Chemical aspects of the cell

Biosynthesis of compounds responsible for biochemical pathways

Two types of intracellular signaling events

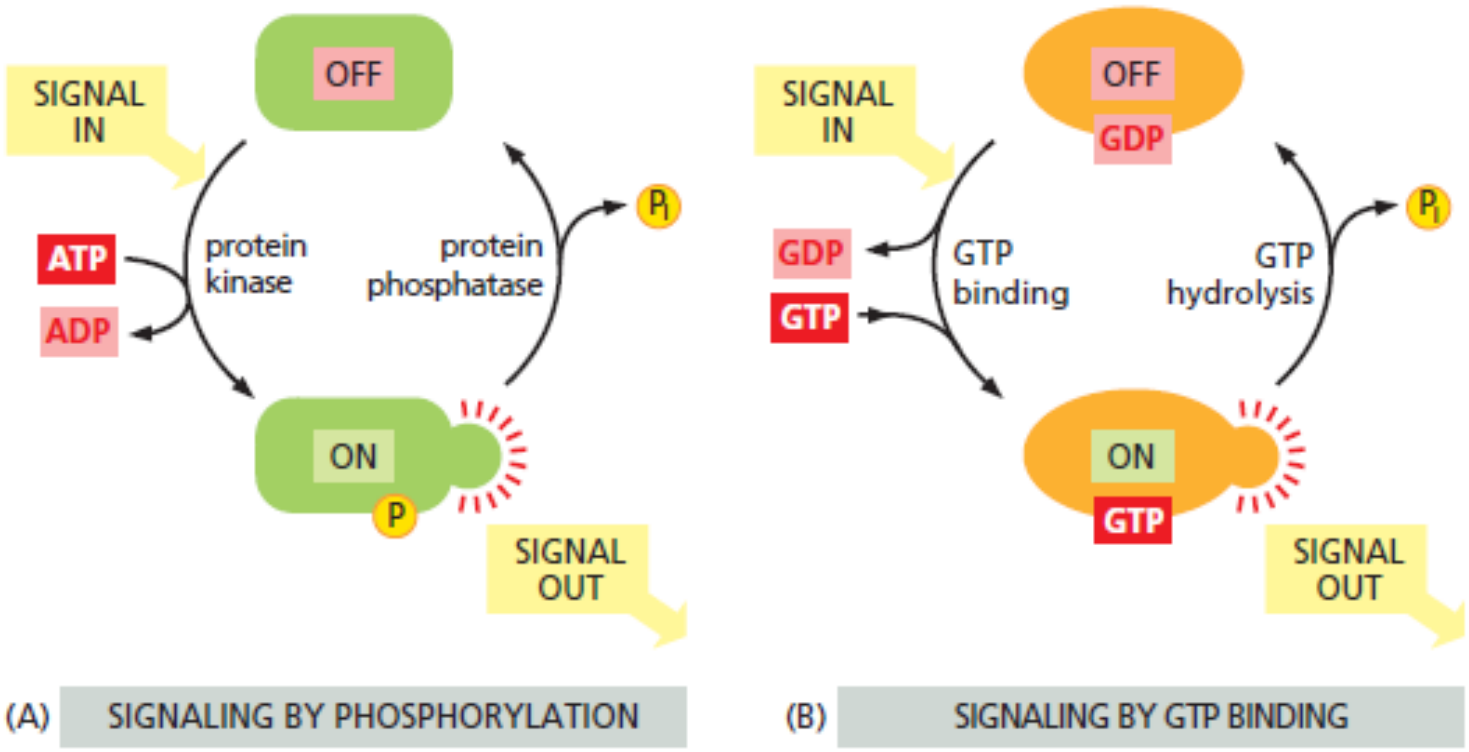


Fig. 15.7 – Molecular Biology of the Cell
http://www.genome.jp/kegg/

Signal transduction

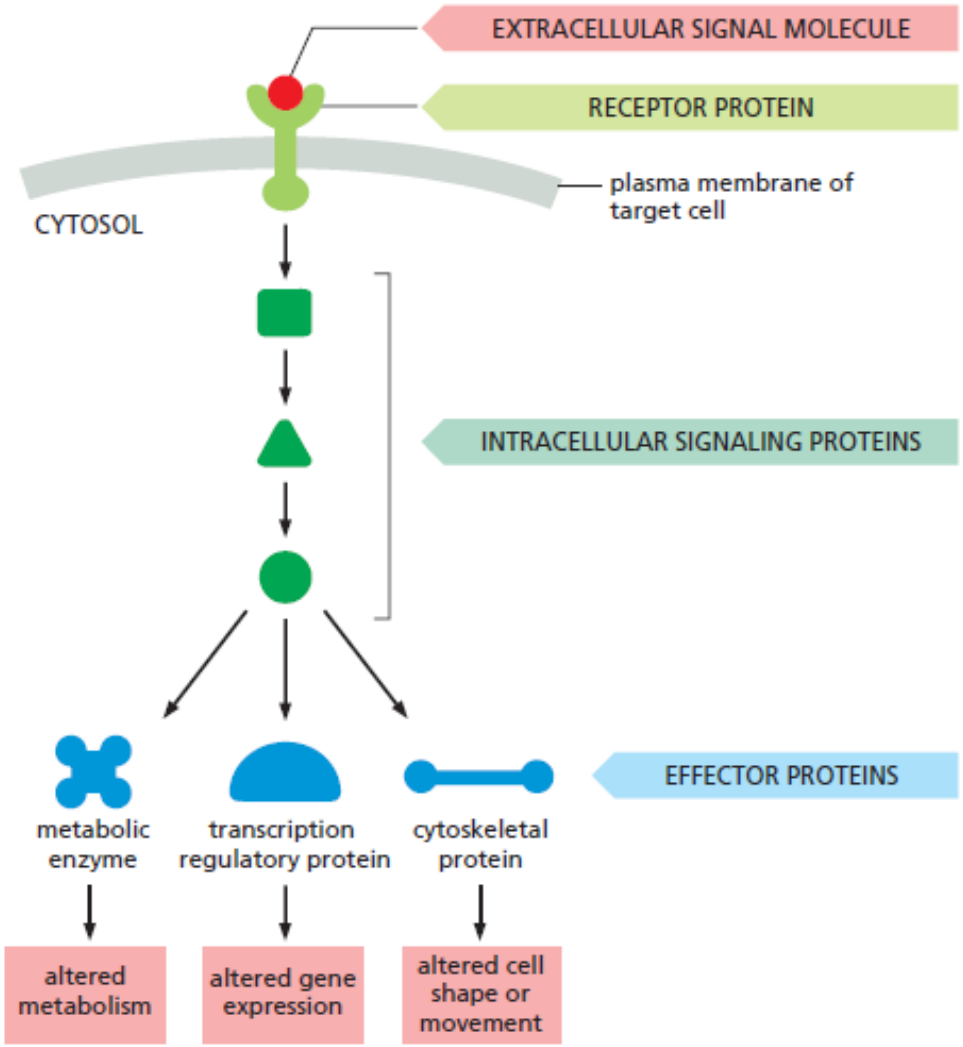


Fig. 15.1 & 15.27 – Molecular Biology of the Cell
https://pt.slideshare.net/AngelVega24/chapter-11-cell-communication?ref=&smtNoRedir=1

Cyclic adenosine monophosphate (cAMP)

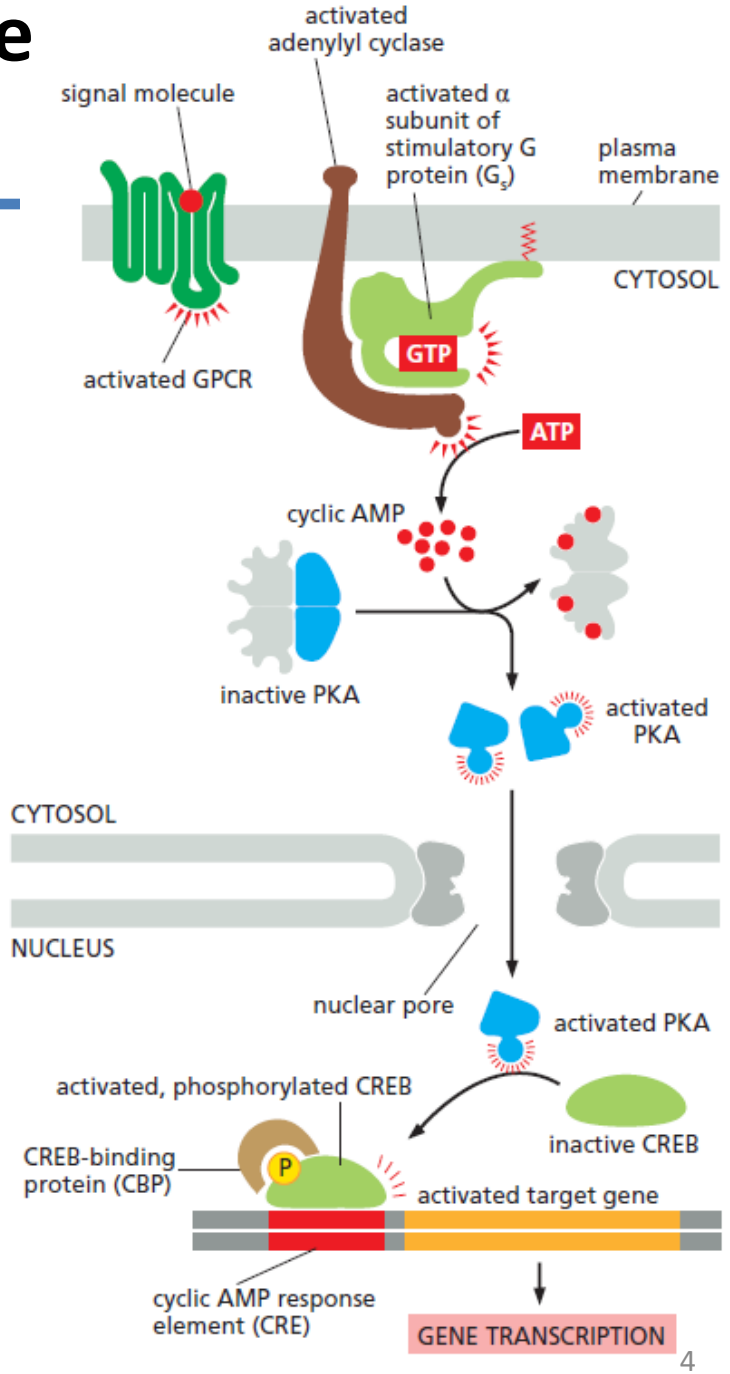
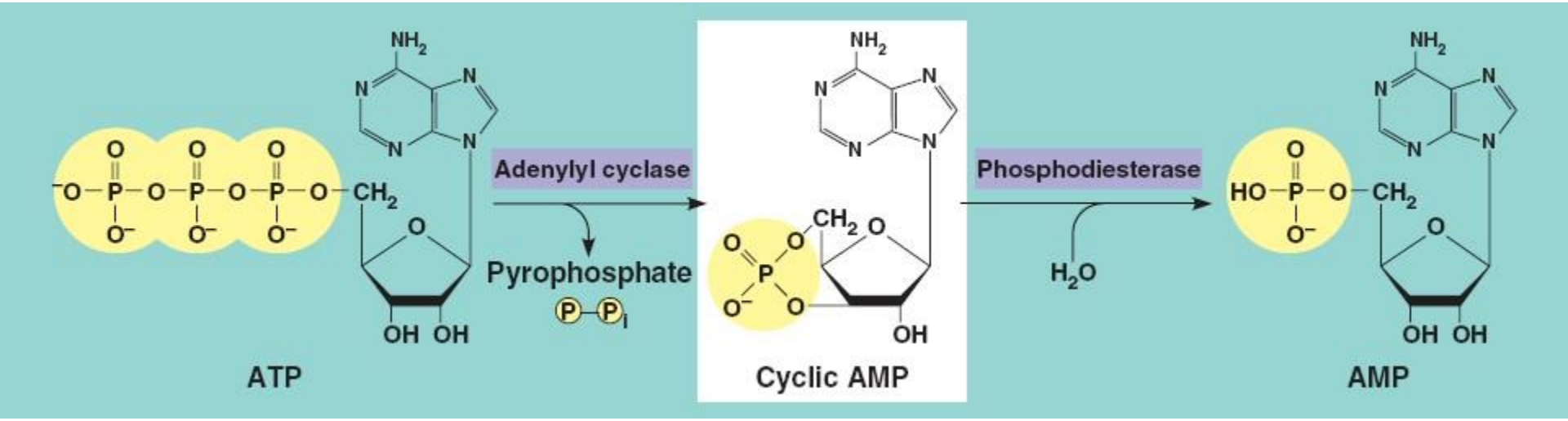


Fig. 15.1 & 15.27 – Molecular Biology of the Cell
https://www.youtube.com/watch?v=Y2er_Dfgg44

Cyclic adenosine monophosphate (cAMP)



1S6K: Crystal structure of the adenylyl cyclase domain of anthrax edema factor (EF)

http://bio1903.nicerweb.com/doc/class/bio1903/Locked/media/ch11/11_09CyclicAMP.jpg

Cyclic adenosine monophosphate (cAMP)

TABLE 15–1 Some Hormone-induced Cell Responses Mediated by Cyclic AMP		
Target tissue	Hormone	Major response
Thyroid gland	Thyroid-stimulating hormone (TSH)	Thyroid hormone synthesis and secretion
Adrenal cortex	Adrenocorticotrophic hormone (ACTH)	Cortisol secretion
Ovary	Luteinizing hormone (LH)	Progesterone secretion
Muscle	Adrenaline	Glycogen breakdown
Bone	Parathormone	Bone resorption
Heart	Adrenaline	Increase in heart rate and force of contraction
Liver	Glucagon	Glycogen breakdown
Kidney	Vasopressin	Water resorption
Fat	Adrenaline, ACTH, glucagon, TSH	Triglyceride breakdown

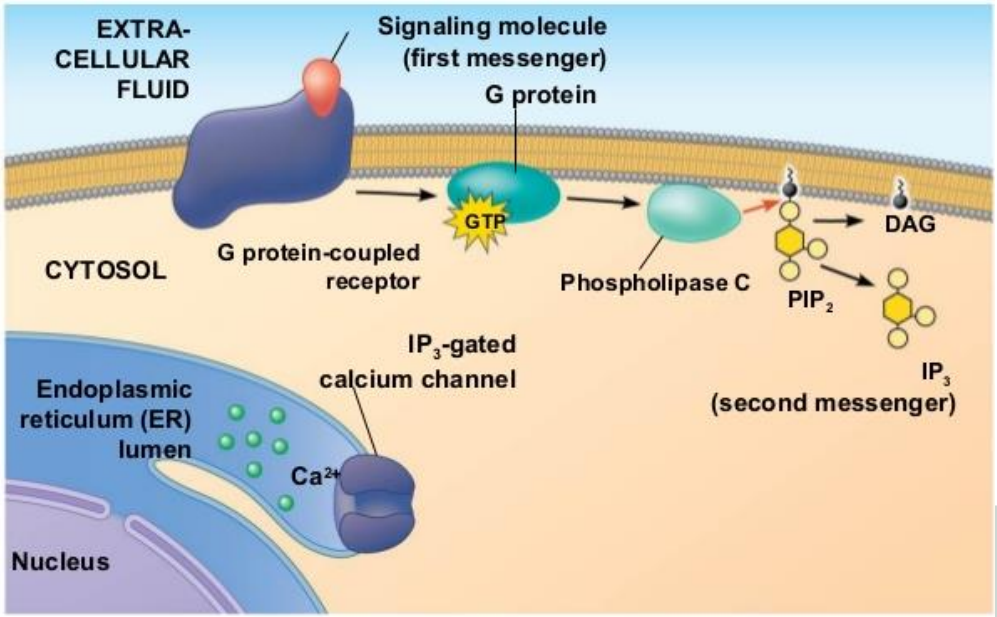
The use of phospholipids

Many GPCRs exert their effects through G proteins that activate the plasma-membrane-bound enzyme phospholipase C-β (PLCβ).

The phospholipase acts on a phosphorylated inositol phospholipid (a *phosphoinositide*) called phosphatidylinositol 4,5-bisphosphate [PI(4,5)P2], which is present in small amounts in the inner half of the plasma membrane lipid bilayer.

IP_3 signaling then splits in two pathways…

Inositol 1,4,5-triphosphate (IP_3)



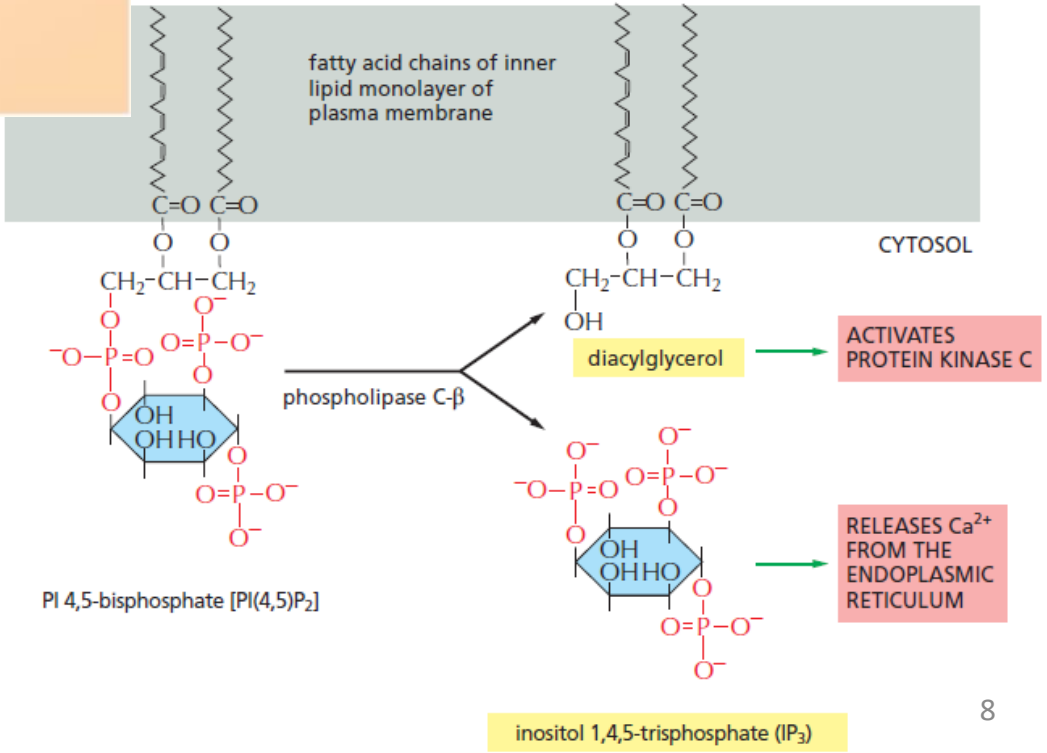


Fig. 15.28 – Molecular Biology of the Cell

https://pt.slideshare.net/AngelVega24/chapter-11-cell-communication?ref=&smtNoRedir=1

https://www.youtube.com/watch?v=lsYBeFqEwzk

Calcium ion (Ca^{2+})

IP3-gated Ca^{2+}-release channels (also called IP3 receptors) opening deliver calcium from the endoplasmatic reticulum.

Ca^{2+} can be transported intracellularly via plasma membrane proteins.

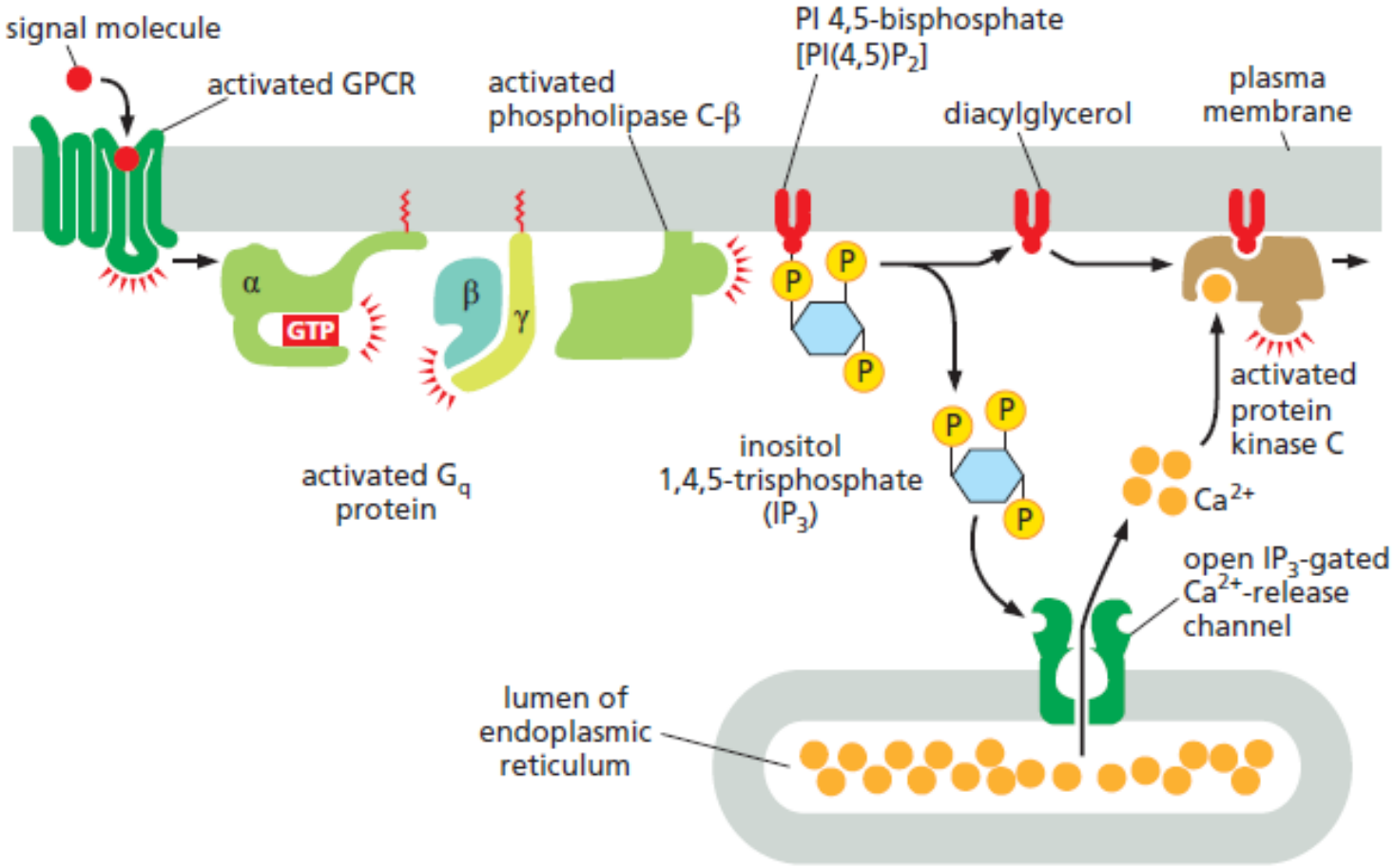


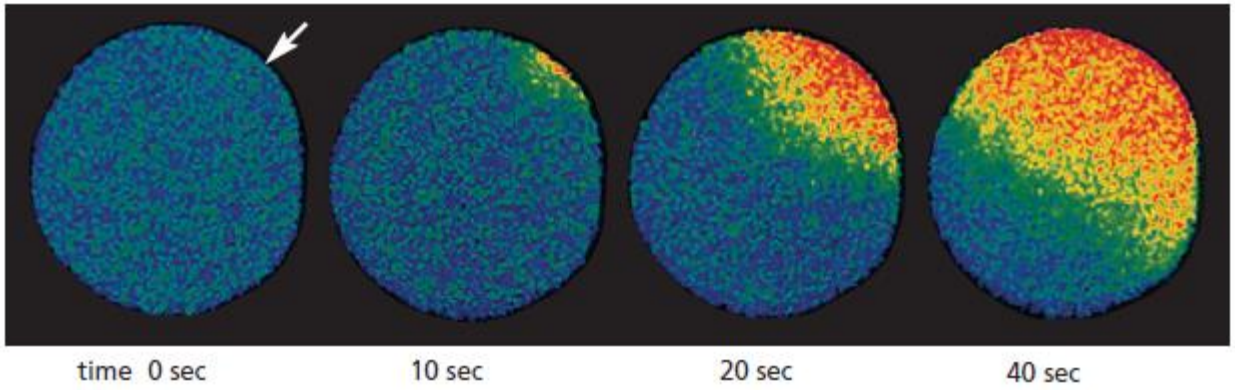
Fig. 15.29 – Molecular Biology of the Cell

Calcium ion (Ca^{2+})

Ca^{2+} concentration in the cytosol is normally very low (~10–7 M), whereas its concentration in the extracellular fluid (~10–3 M) and in the lumen of the ER [and sarcoplasmic reticulum (SR) in muscle] is high.

There is a large gradient tending to drive Ca^{2+} into the cytosol across both the plasma membrane and the ER or SR membrane.

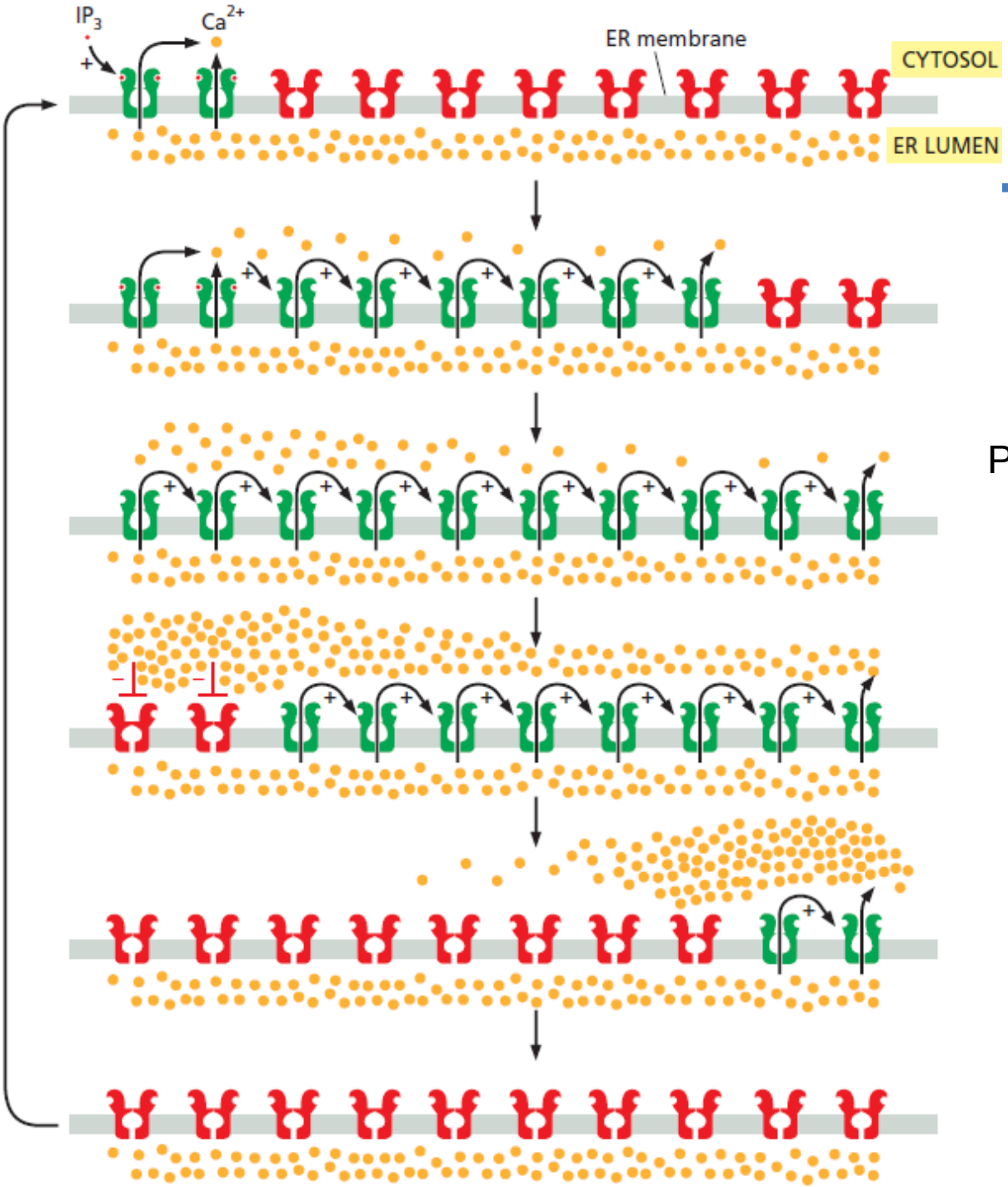
Several mechanisms rapidly terminate the Ca^{2+} signal and are also responsible for keeping the concentration of Ca^{2+} in the cytosol low in resting cells.



The fertilization of an egg by a sperm triggers a wave of cytosolic Ca^{2+}

Fig. 15.30 – Molecular Biology of the Cell

Waves of calcium ion (Ca^{2+})



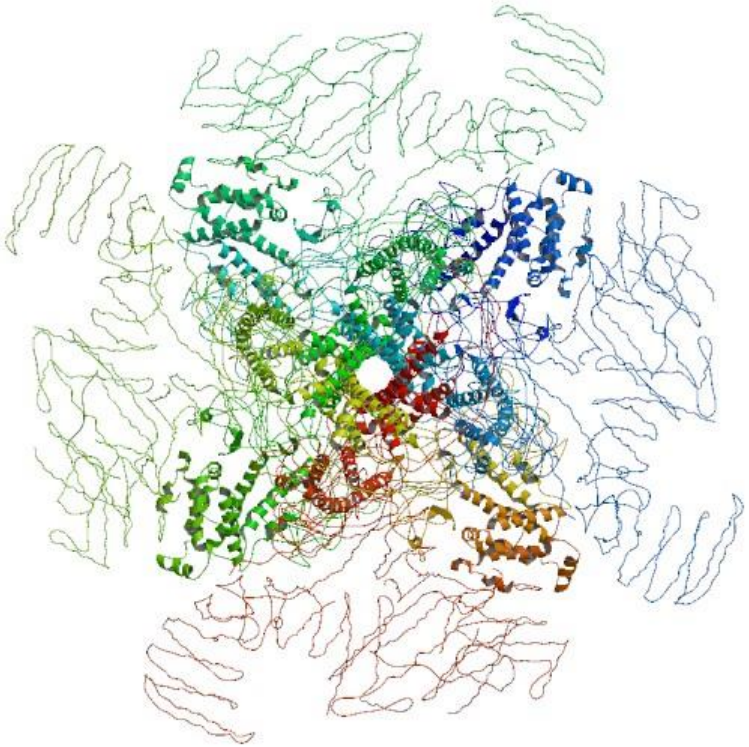
Positive and negative feedback produce Ca^{2+} waves and oscillations.

Fig. 15.31
Molecular Biology of the Cell

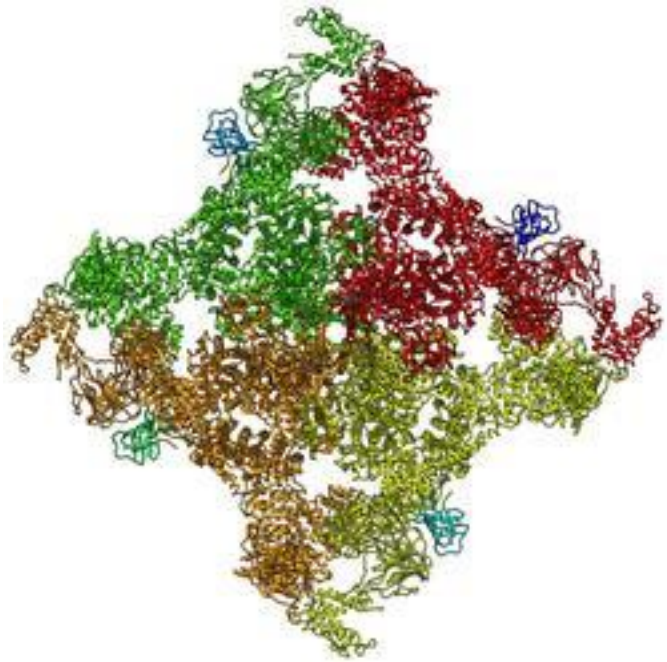
Calcium ion (Ca^{2+}) receptors

There are many receptors, mainly characterized by voltage-gated and ligand-gated.
Two ligand-gated receptors are shown below:

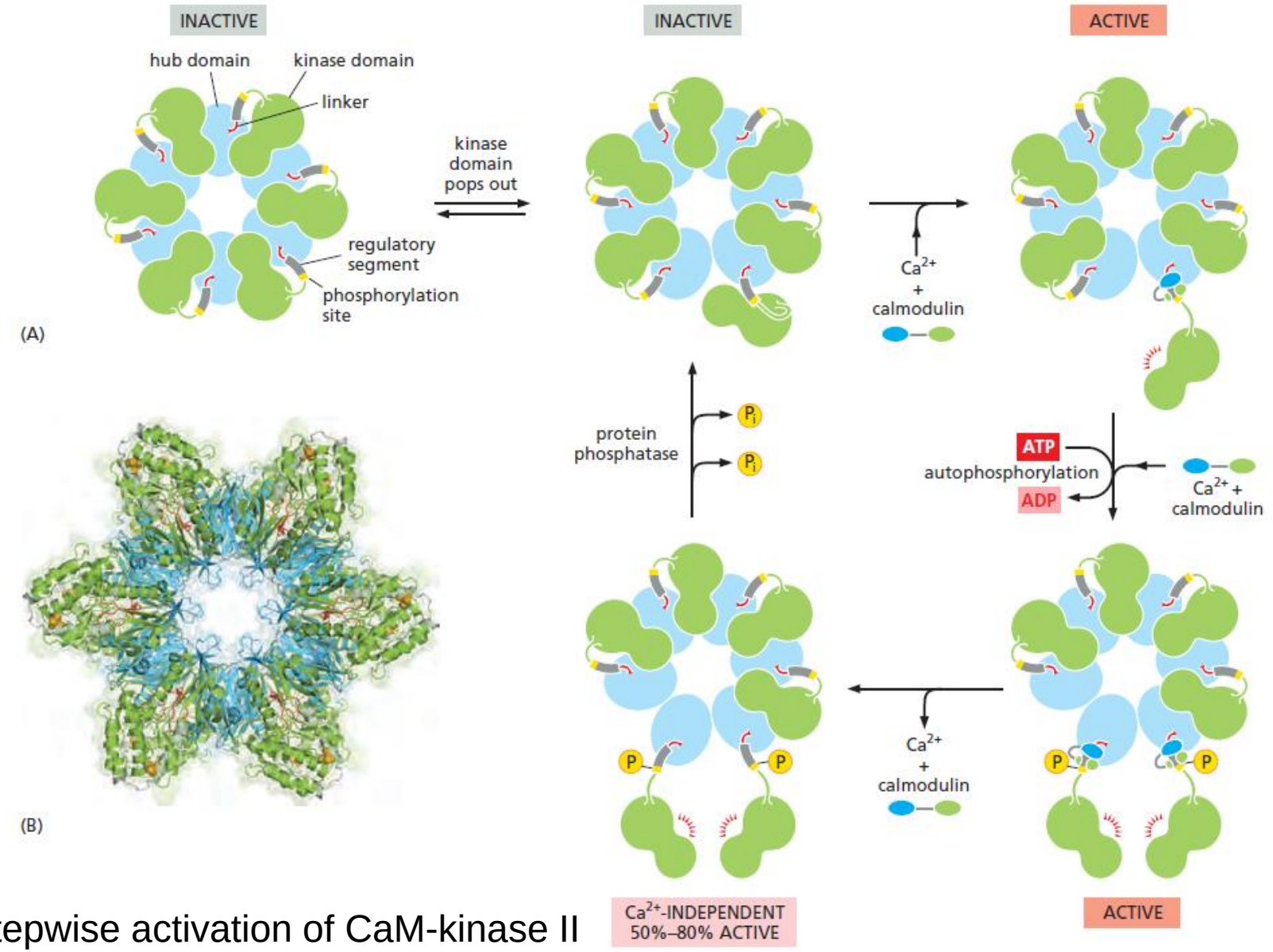
Inositol Triphosphate Receptor (InsP3R1)
1N4K & 3JAV



Ryanodine Receptor (RYR1)
5TA3



Calcium ion (Ca^{2+}) receptors



The stepwise activation of CaM-kinase II

Effects of the calcium ion (Ca^{2+})

One example is the vasopressin release in a liver cell:

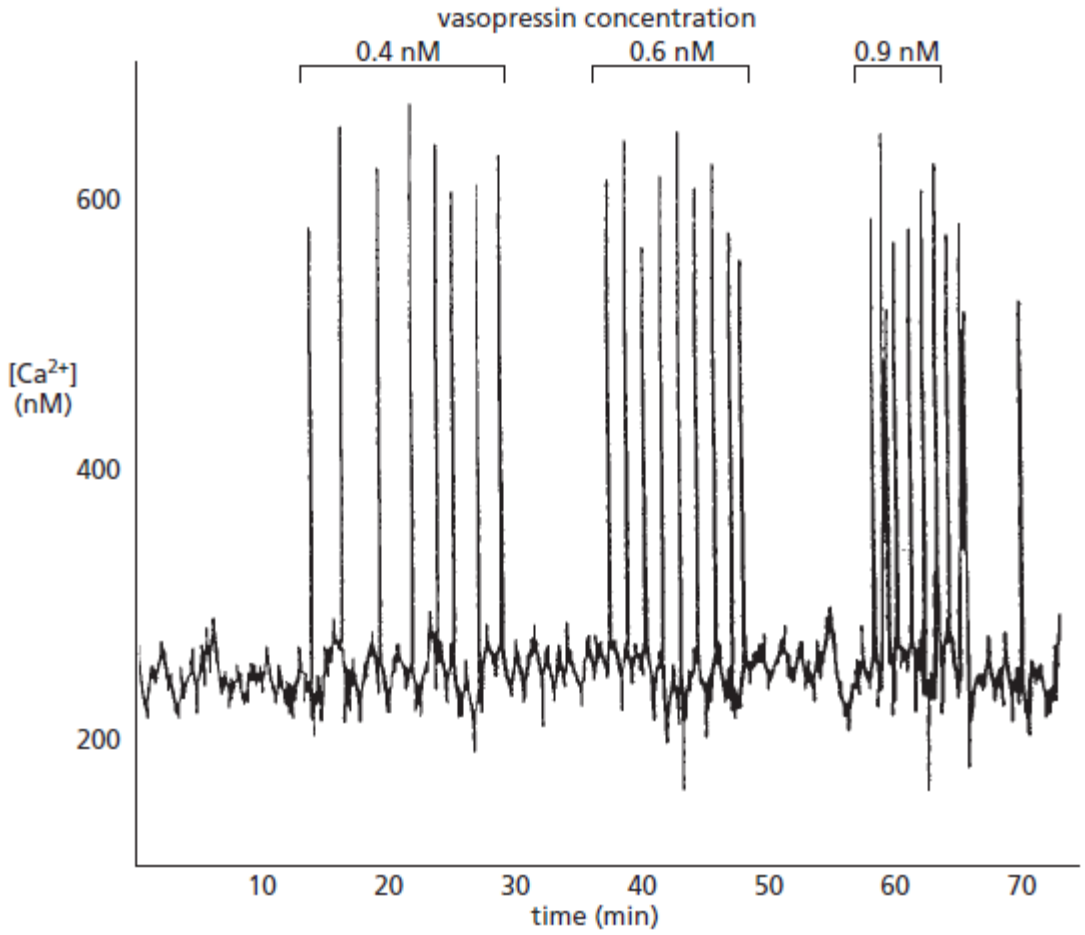


Fig. 15.32 – Molecular Biology of the Cell

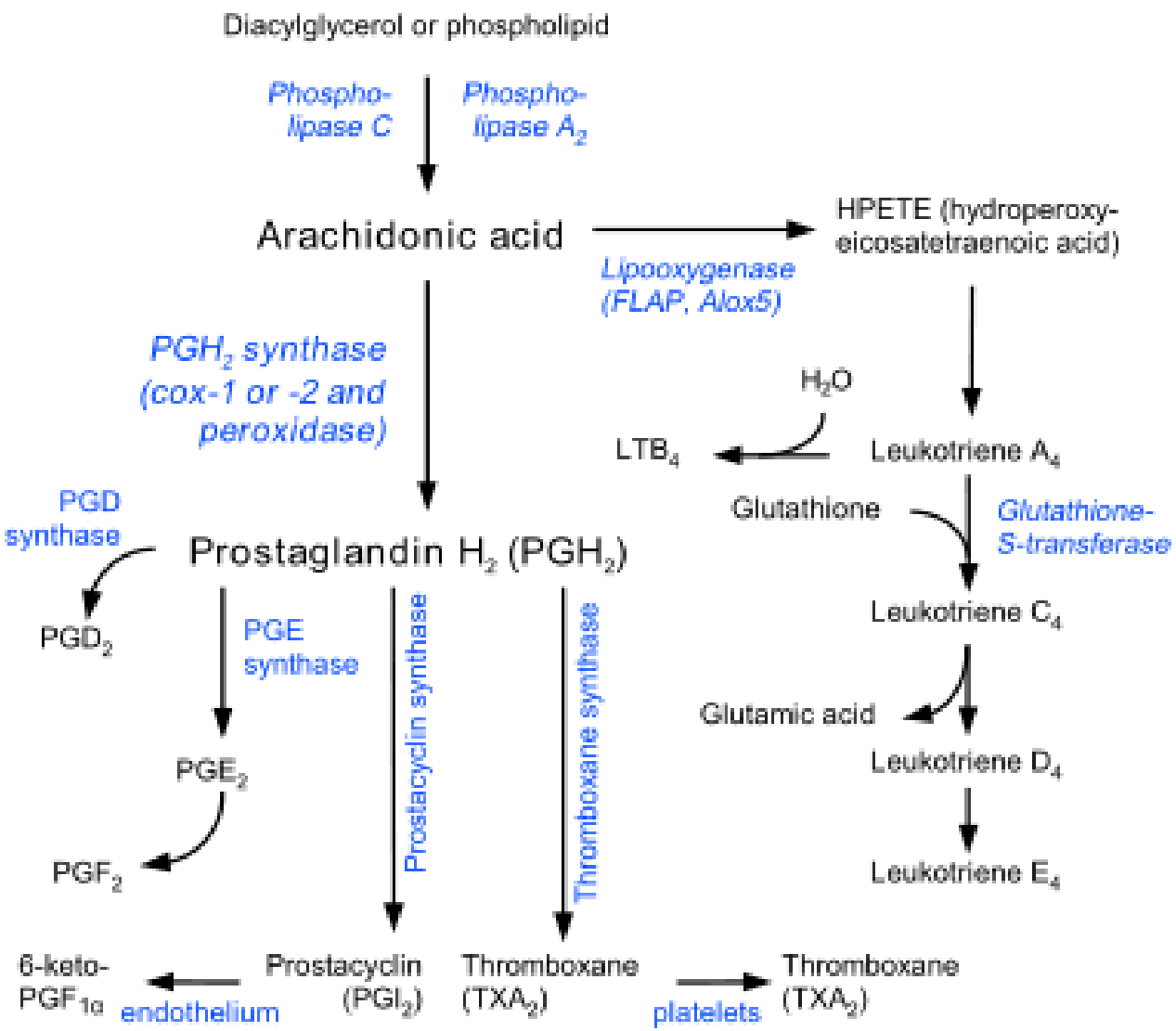
Diacylglycerol

It also acts as a second messenger, but it remains embedded in the plasma membrane, where it has several potential signaling roles. One of its major functions is to activate a protein kinase called protein kinase C (PKC), so named because it is Ca^{2+}-dependent.

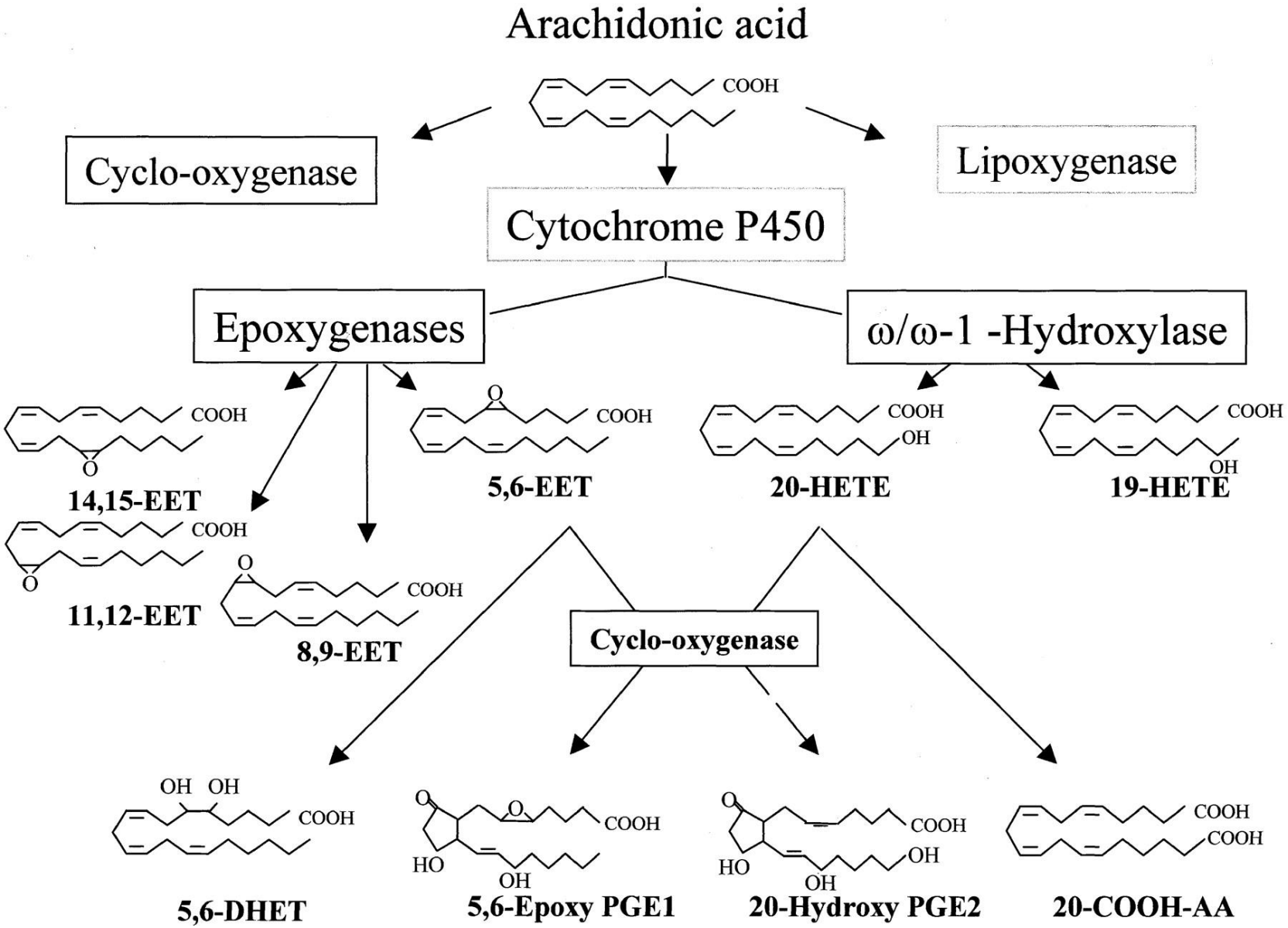
PKC is activated by the combination of Ca2+, diacylglycerol, and the negatively charged membrane phospholipid phosphatidylserine.

Diacylglycerol can be further cleaved to release arachidonic acid, which can either act as a signal in its own right or be used in the synthesis of other small lipid signal molecules called *eicosanoids.*

Eicosanoids



Eicosanoids



http://circres.ahajournals.org/content/89/9/753