

Chapter 16

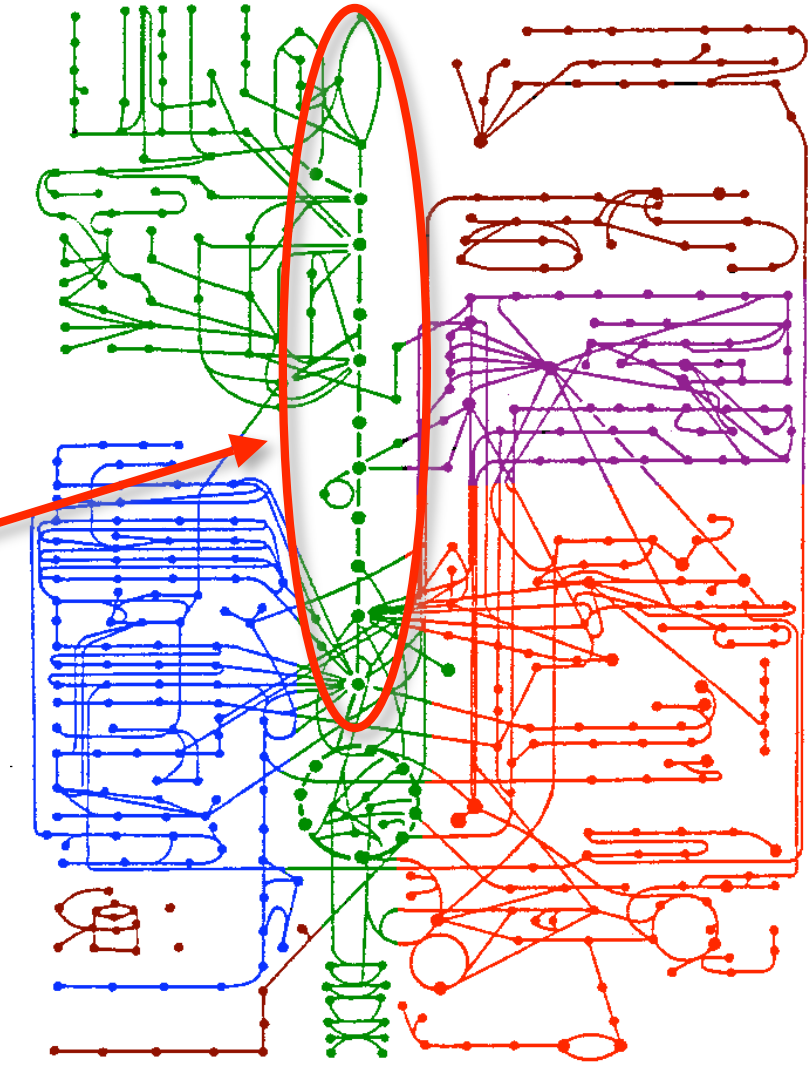
Glycolysis and Gluconeogenesis

The Musical?



Chapter 16

We Are Here



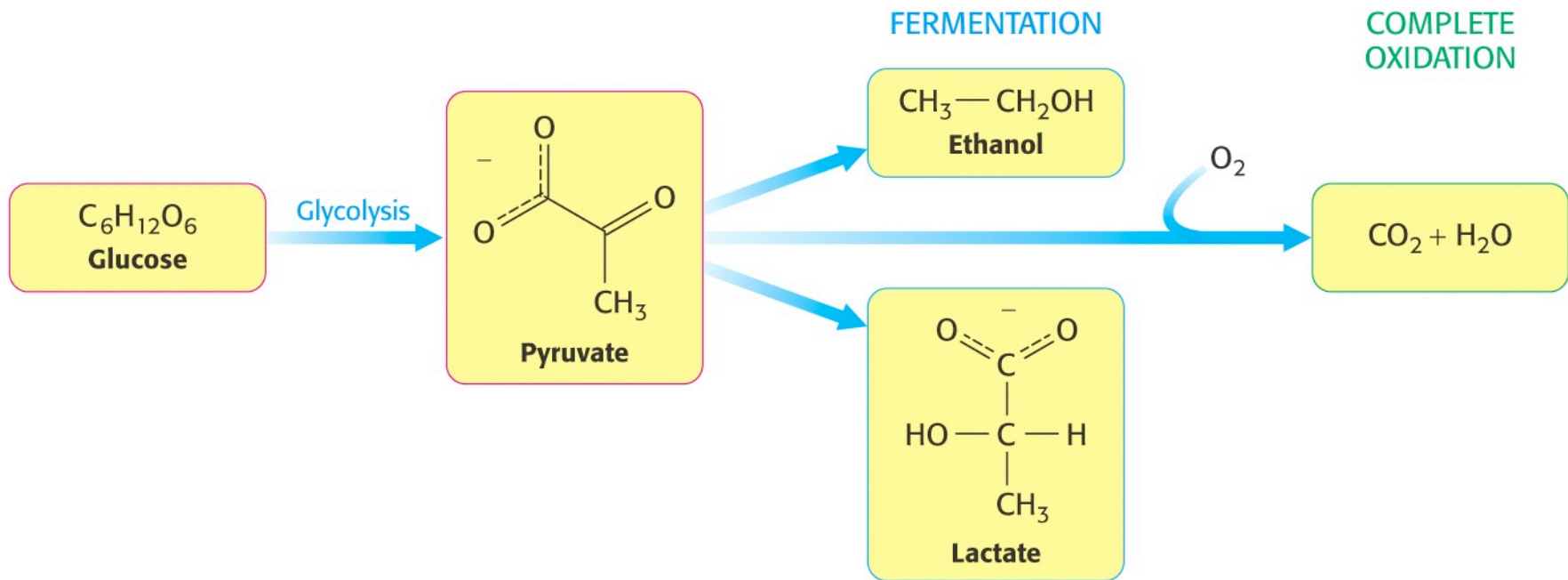
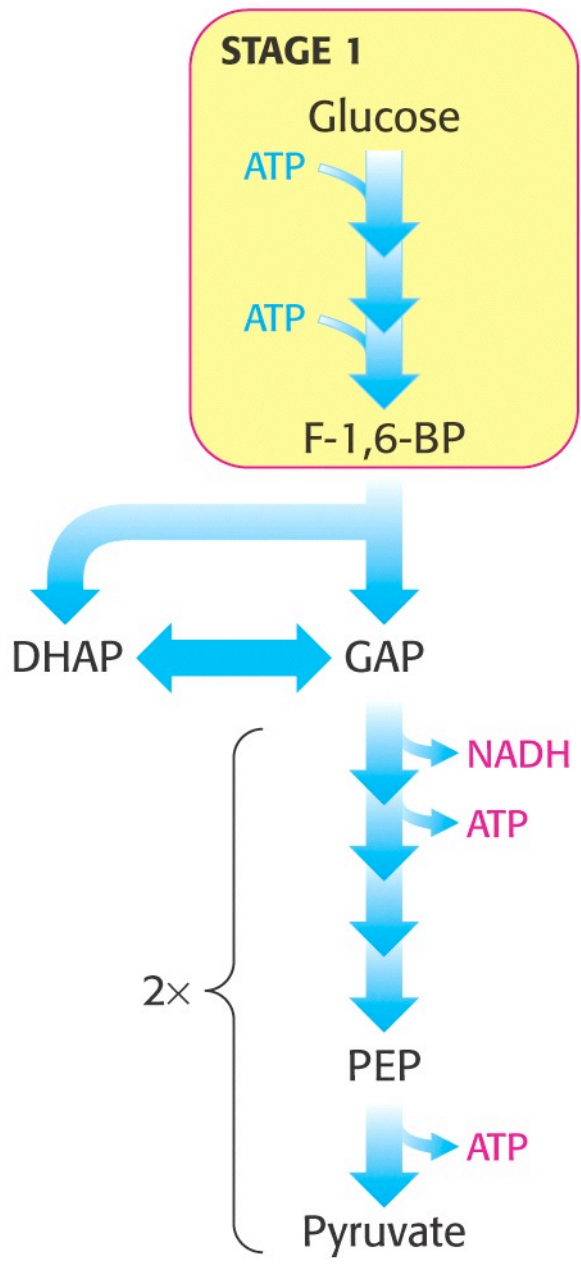


TABLE 16.1 Starting and ending points
of various fermentations

Glucose	—————→	lactate
Lactate	—————→	acetate
Glucose	—————→	ethanol
Ethanol	—————→	acetate
Arginine	—————→	carbon dioxide
Pyrimidines	—————→	carbon dioxide
Purines	—————→	formate
Ethylene glycol	—————→	acetate
Threonine	—————→	propionate
Leucine	—————→	2-alkylacetate
Phenylalanine	—————→	propionate

Note: The products of some fermentations are the substrates for others.



Stage 1

Glucose



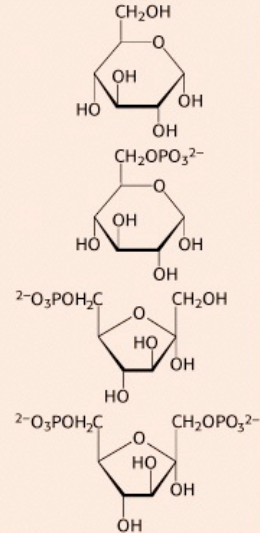
Glucose-6-phosphate



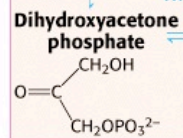
Fructose-6-phosphate



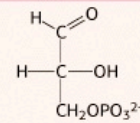
Fructose-1,6-bisphosphate



Stage 2



Glyceraldehyde 3-phosphate



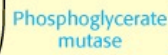
Stage 3



1,3-Bisphosphoglycerate



3-Phosphoglycerate



2-Phosphoglycerate

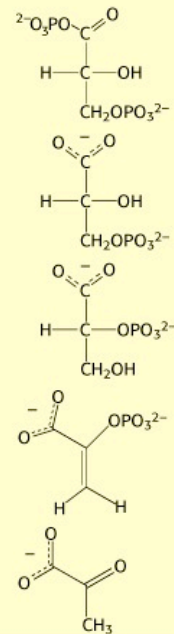


Phosphoenolpyruvate



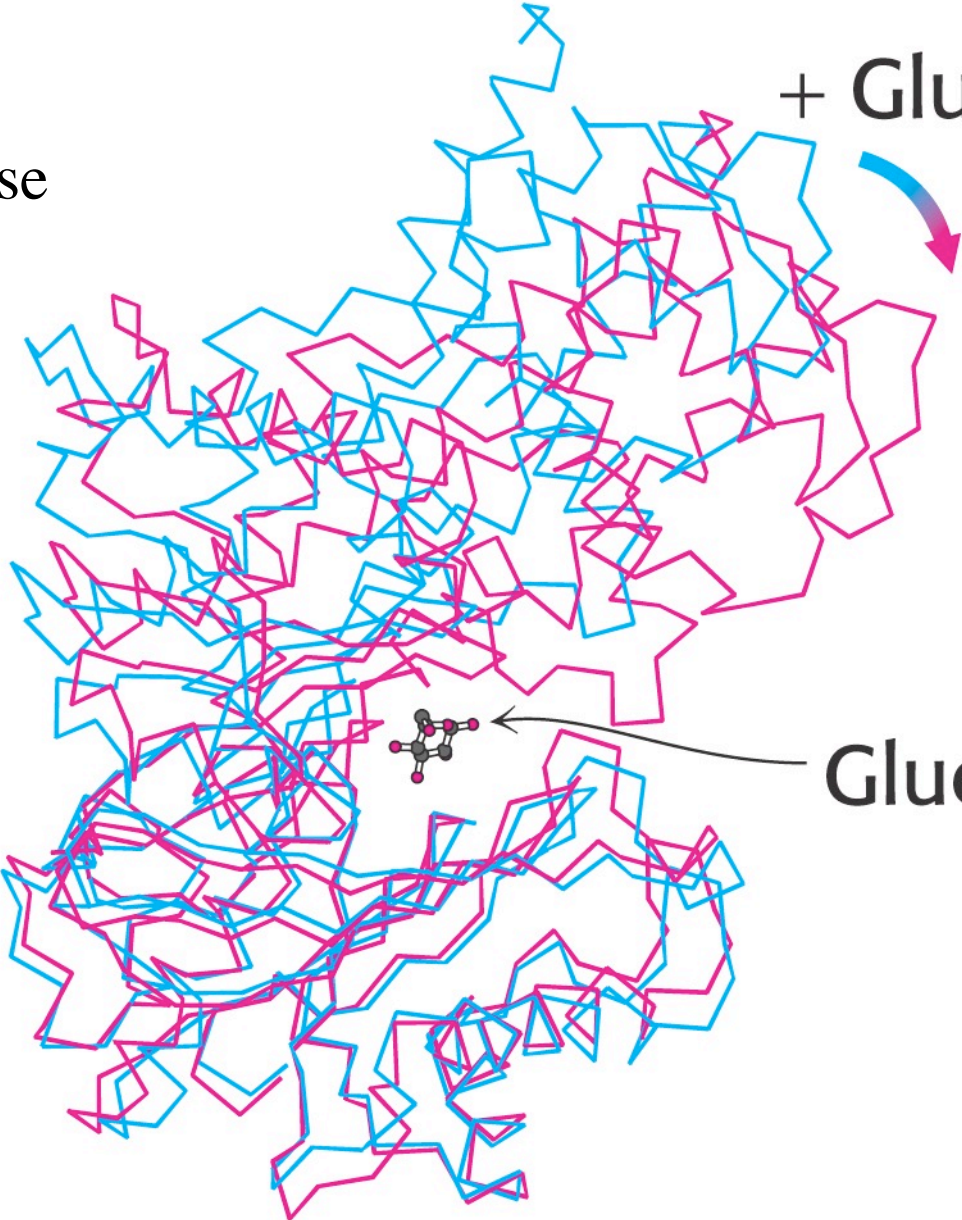
Pyruvate

2 X

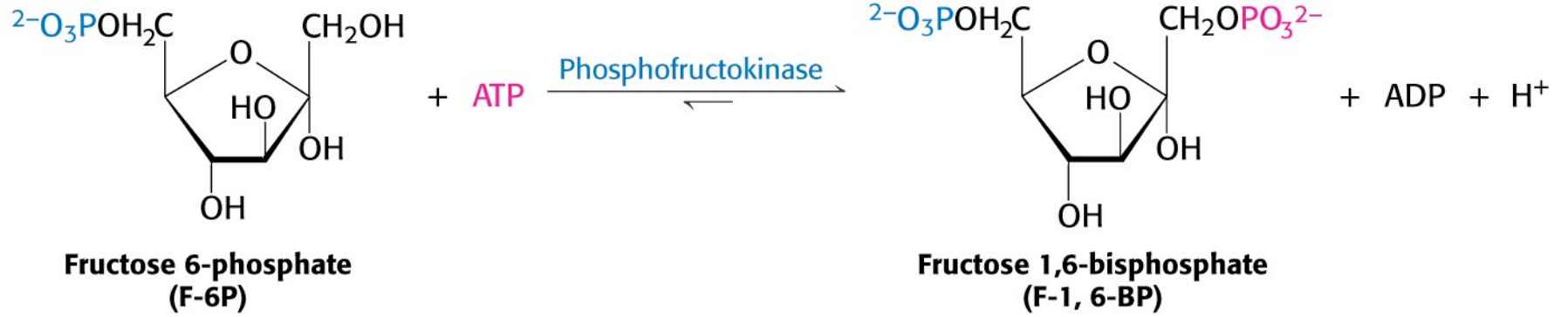


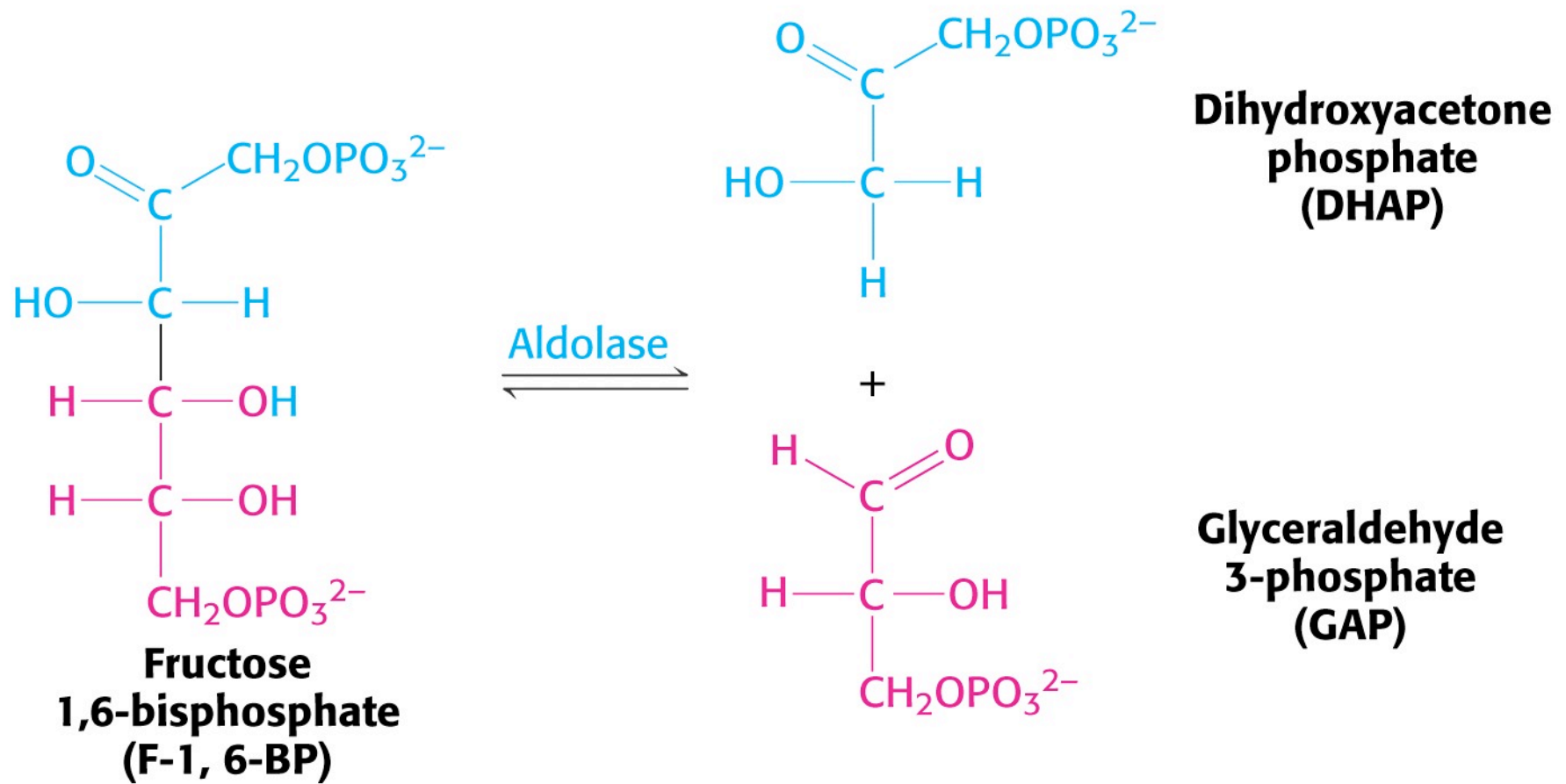
Hexokinase

+ Glucose

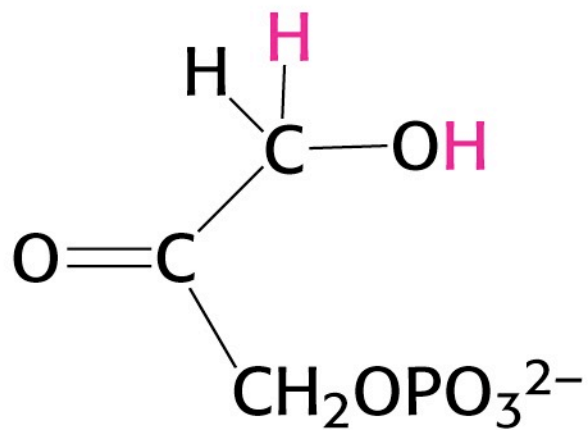


Glucose

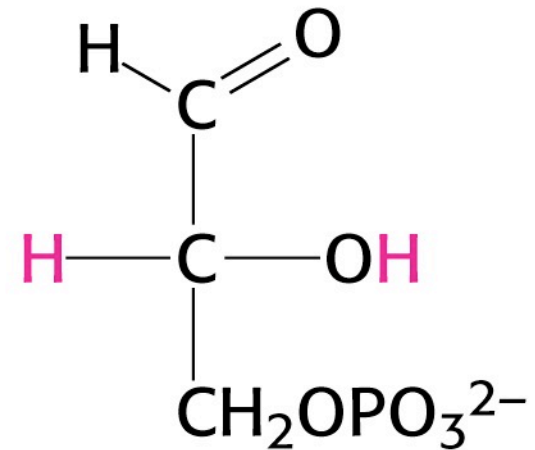




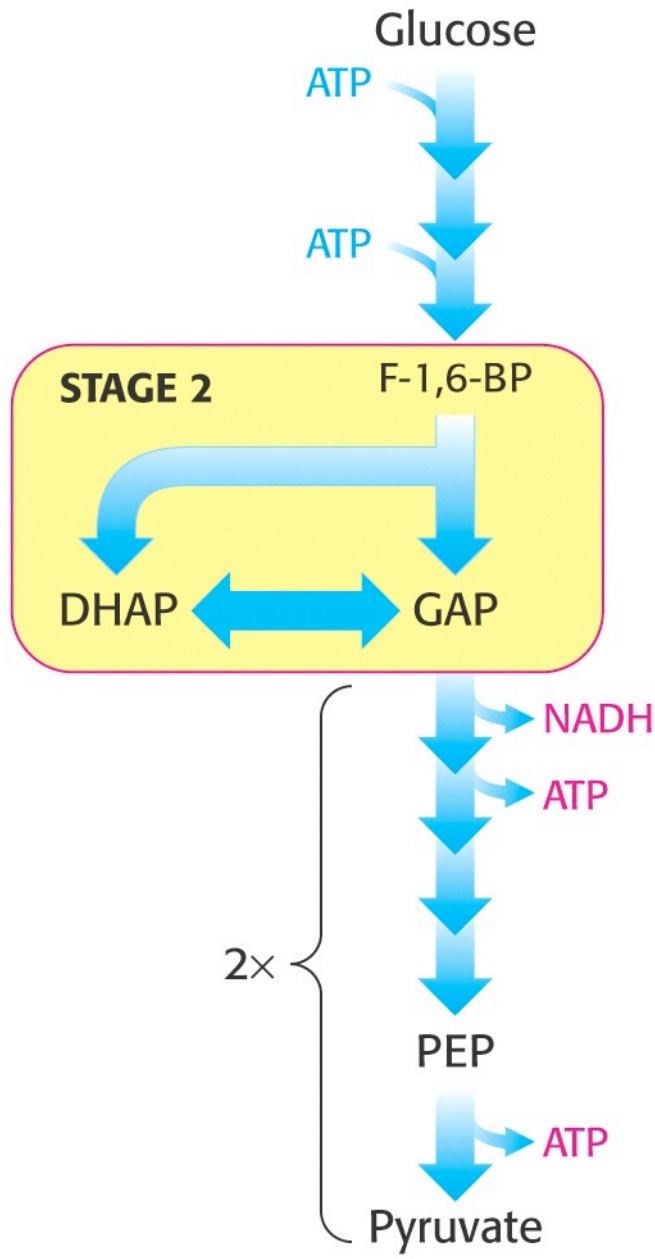
Reverse aldol condensation



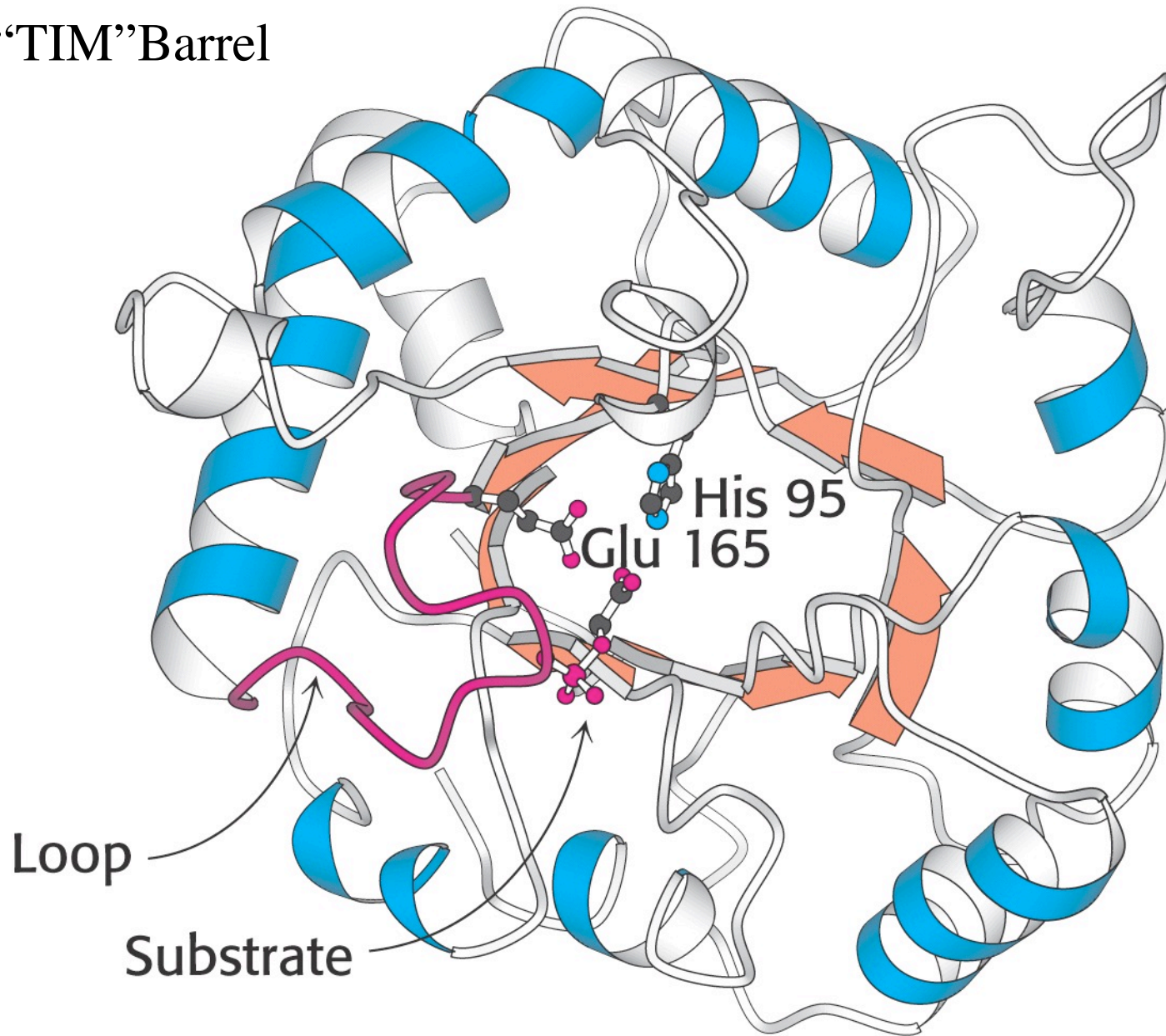
**Dihydroxyacetone
phosphate**



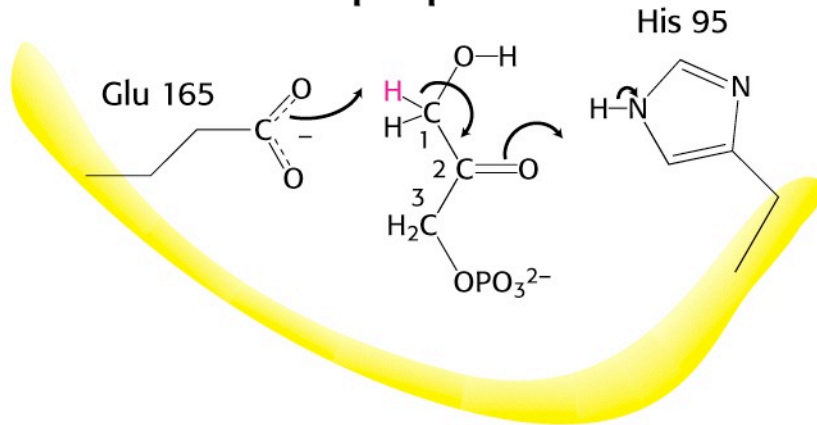
**Glyceraldehyde
3-phosphate**



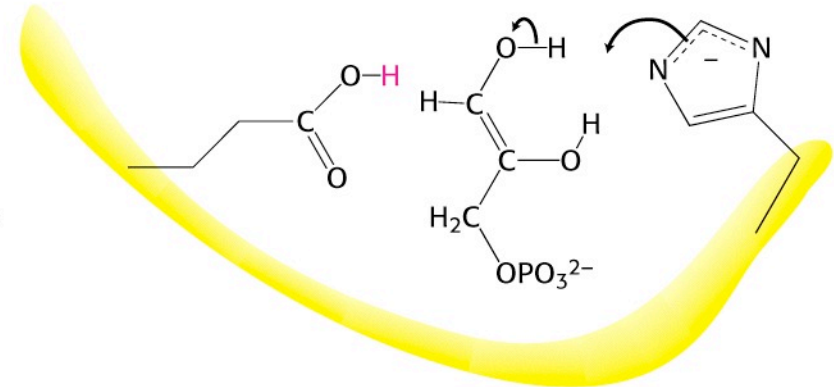
“TIM” Barrel



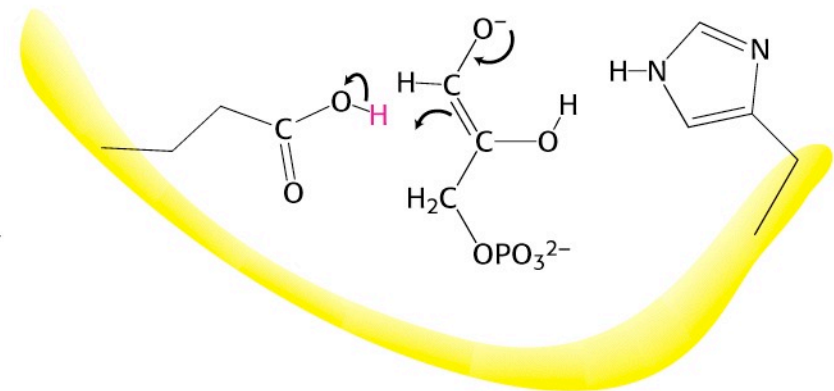
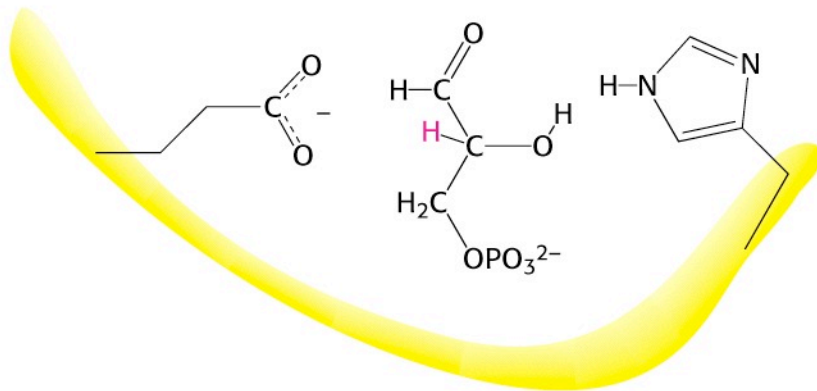
Dihydroxyacetone phosphate



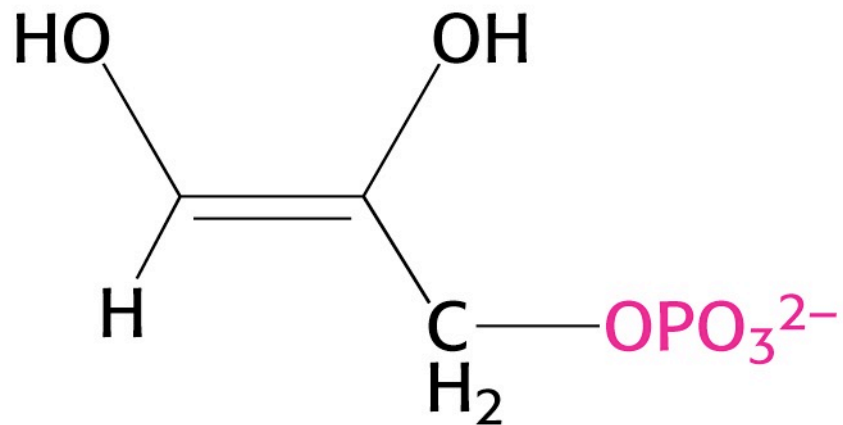
Enediol intermediate



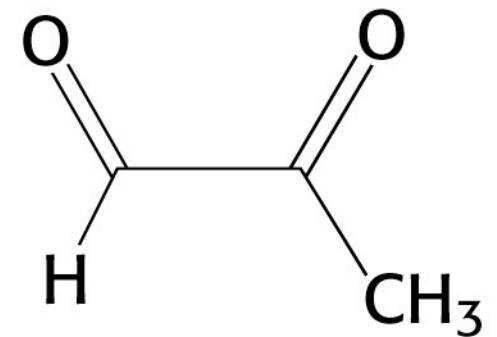
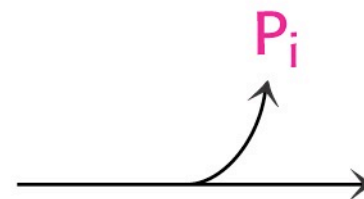
Glyceraldehyde 3-phosphate



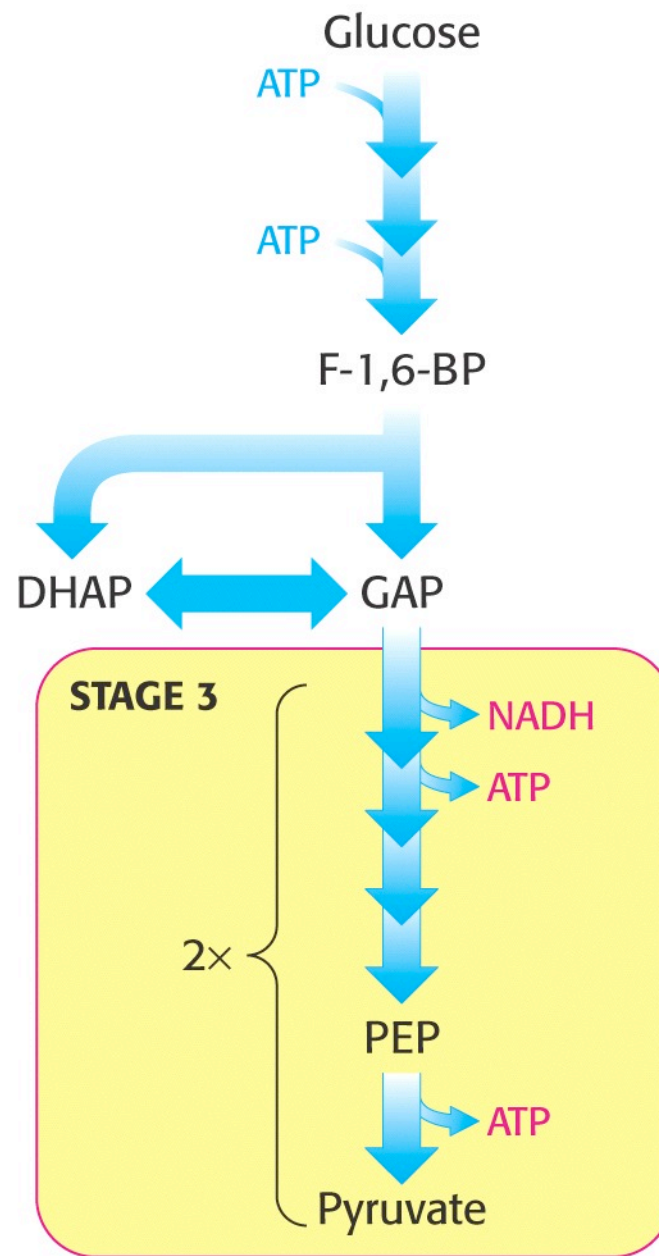
TIM prevents this!

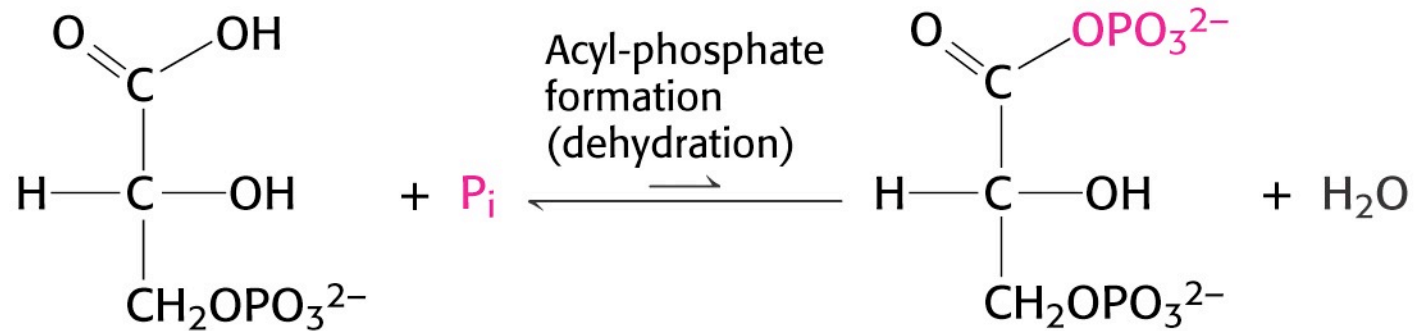
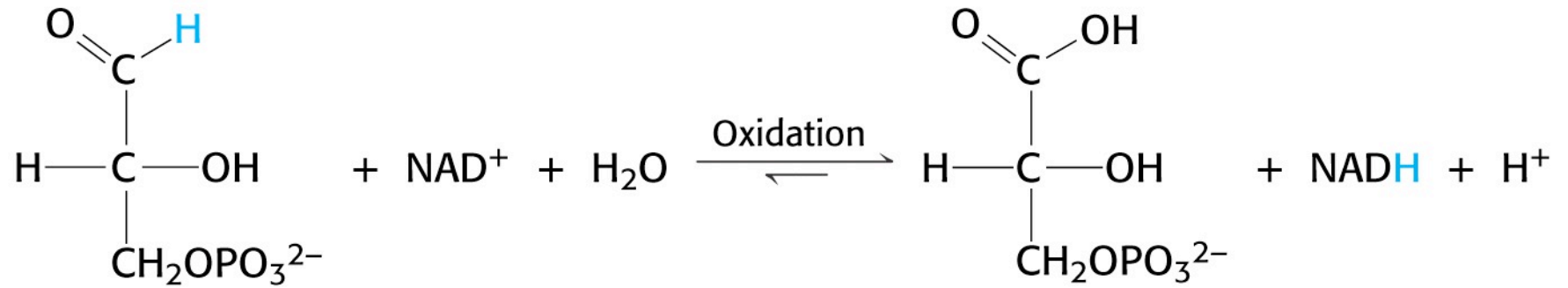


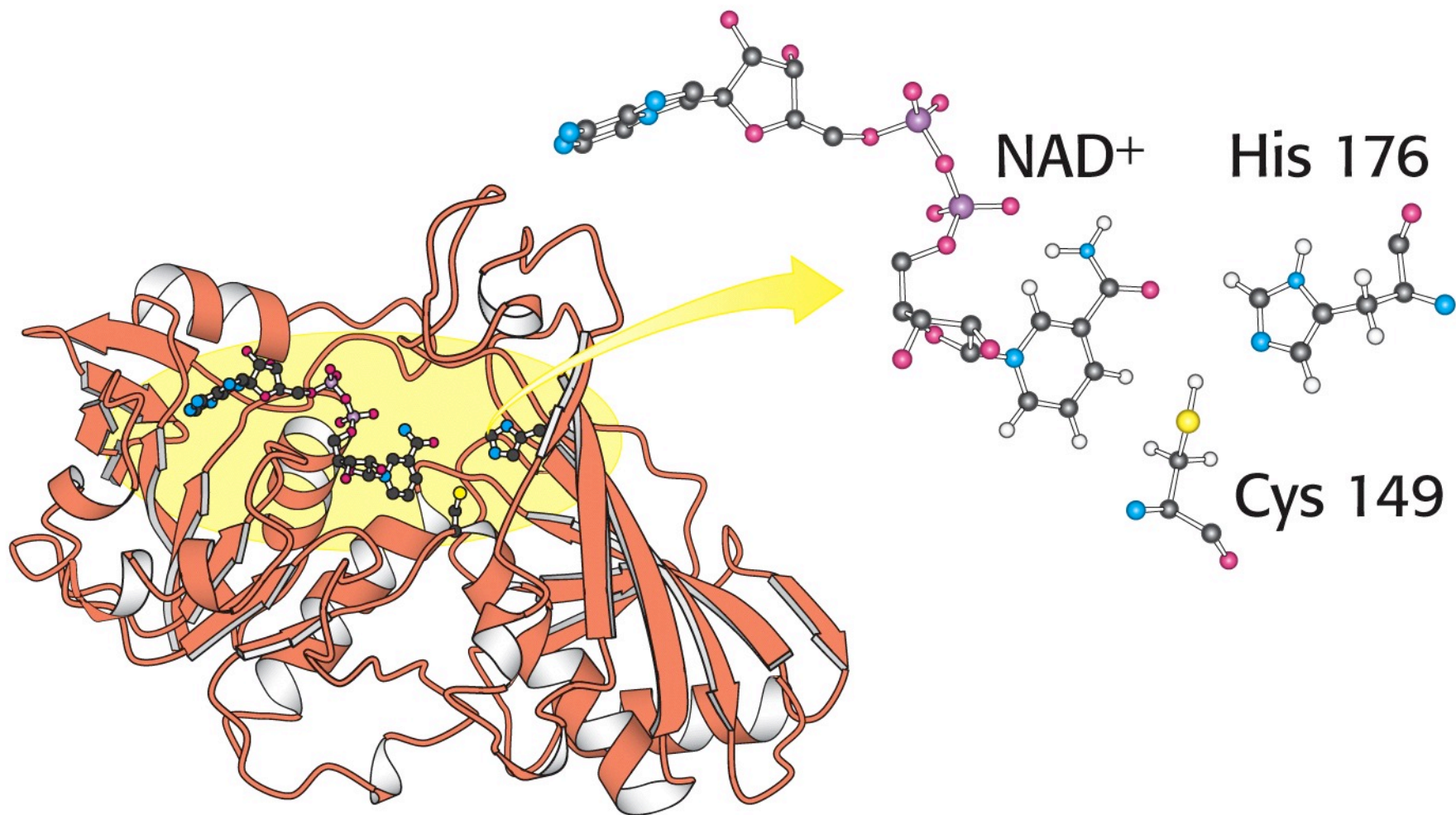
Enediol intermediate

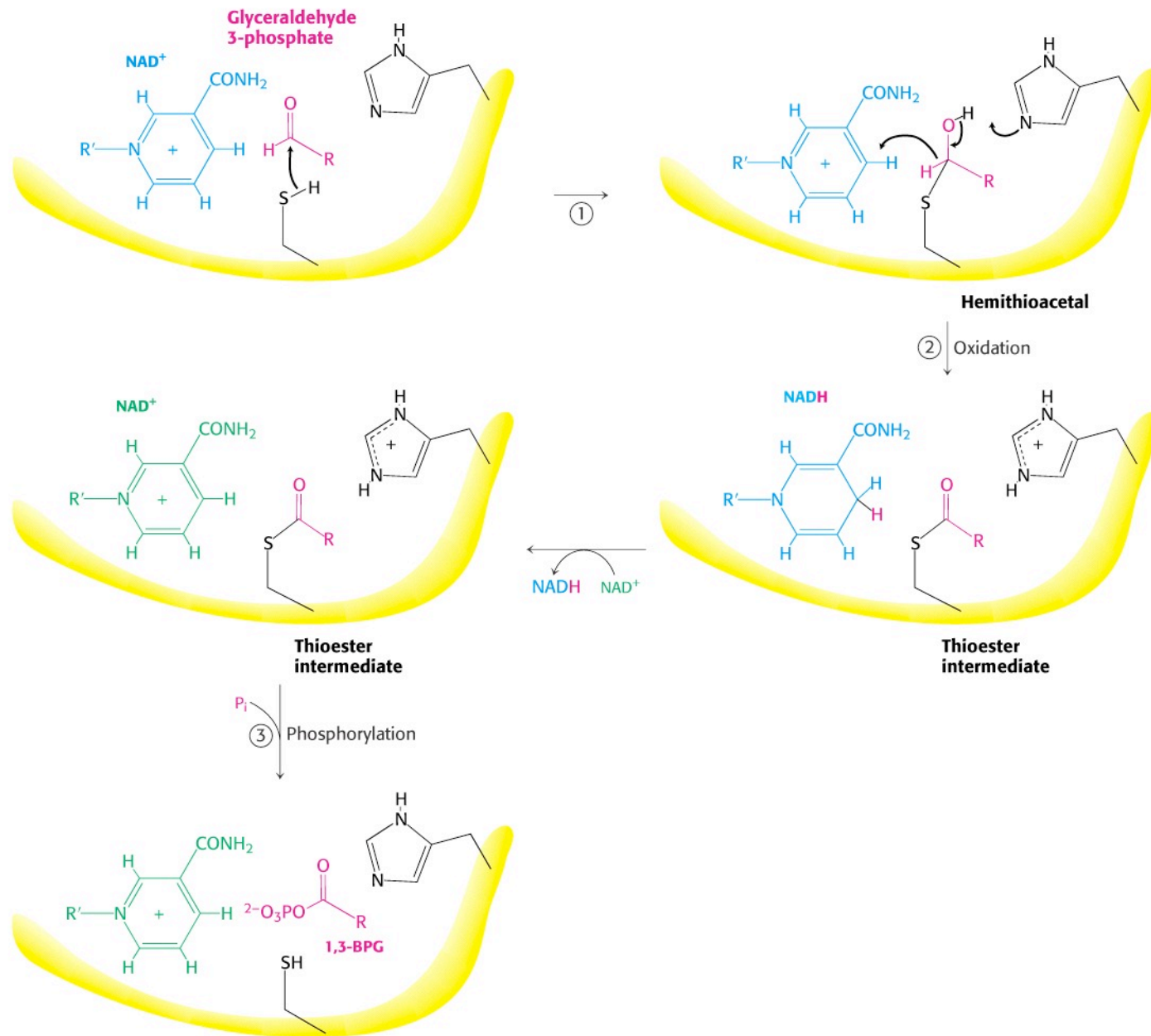


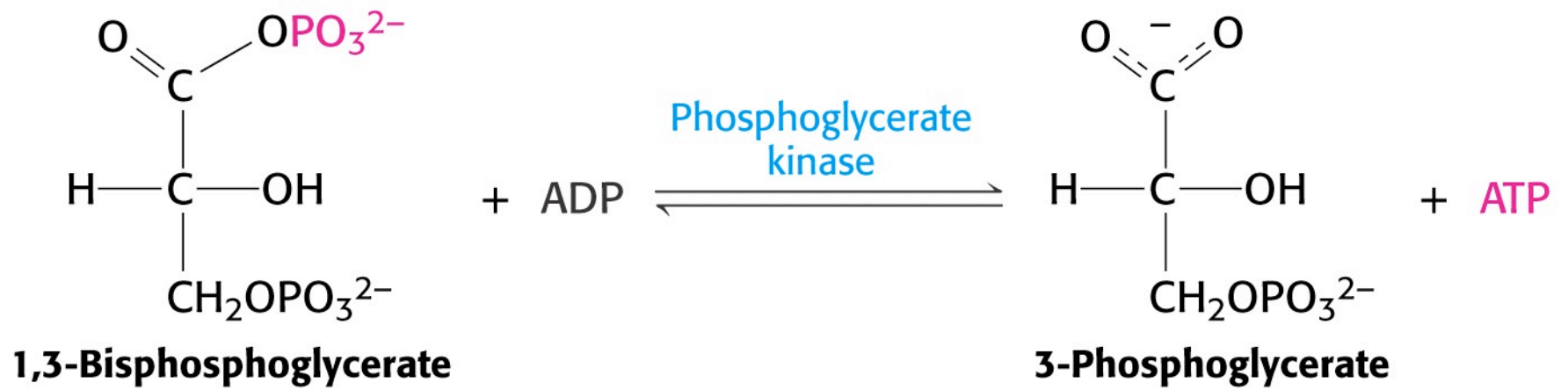
Methyl glyoxal

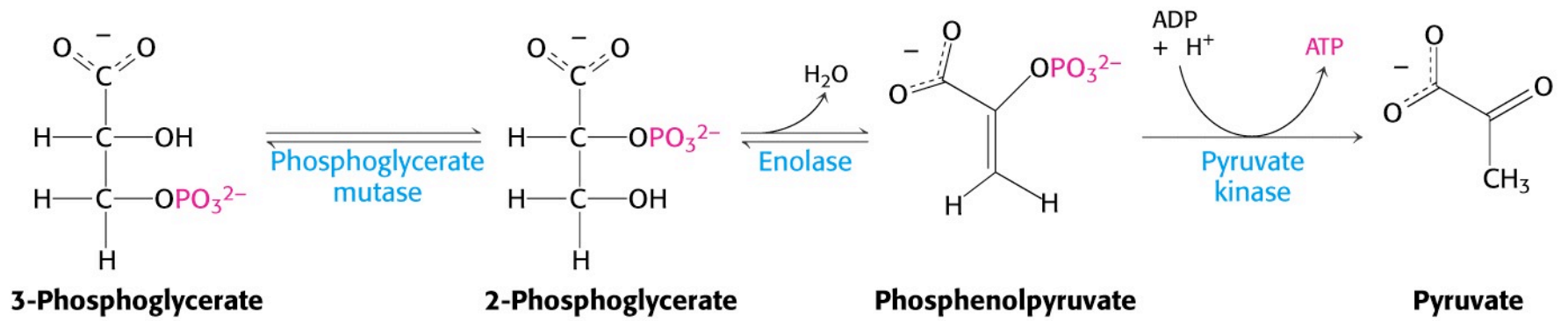


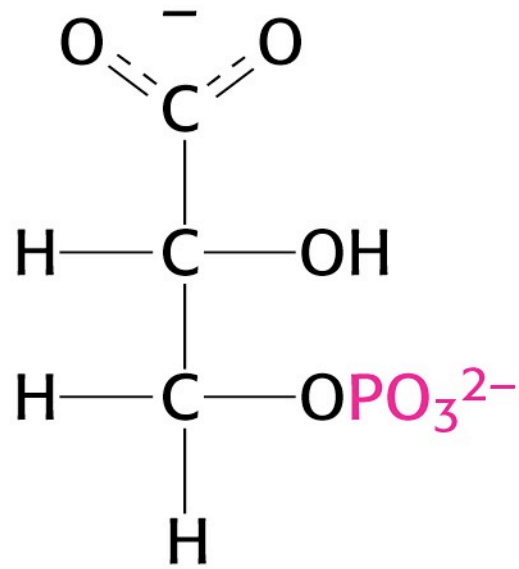




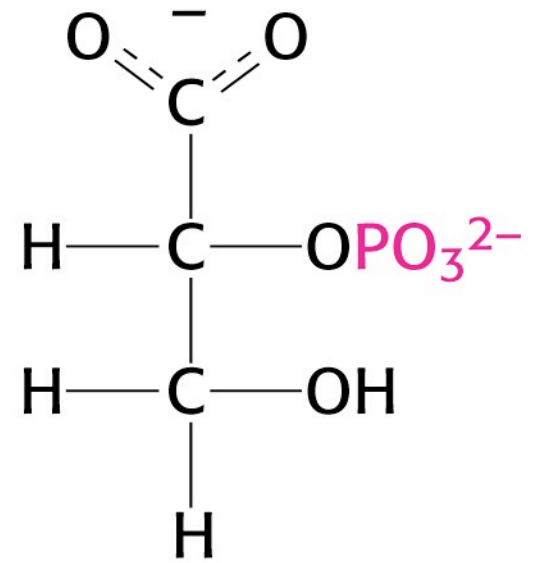
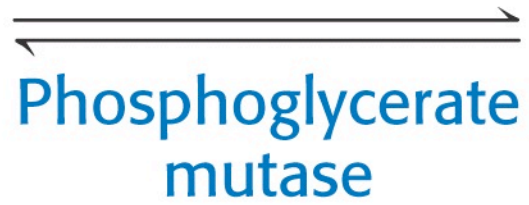




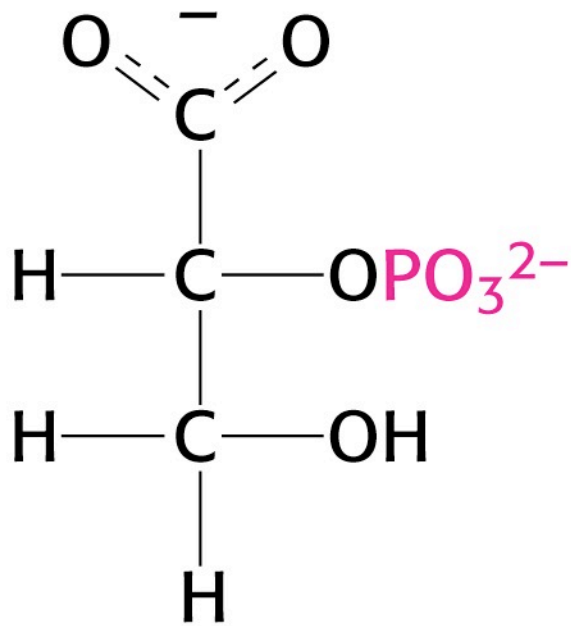




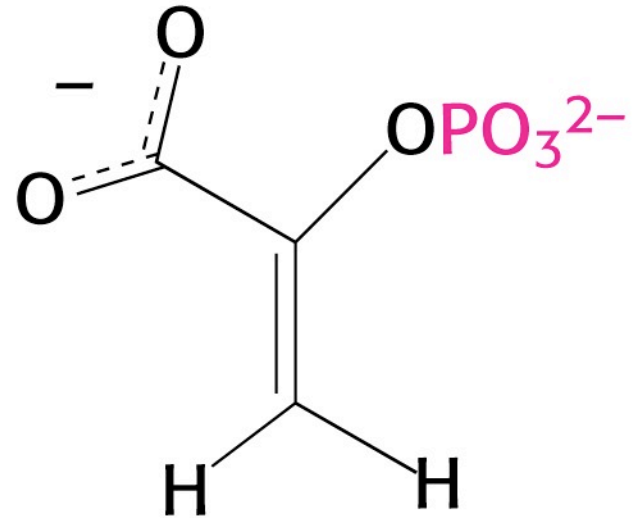
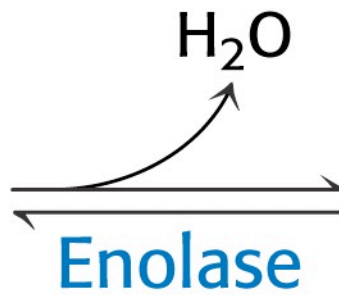
3-Phosphoglycerate



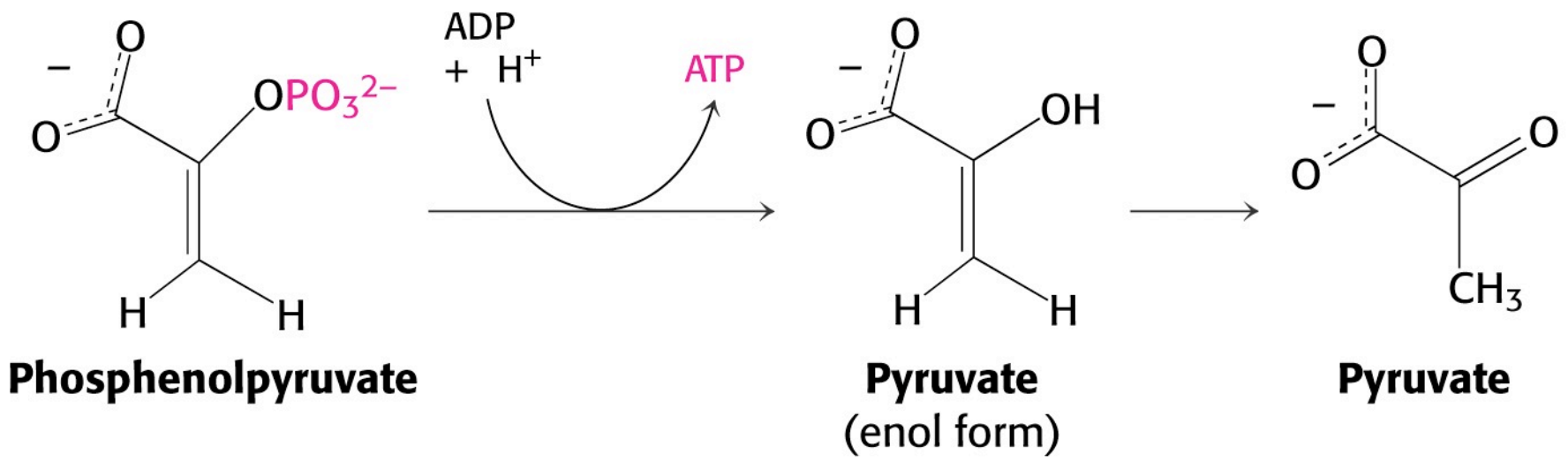
2-Phosphoglycerate



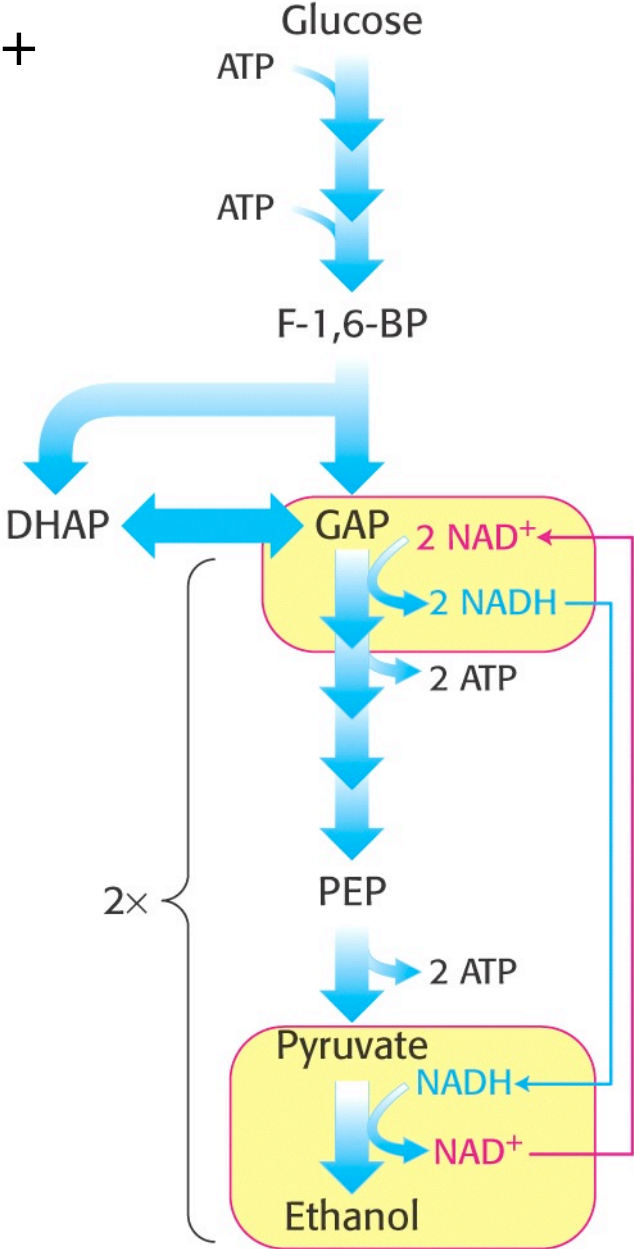
2-Phosphoglycerate



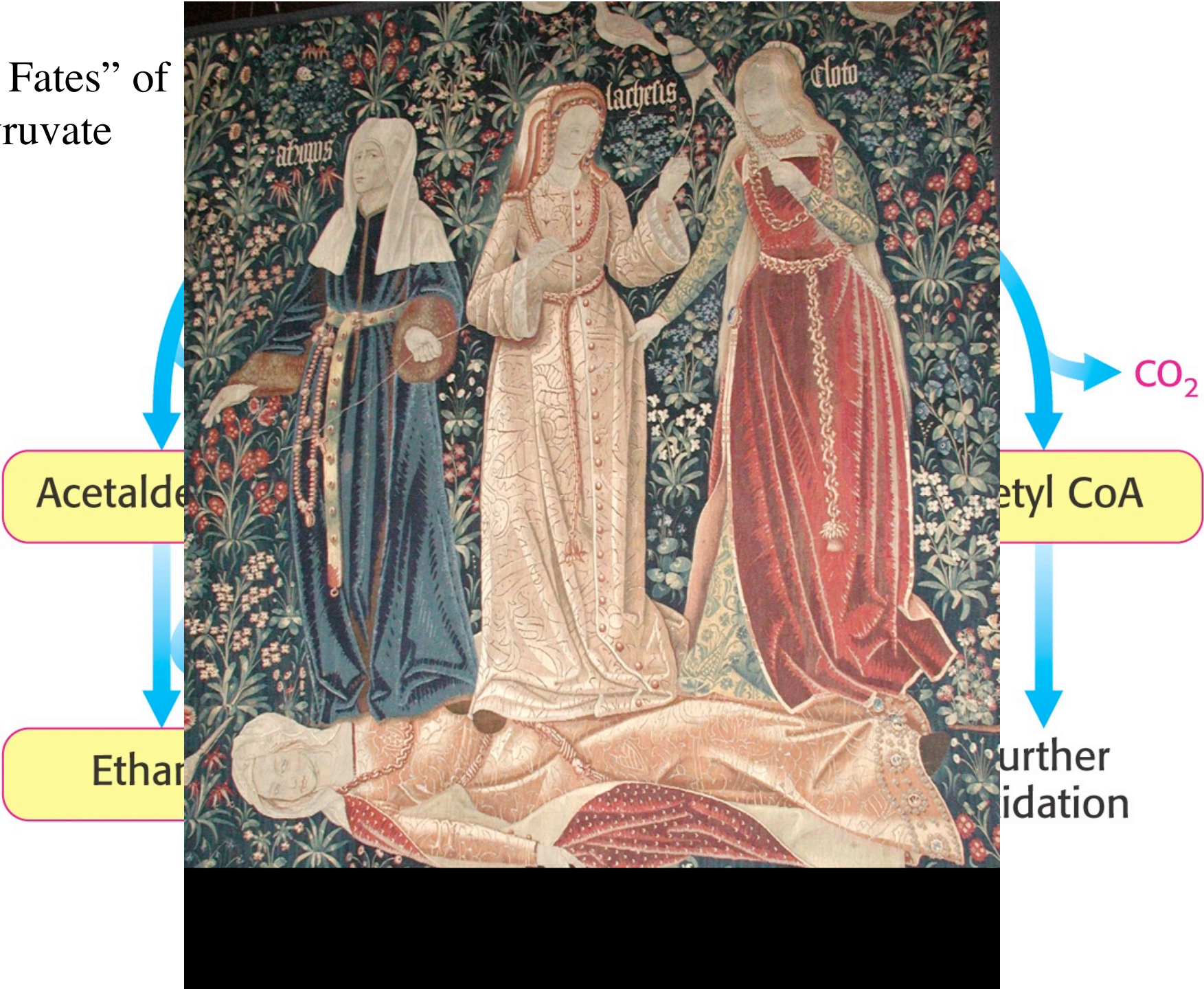
Phosphoenolpyruvate

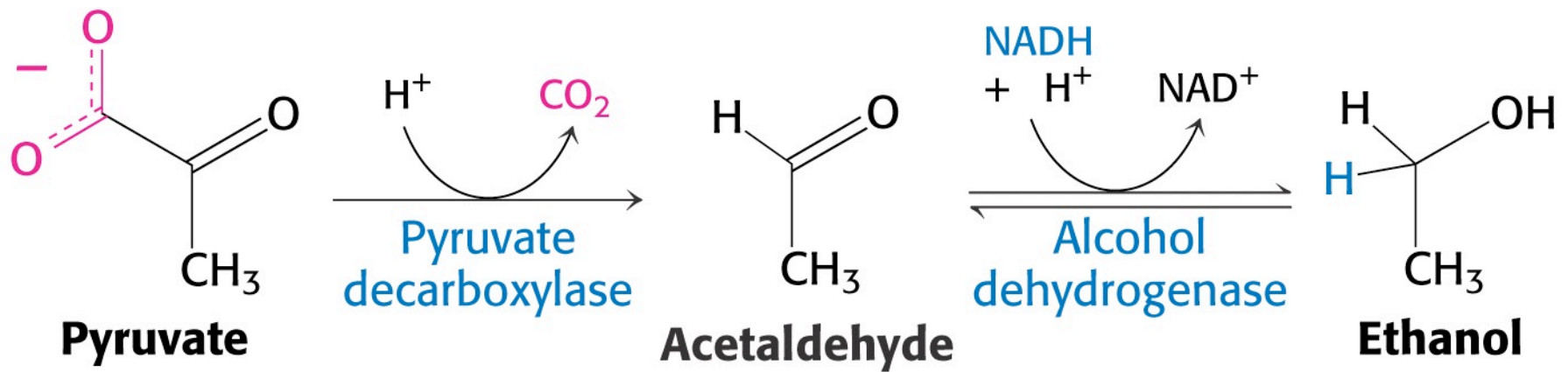


Reoxidizing NAD⁺

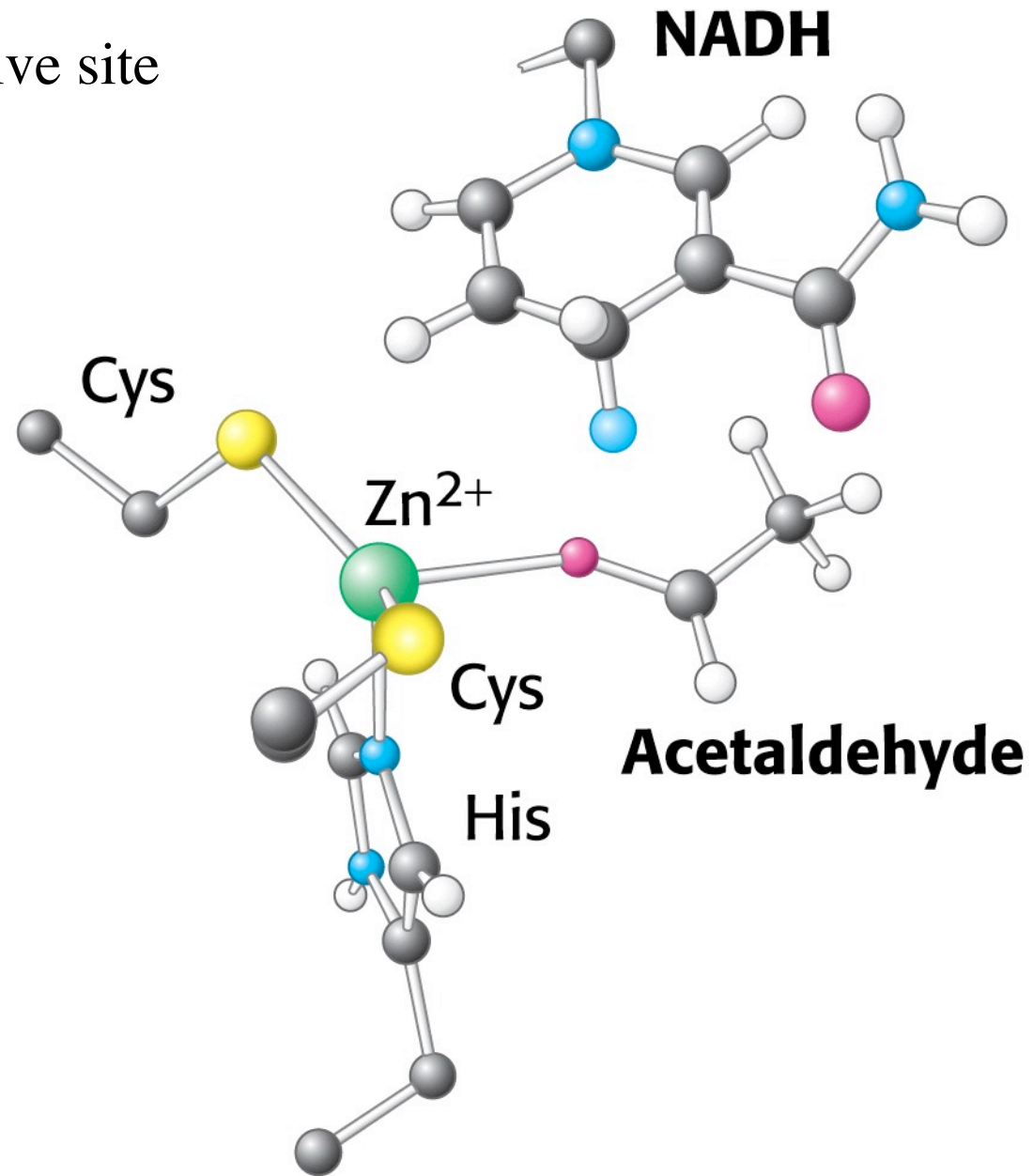


“3 Fates” of Pyruvate

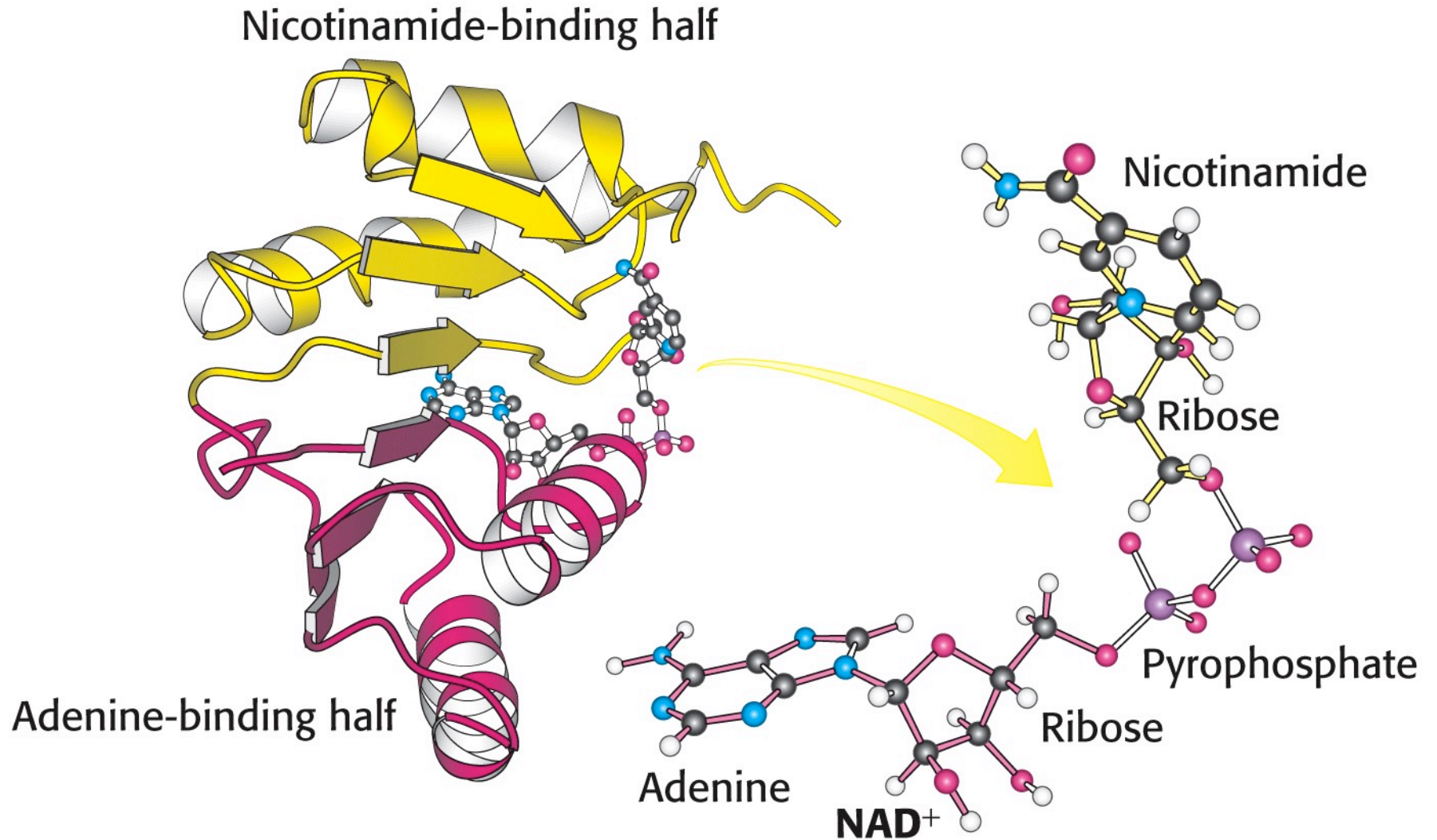


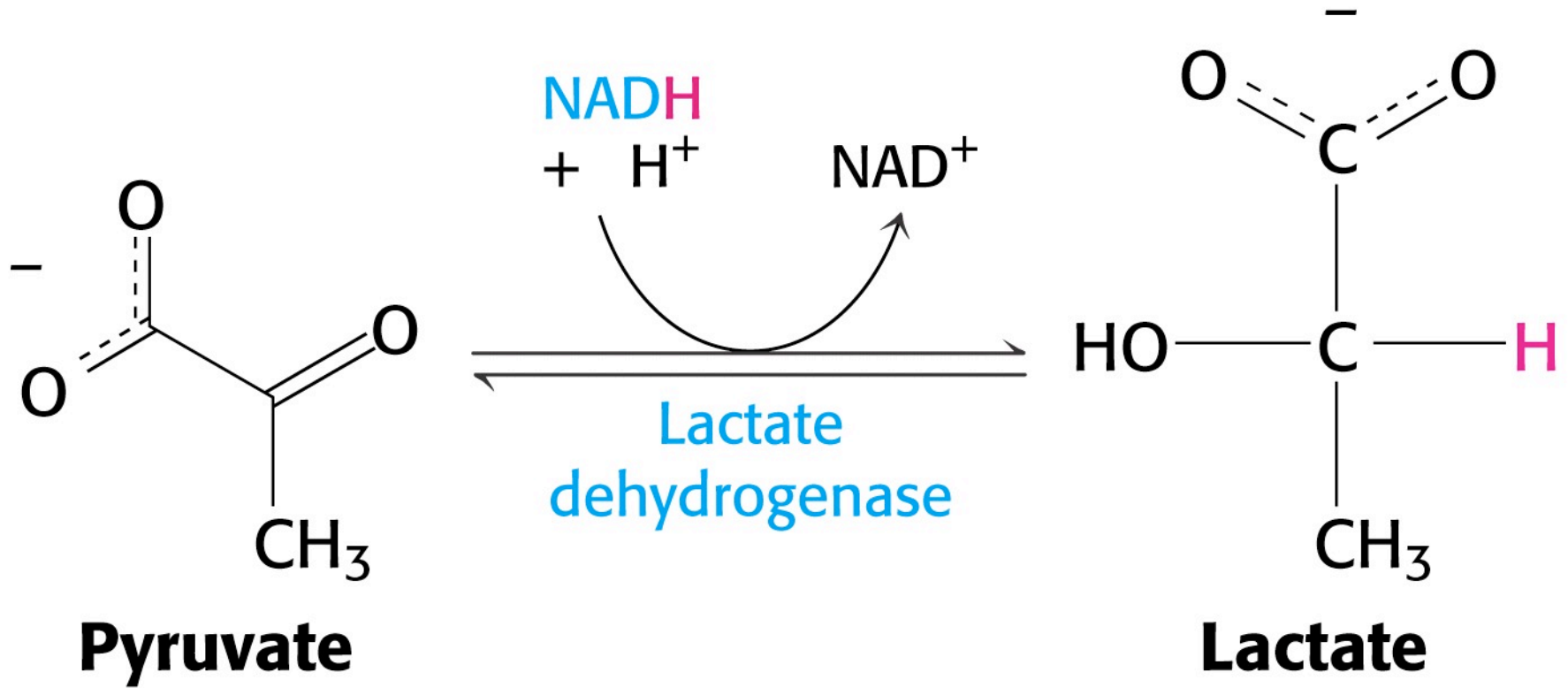


ADH active site

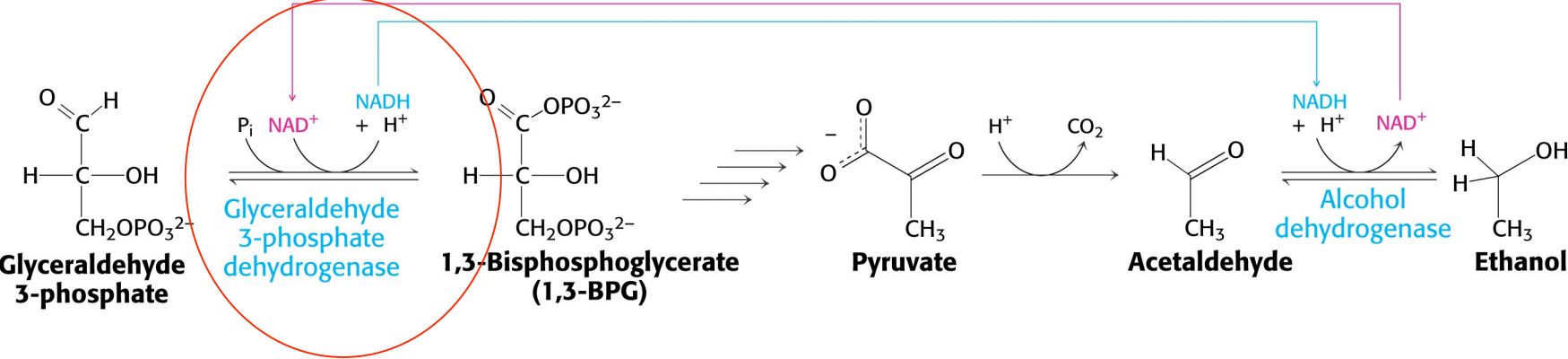


Dehydrogenase NAD binding motif: the Rossmann fold

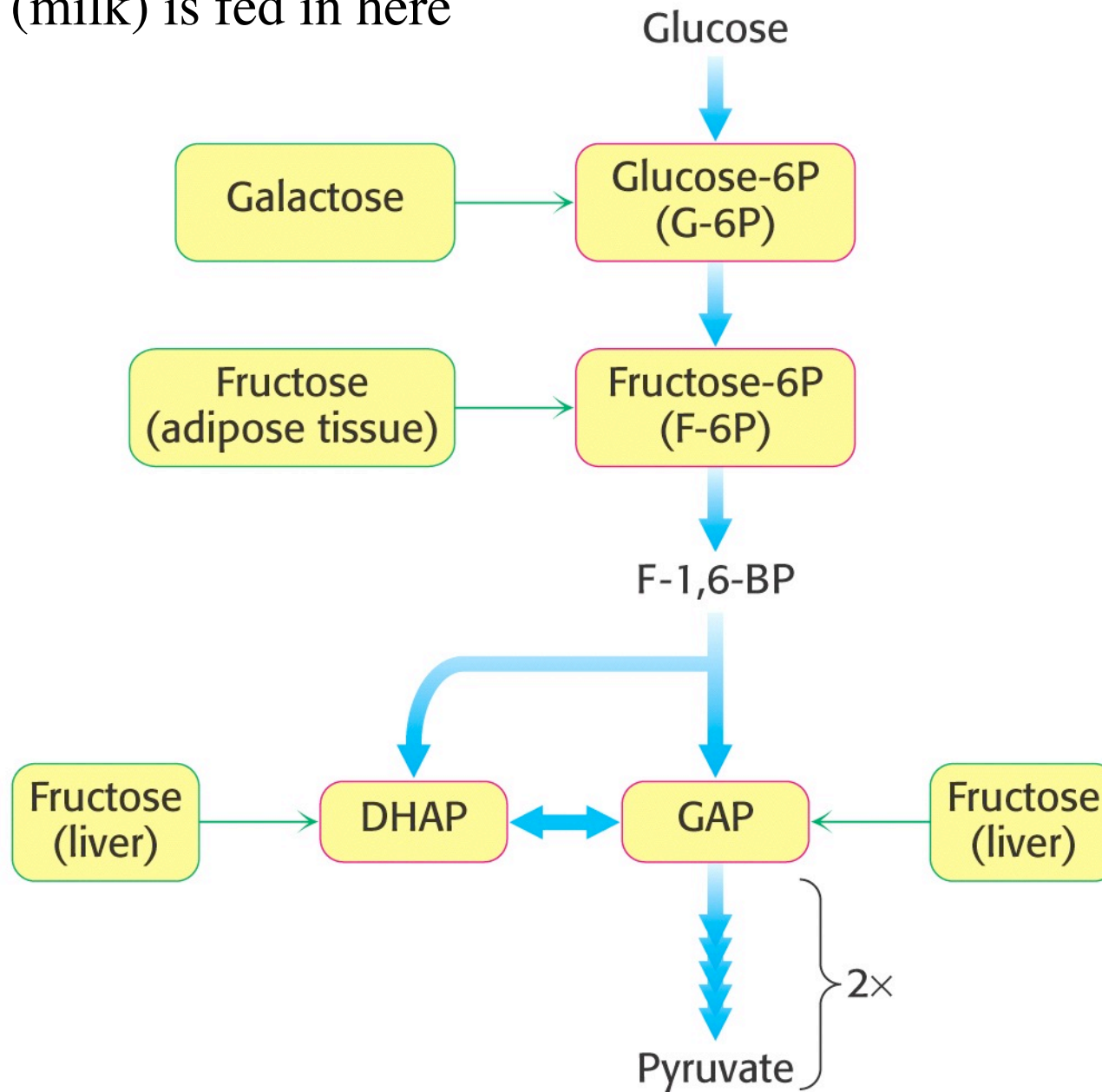




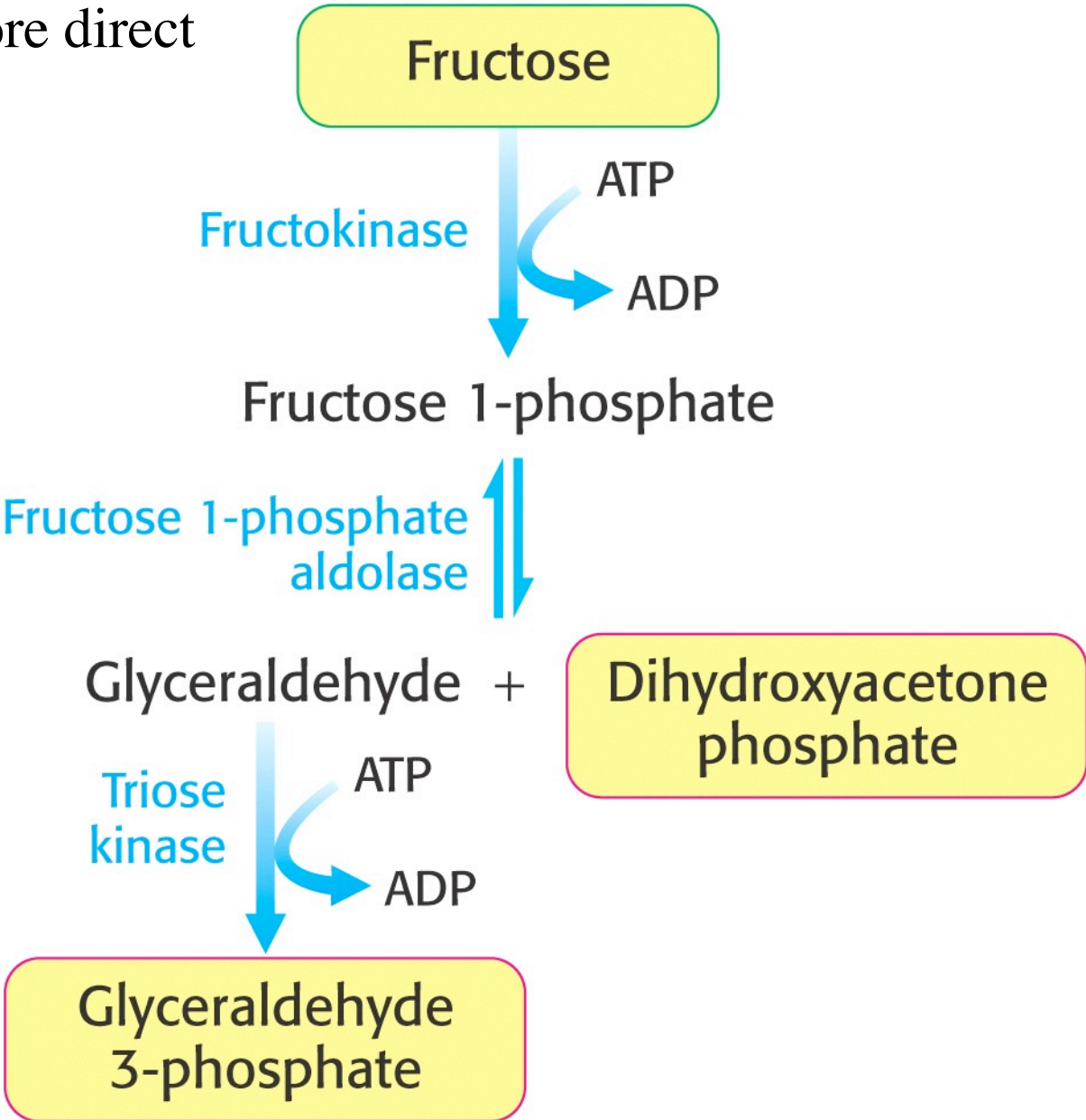
Reoxidation of NAD+ is very important to keep this reaction going



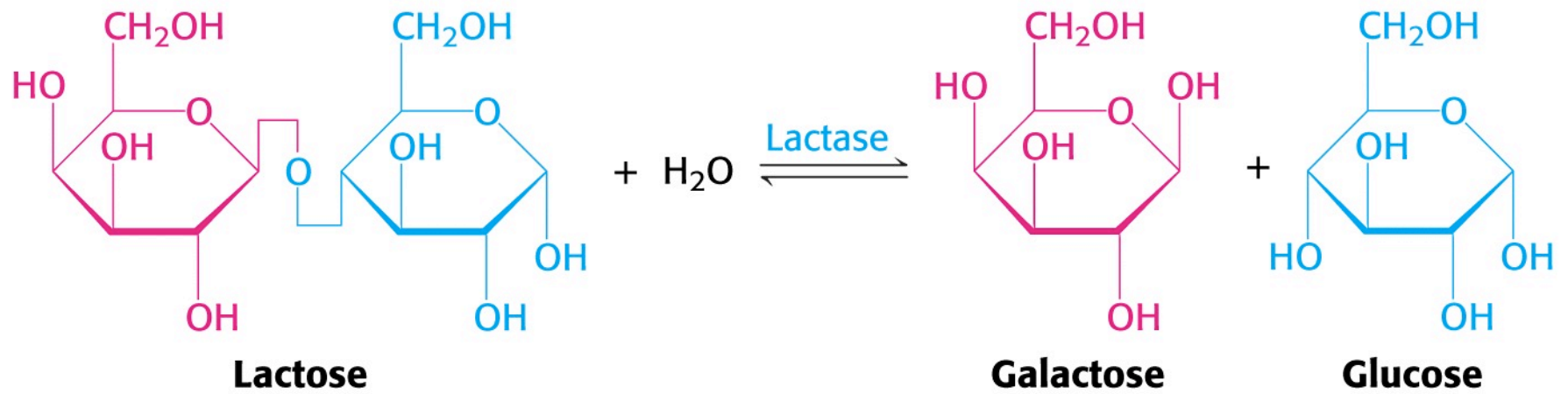
Galactose (milk) is fed in here



Fructose is more direct

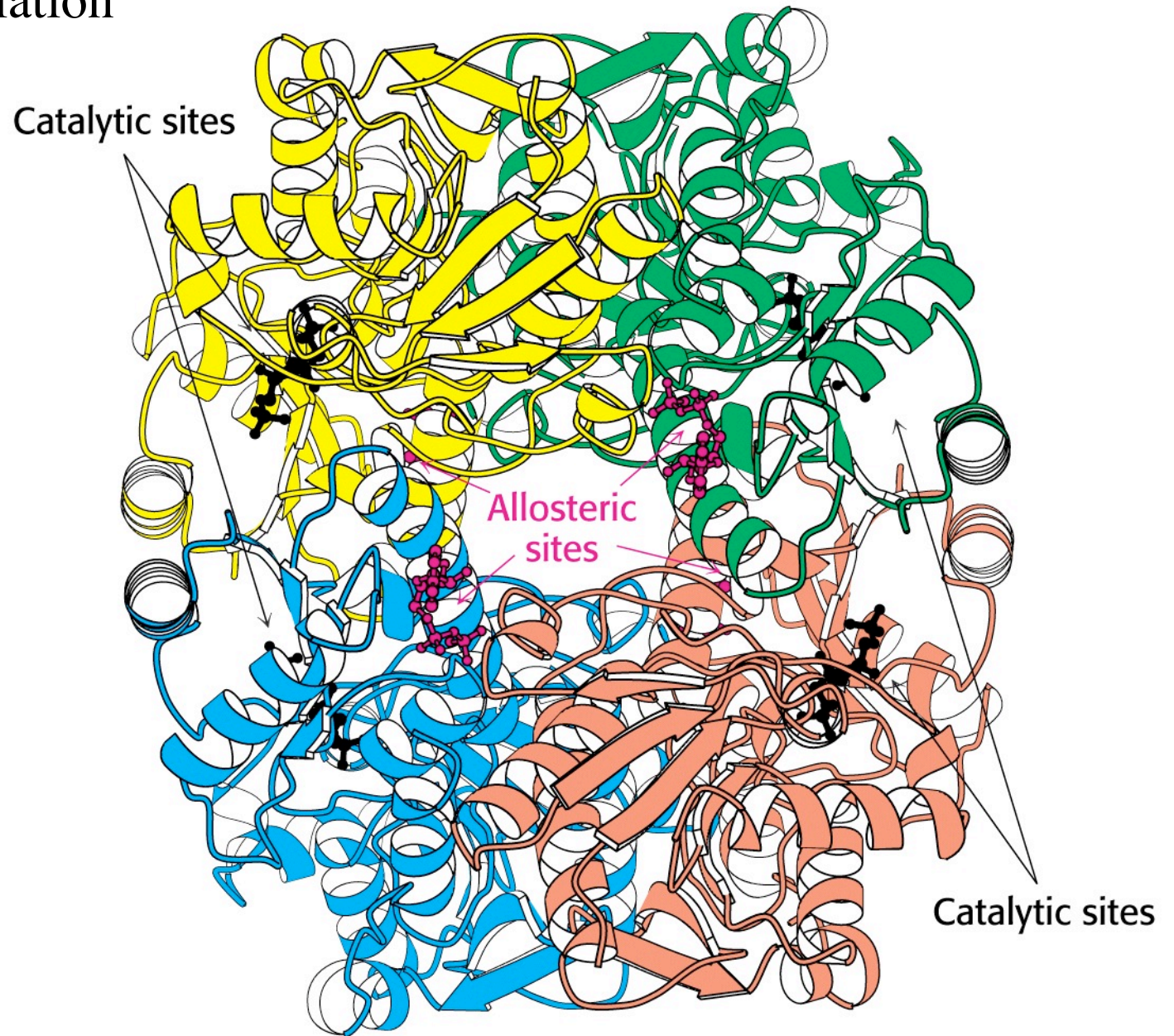


If you are Lactose intolerant.....



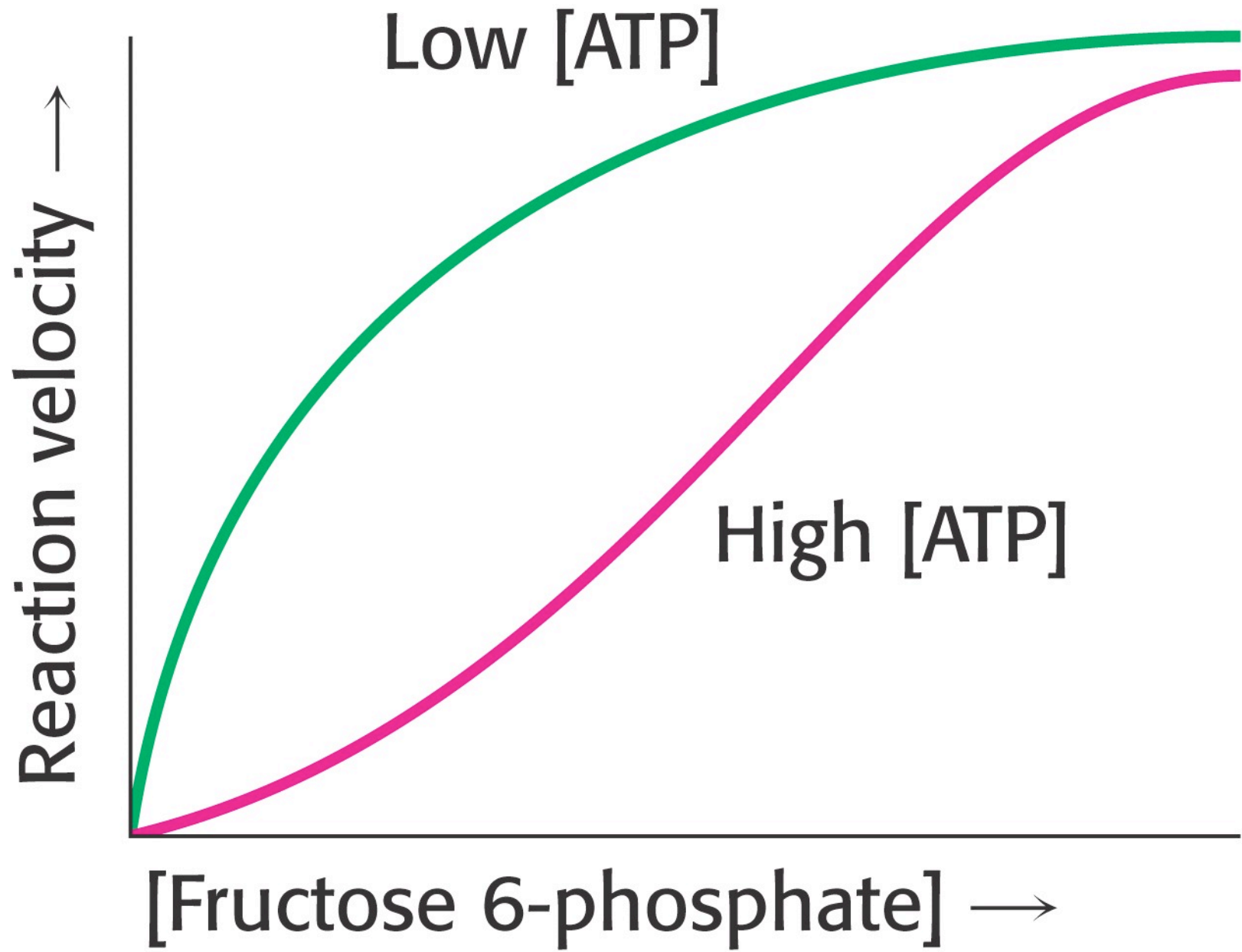
PFK (1):
EXTREME regulation

ATP -
AMP+
pH-
Citrate-
F2,6 BP



Marmite..Yummmm....

Water Soluble Vitamins	Fat Soluble Vitamins
<p>Thiamin (B₁) B₁ Deficiency and Disease</p> <p>Riboflavin (B₂) B₂ Deficiency and Disease</p> <p>Niacin (B₃) B₃ Deficiency and Disease</p> <p>Pantothenic Acid (B₅)</p> <p>Pyridoxal, Pyridoxamine, Pyridoxine (B₆)</p> <p>Biotin</p> <p>Cobalamin (B₁₂) B₁₂ Deficiency and Disease</p> <p>Folic Acid Folate Deficiency and Disease</p> <p>Ascorbic Acid</p>	<p>Vitamin A Gene Control by Vitamin A Role of Vitamin A in Vision Additional Roles of Vitamin A Clinical Significances of Vitamin A</p> <p>Vitamin D Clinical Significances of Vitamin D</p> <p>Vitamin E Clinical Significances of Vitamin E</p> <p>Vitamin K Clinical Significance of Vitamin K</p>



Overall Muscle Regulation

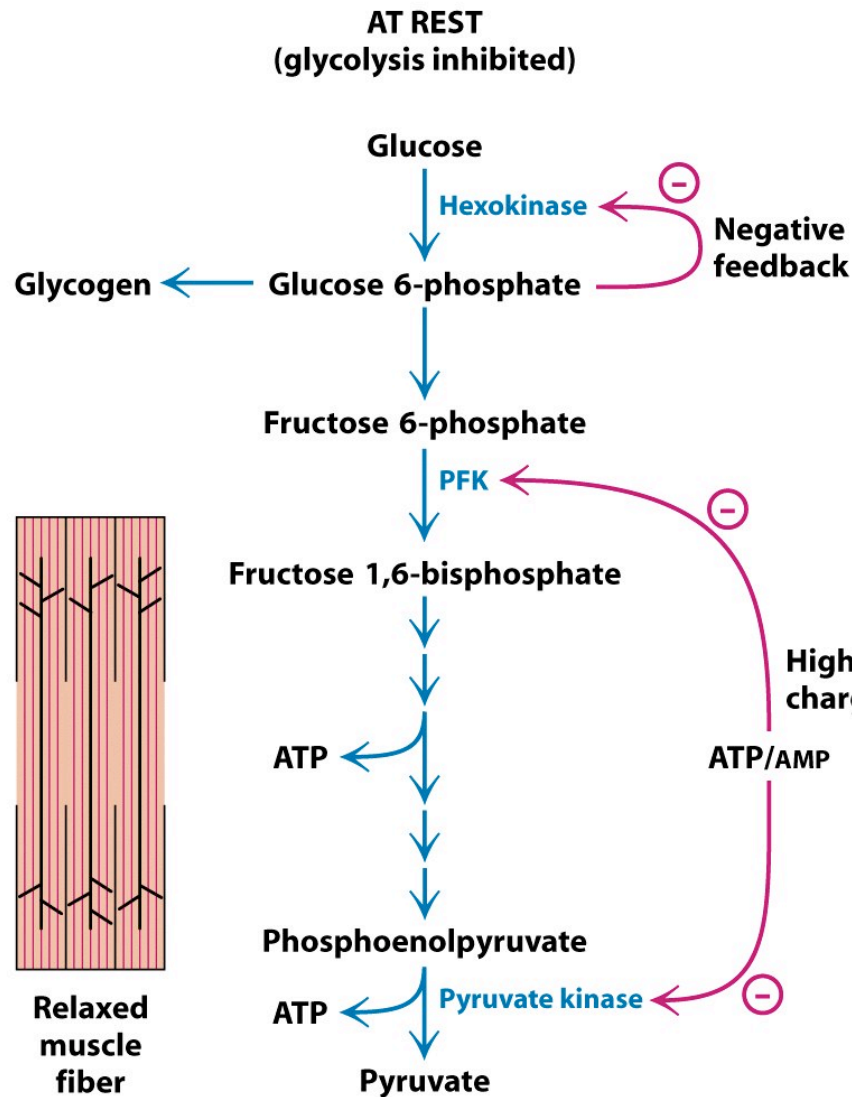


Figure 16-17 part 1
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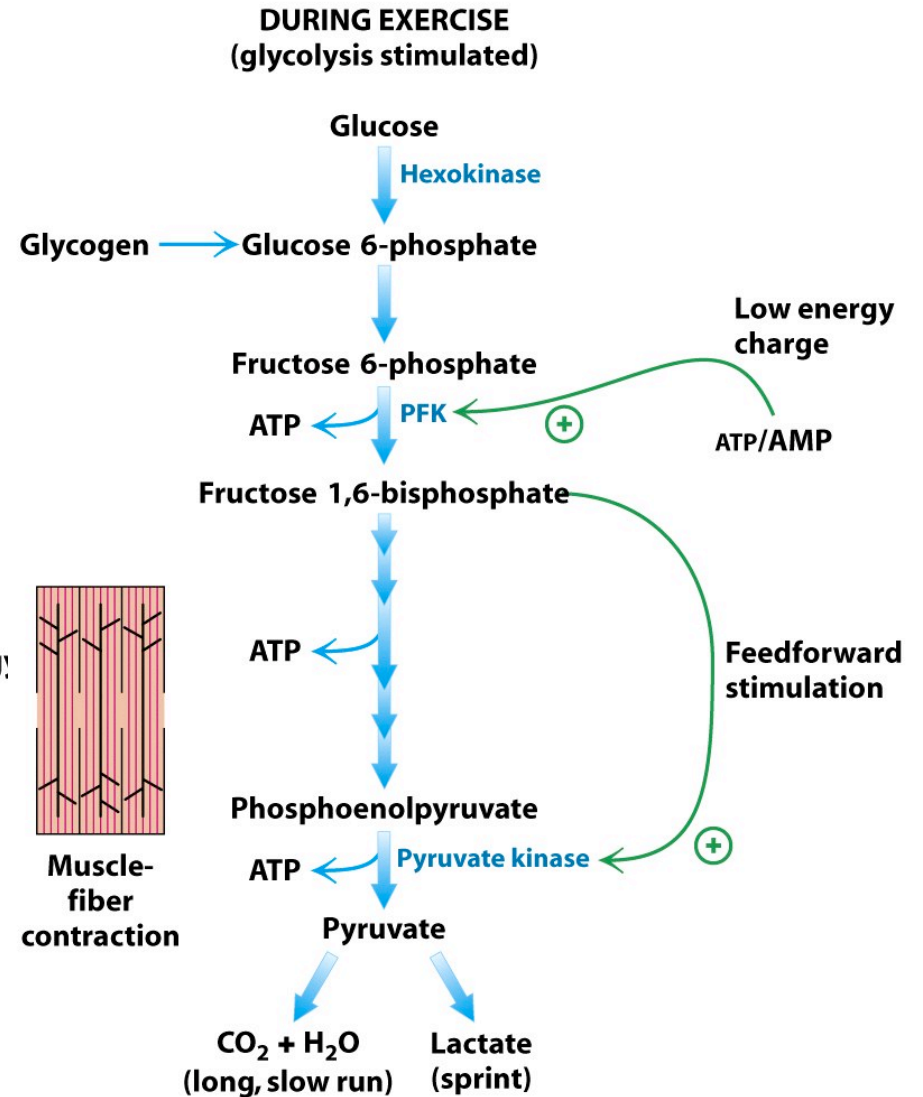
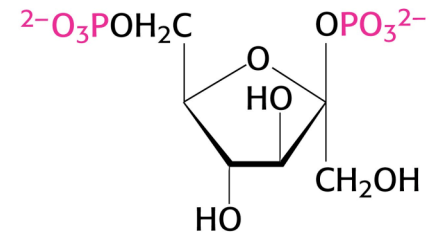


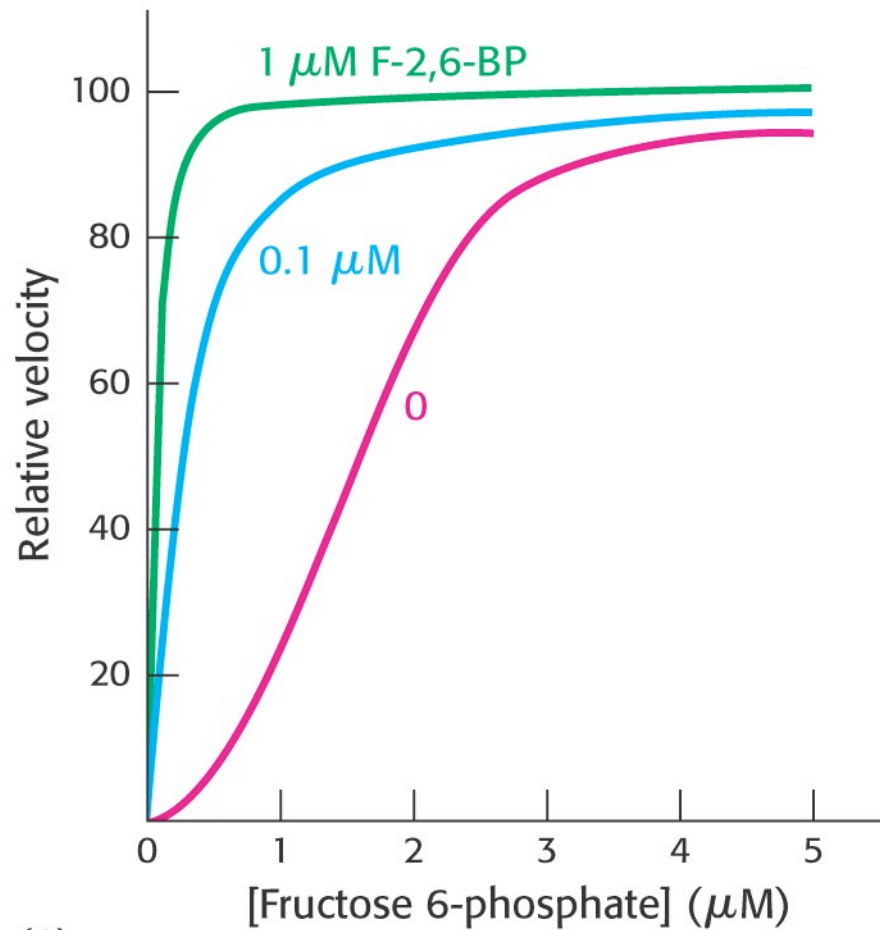
Figure 16-17 part 2
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Liver Regulation of Glycolysis

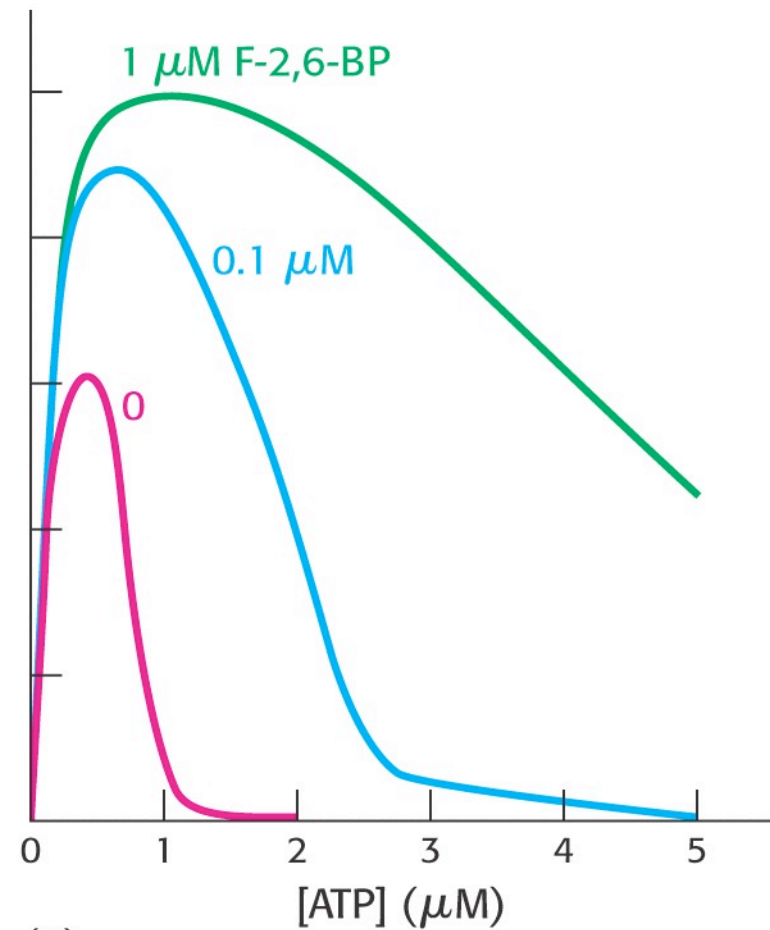


Fructose 2,6-bisphosphate

F2,6 BP is key

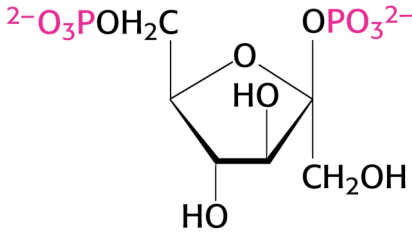


(A)

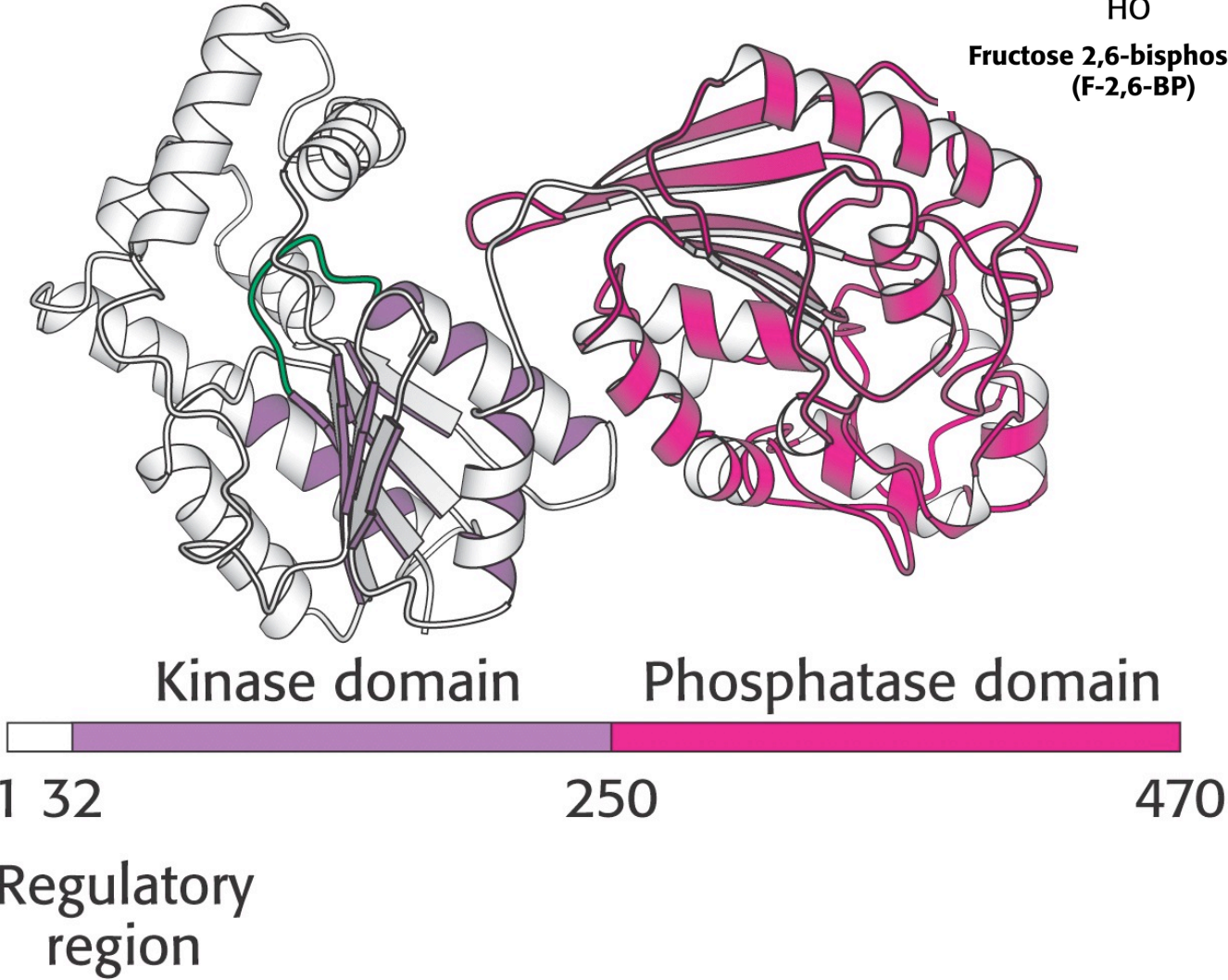


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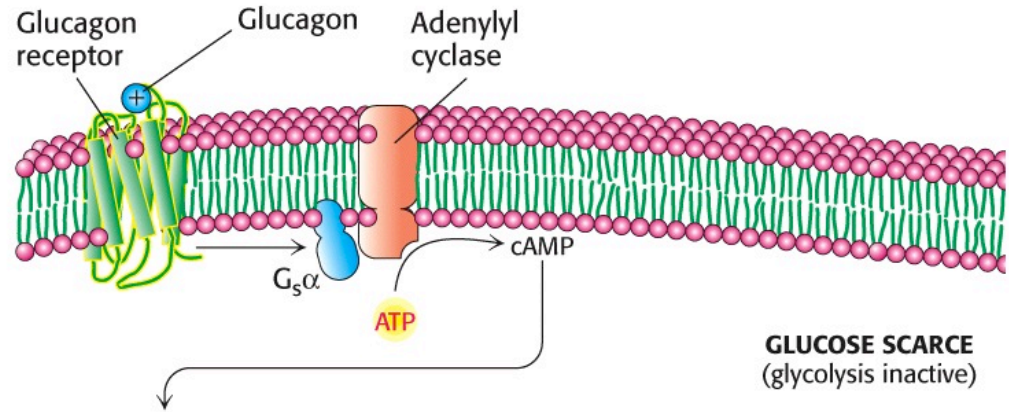
The plot thickens!: PFK-2



Fructose 2,6-bisphosphate (F-2,6-BP)



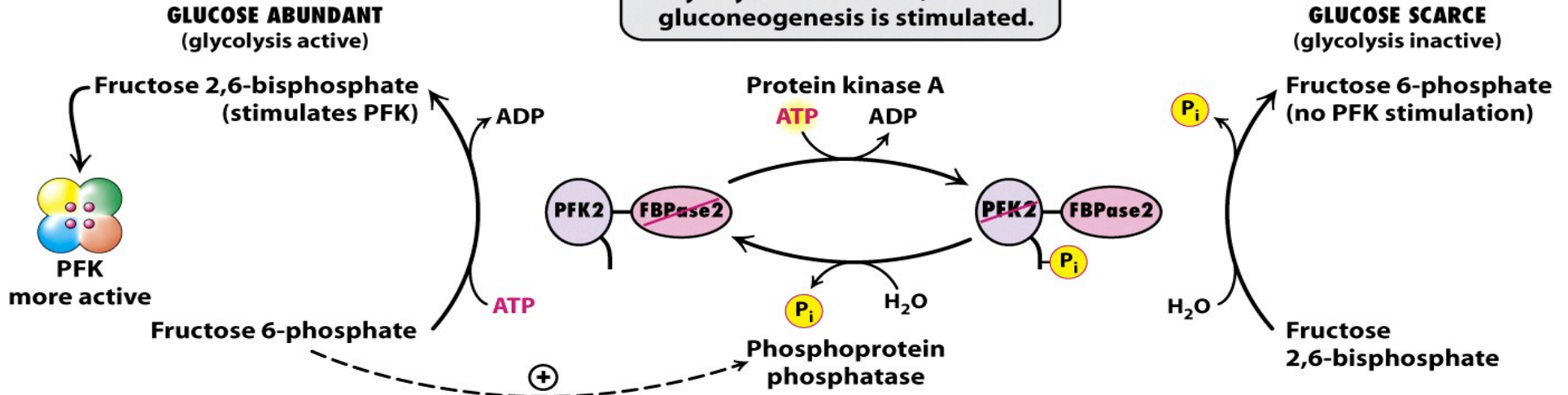
Regulation of glycolysis by overall hormonal levels



GLUCOSE ABUNDANT
(glycolysis active)

GLUCOSE SCARCE
(glycolysis inactive)

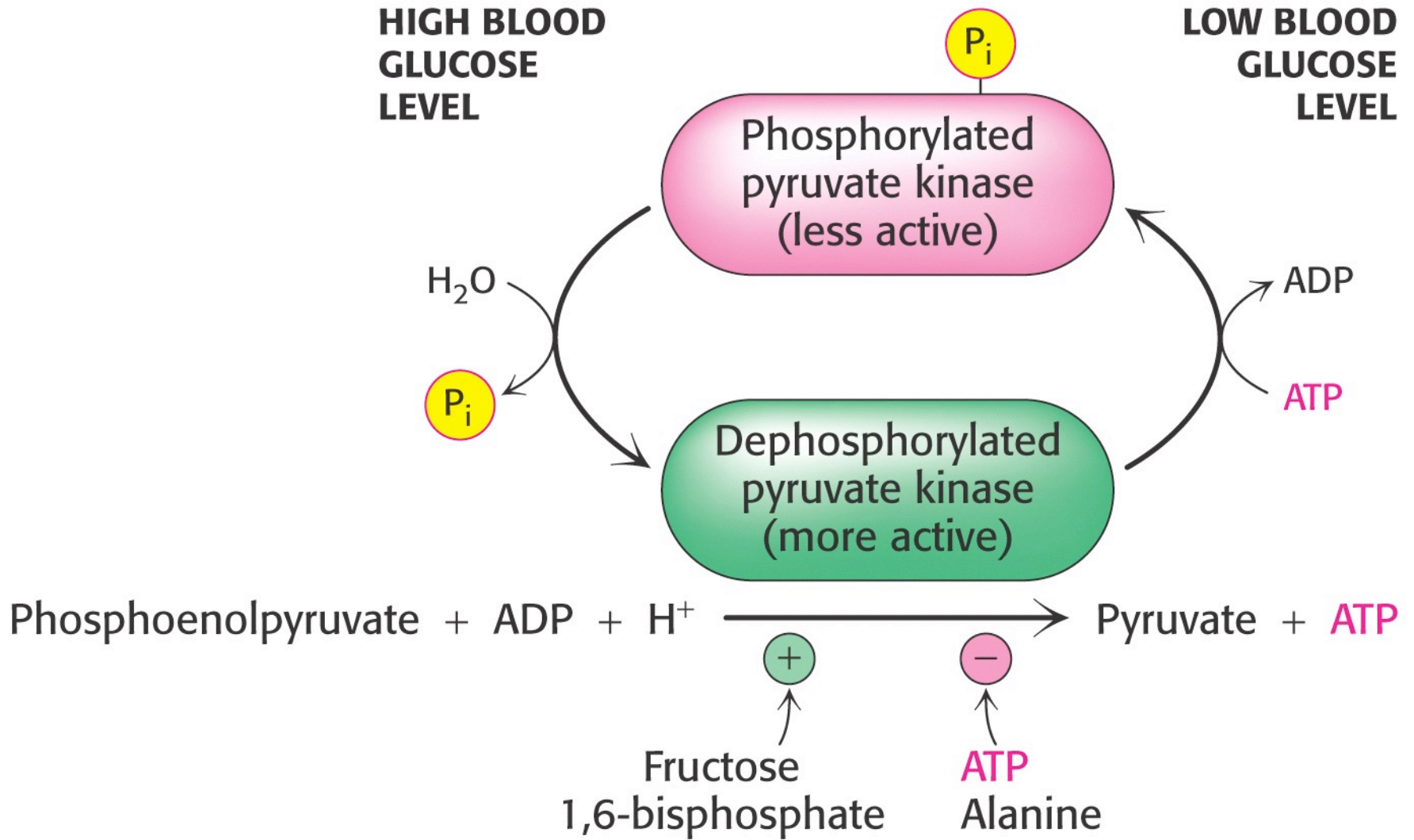
Glucagon stimulates PKA when blood glucose is scarce. FBPase 2 is activated. Glycolysis is inhibited, and gluconeogenesis is stimulated.



High levels of fructose 6-phosphate stimulate phosphoprotein phosphatase. PFK2 is activated. Glycolysis is stimulated, and gluconeogenesis is inhibited.

Figure 16-30
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Another regulator: Pyruvate Kinase



Getting Glucose into cells

TABLE 16.4 Family of glucose transporters

Name	Tissue location	K_m	Comments
GLUT1	All mammalian tissues	1 mM	Basal glucose uptake
GLUT2	Liver and pancreatic β cells	15–20 mM	In the pancreas, plays a role in regulation of insulin In the liver, removes excess glucose from the blood
GLUT3	All mammalian tissues	1 mM	Basal glucose uptake
GLUT4	Muscle and fat cells	5 mM	Amount in muscle plasma membrane increases with endurance training
GLUT5	Small intestine	—	Primarily a fructose transporter

Glycolysis related enzymes (HIF induced) can increase viability of tumors

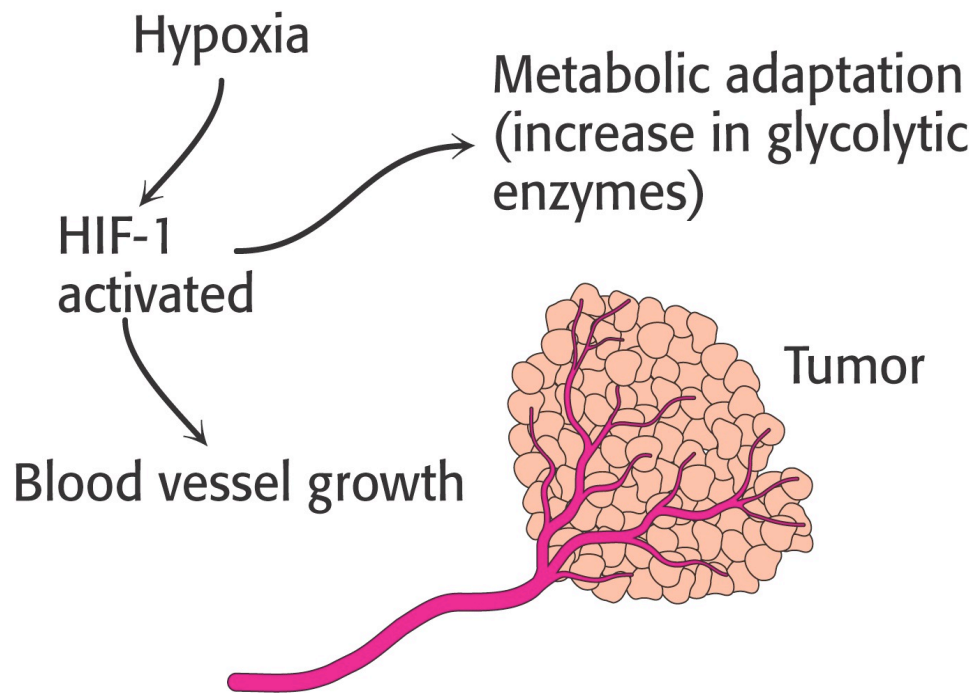
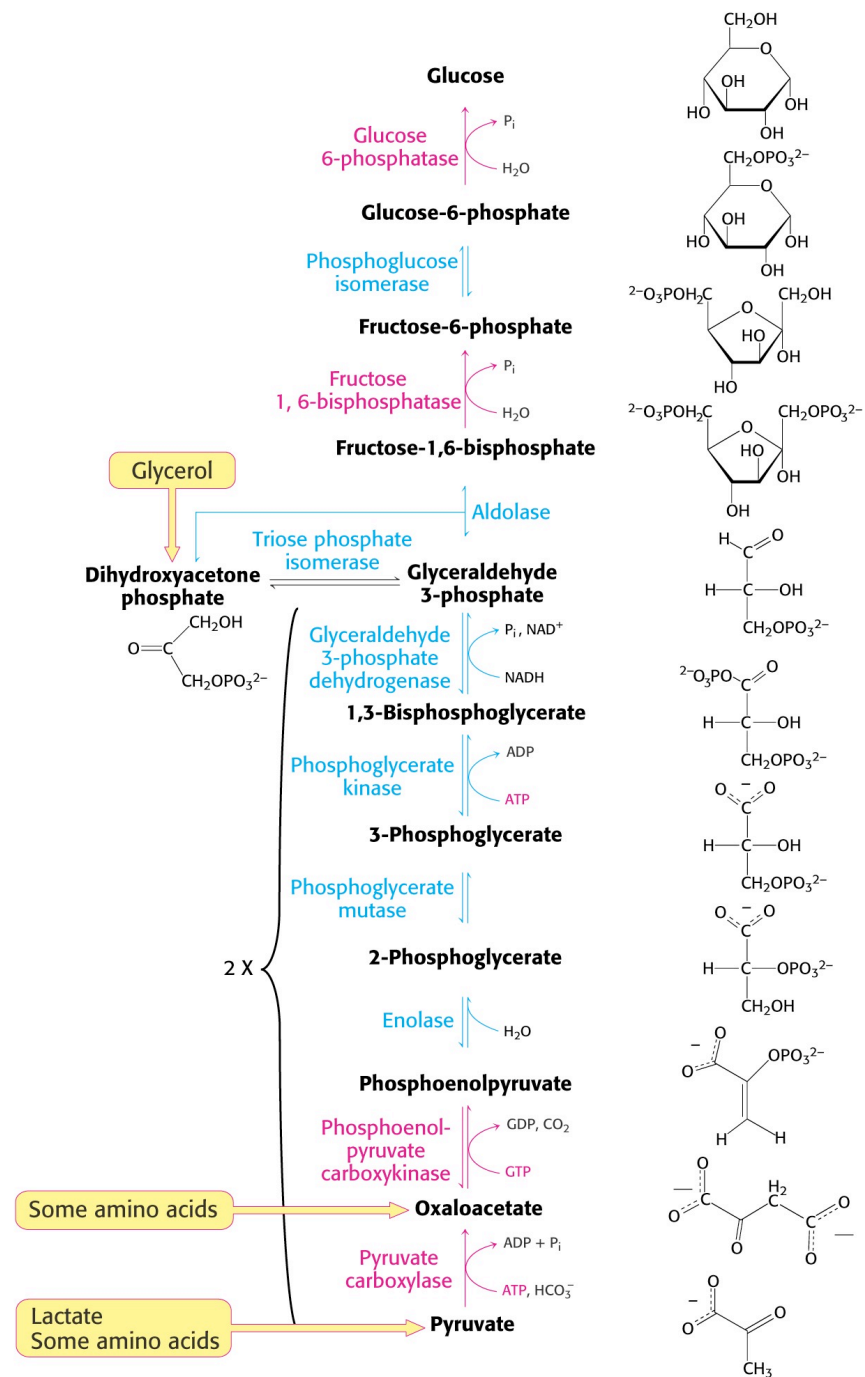


TABLE 16.5 Proteins in glucose metabolism encoded by genes regulated by hypoxia-inducible factor

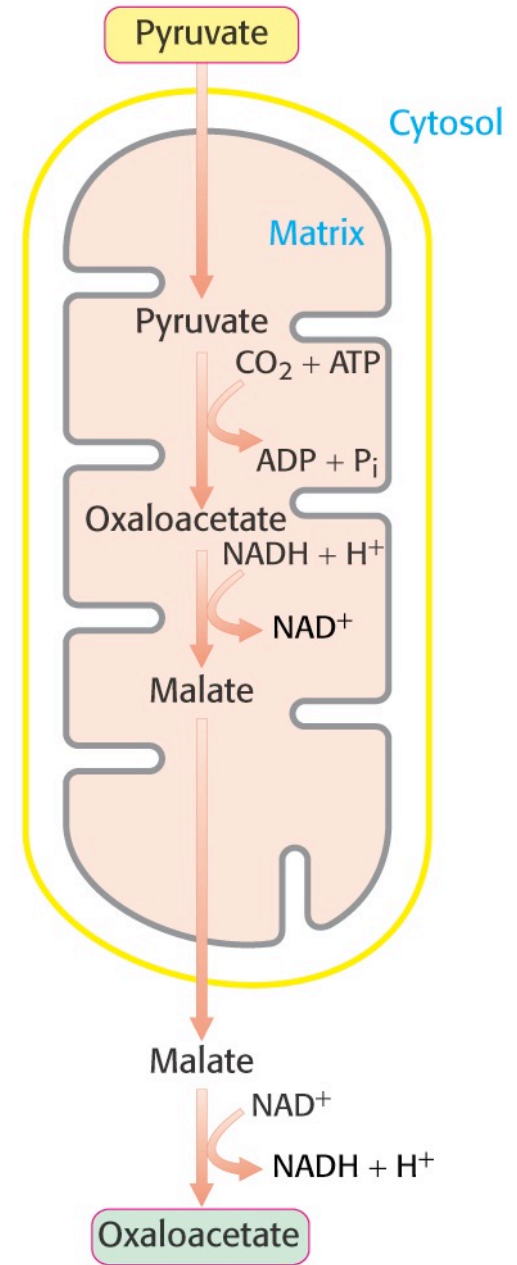
GLUT1
GLUT3
Hexokinase
Phosphofructokinase
Aldolase
Glyceraldehyde 3-phosphate dehydrogenase
Phosphoglycerate kinase
Enolase
Pyruvate kinase
Lactate dehydrogenase

When times are tough: the tough make glucose!

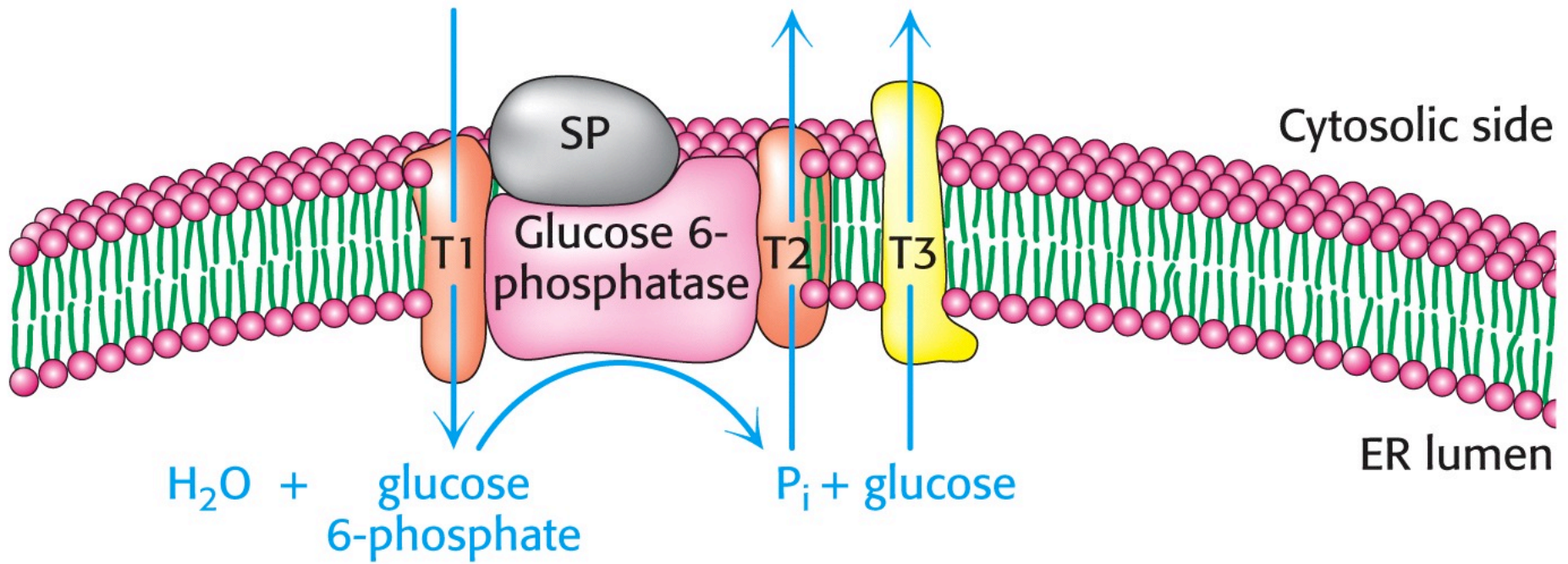
Balance Sheet:



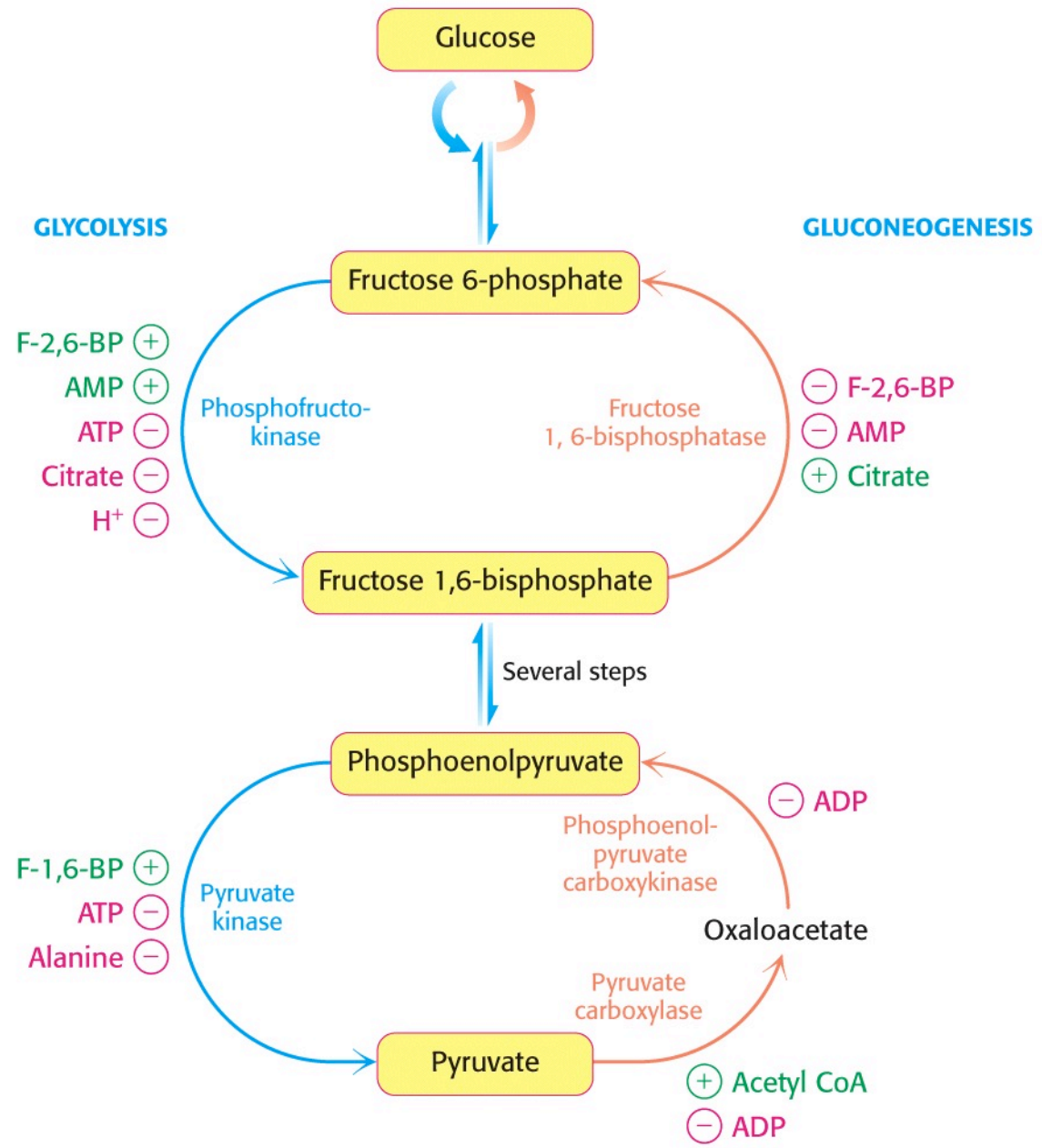
Making glucose from pyruvate:



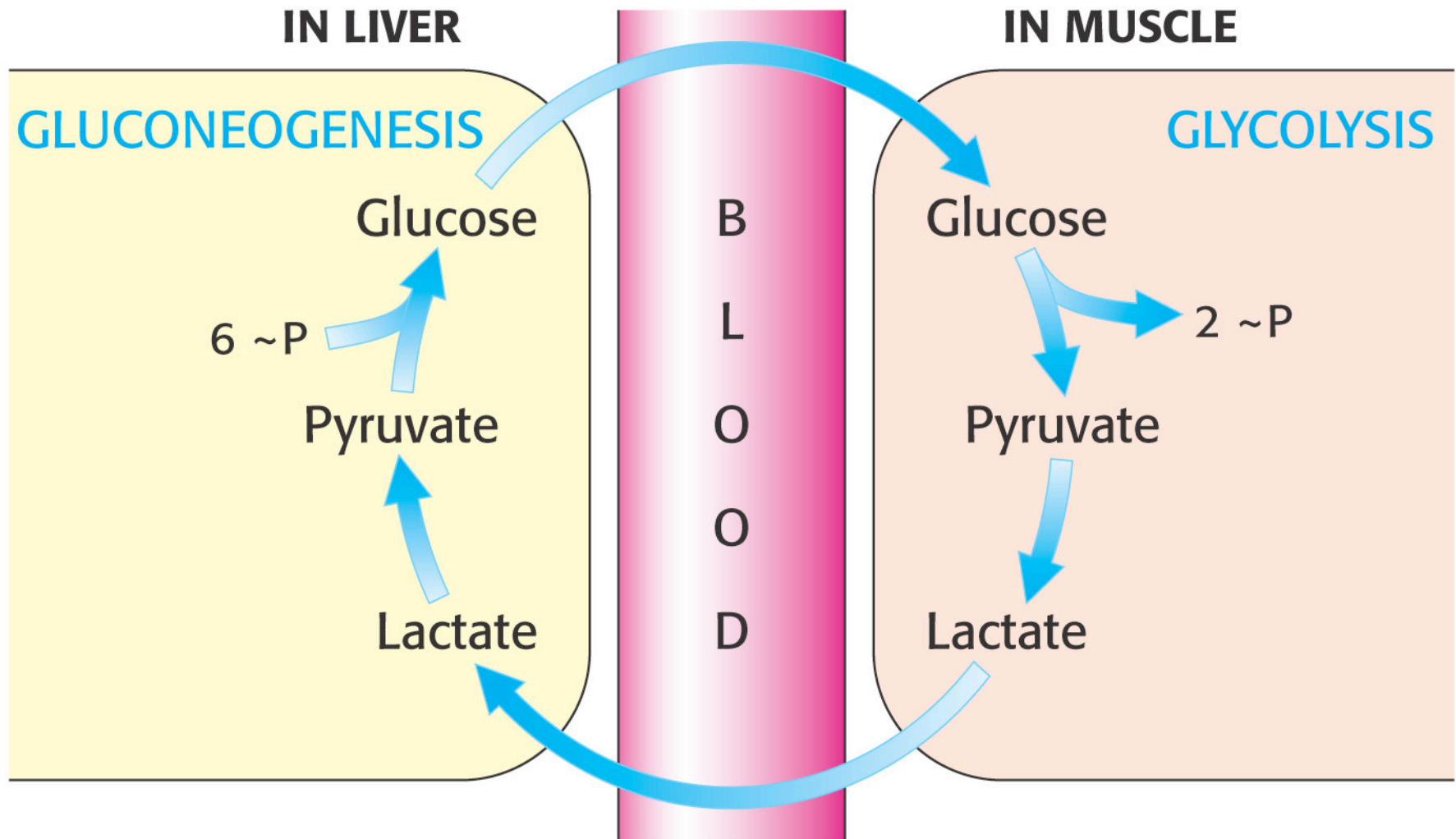
Putting glucose into the bloodstream: liver only need apply



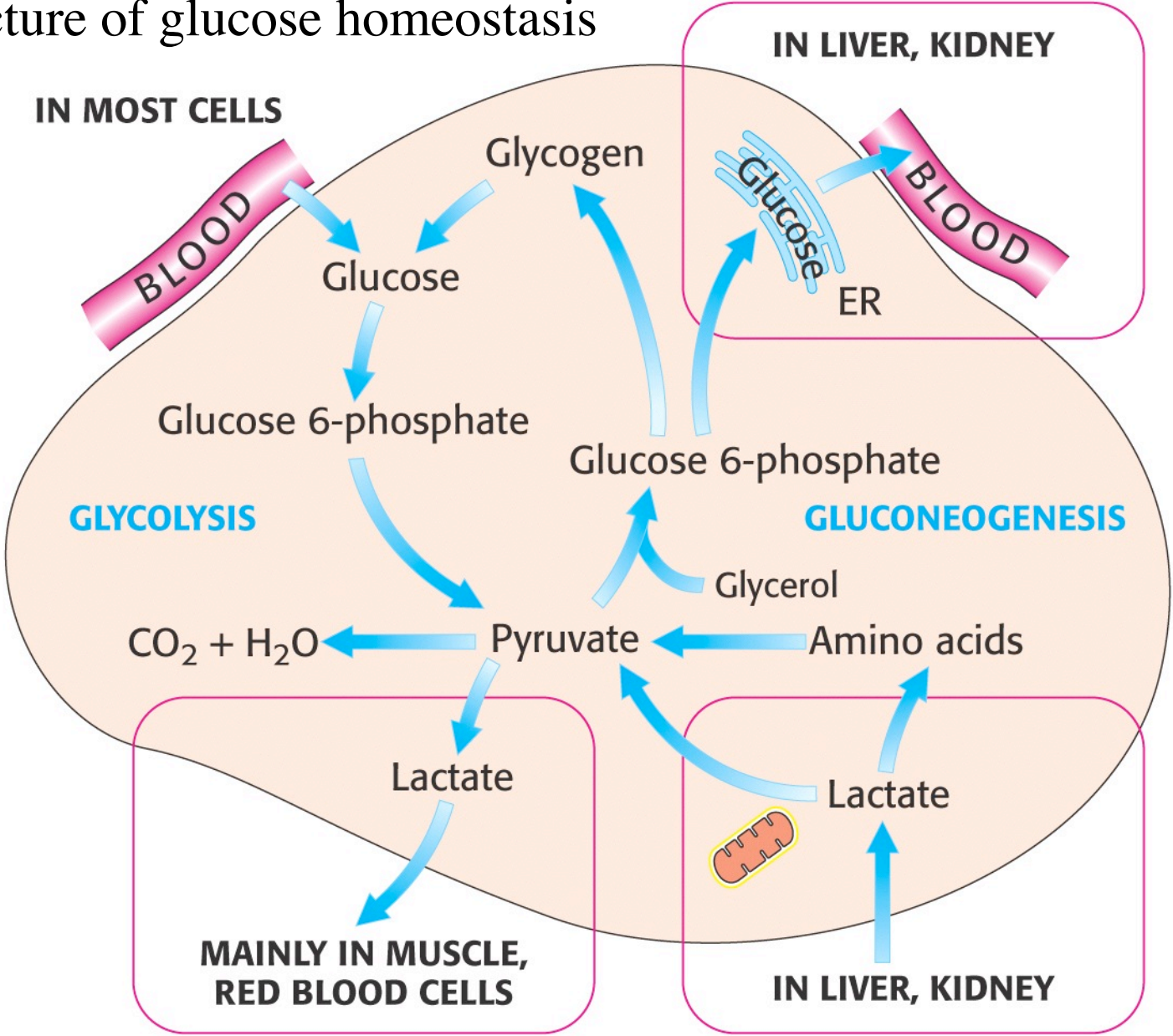
Reciprocal
regulation:
Know metabolic
logic behind these



The Cori Cycle: Oh my aching legs!!



The Big Picture of glucose homeostasis



Interconnections

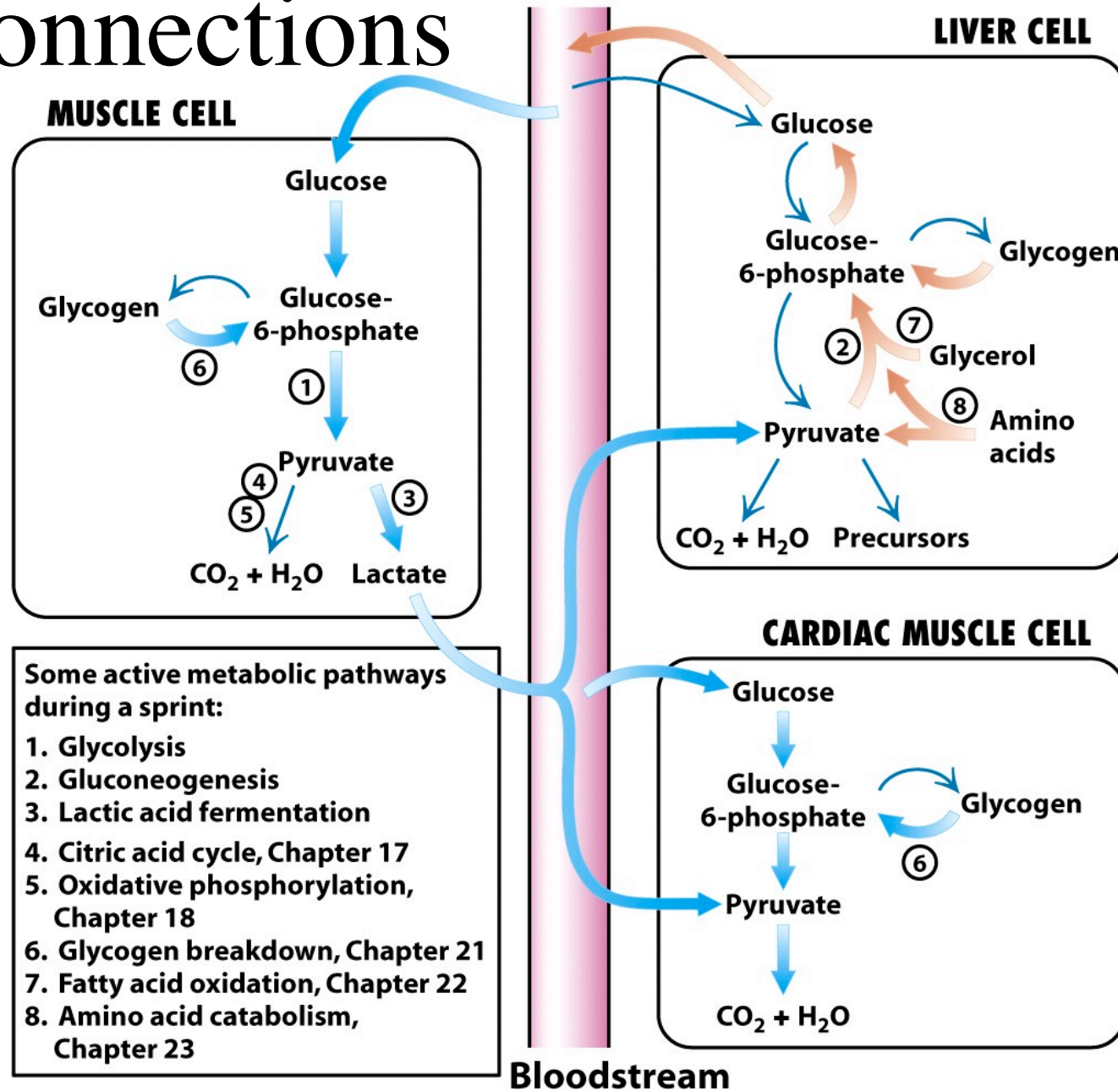


Figure 16-34
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