

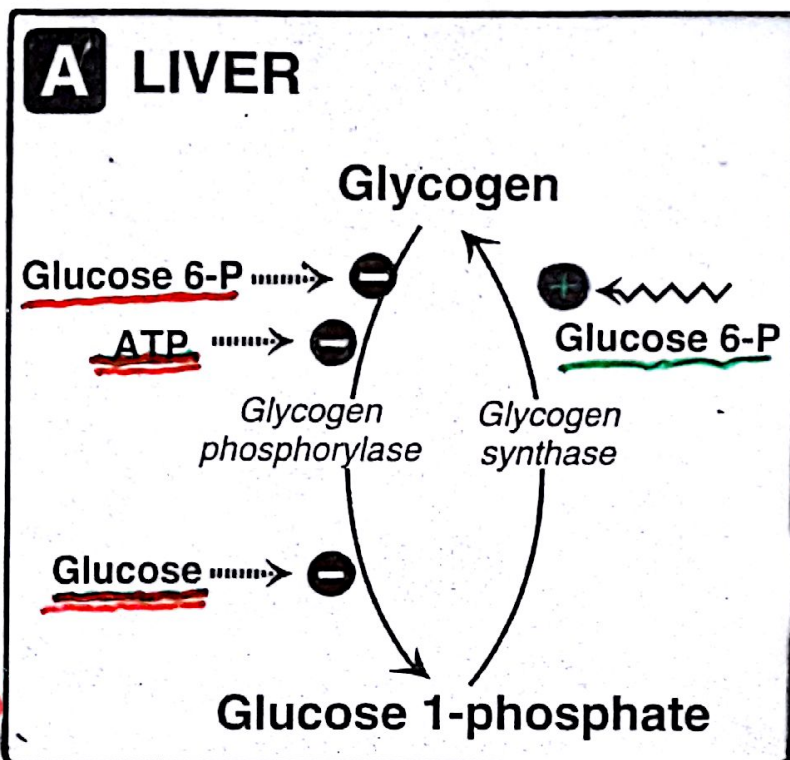
Regulation of Glycogen Synthesis and Degradation

A. Allosteric Regulation

- During Well-Fed state
 Glu \uparrow , G6P \uparrow
 ATP \uparrow

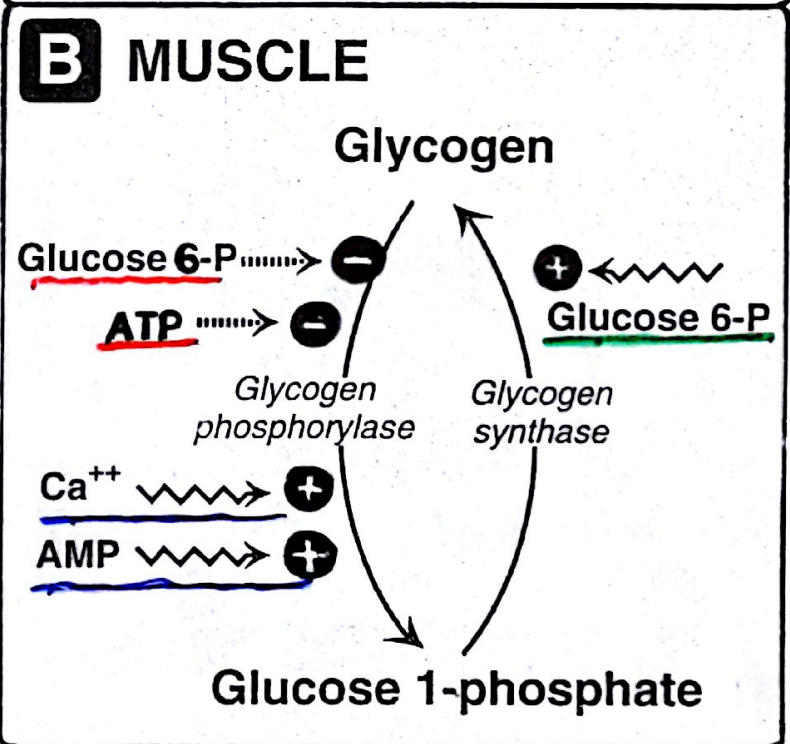
- Activation of glycogen degradation in muscle by Ca^{2+}

- Activation of Glycogen degradation in muscle by 5'-AMP



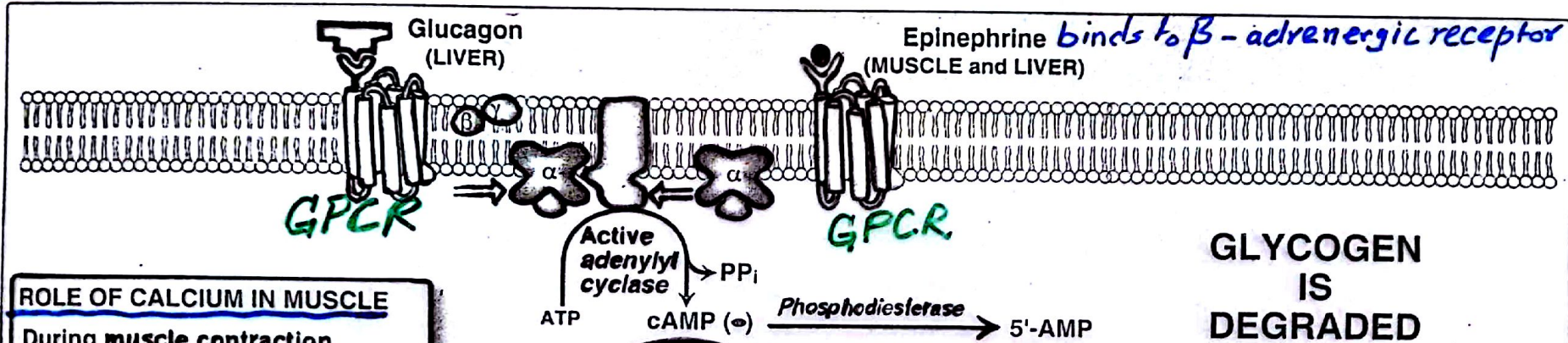
Well Fed:-
 synthesis \uparrow
 Degradation \downarrow
 High Energy
 High [S] = Glu

Fasting:-
 Synthesis \downarrow
 Degradation \uparrow
 (low energy, low glu)

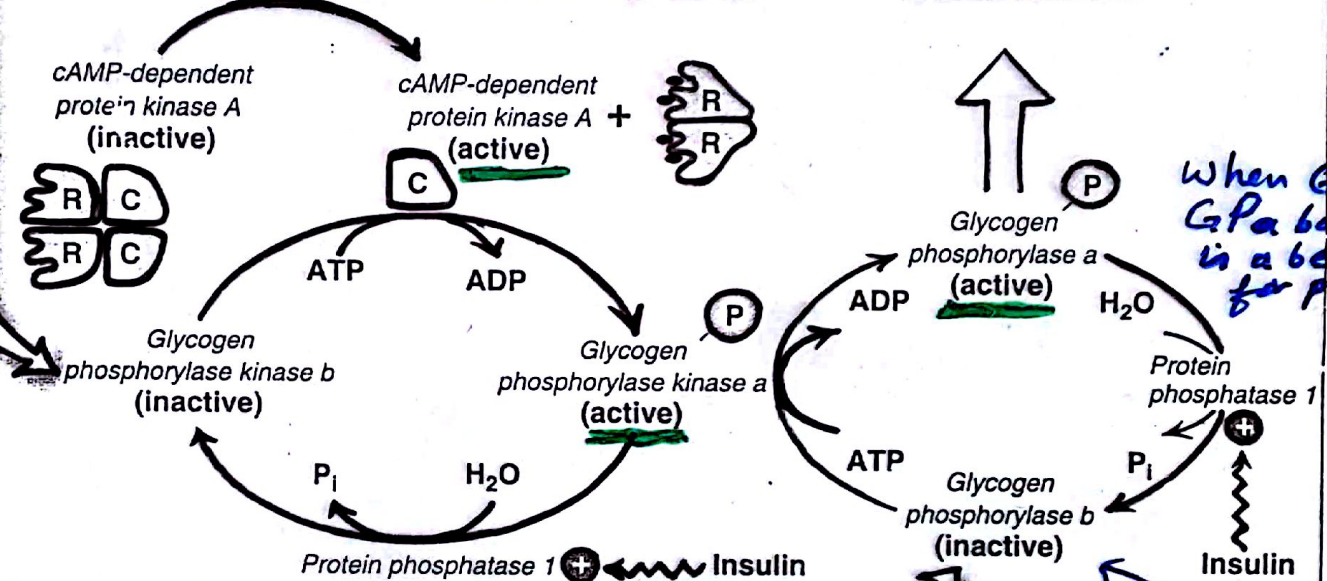


Exercise:-
 Degradation \uparrow

Activation of Glycogen Degradation by a cAMP-directed Pathway



ROLE OF CALCIUM IN MUSCLE
 During muscle contraction, Ca^{2+} is released from the sarcoplasmic reticulum. The Ca^{2+} binds to the calmodulin subunit of phosphorylase kinase, activating it without phosphorylation. Phosphorylase kinase can then activate glycogen phosphorylase, causing glycogen degradation.



GLYCOGEN IS DEGRADED

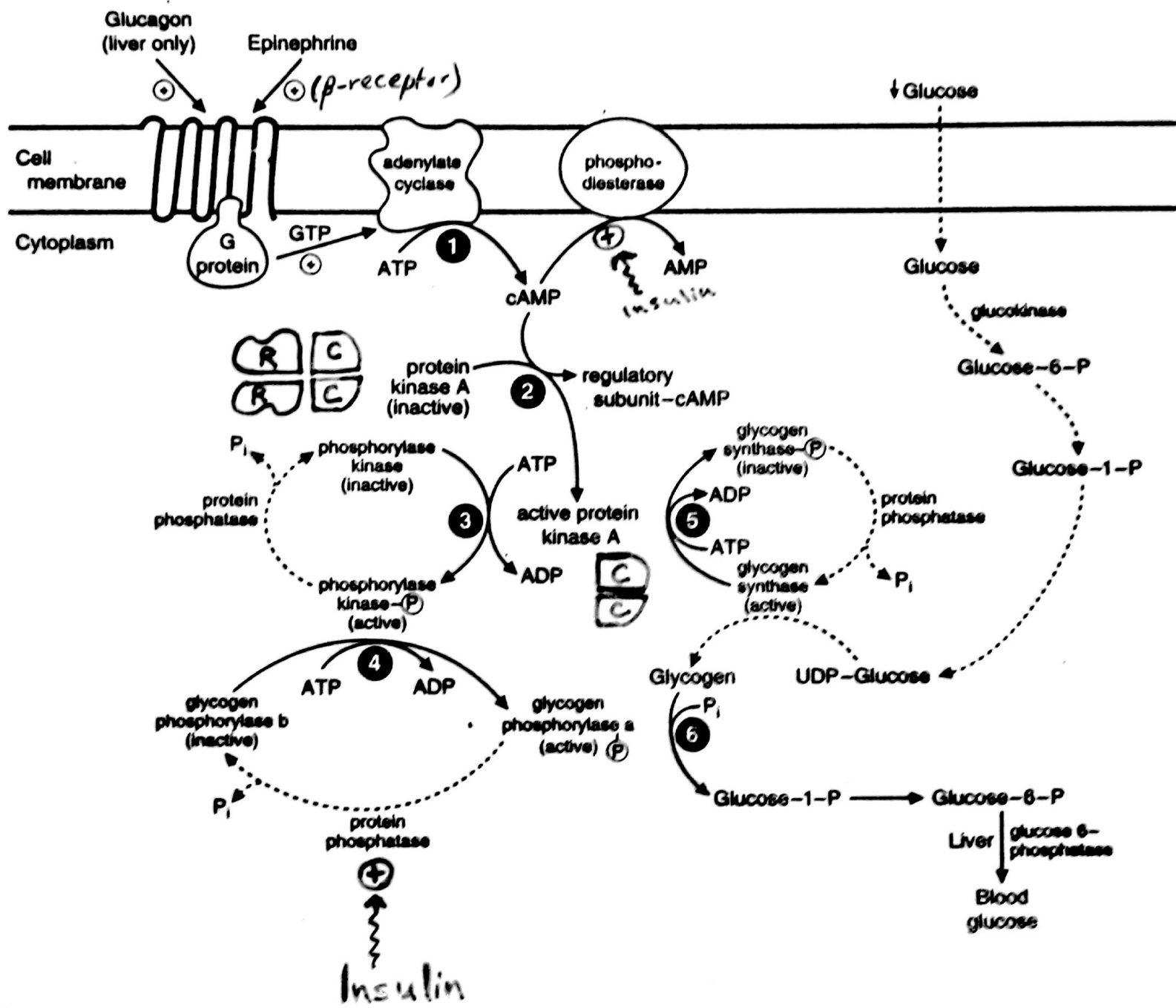
When Glu-1-P is a better [S] for phosphatase

ROLE OF AMP IN MUSCLE
 In muscle under extreme conditions of anoxia and depletion of ATP, AMP activates glycogen phosphorylase b without it being phosphorylated.

When bound to Glu, no response to 5'-AMP

- 1- Activation of Protein Kinase A
- 2- Activation of phosphorylase Kinase
- 3- Activation of Glycogen phosphorylase

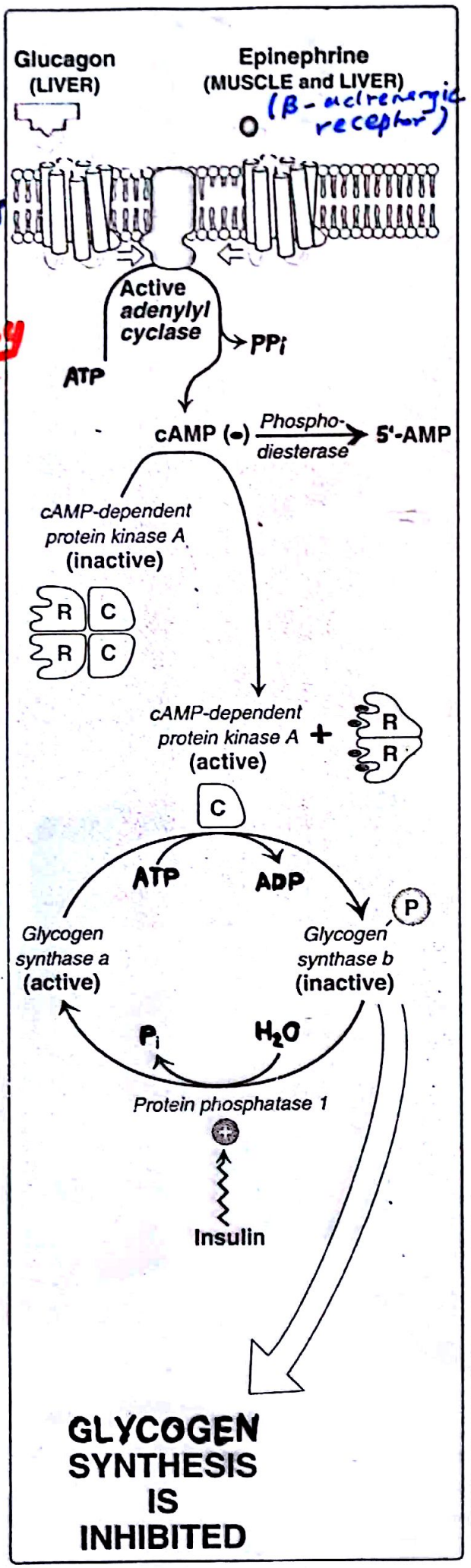
Regulation of Glycogen Synthesis and Degradation in the Liver :-



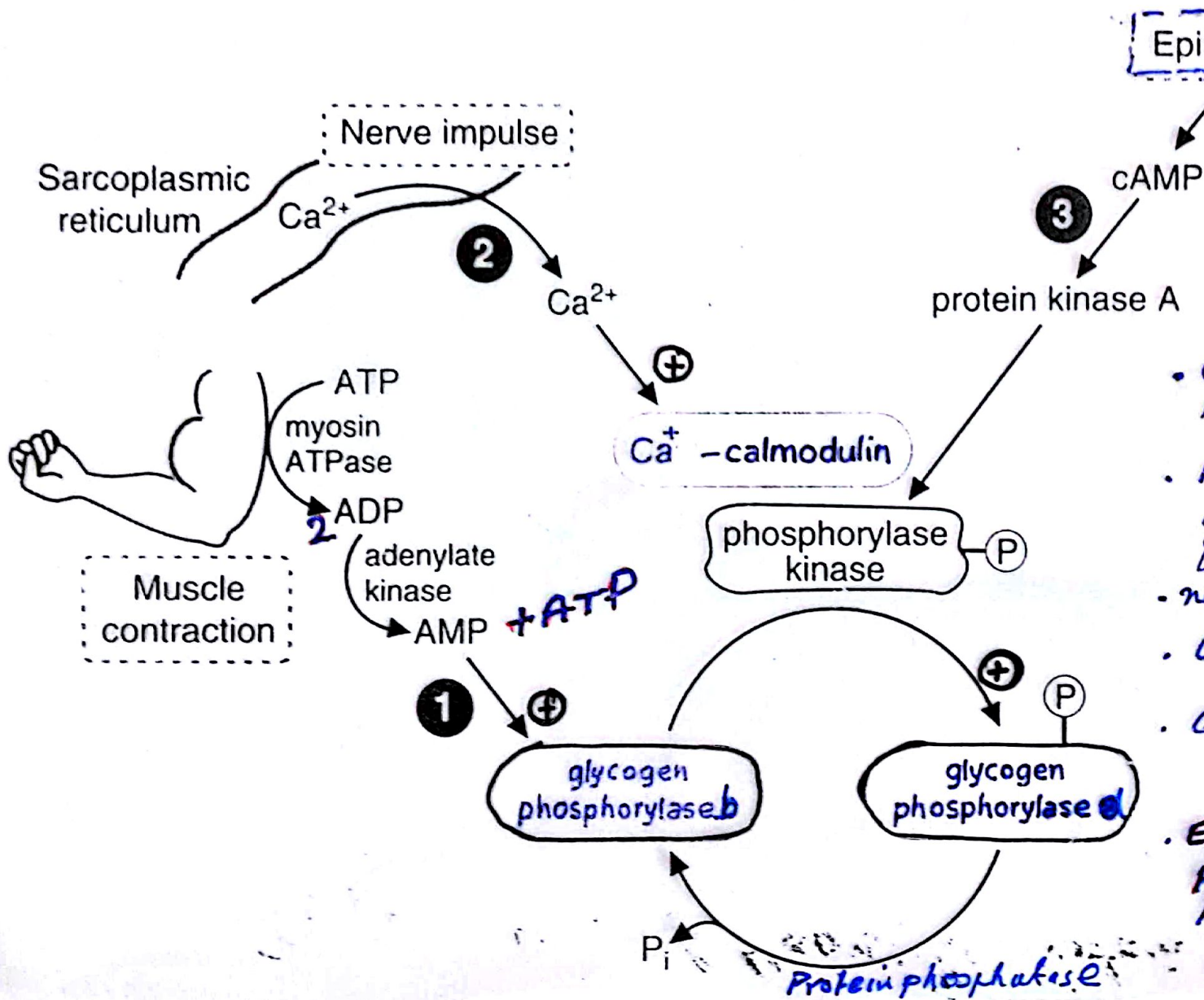
Hormonal Regulation of Glycogen Synthesis

- Inhibition by cAMP mediated process

+ - Inhibition by other Protein Kinases (cAMP indep. endant)



Activation of Muscle Glycogen Phosphorylase During Exercise 35



Differences in Regulation of Glycogen Deg. + Syn. between Liver & muscle:-

- Glucagon has no effect on muscle
- AMP is an allosteric effector of muscle GP only (not liver)
- neural stimulation ↑ Ca⁺
- Glu is not a physiological stimulator of GS in muscle
- Glycogen is stronger inhibitor of GS in muscle than in liver
- Effect of epinephrine - stimulated Protein Kinase A is similar in liver & muscle.

Calmodulin mediates many effects of intracellular Ca^{2+}

Epinephrine \rightarrow α -agonist receptor
 \rightarrow \uparrow phospholipase C

$PIP_2 \xrightarrow{\text{phospholipase C}} \begin{cases} \uparrow \text{ DAG} \\ \downarrow \text{ IP}_3 \end{cases}$

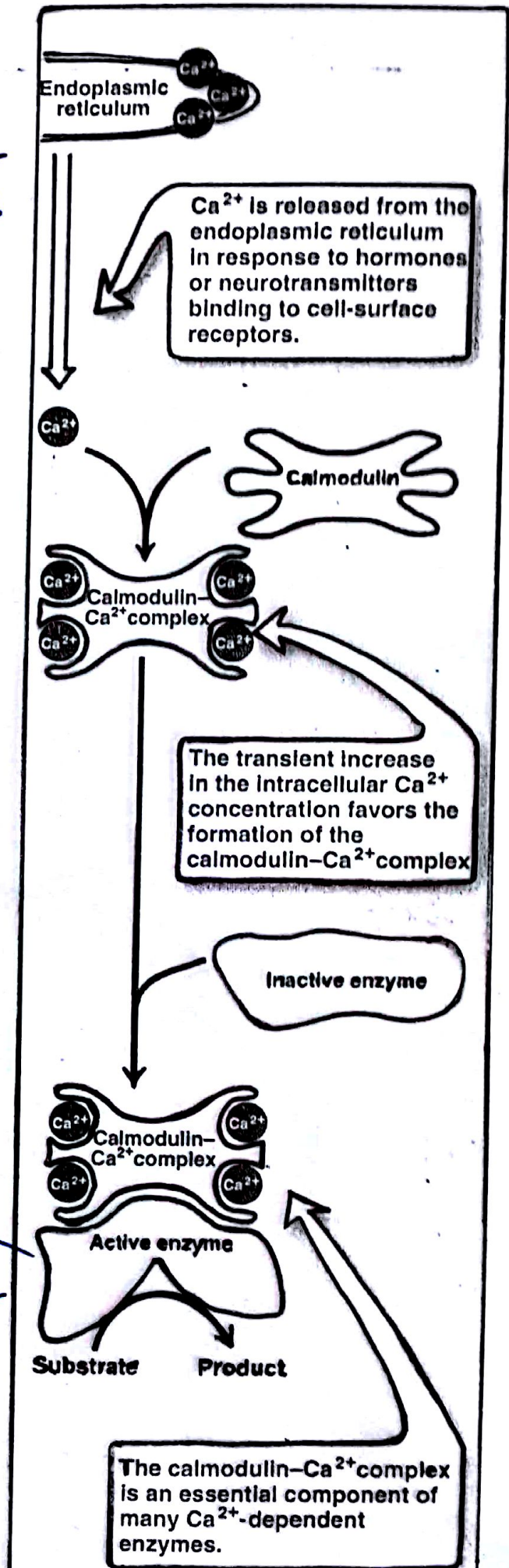
$IP_3 \rightarrow \text{E.R.} \rightarrow Ca^{2+}$

Ca^{2+} also activate protein kinase C

e.g. :-

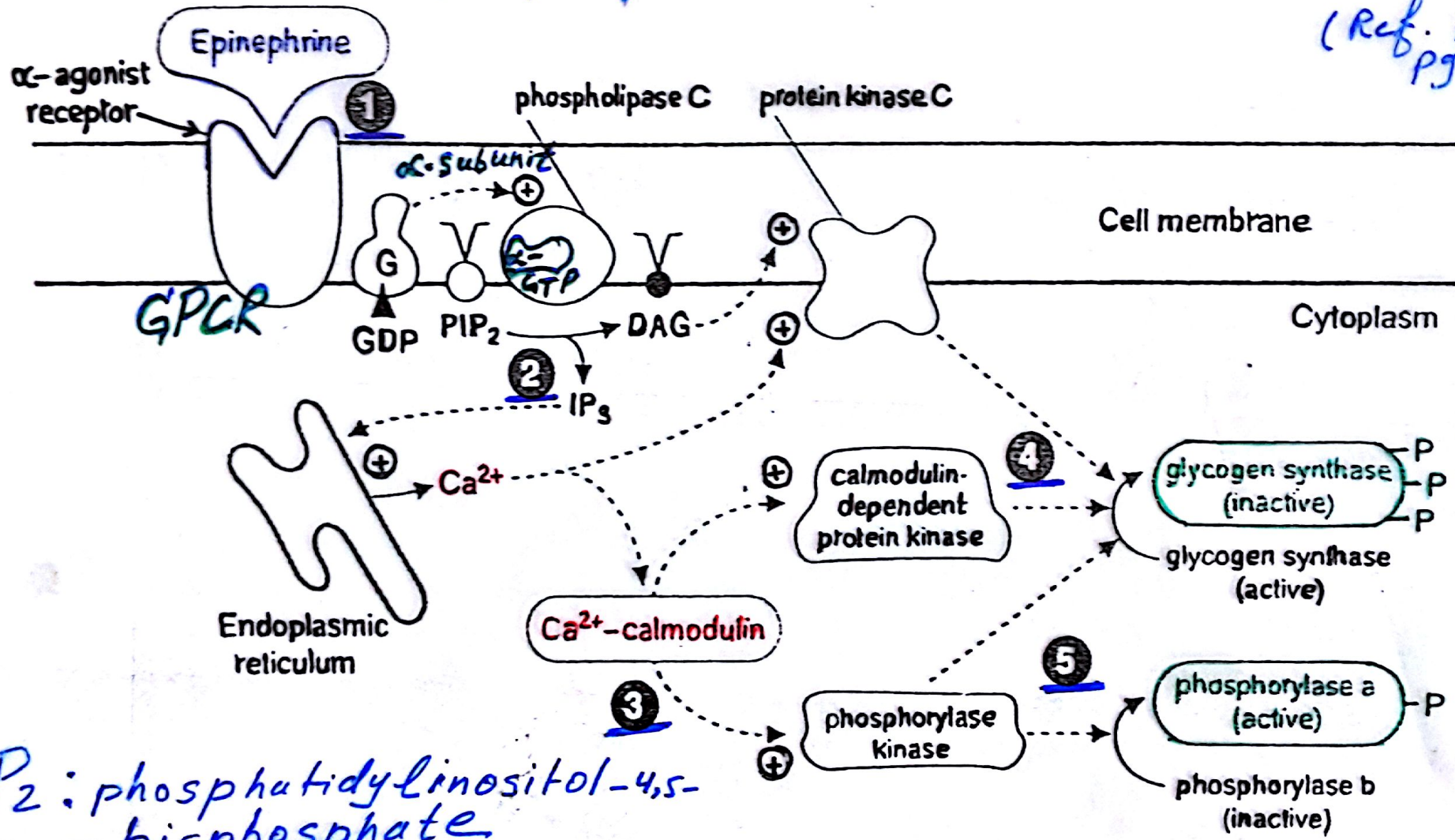
(1) Calmodulin-dependent protein kinase

(2) phosphorylase kinase



Regulation of Glycogen Synthesis and Degradation by Epinephrine and Ca^{2+} in the Liver

(Ref. fig 17.8, pg 205)



PIP_2 : phosphatidylinositol-4,5-bisphosphate
 IP_3 : Inositol 1,4,5-trisphosphate
 DAG: Diacylglycerol