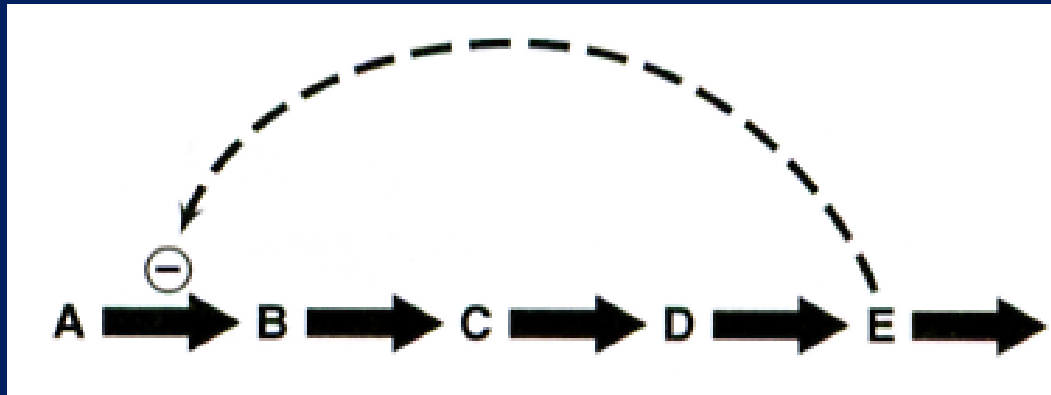
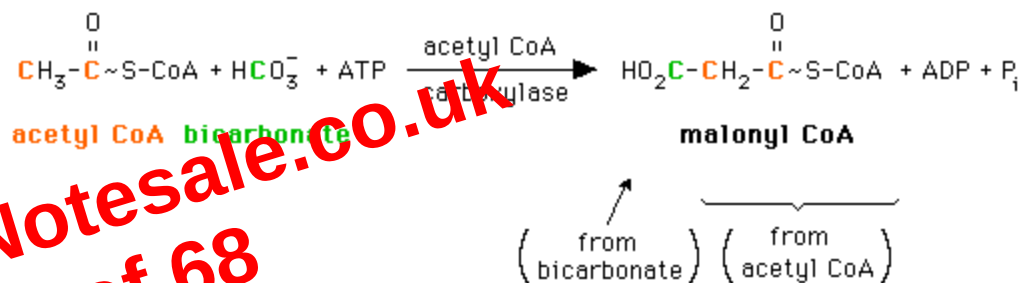
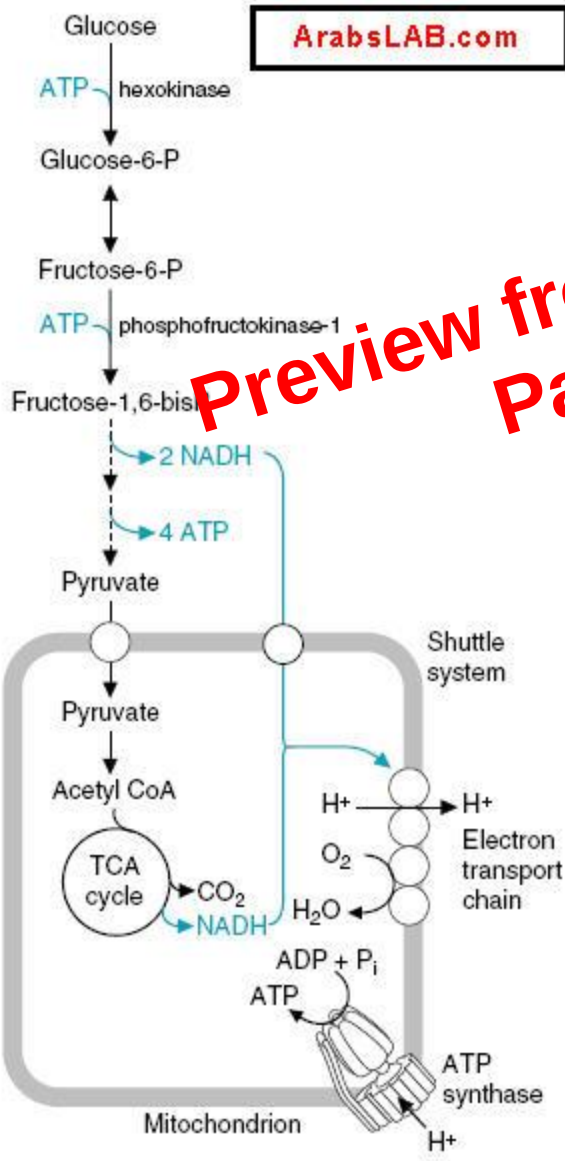


Feed back inhibition

- ✓ The **ultimate product** of a long metabolic pathway **inhibits the first enzyme** in the early step in the pathway.
- ✓ Some products of a pathway repress the synthesis of the enzyme, it called (FB repression).



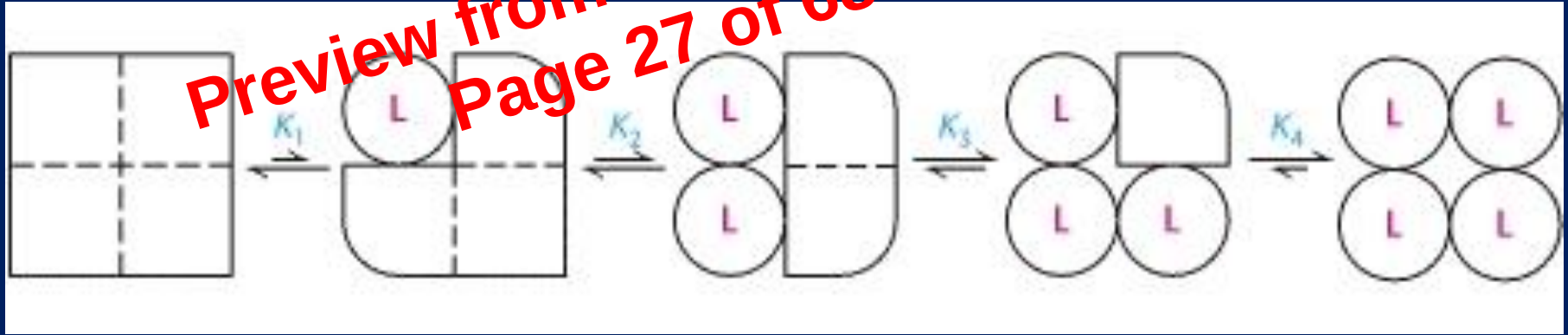


This is the first and the committed step in the biosynthesis of long-chain fatty acids.

It is down-regulated by:
 palmitoyl CoA (endproduct regulation).
 phosphorylation of the enzyme
 (through a glucagon-cAMP cascade).

It is up-regulated by:
 citrate (allosteric)
 dephosphorylation of the enzyme
 (influenced by the insulin/glucagon ratio).

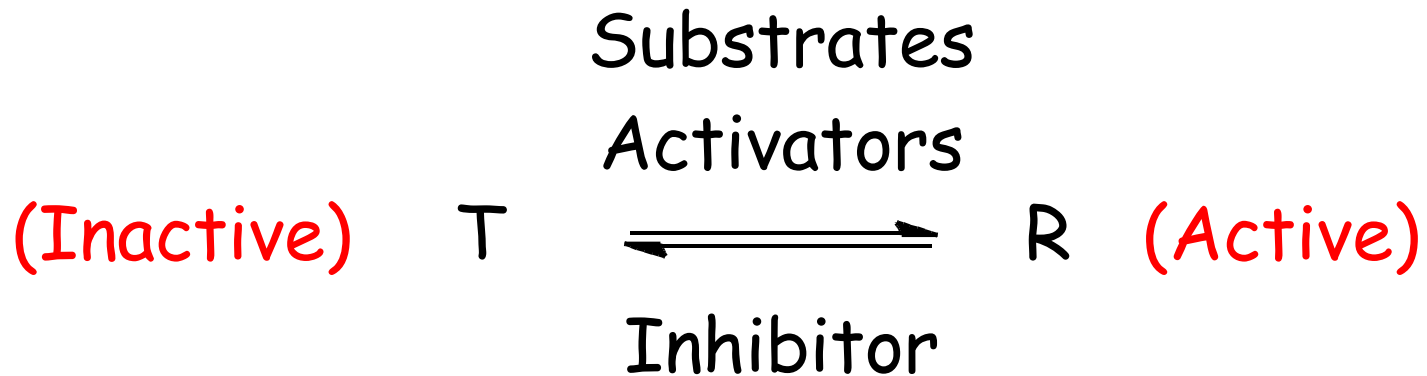
Simple Sequential Model for a Tetrameric Allosteric Enzyme



- ✓ The binding of a ligand (L) to a subunit changes the conformation of that particular subunit from the T (square) to the R (circle) form.
- ✓ This transition affects the affinity of the other subunits for the ligand.

Allosteric (Regulatory) Enzymes

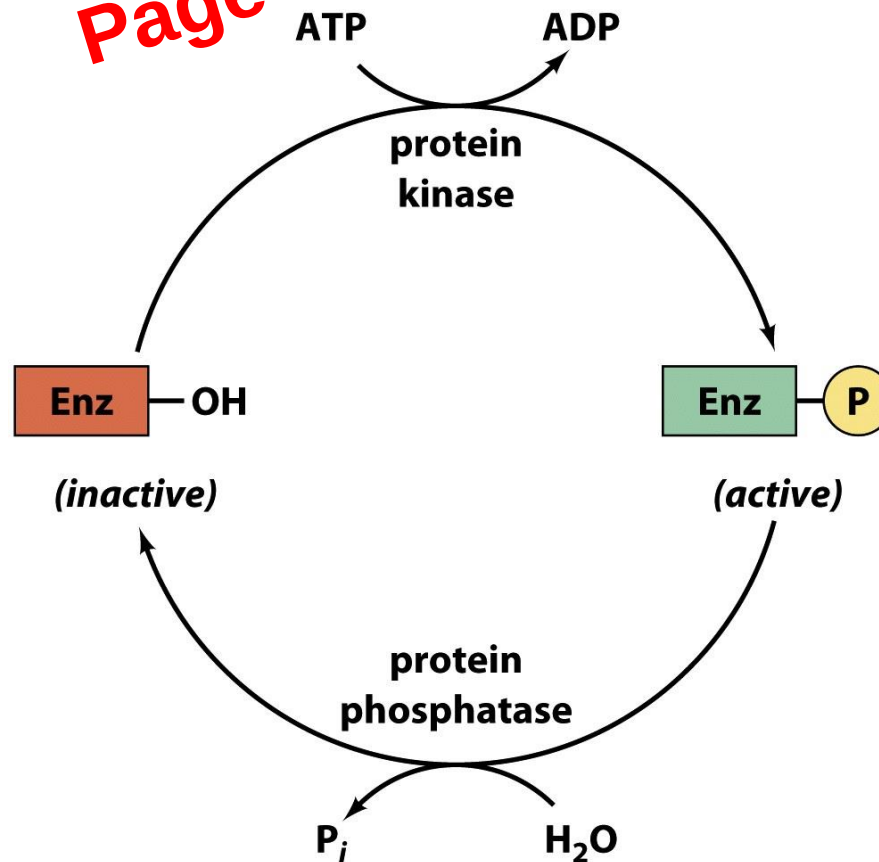
Preview from Notesale.co.uk
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Protein Modification

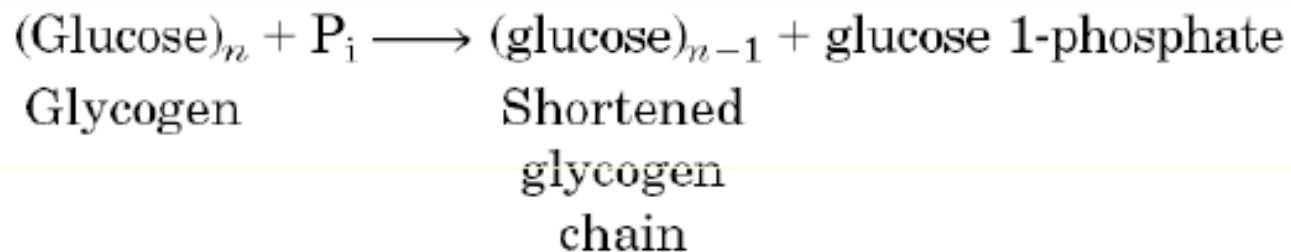
(Phosphorylation/Dephosphorylation)

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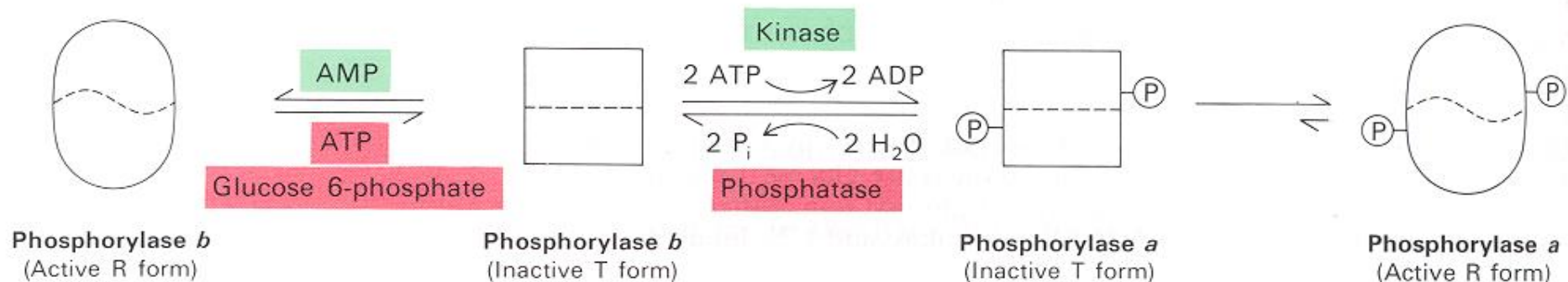
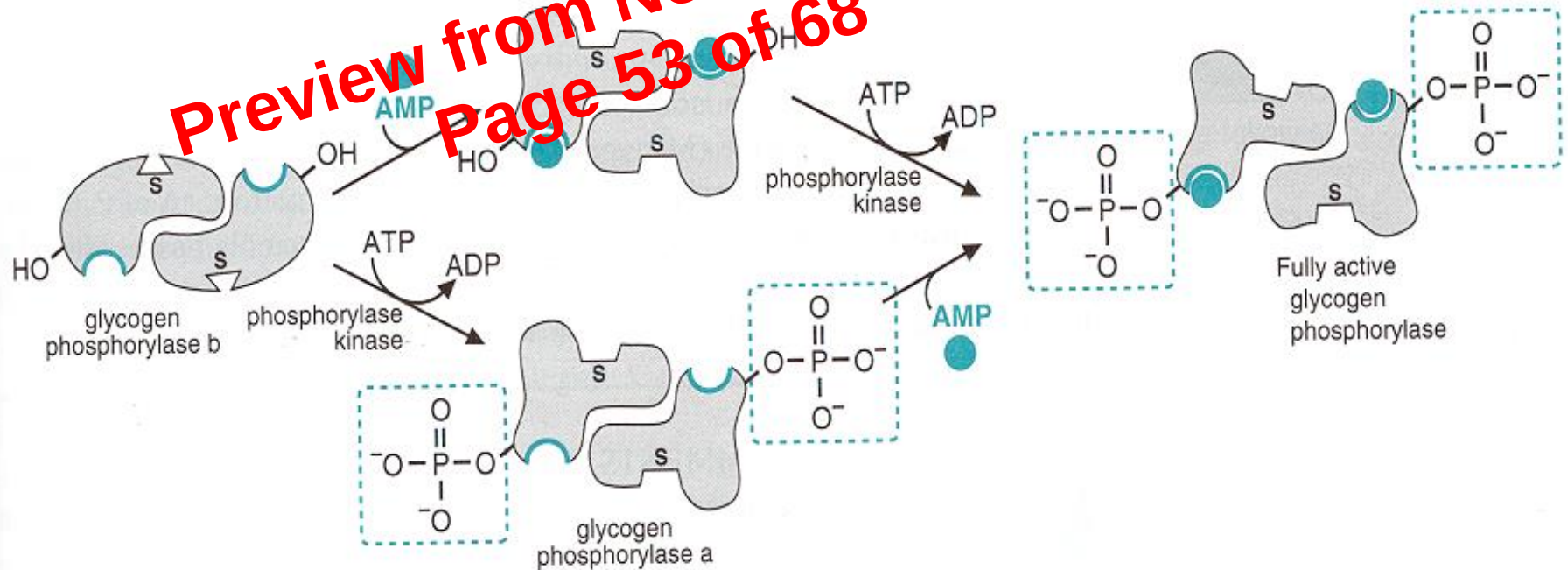
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An important example of regulation by phosphorylation is seen in glycogen phosphorylase (M_r 94,500) of muscle and liver (Chapter 15), which catalyzes the reaction



The glucose 1-phosphate so formed can be used for ATP synthesis in muscle or converted to free glucose in the liver. Glycogen phosphorylase occurs in two forms: the more active phosphorylase *a* and the less active phosphorylase *b* (Fig. 6-31). Phosphorylase *a* has two

Allosteric and Phosphorylation Regulation - Glycogen Phosphorylase



Medical Apps: Diagnosis-3

- LDH is a tetramer composed of two protomers, heart (H) and muscle (M). Of the five LDH isozymes, LDH₁ (H₄) and LDH₂ (H₃M) are found only in heart muscle and red blood cells.
- Again, electrophoresis patterns can be used to diagnose an infarct. The next slide shows normal and abnormal patterns for LDH₁₋₅.

Medical Apps: Therapy

- Streptokinase and human tissue plasminogen activator (tPA) are both used to treat heart attack because they dissolve blood clots
- Asparaginase does not occur in human blood. Some cancer cells (eg some adult leukemias) cannot synthesize asparagine. Infusing the enzyme can cause cancer cell death due to lack of asparagine. Serious side effects can occur.

Zymogens (cont)

- Activation of zymogens by proteolytic cleavage result in irreversible activation. Zymogen forms allow proteins to be transported or stored in inactive forms that can be readily converted to active forms in response to some type of cellular signal. Thus they represent a mechanism whereby the levels of an enzyme/protein can be rapidly increased (post-translationally). Other examples of zymogens include proinsulin, procollagen and many blood clotting enzymes (the latter will be discussed in the next lecture).

Allosteric and Phosphorylation Regulation

- Glycogen Phosphorylase

