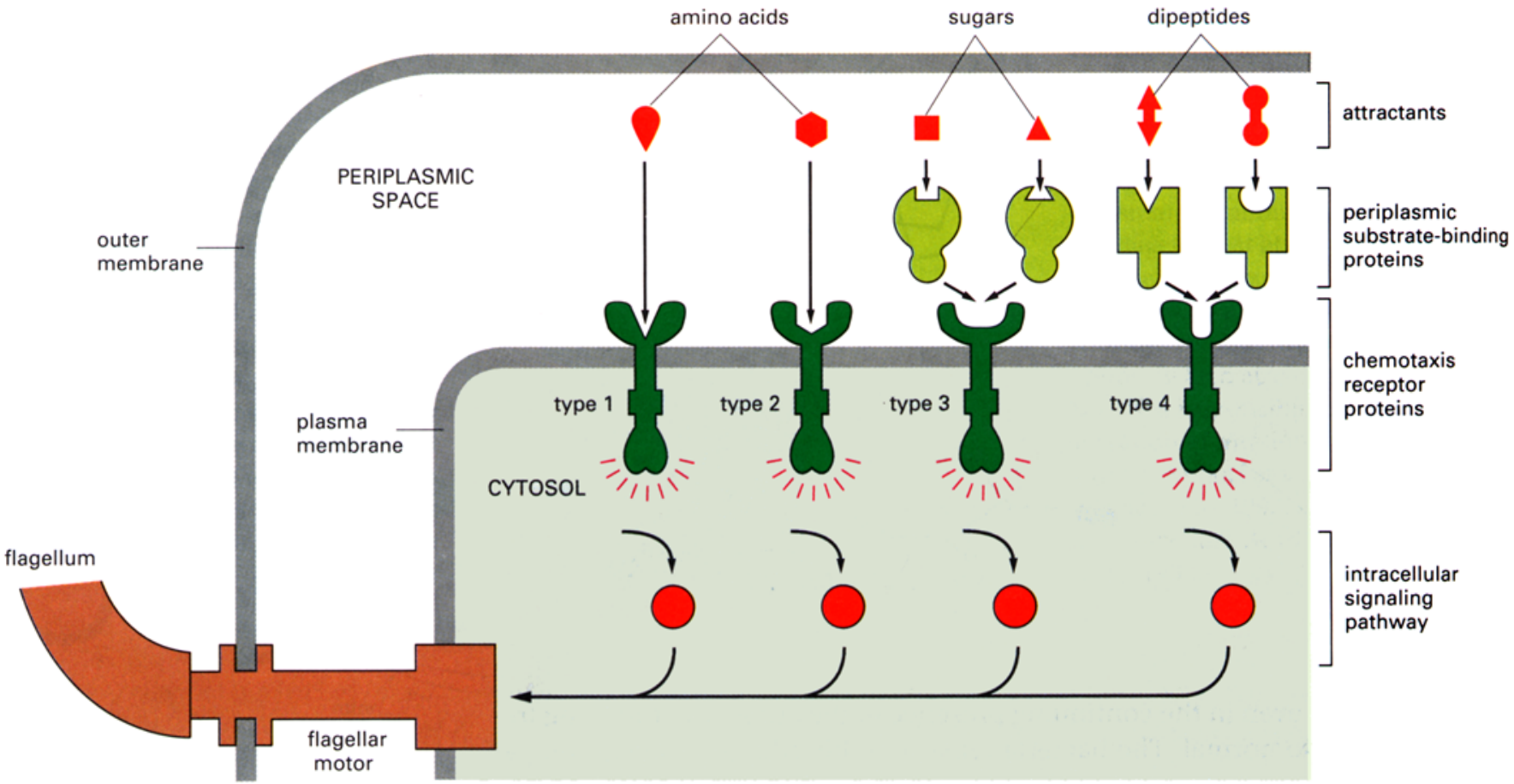
Information processing by cells

- Two types of information available
  - Direct physical aspects of the environment
  - Symbolic information encoded by other cells
- Analogous to physical senses versus social communication

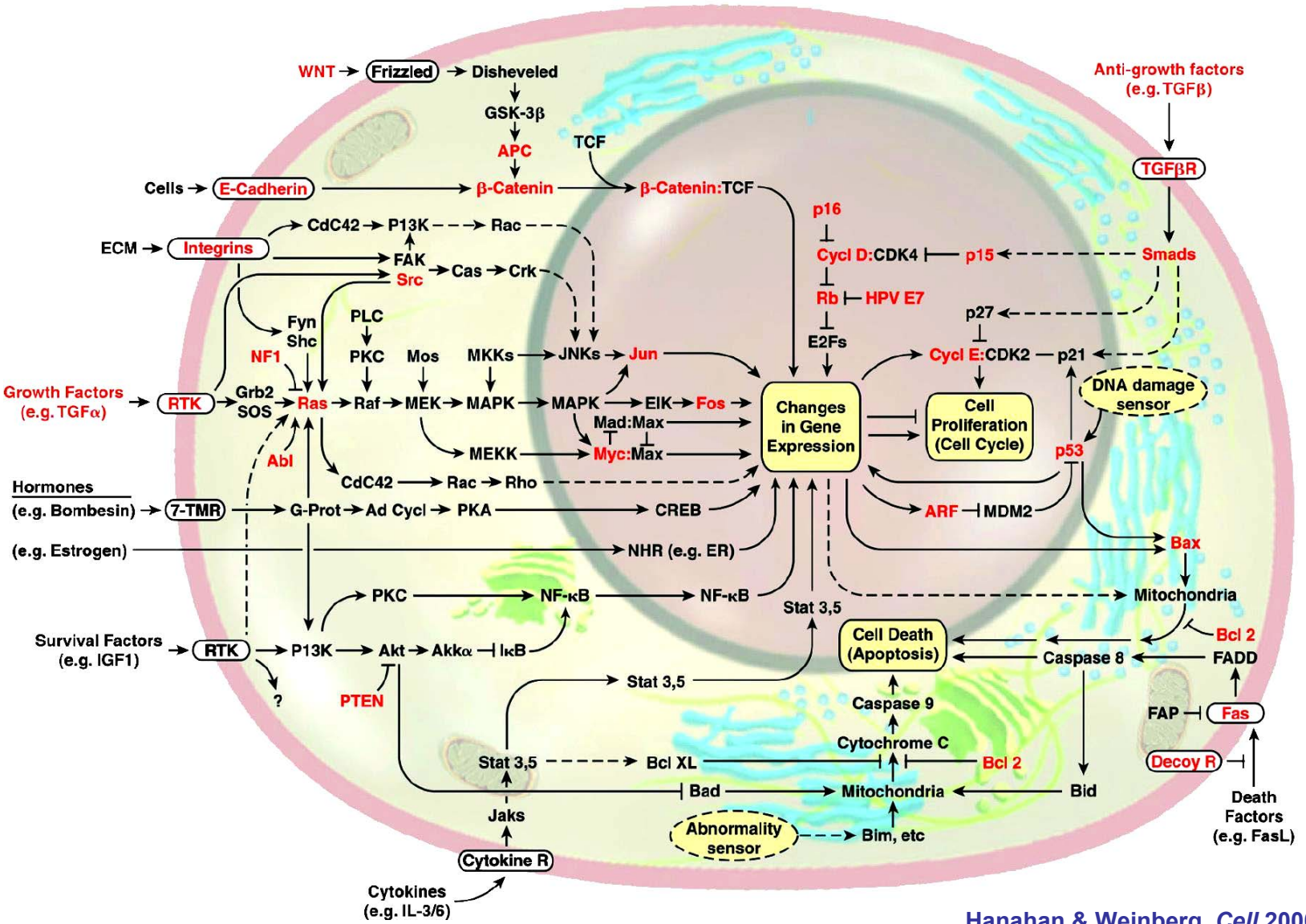
Symbolic information is required for multicellular organisms

- Bacteria (unicellular organisms) sense their environment and change their behavior (i.e. chemotaxis).
- To coordinate the behavior of populations of cells, cells in multicellular organisms must exchange data.
- There are exceptions to all rules. How much do bacterial communities talk to each other?

Environmental sensing in bacteria



Networks of proteins mediate cell signaling



Hanahan & Weinberg, *Cell* 2000
"Hallmarks of Cancer"

Terminology
(names for cell signals)

- Hormone – circulating, global regulator made by endocrine glands
- Growth factor - polypeptide that promotes cell growth and/or proliferation
- Cytokine - general term for a growth factor, derived from immunology
- Chemokine - small factor involved in cell attraction and migration

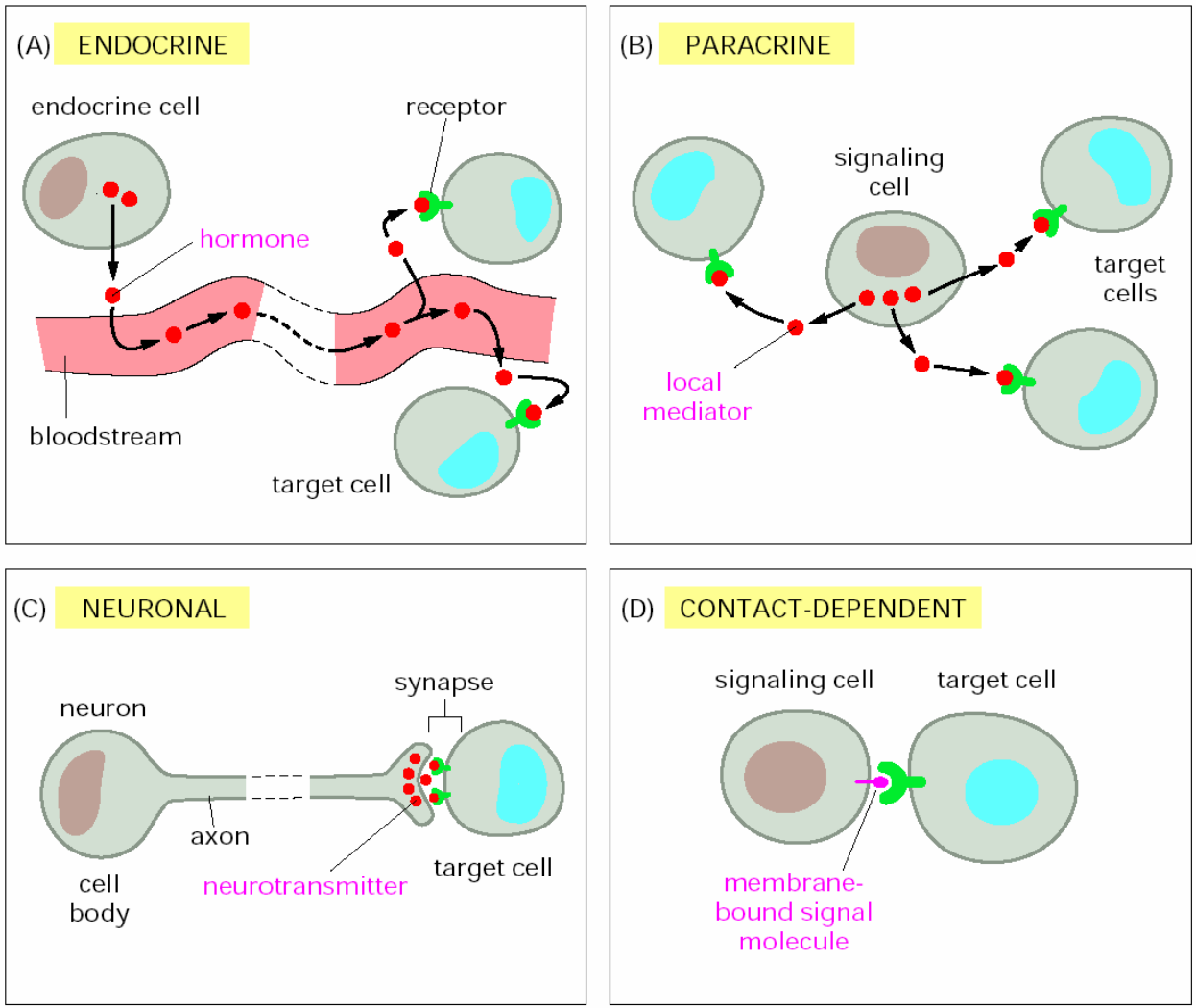
What types of information do cells exchange?

- Global - What is going on within the organism?
- Local - What is going on between cells?
- Coordination - Make sure different parts work together

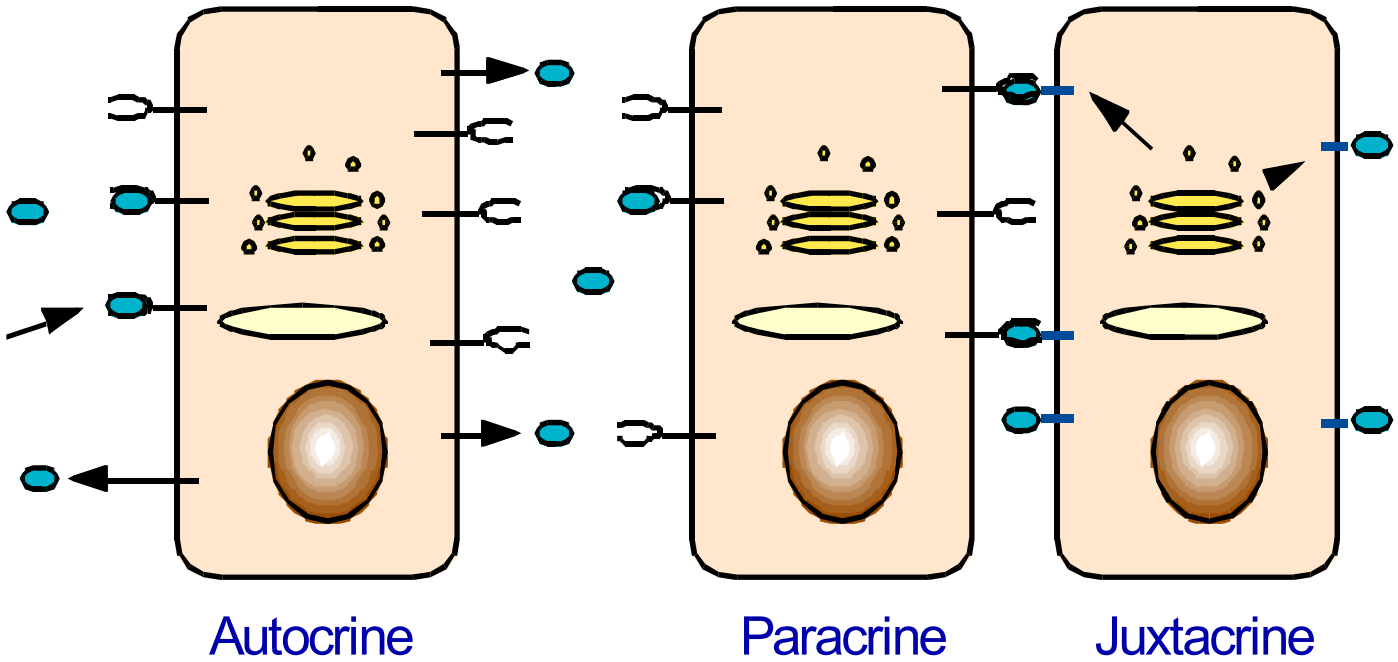
The types of information constrain the system

- You can infer a lot about a system by looking at its physical properties
  - For example: Can't communicate *spatial* information by a factor that can't be *localized*
  - The *kinetics* of the system are appropriate to the *time-scale* of the controlled process

Modes of signaling



Different modes of ligand presentation

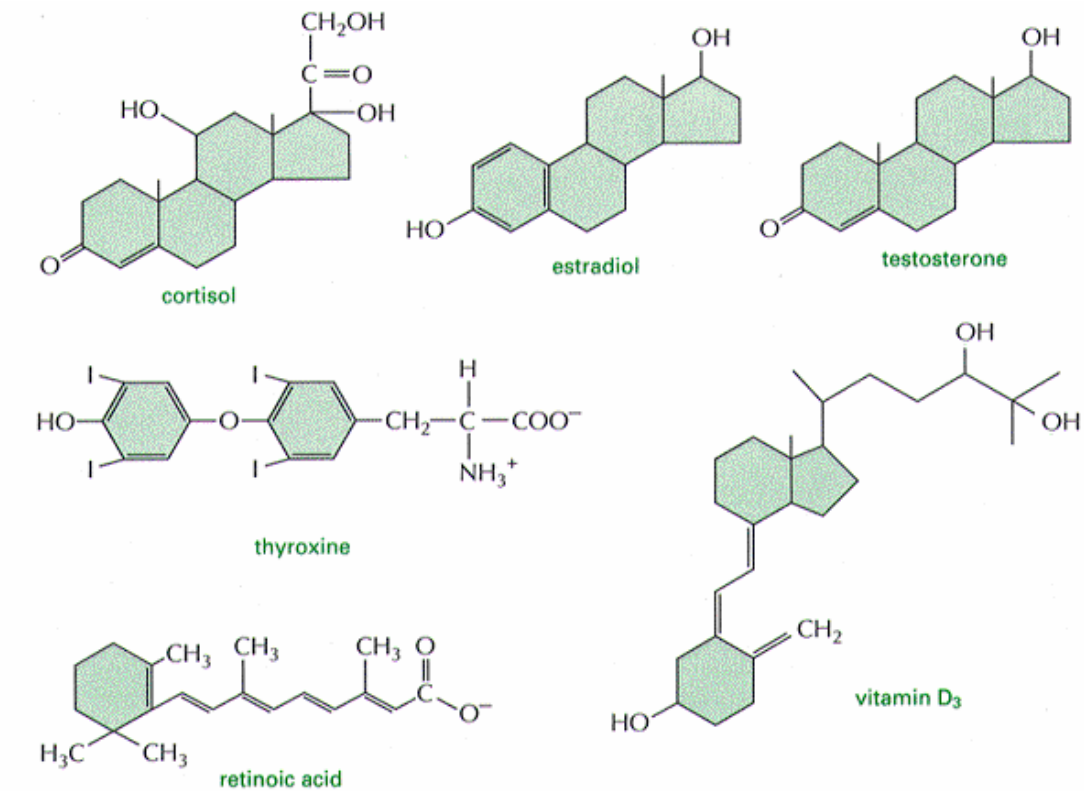


Hormones

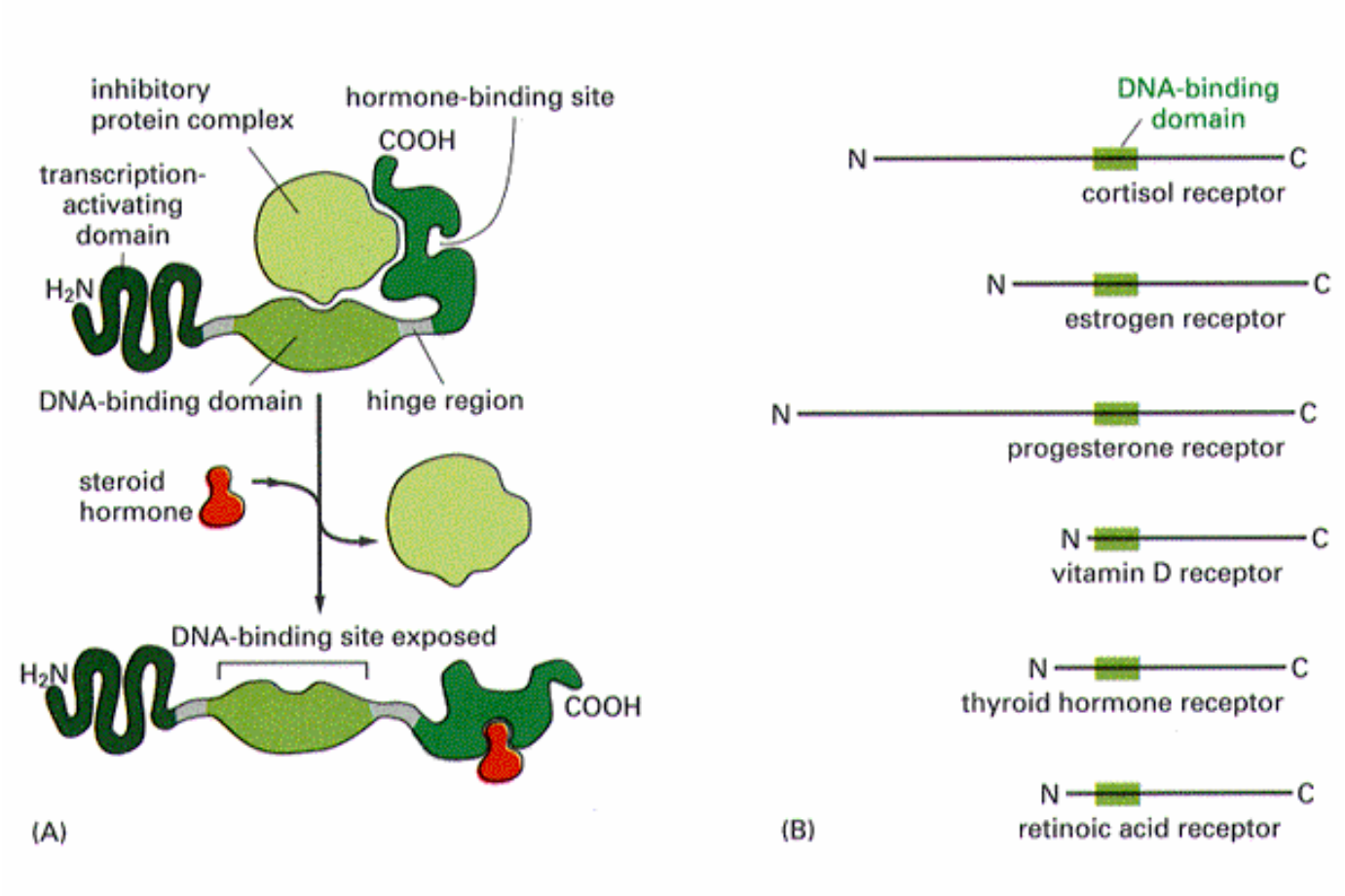
- Convey important information to the entire organism
- Work in the cell nucleus (transcriptional level) or at the cell surface
- In general, nuclear is slow, surface is fast
- Information can be encoded in the pattern (changing rates) of production as well as level (concentration)

Intracellular receptors

Ligands that bind to intracellular receptors



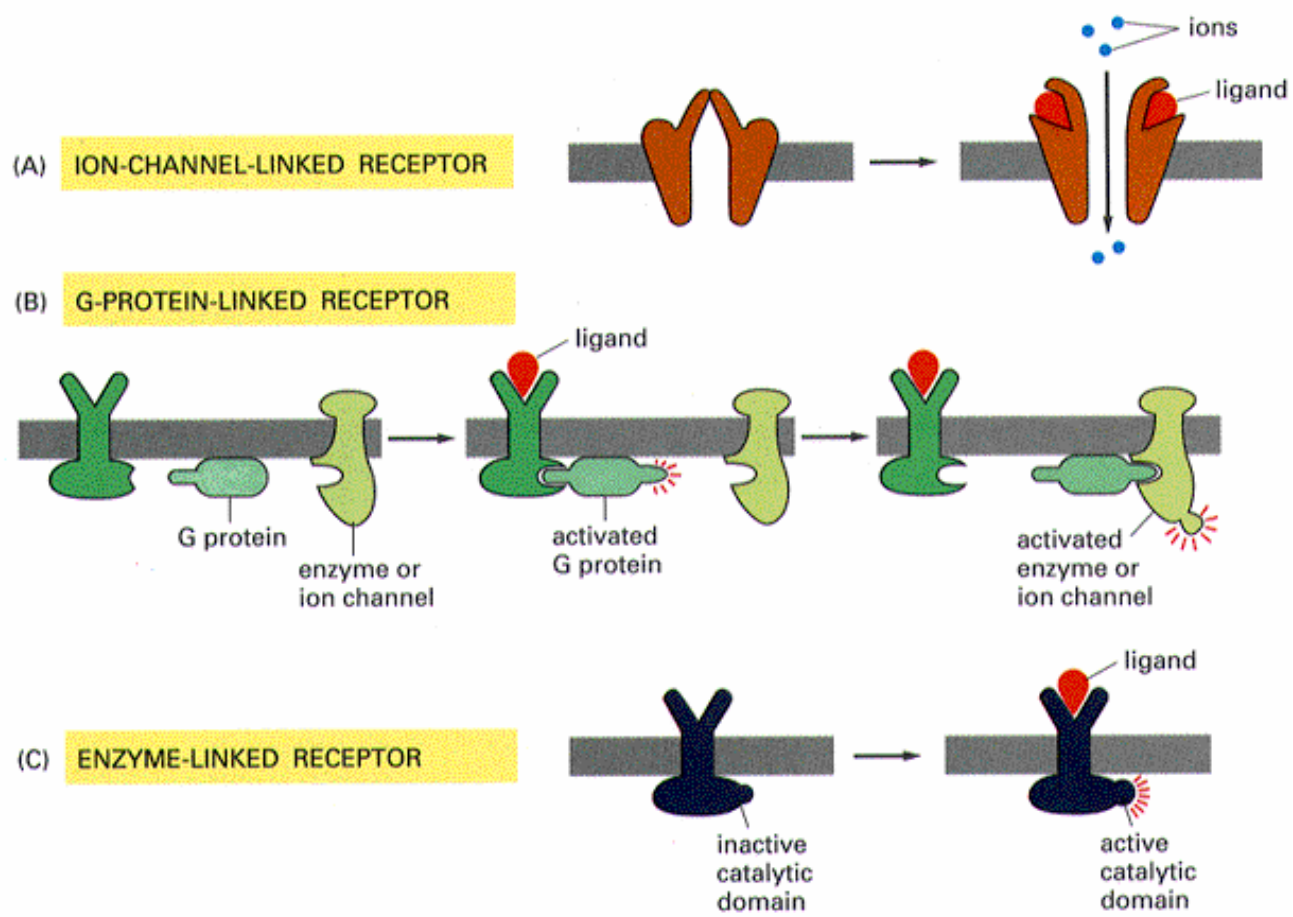
Activation of steroid receptors (nuclear level)



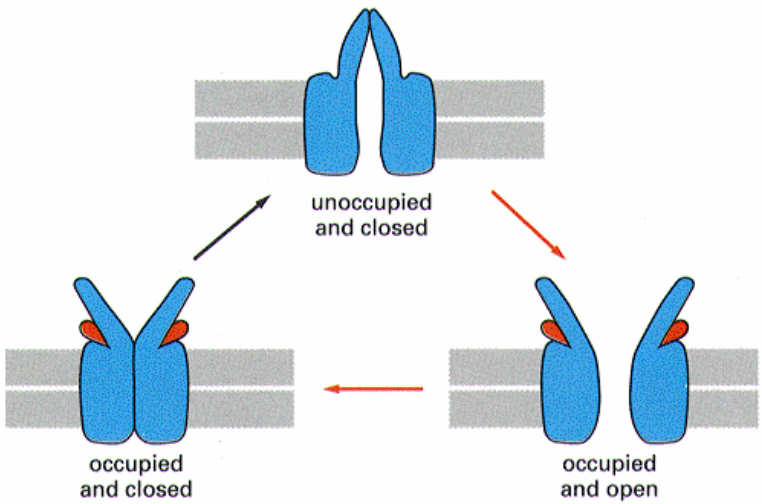
Cell-surface receptors

- This receptor class is spatially restricted, and can therefore convey information on signal source
- There are three known classes of cell-surface receptor proteins
  A) ion channel-linked
  B) *G* protein-linked (or, *G* protein-coupled)
  C) enzyme-linked

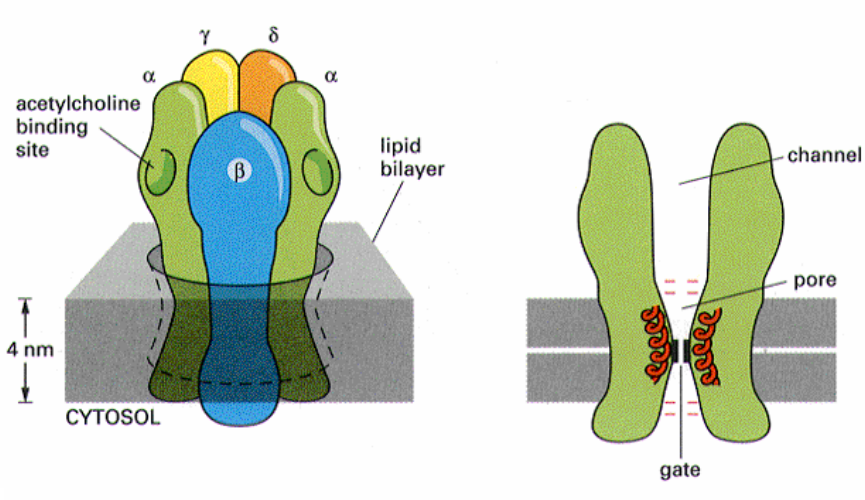
Three types of cell-surface receptors



A) Ion channel-linked receptors

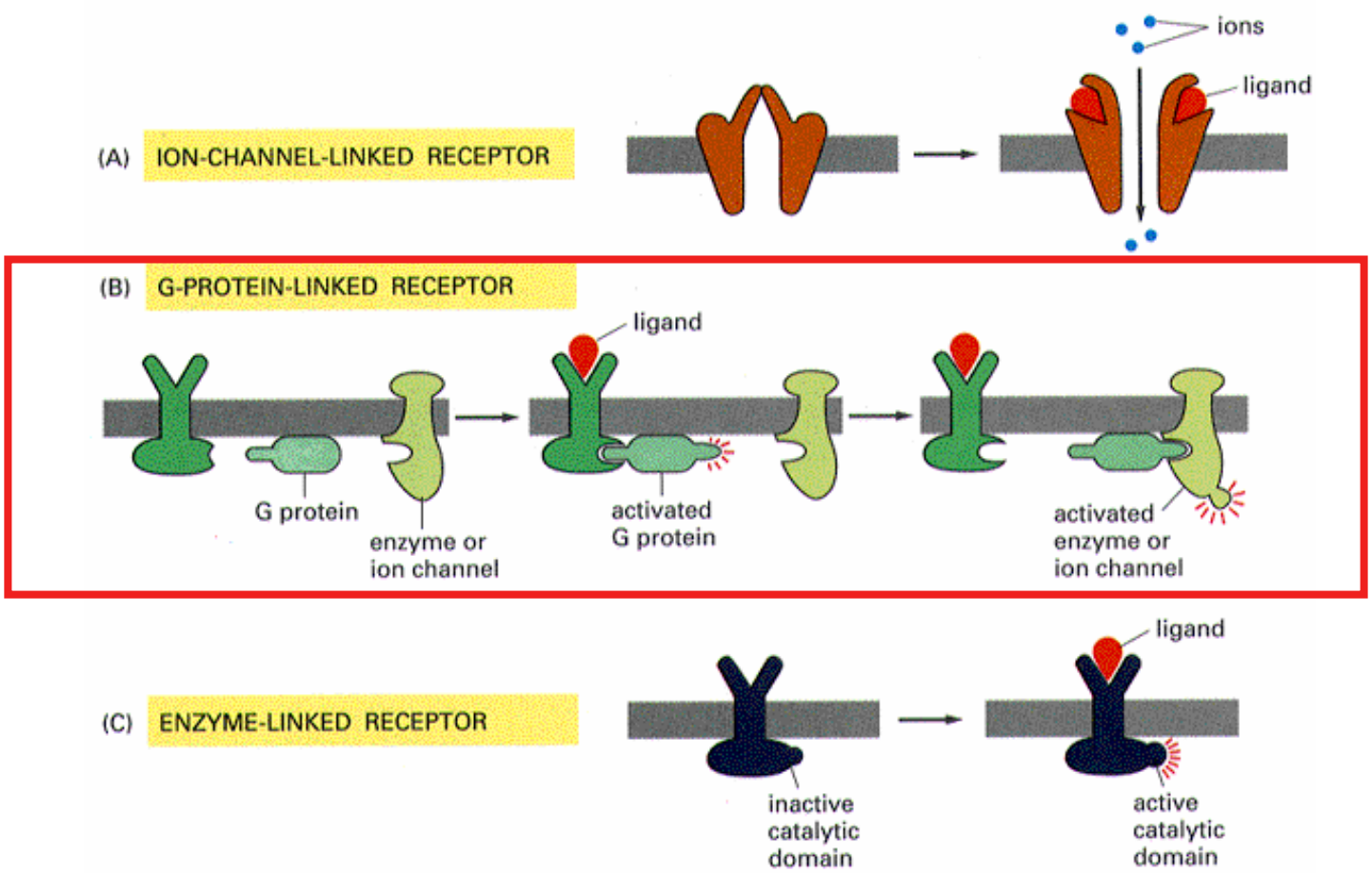


Example: acetylcholine receptor

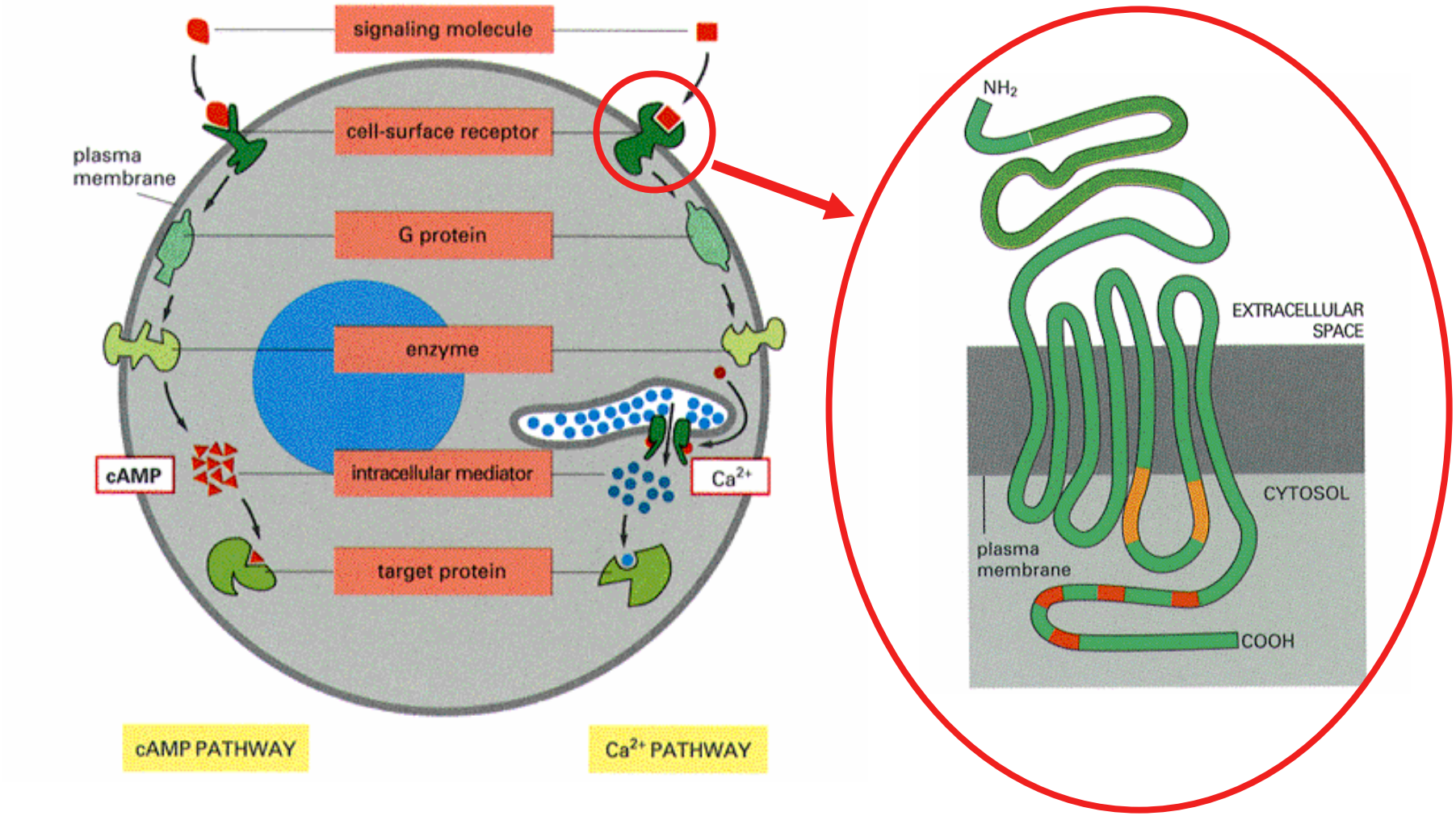


Structure and mechanism

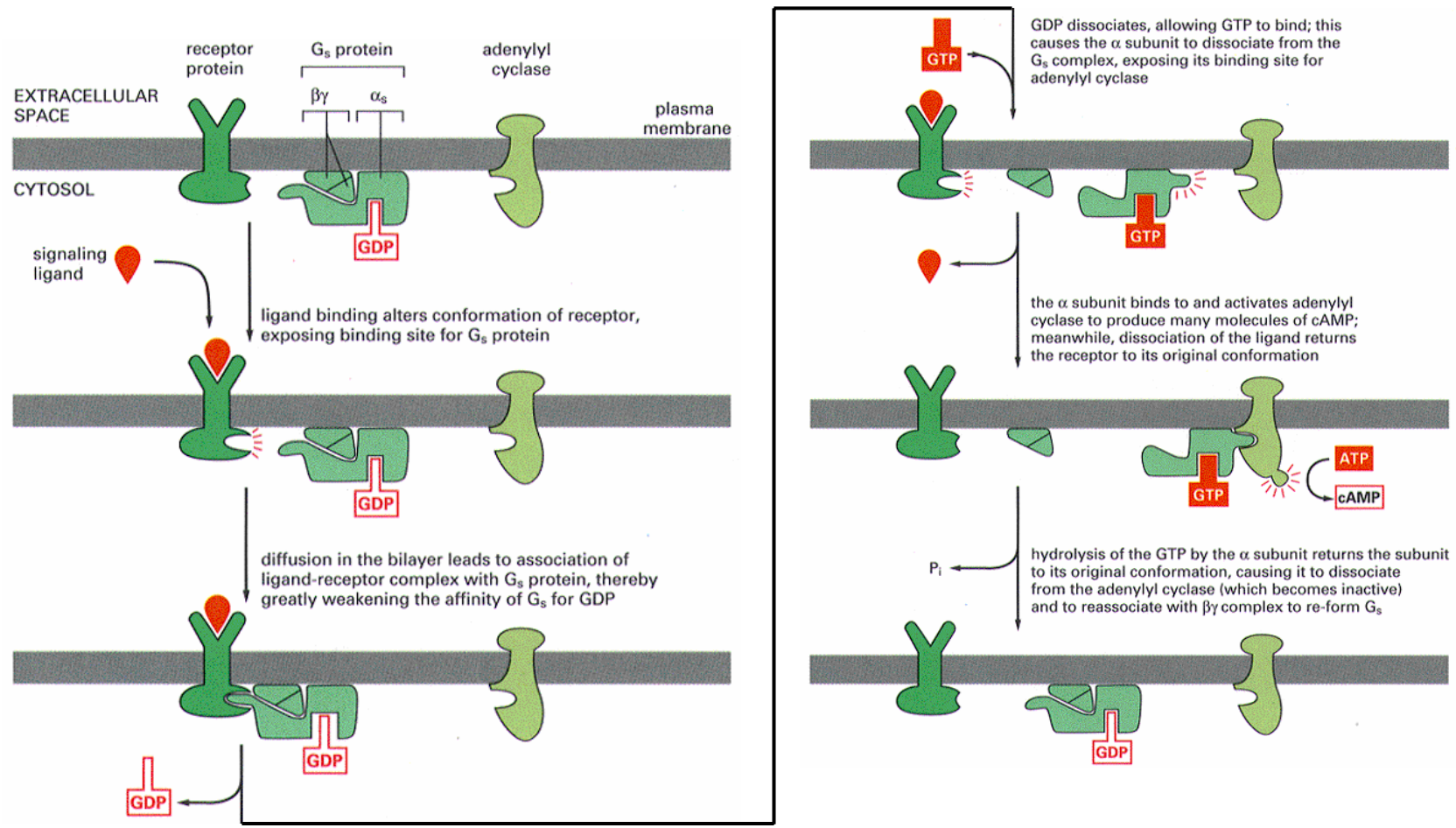
Three types of cell-surface receptors



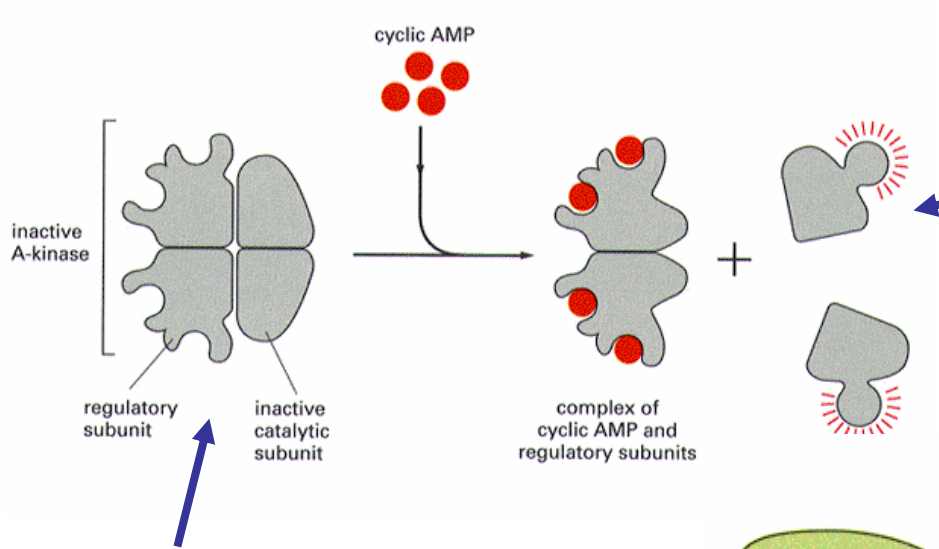
B) G protein-coupled receptors (GPCR)



Mechanisms of GPCR action

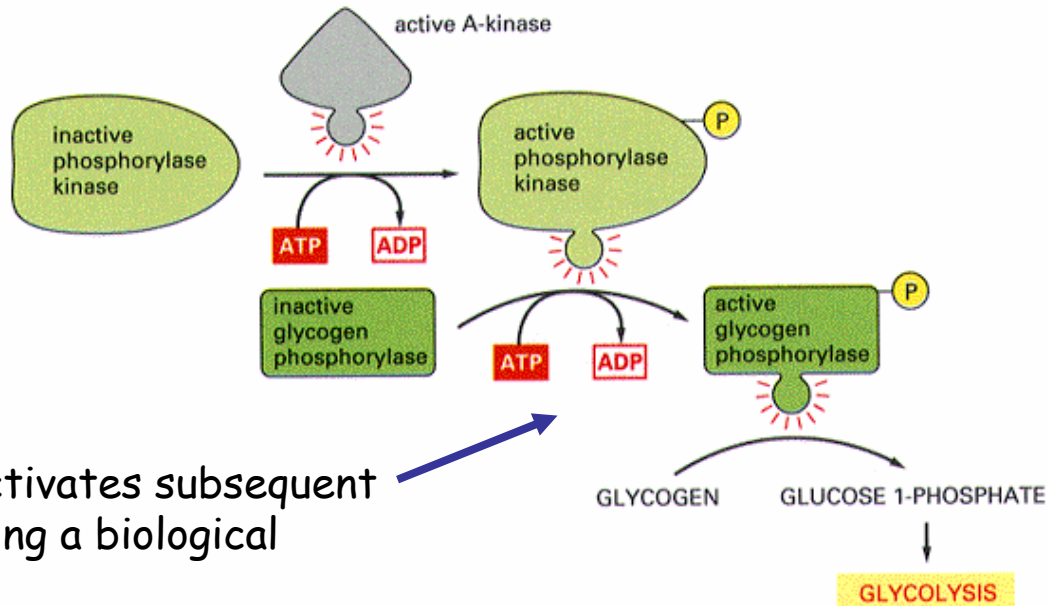


Activation of the cAMP signal cascade



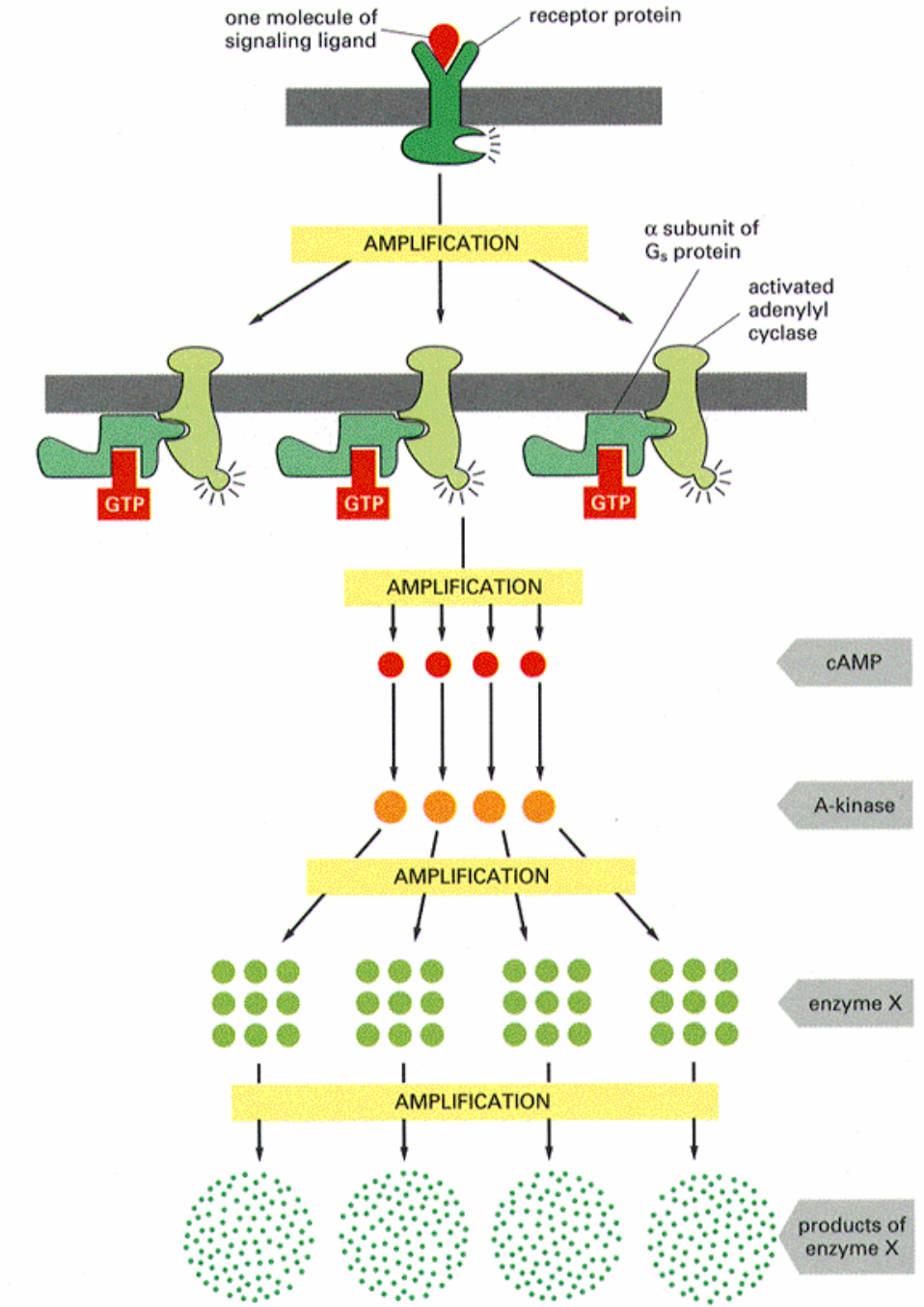
cAMP causes the dissociation of the catalytic subunits, which activates the kinase

cAMP-dependent protein kinase (A-kinase is initially in an inactive protein complex, shown here)

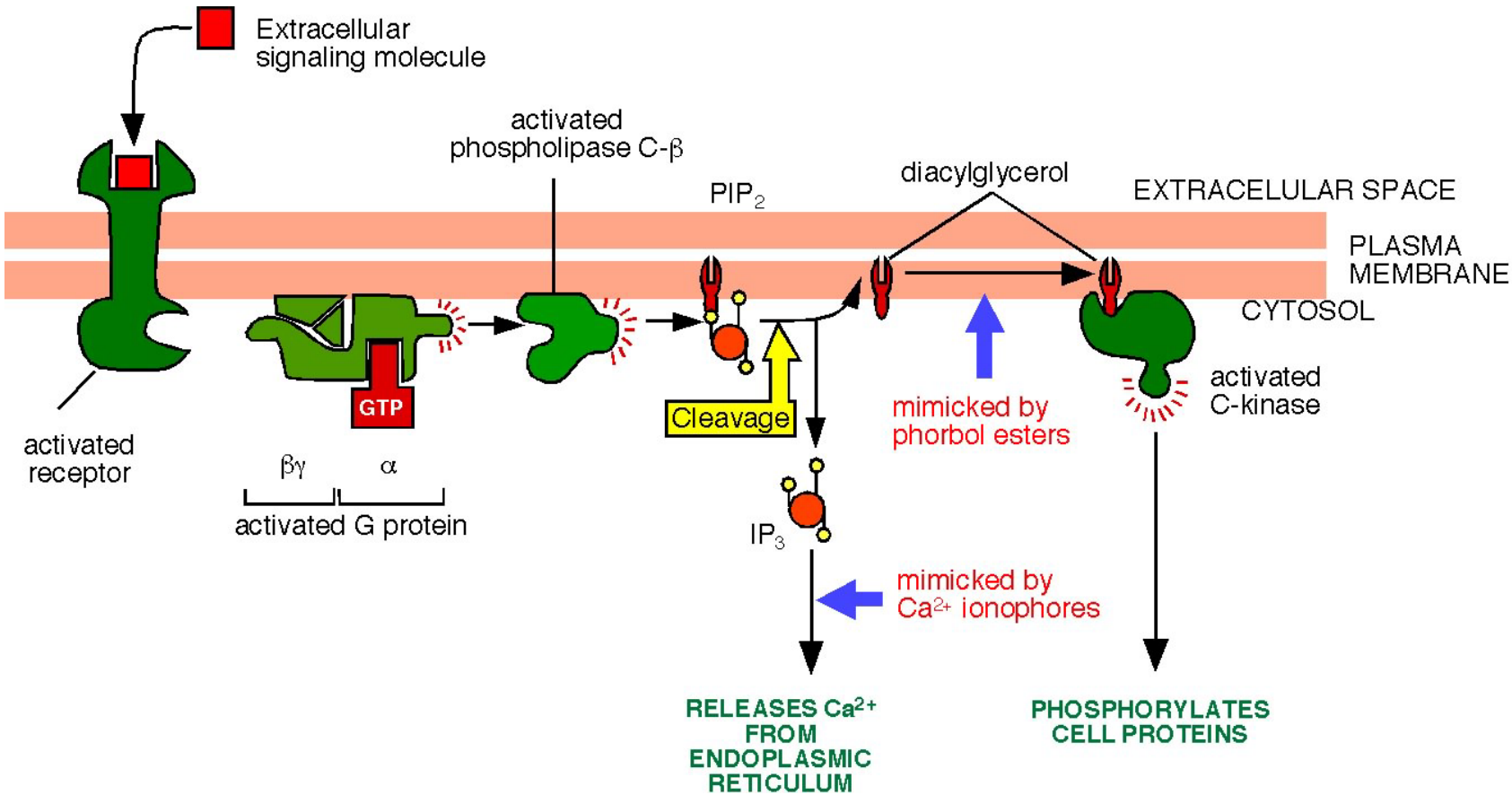


The activation of the first kinase activates subsequent kinases/enzymes, eventually activating a biological response (here, glycolysis)

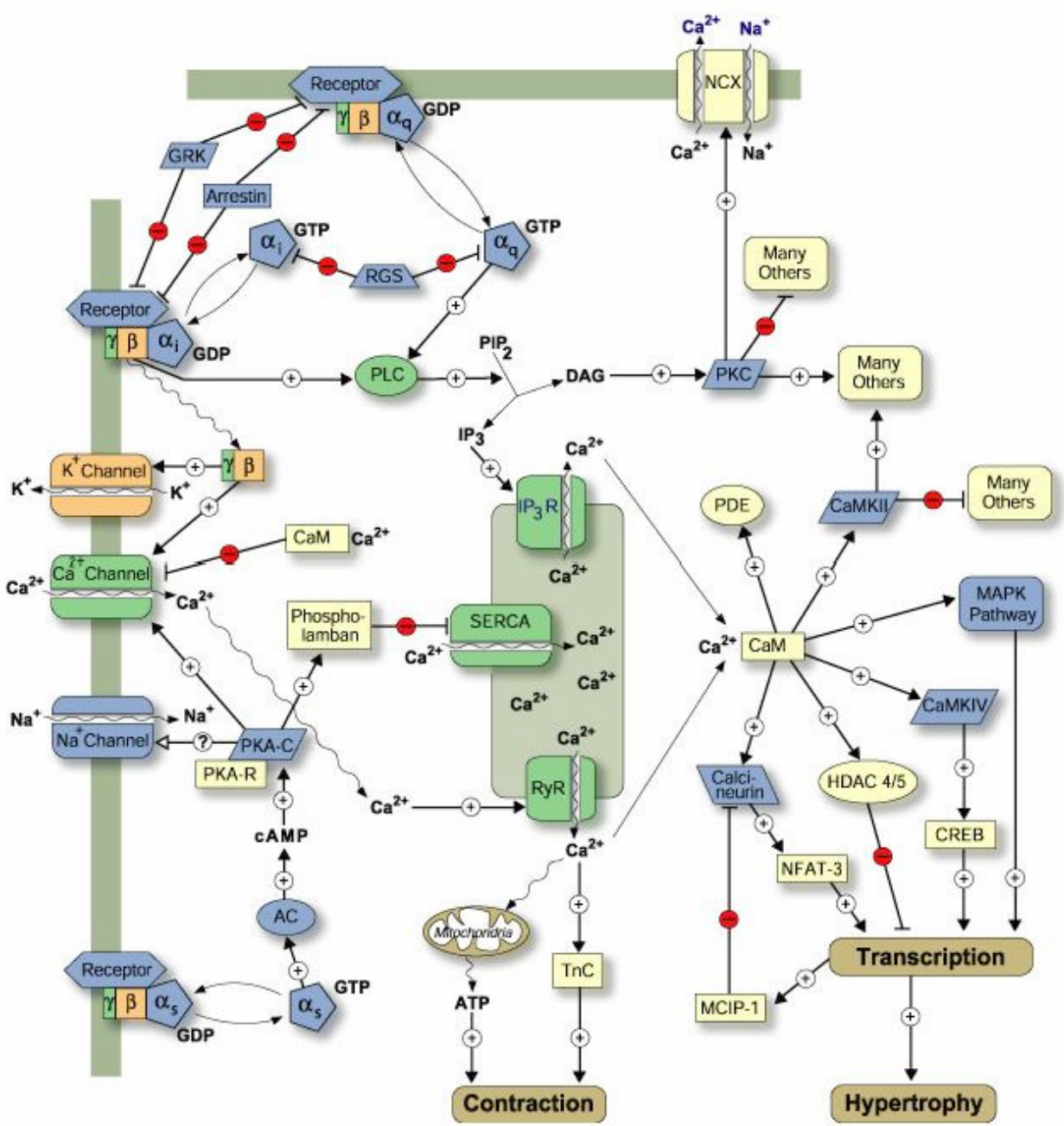
Principles of signaling cascades: amplification



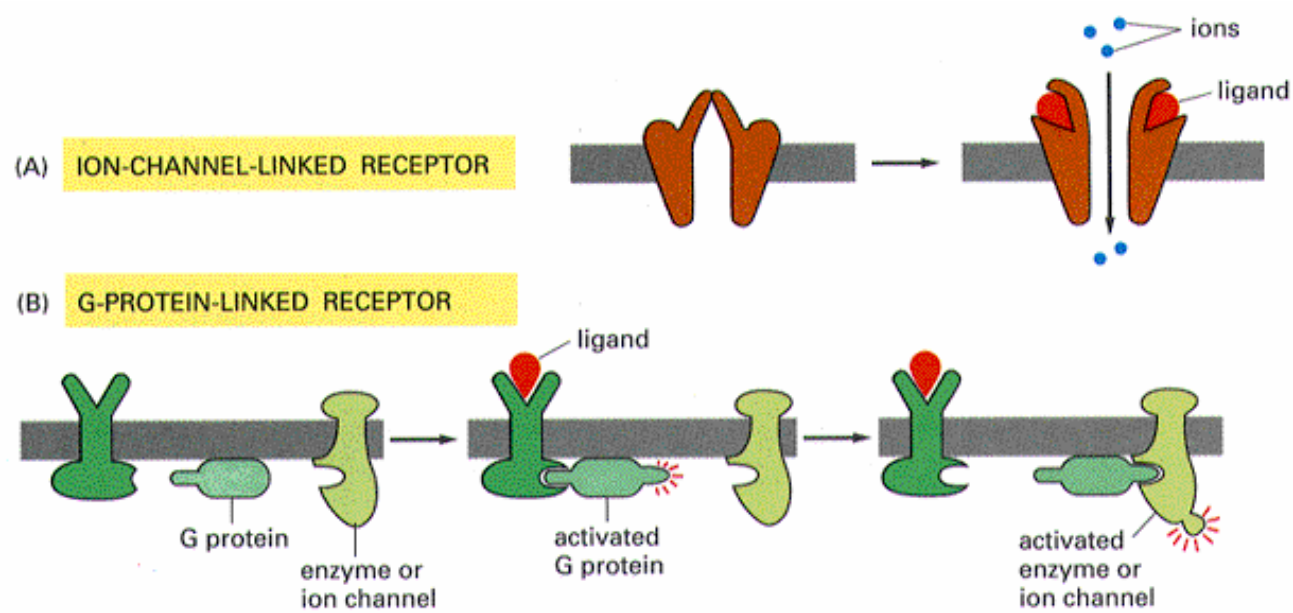
Activation of calcium signaling



Calcium activates a bunch of things in cells

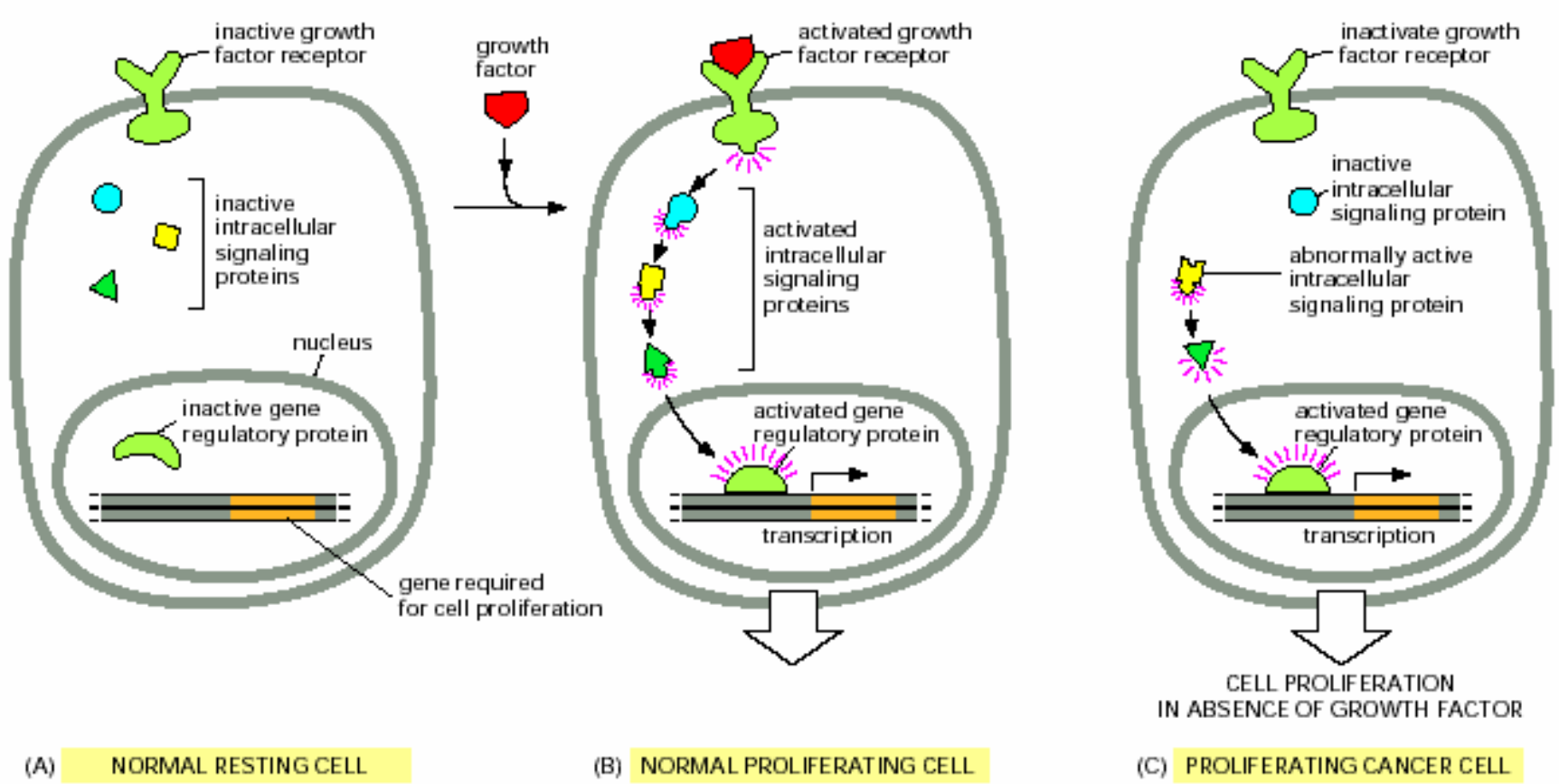


Three types of cell surface receptors



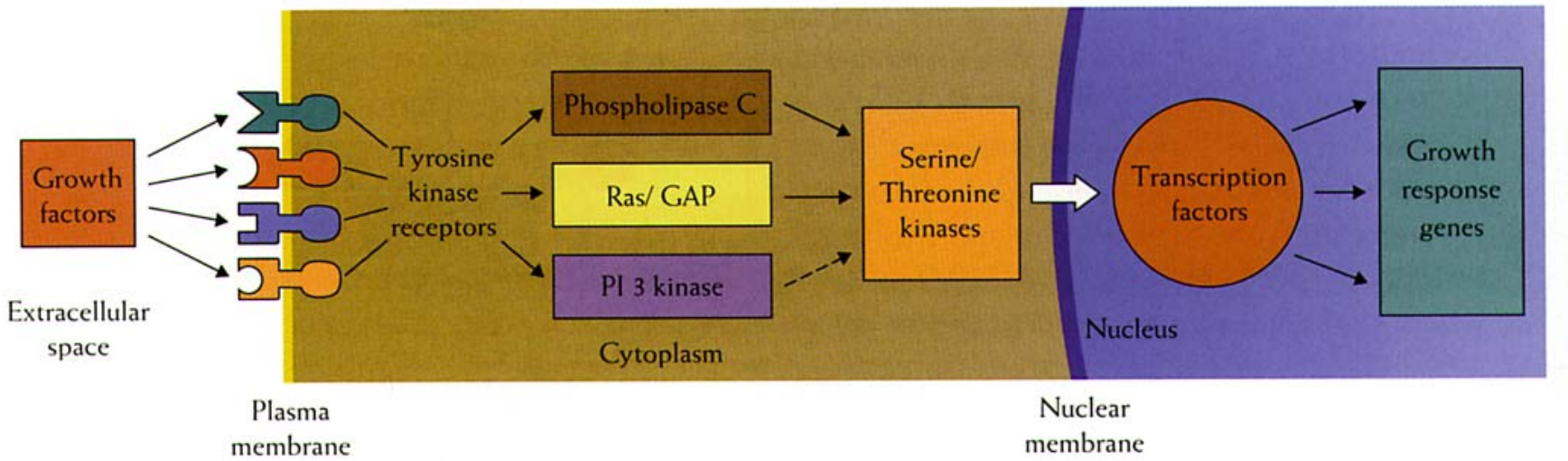
C) Enzyme-linked receptors

Activate gene transcription

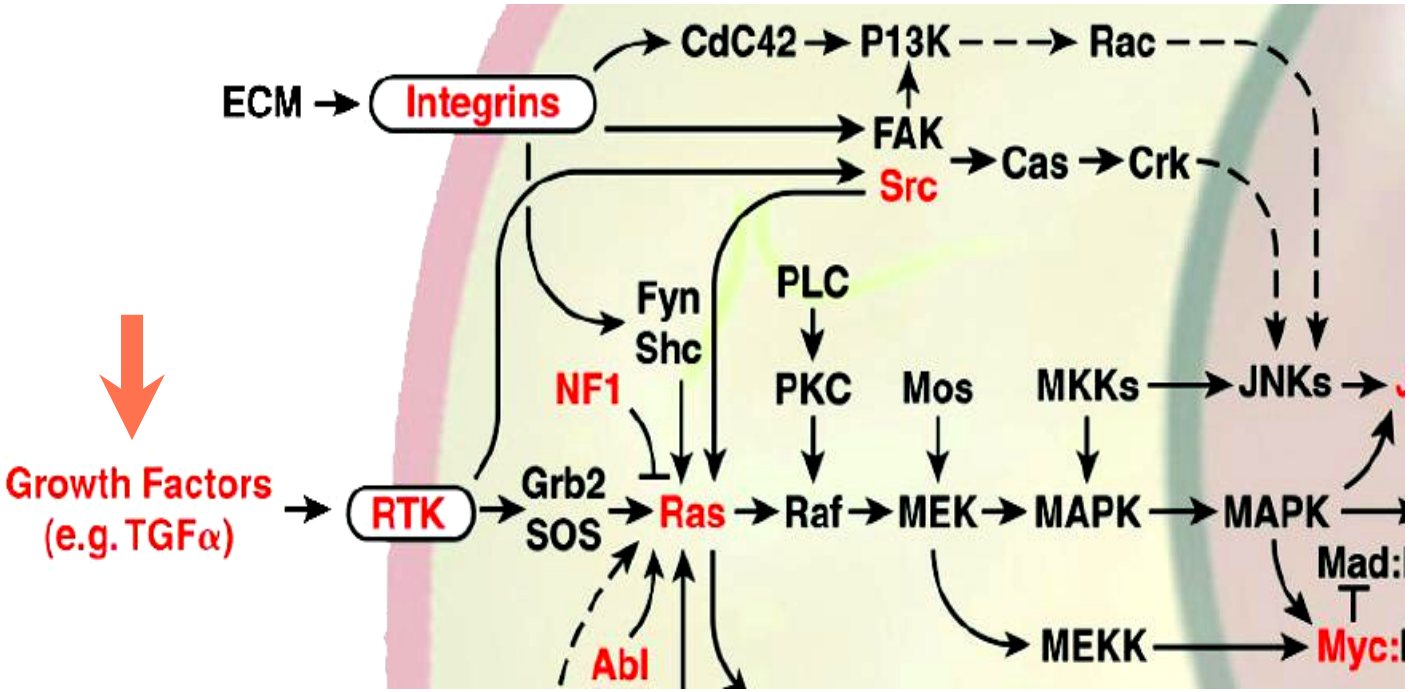


Growth factors

pathways of growth factors



Signaling through growth factor receptors

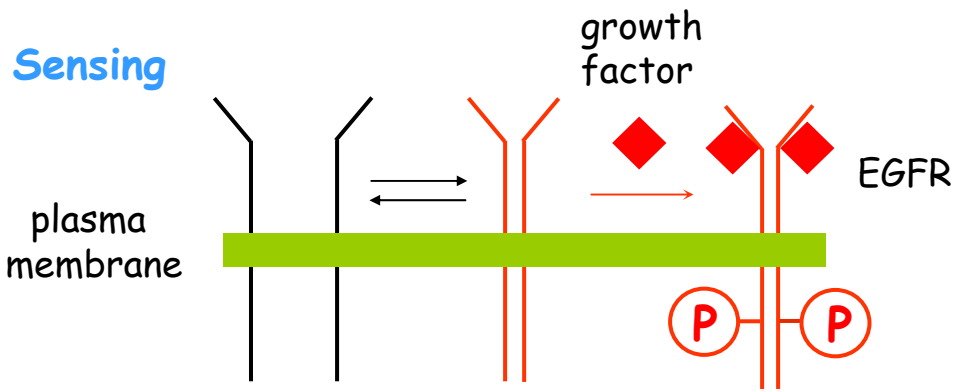


ligand (extracellular molecule)	membrane **receptor**	intracellular signaling cascade	physiological response
INPUT	SENSOR	ACTUATOR	OUTPUT

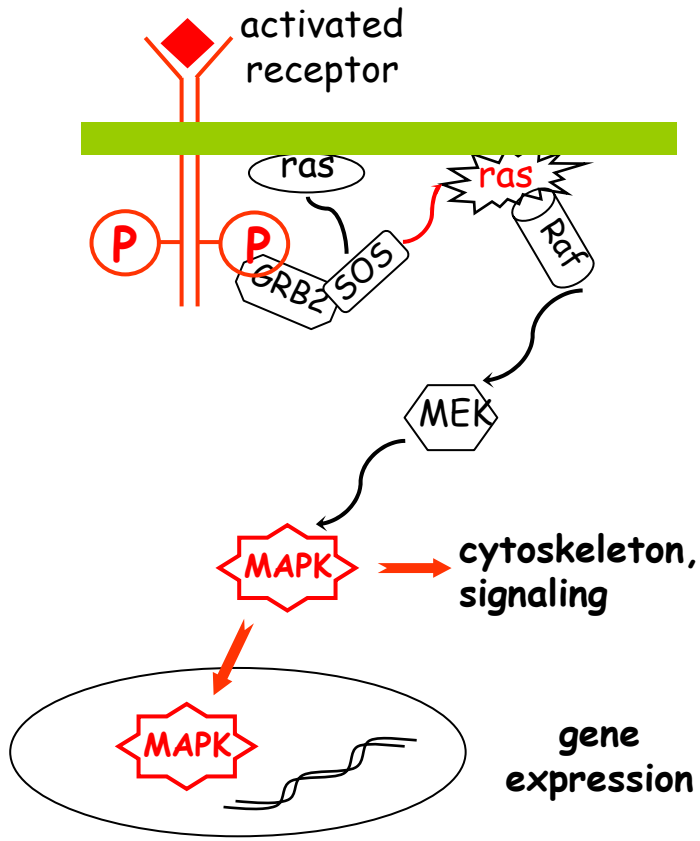
Epidermal growth factor receptor (EGFR): cellular level

- Large transmembrane protein (>1000 amino acids)
- 3 parts: extracellular, transmembrane, and cytoplasmic
- Sensing: specific binding of the peptide growth factors
- Actuation: ligand-receptor binding leads to changes in cellular biochemistry

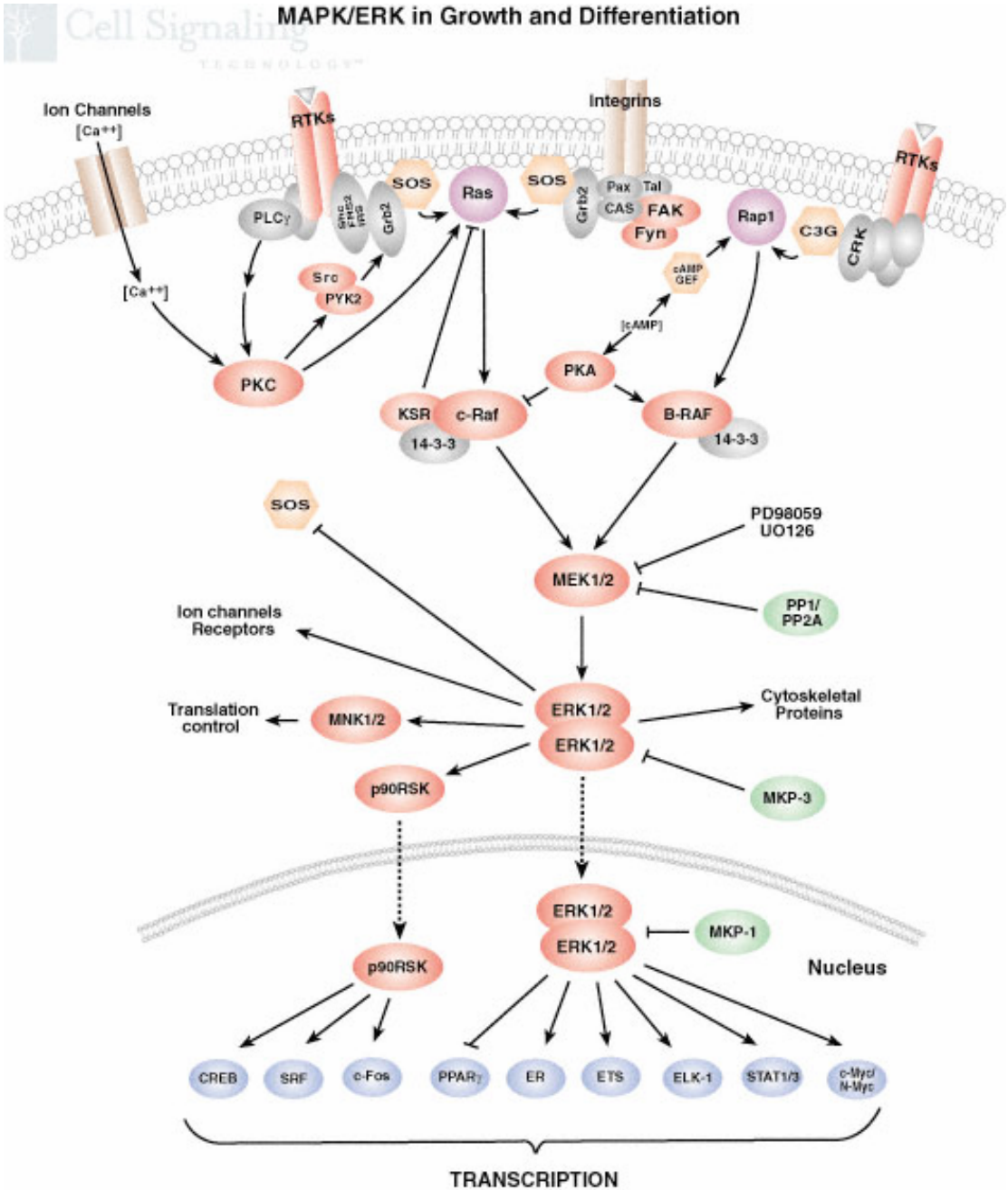
Sensing



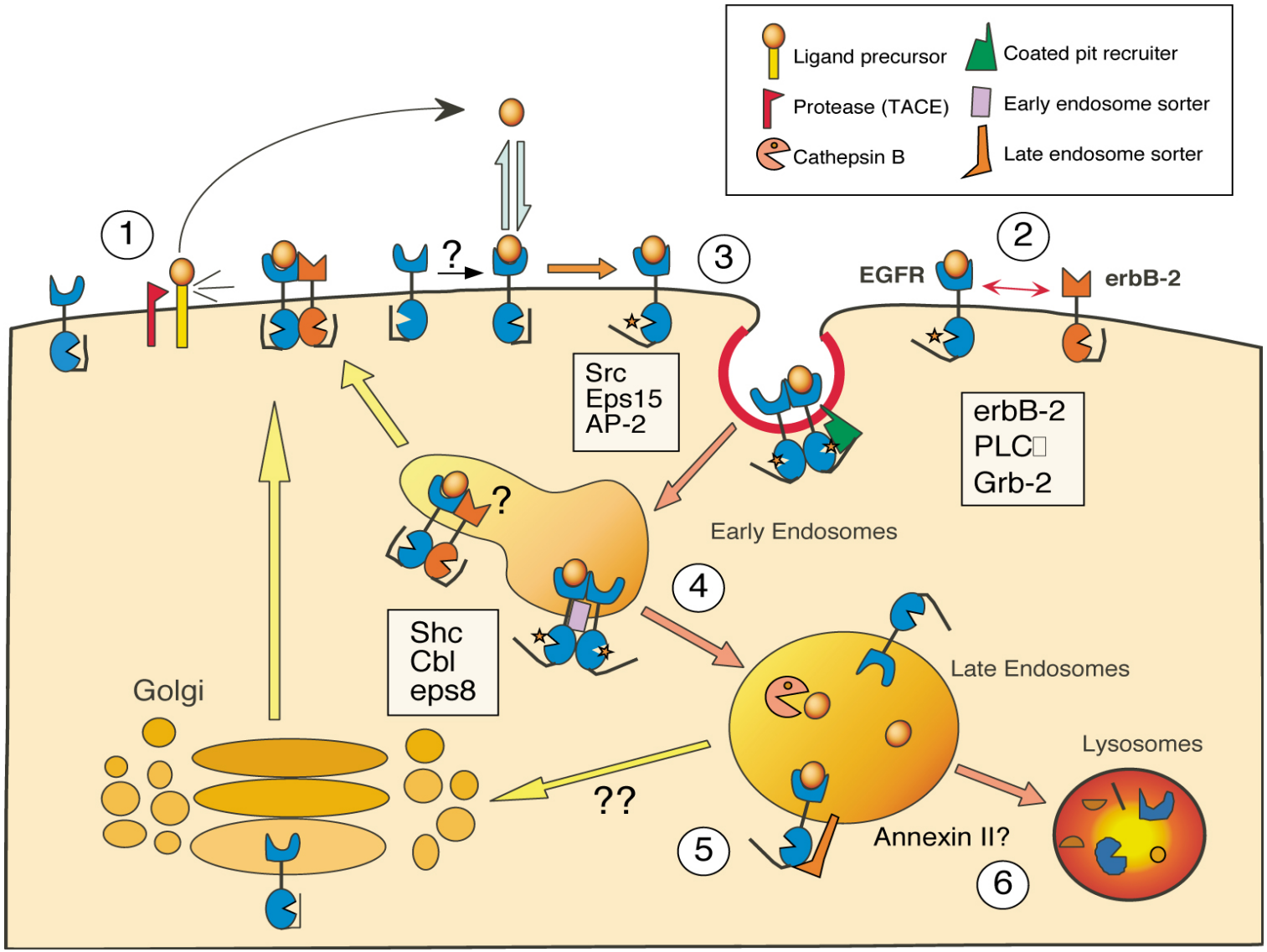
Actuation



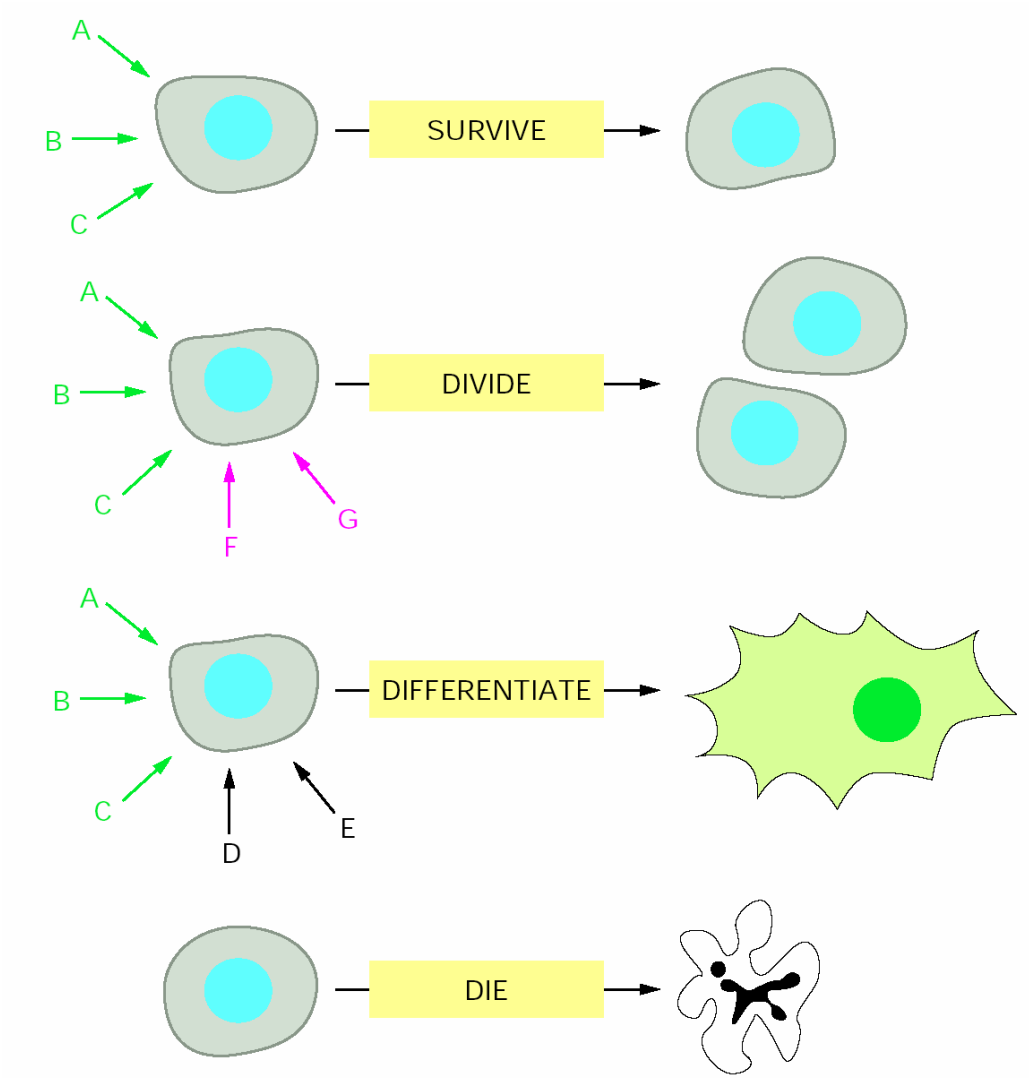
The MAP-kinase cascade



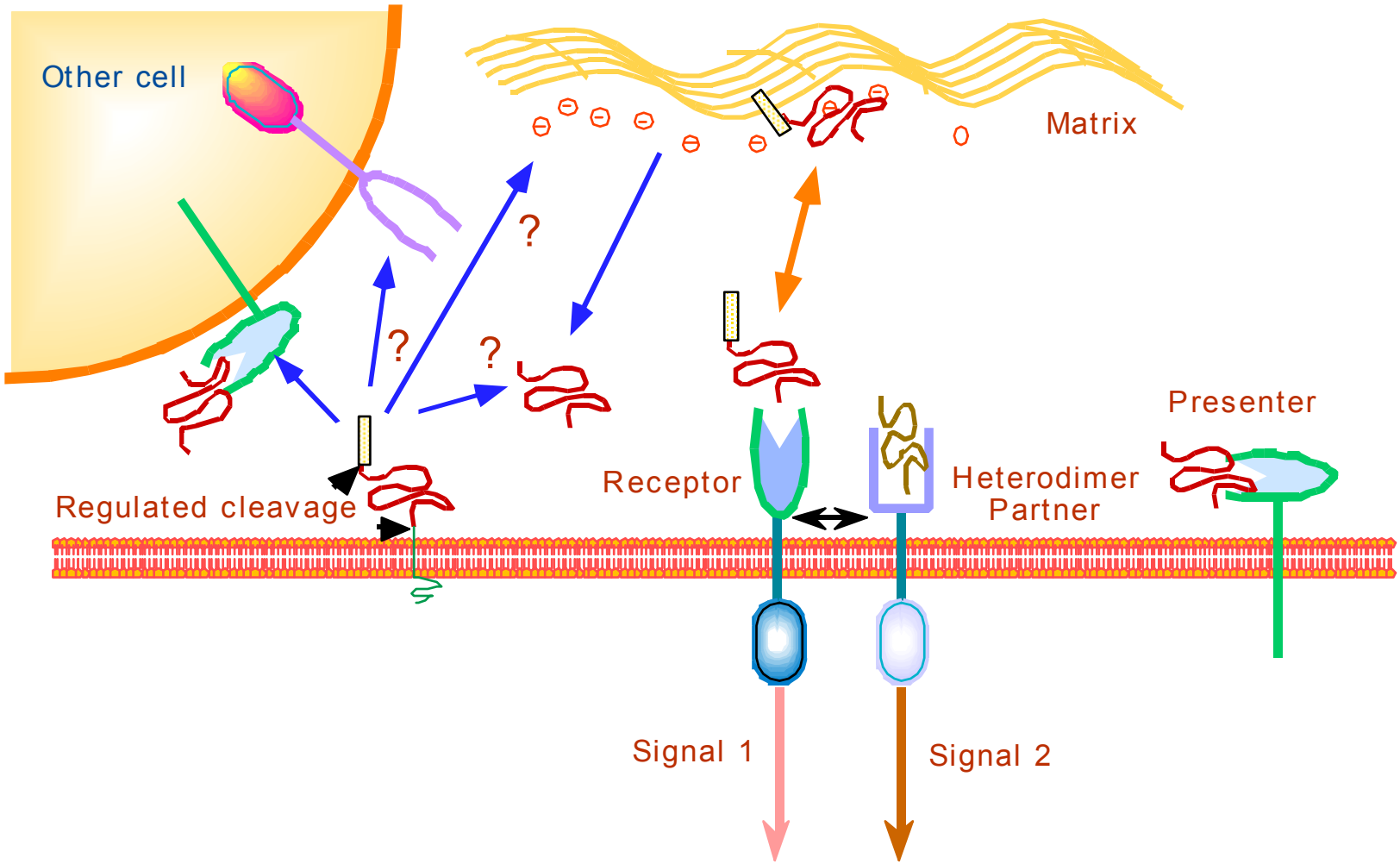
Surface receptors are dynamic



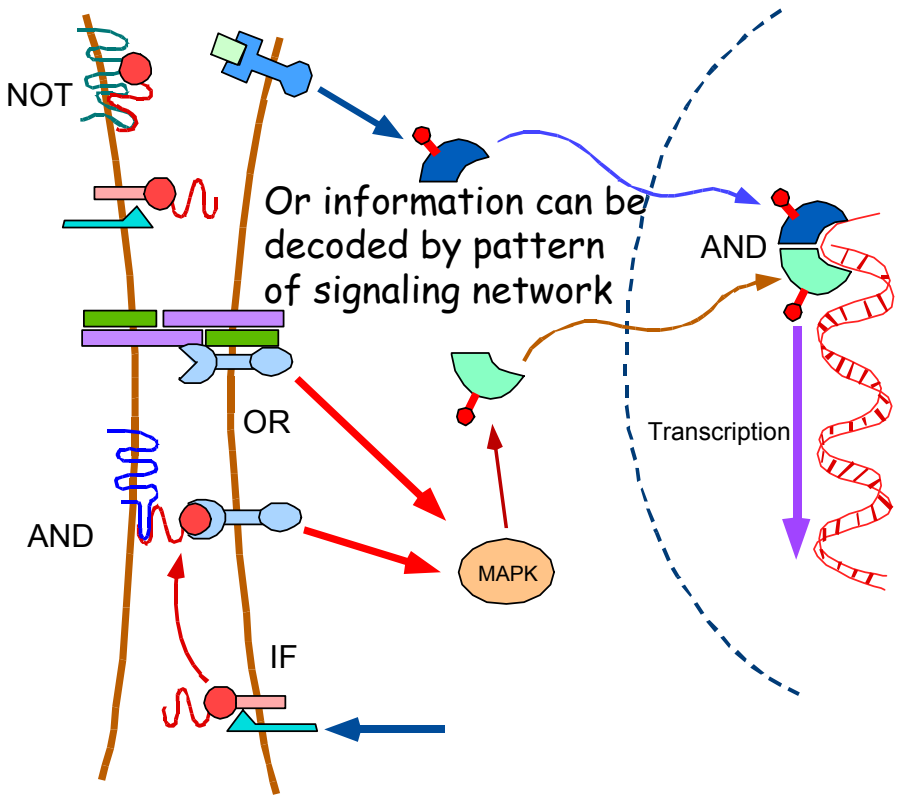
Cells make different decisions depending on the input

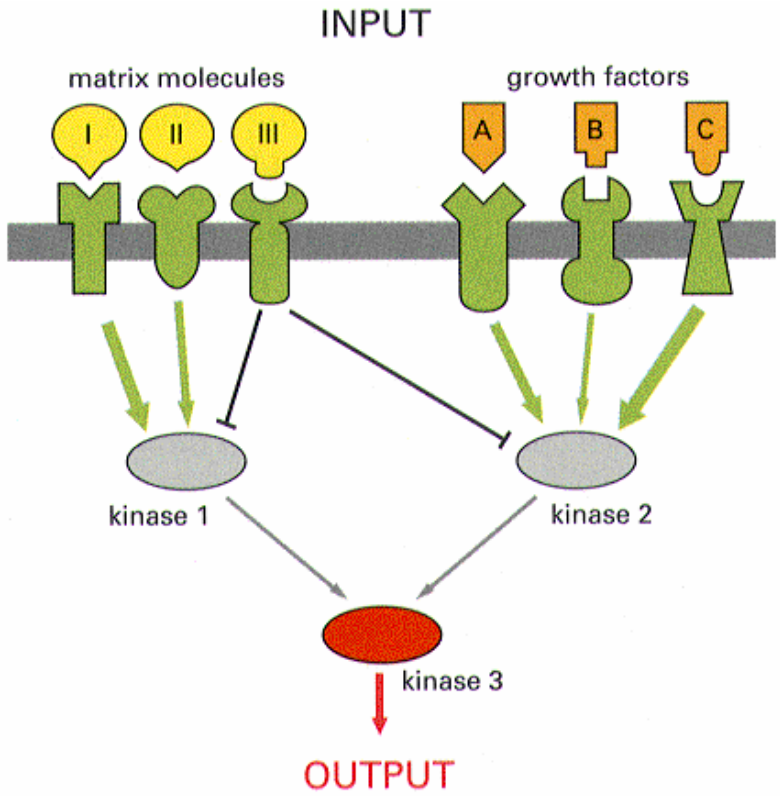


Complex extracellular interactions regulate the availability of signaling molecules

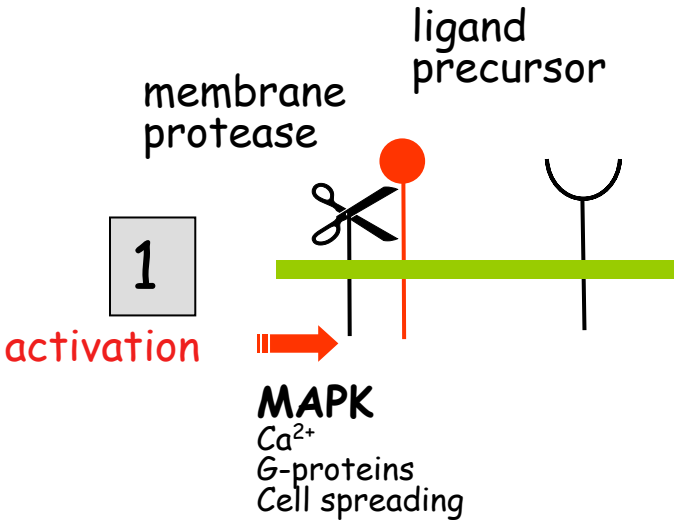


Different modes of information processing



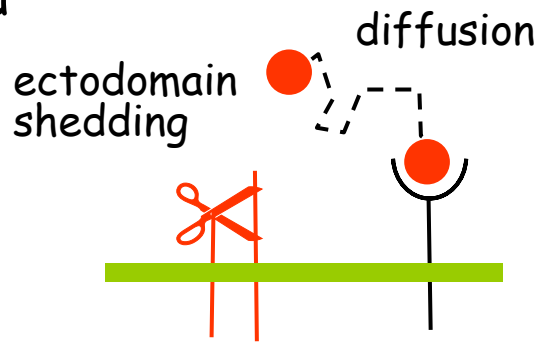


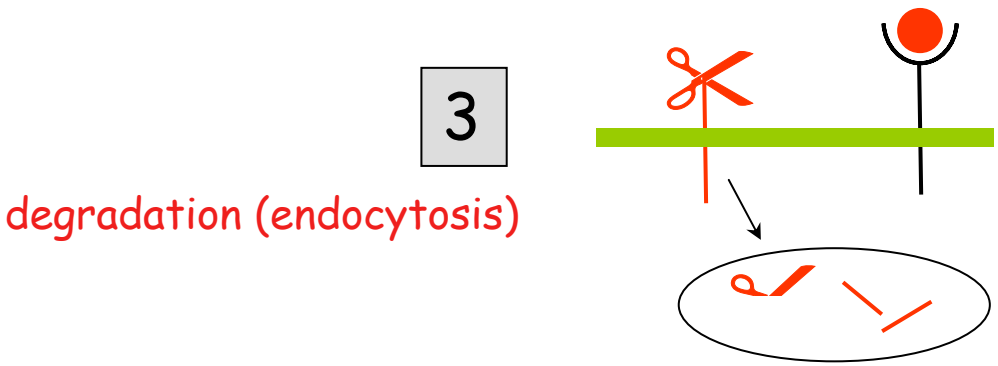
Where do some growth factors come from?
Regulated Proteolysis



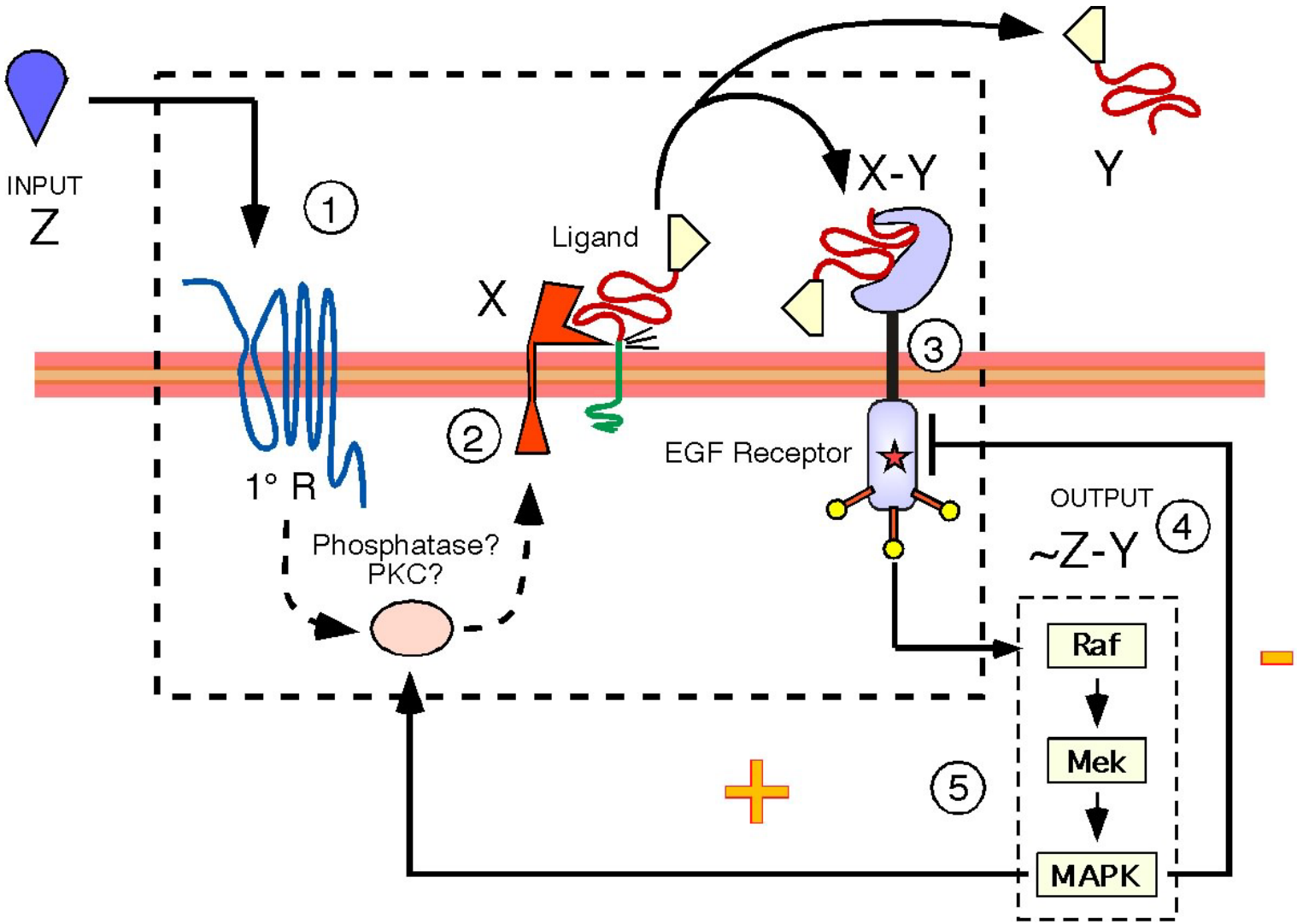
Ectodomain Shedding:

- broad specificity
- regulated
- dynamic





Autocrine control loops



Understanding cell signaling: Where are we going?

- We have identified a lot of "cell words"
  - What is the context in which they are used?
  - What is the grammar and syntax of cellular language?
- Can we talk to cells?
  - What can we say to them?
  - Can we make them understand?