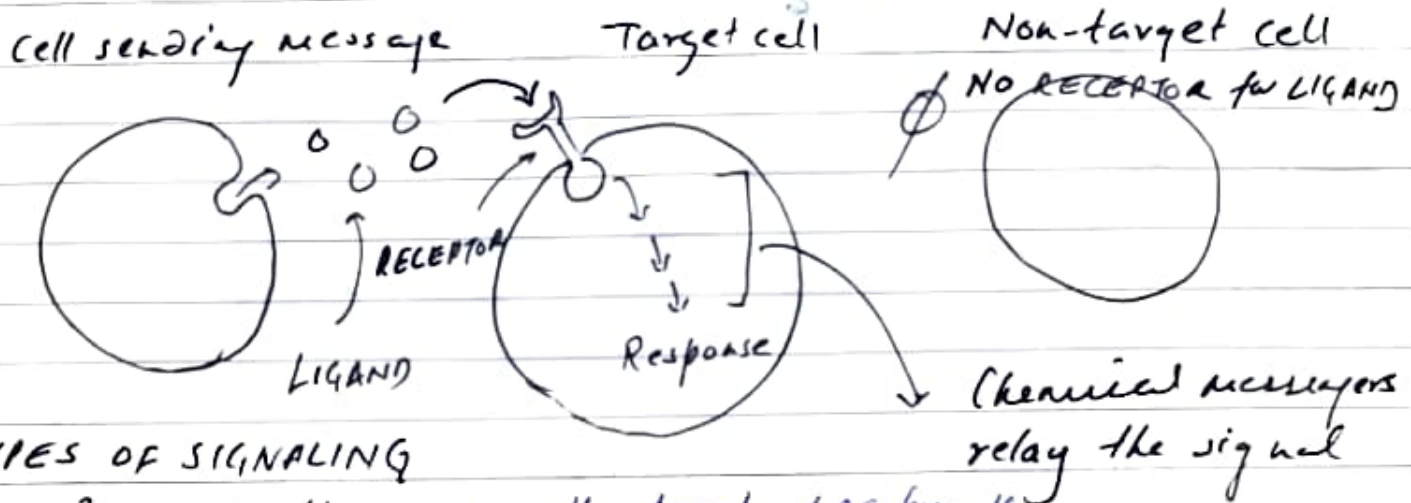


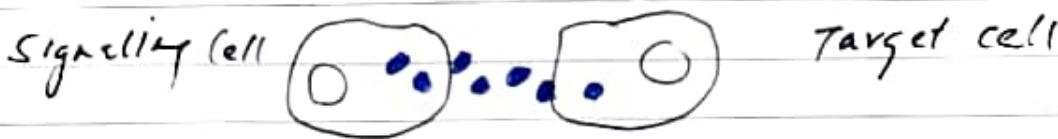
- Signaling
- I Introduction
 - II Ligands & Receptors
 - III Signal relay pathways
 - IV Response to signal

①

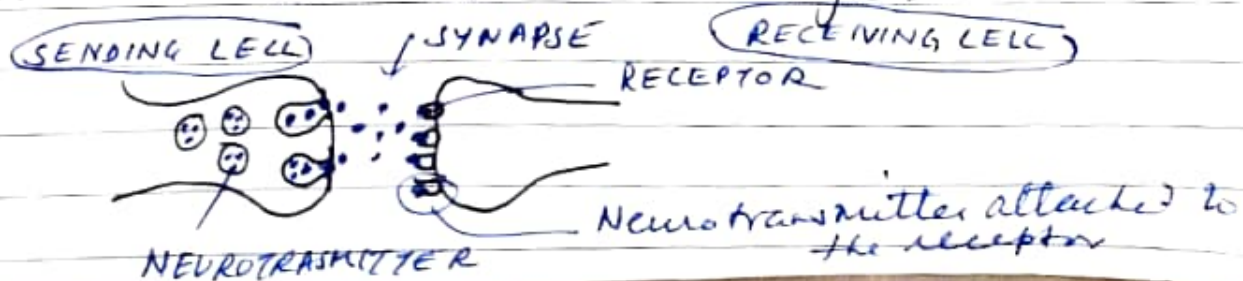


TYPES OF SIGNALING

- (a) **Paracrine signaling** - a cell targets nearby cells.
- cells are near one another
 - i.e. short distance communication
 - it allows cells to locally coordinate activities with their neighbours
 - important during development



(b) **Synaptic signaling** is an example of paracrine signaling wherein the nerve cells transmit signals.



⑥ AUTOCRINE SIGNALING

②

Self signaling via release of a ligand that binds to receptors on its own surface



⑦ ENDOCRINE SIGNALING

Signals produced by specialized cells and released into the bloodstream which carries them to target cells in distant parts of the body.

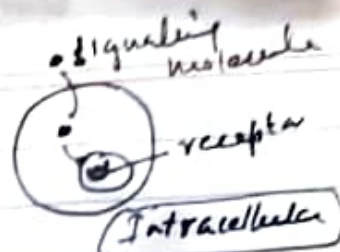
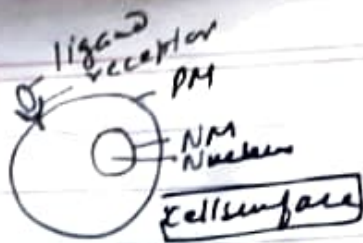


GAP JUNCTIONS in animals } are tiny channels that
PLASMODESMATA in plants } directly connect neighbouring cells.

These are the water filled channels that allow small signaling molecules (intracellular mediators) to diffuse between cells. e.g. Ca^{2+} ions.

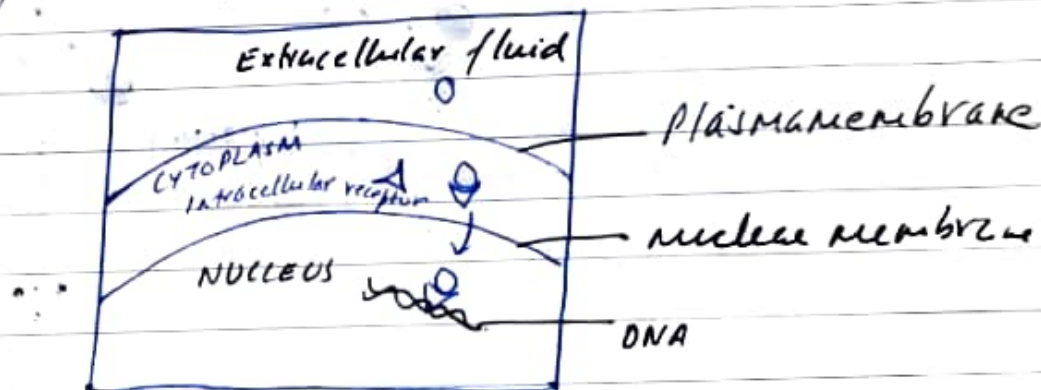
③

TYPES OF RECEPTORS



→ INTRACELLULAR

- found inside the cell typically in the cytoplasm or nucleus
- mostly hydrophobic molecules, small in size
eg. receptors for steroid hormones
- binding of ligand changes the receptor shape
- Receptor-ligand complex enters the nucleus
- Regulates gene activity



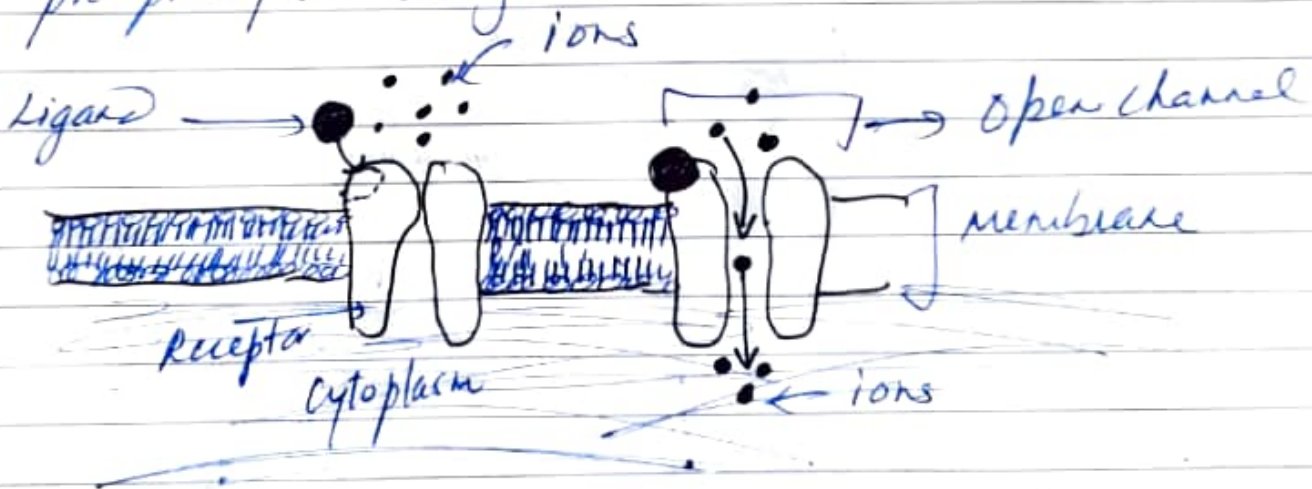
→ CELL-SURFACE RECEPTOR

- membrane anchored proteins that bind to ligands on the outside surface of the cell
- ligand does not need to cross the plasma membrane
- cell-surface receptor has three different domains
 - an extracellular ligand-binding domain
 - a hydrophobic domain extending through the membrane
 - an intracellular domain which often transmits the signal.

- cell surface receptors
 - ↳ ligand gated ion channels
 - G protein-coupled receptors
 - receptors tyrosine kinases

LIGAND GATED ION CHANNELS

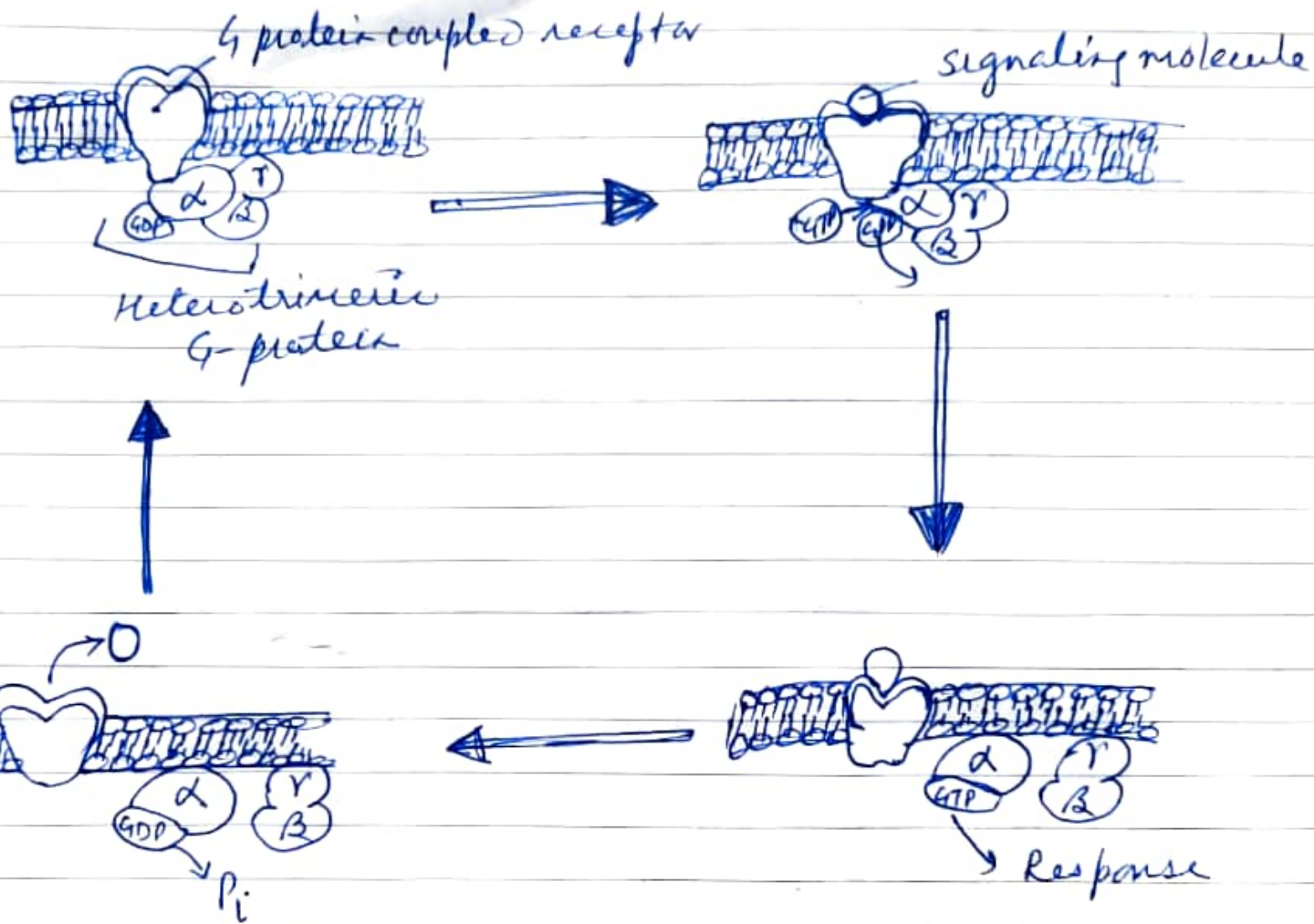
- open in response to the binding of a ligand
- has a membrane spanning region with a hydrophobic channel through its middle
- it lets ion to cross the membrane without having to touch hydrophobic core of the phospholipid bilayer



G- PROTEIN COUPLED RECEPTORS (GPCRs)

- large family
- seven different protein segments that span the membrane
- signaling via G-Protein
- GPCRs are diverse & binds to different types of ligands.
- G-proteins → bind GTP → hydrolysed to GDP

GTP bound G-protein is ACTIVE or 'ON' (5)
 GDP " " " INACTIVE or 'OFF'



RECEPTOR TYROSINE KINASES

- Type of Enzyme linked receptors
- It's intracellular domain associated with enzyme or sometimes it itself is an enzyme.

RTKs are found in humans and many other sp.

Plants lack classical tyrosine kinase from the TK gr. but do contain phosphotyrosine.

Brassinosteroid receptor BRI1 and its co-receptor BAK1 have been shown to auto-phosphorylate on tyrosine.

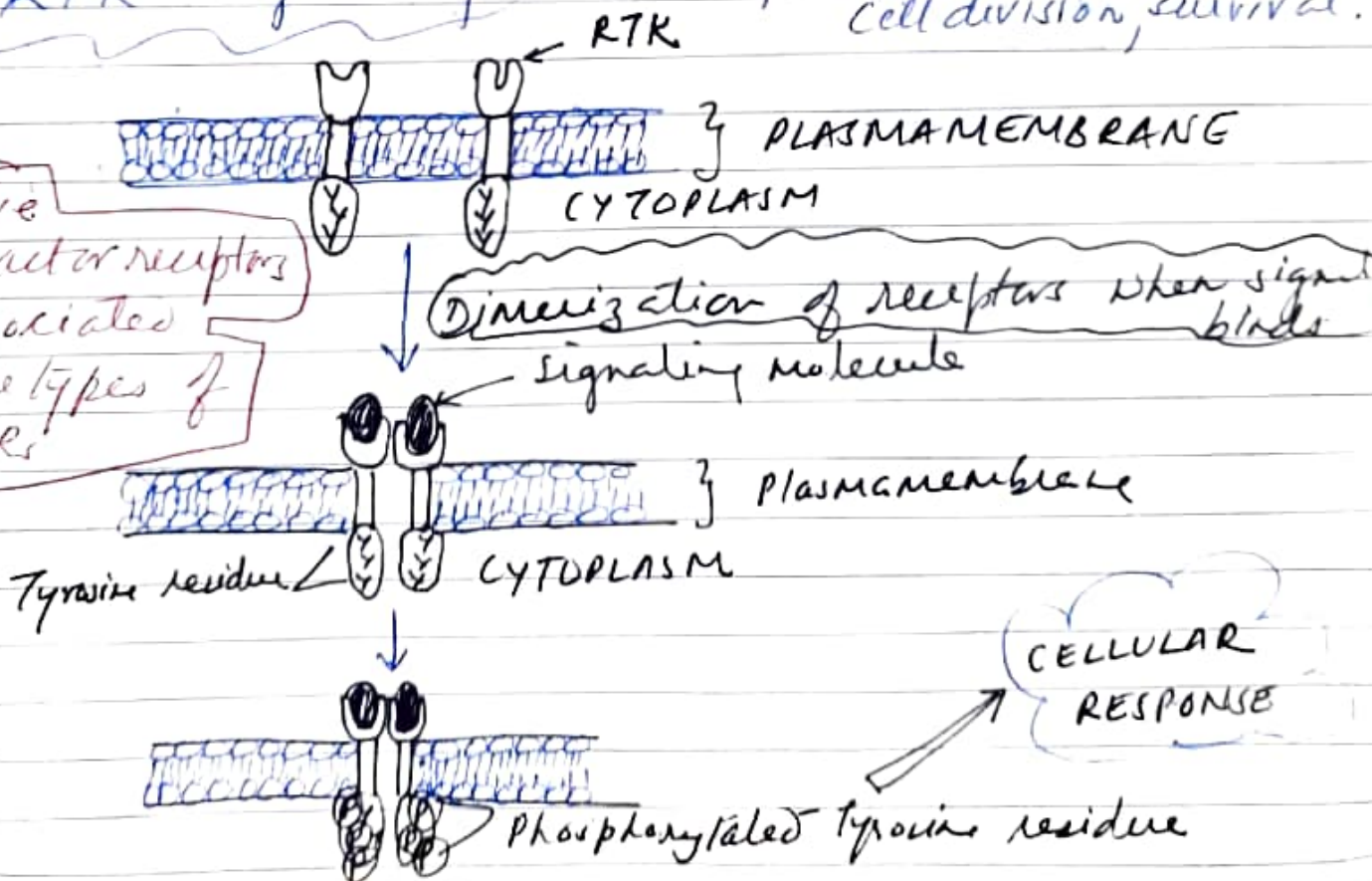
A KINASE is an enzyme that transfers phosphate group to a protein or other target and a -

- Receptor tyrosine kinase transfers phosphate groups specifically to amino acid TYROSINE

↳ IMPORTANT to many processes in humans like cell division, survival.

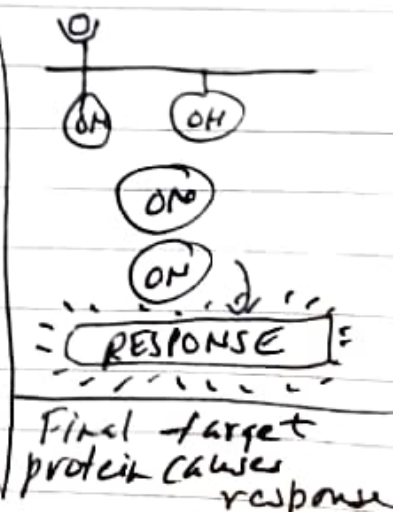
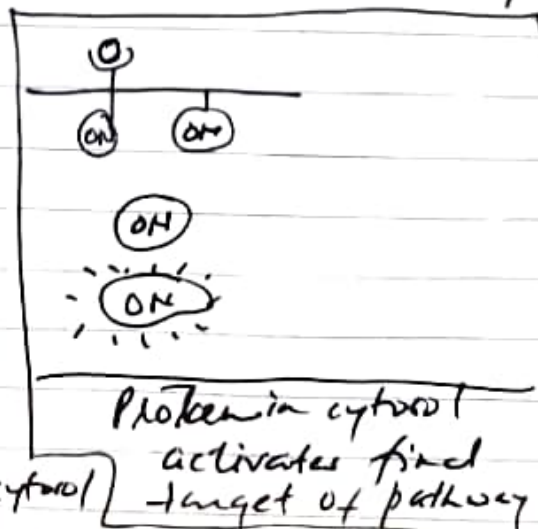
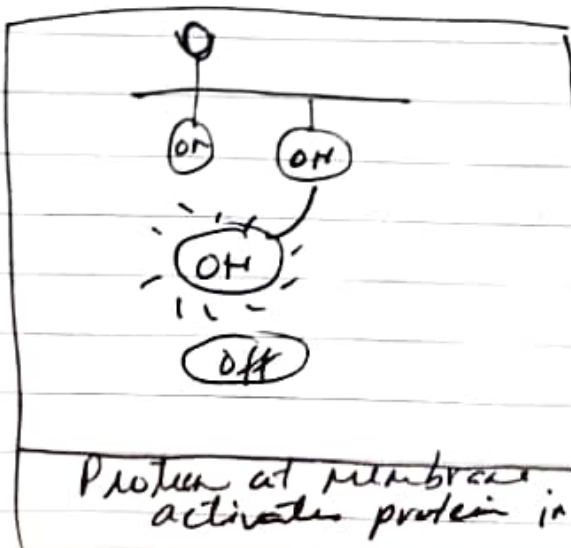
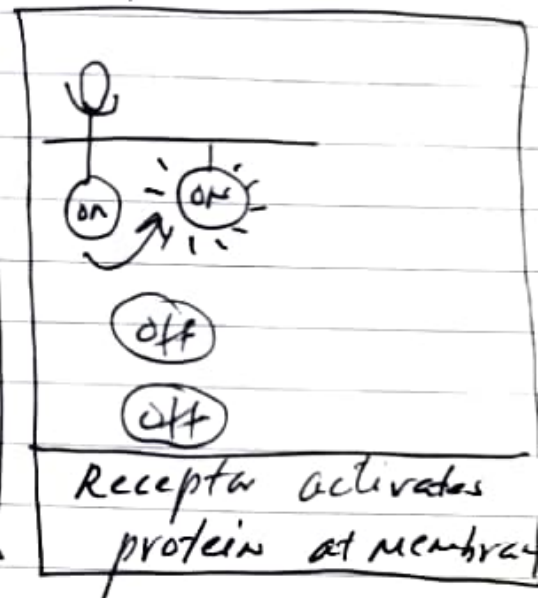
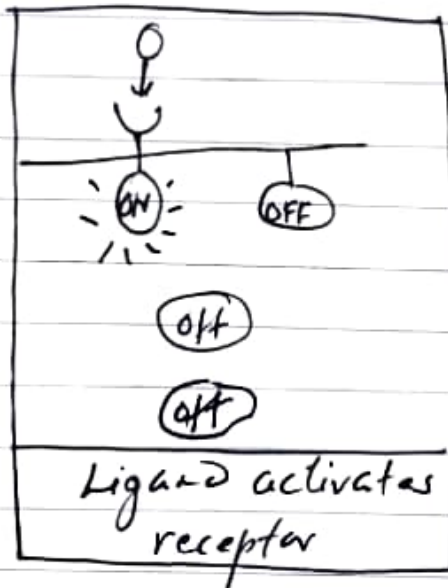
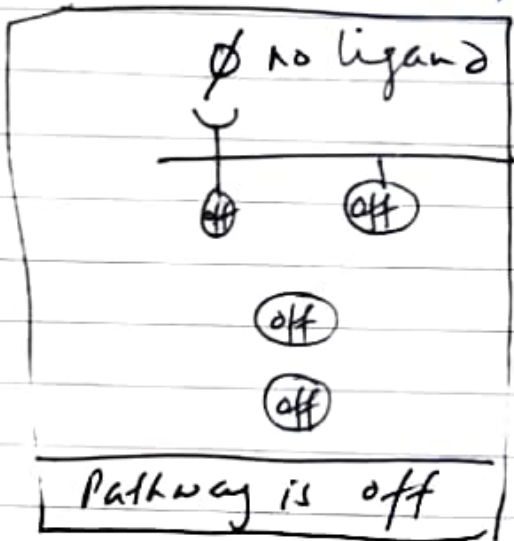
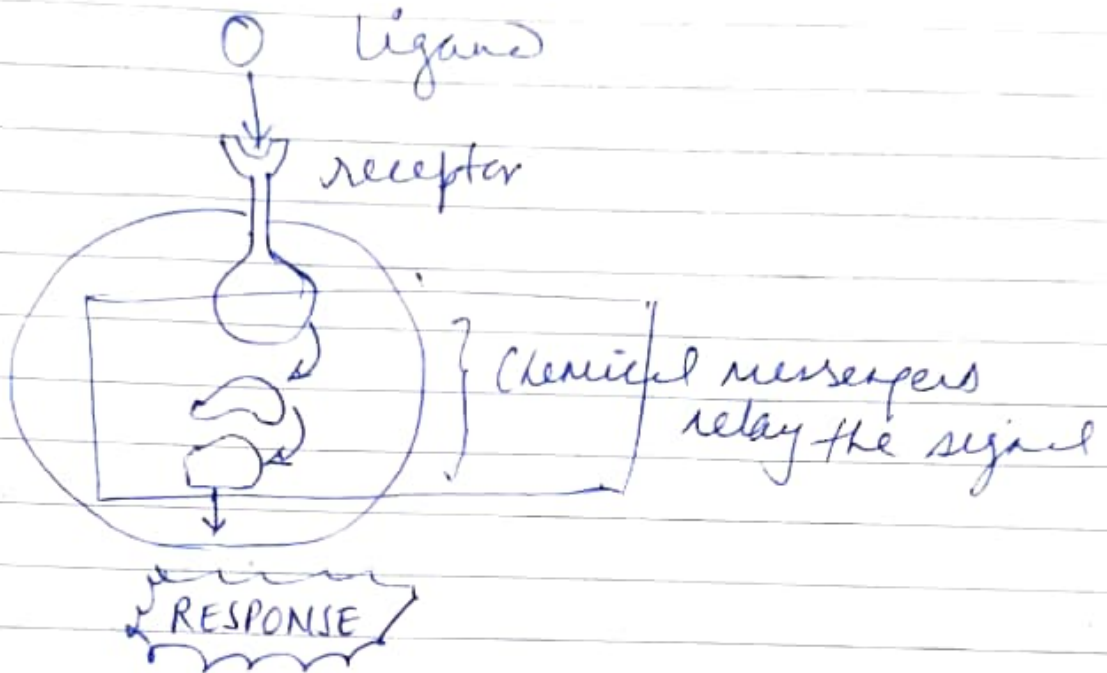
R.T.K. signaling

* Overactive growth factor receptors are associated with some types of CANCERS



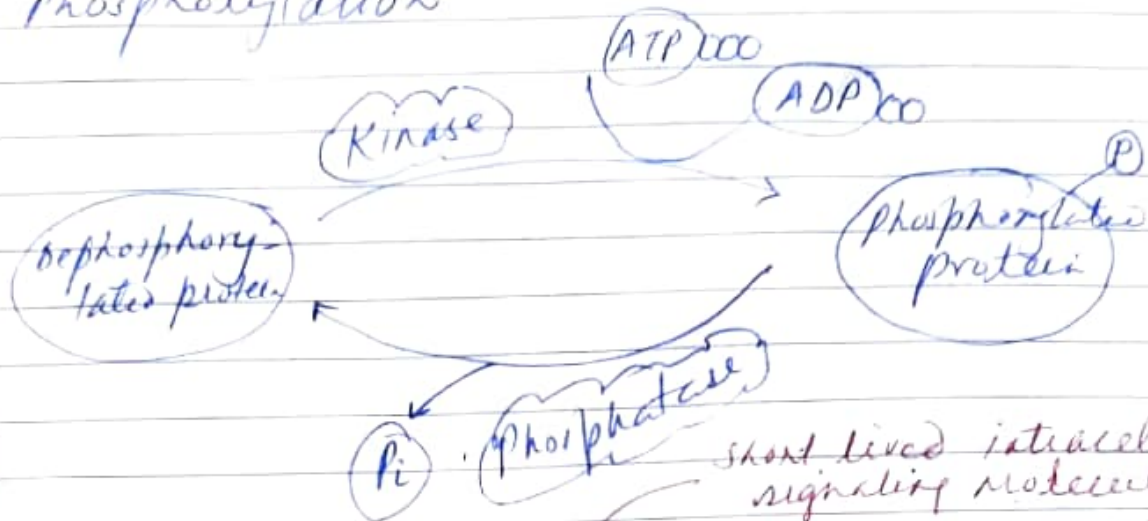
SIGNAL RELAY PATHWAYS

7



Phosphorylation

(8)



I Hydrophilic
cAMP
cGMP
IP₃
Ca²⁺

II Hydrophobic

Diacylglycerol
Phosphatidylinositol

Gas

NO
H₂S
CO

Second messengers

short lived intracellular signaling molecule

Earl Wilbur Sutherland Jr
1971, Nobel Prize

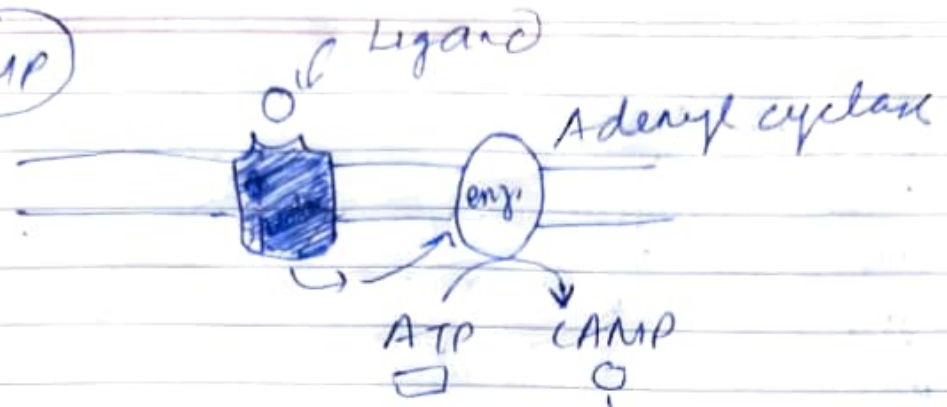
Molecules that relay signals from receptors on the cell surface to target molecules inside the cell.

① Calcium ions; Ca²⁺ ions

- conc. of Ca²⁺ in the cytosol is very low inside the cell.
- Ca²⁺ ions restored in ER
- Upstream signaling events release a ligand that binds to and opens ligand-gated Ca²⁺ ion channel.
- Ca²⁺ ions flow in the cytoplasm
- conc. of Ca²⁺ ions ↑
- These attach to proteins that have binding sites for Ca²⁺ ions.
- Proteins change shape (becomes active)
- and response is produced.

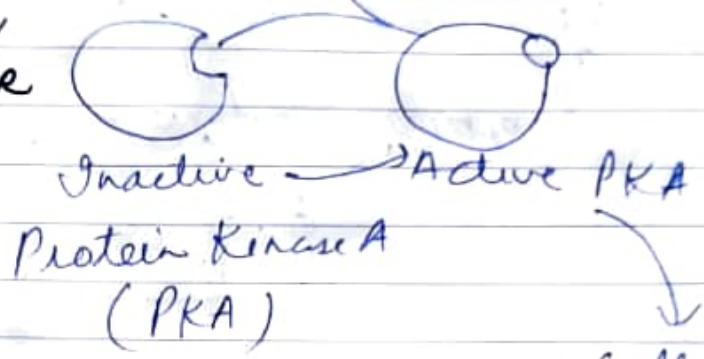
eg. Ca-signaling in muscle cells leads to muscle contraction.

(II) **CAMP**



CAMP binds to a protein called CREB (cAMP response element) Binding Protein

Either/or

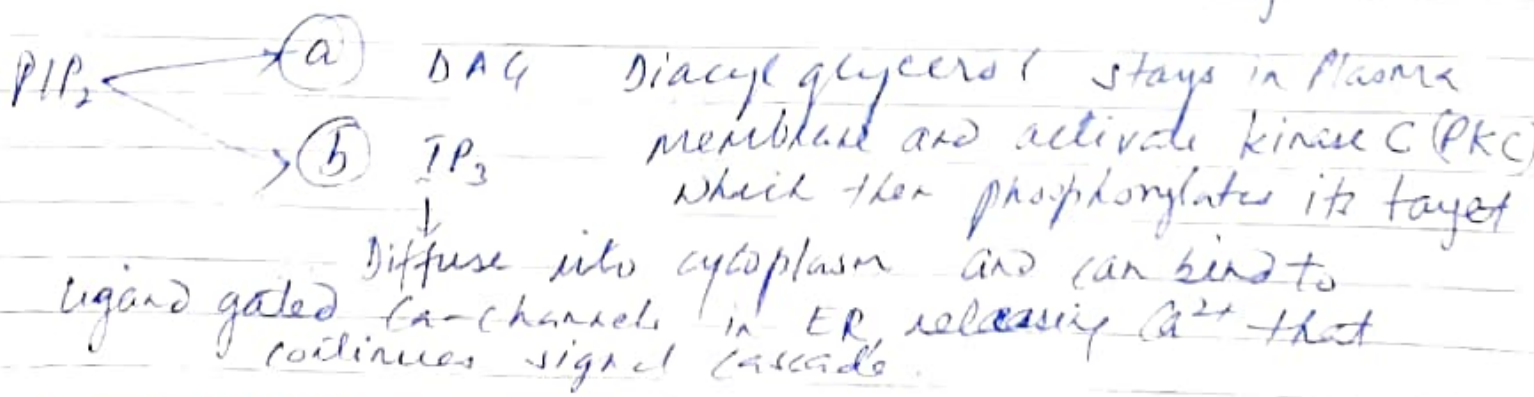


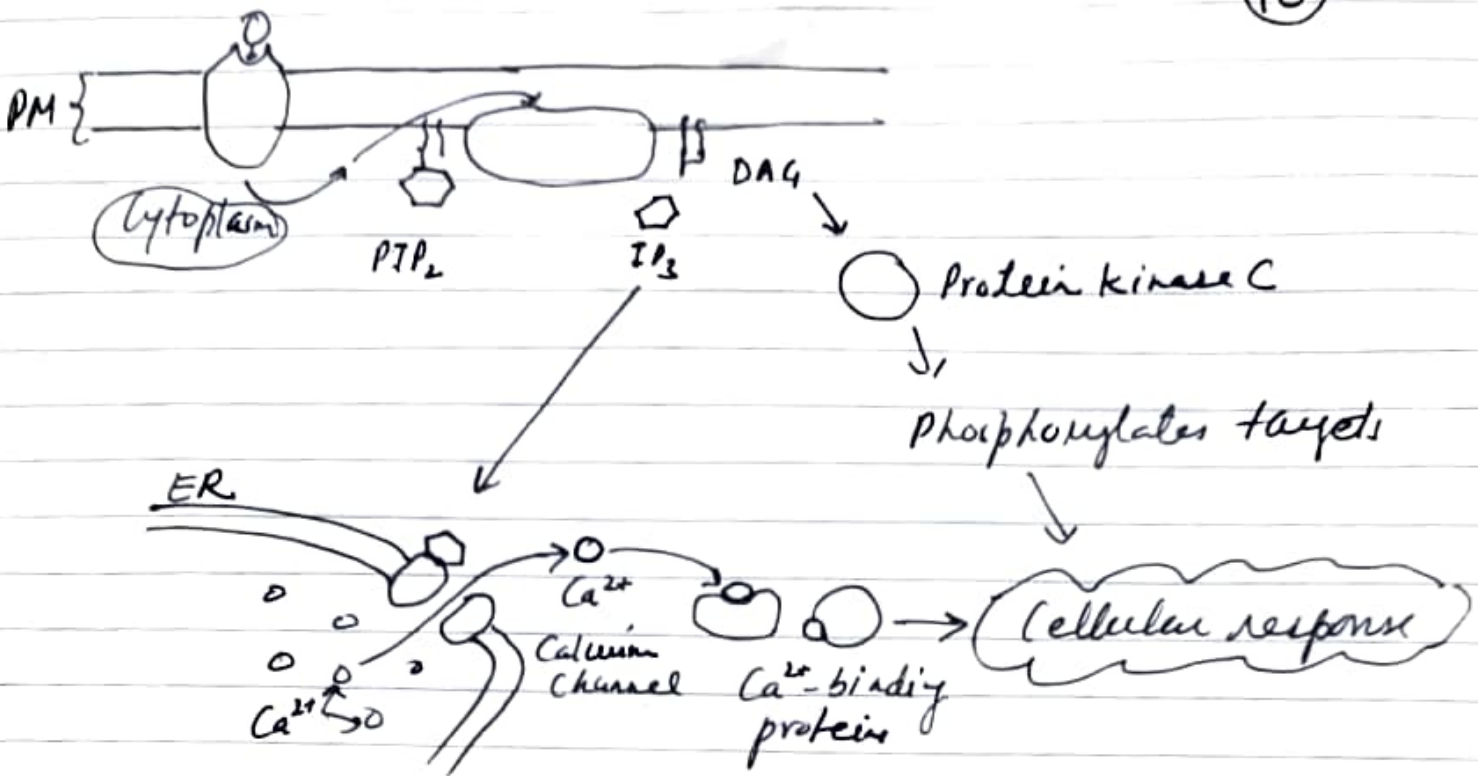
Cellular response

CAMP signaling is turned OFF by enzymes phosphodiesterases - enz. that convert CAMP to AMP by breaking the ring of CAMP

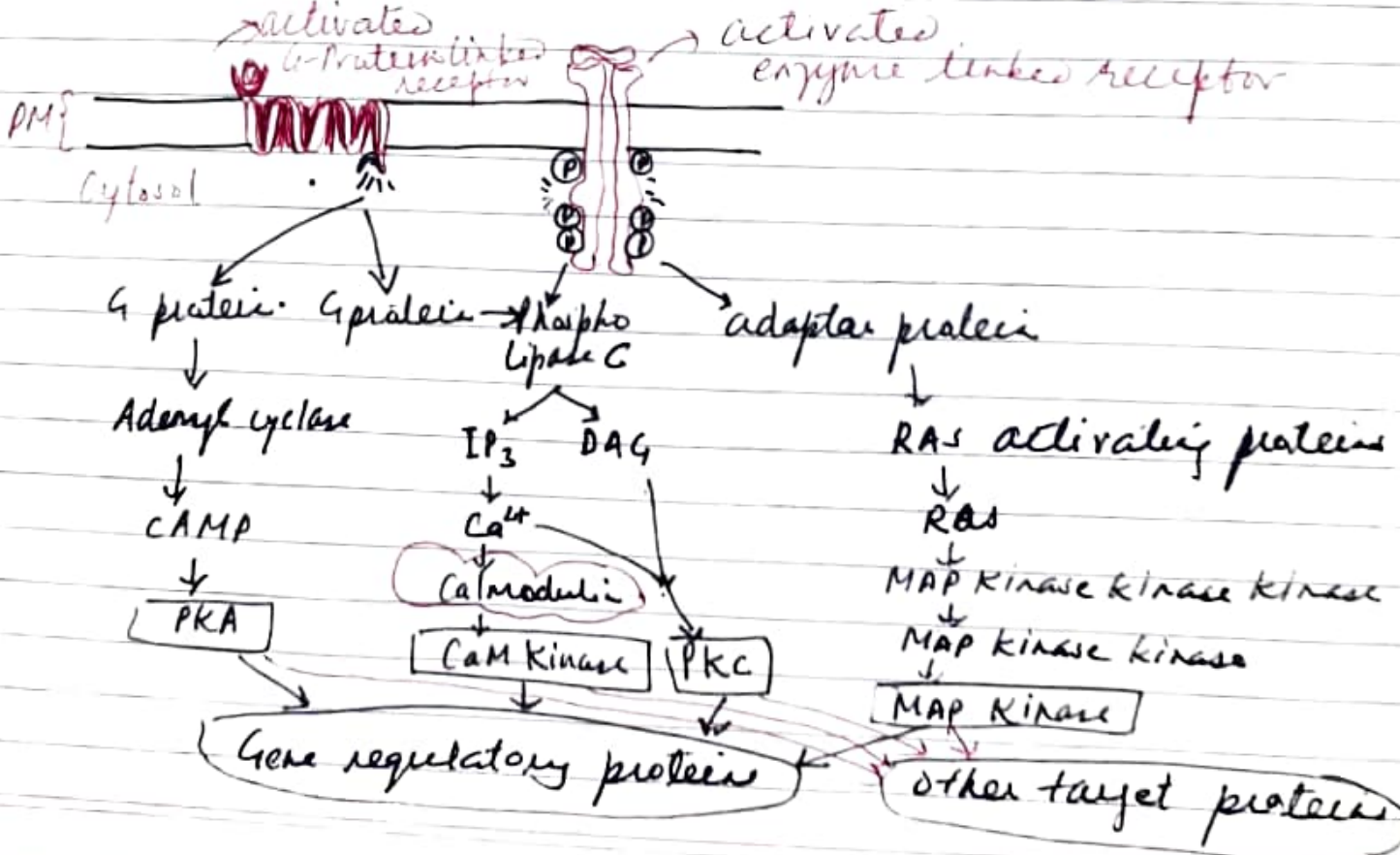
(III) **Inositol Phosphates: IP₃**

Phospholipids called Phosphatidylinositols are phosphorylated and release two fragments that both acts as second messenger.





SIGNALING PATHWAYS ARE HIGHLY INTERCONNECTED



NO Nitric Oxide

ROBERT FURCHGOTT } NOBEL
LOUIS J. IGNORE & } PRIZE
FERID MURAD } 1998

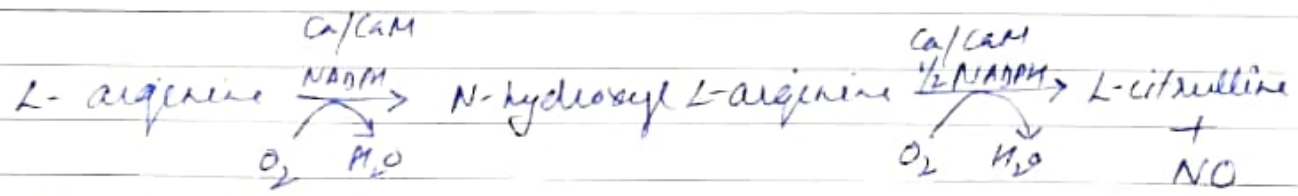
- Environmental Pollutant
- 1st Gas to know as a biological messenger
- 1st described as a potent relaxant of peripheral vascular smooth muscle in 1979.

- NO → small water and lipid soluble gas
- Gaseous free radical
- 3 interchangeable forms

- NO Nitric oxide
- NO⁺ Nitrosonium cation
- NO⁻ Nitroxyl radical

Nitroglycerine → N-O
(used to treat angina)

actually its breakdown prod NO expands the smooth muscle of cells



Enzyme: Nitric oxide Synthase

