The net yield of ATP from glucose oxidation depends on the shuttle

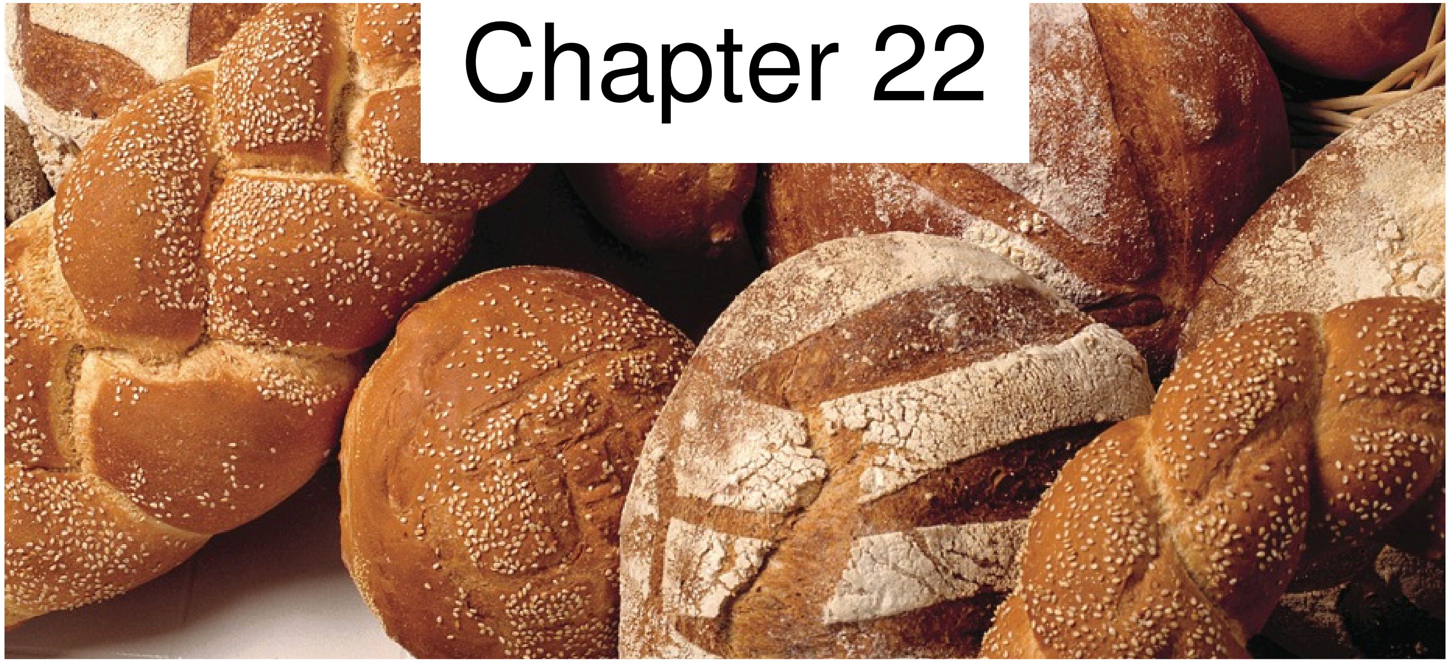
- From complete oxidation of glucose:
- Glycolysis in cytosol:

- Pyruvate to acetyl co-A (mitochondrion)

The net yield of ATP from glucose oxidation depends on the shuttle

- TCA cycle (mitochondrion)
- Oxidative phosphorylation (mitochondrion)

Gluconeogenesis and Glycogen Metabolism



Chapter 22

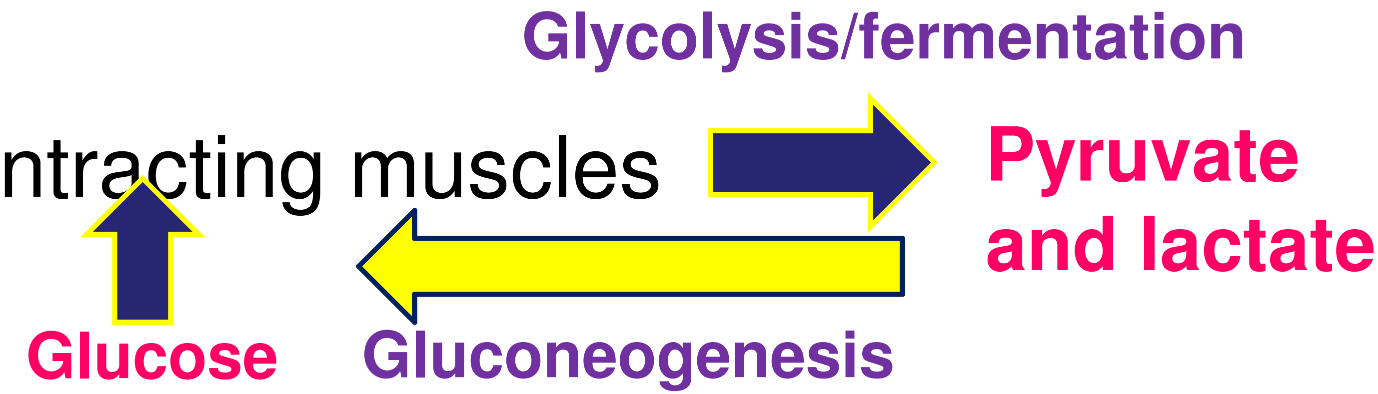
Gluconeogenesis

- Human metabolism consumes
- Body fluids carry
- Glycogen stores provide

→Only day’s supply of glucose in the body

- **New glucose** produced from non-carbohydrate precursors:

- Contracting muscles



Gluconeogenesis

- Which organs consume the most glucose?

Brain and muscles

- Which organs are the major sites of glucose synthesis?

Liver (90%) and kidney (10%)

Gluconeogenesis and Glycolysis

Gluconeogenesis	Glycolysis
• Glucose synthesised	• Glucose catabolised
• ATP consumed	• ATP produced
• NADH oxidised to NAD^+	• NAD^+ reduced to NADH
• **Endergonic?**	
• **Regulation**	• **Regulation**

4 reactions are unique to gluconeogenesis

- 7 of the 10 steps in glycolysis are reversed in gluconeogenesis:

Isomerisation of G-6P to F-6P (reaction 2)
6 reactions between F1,6 BP and PEP (reactions 4 → 9)

- 4 unique reactions

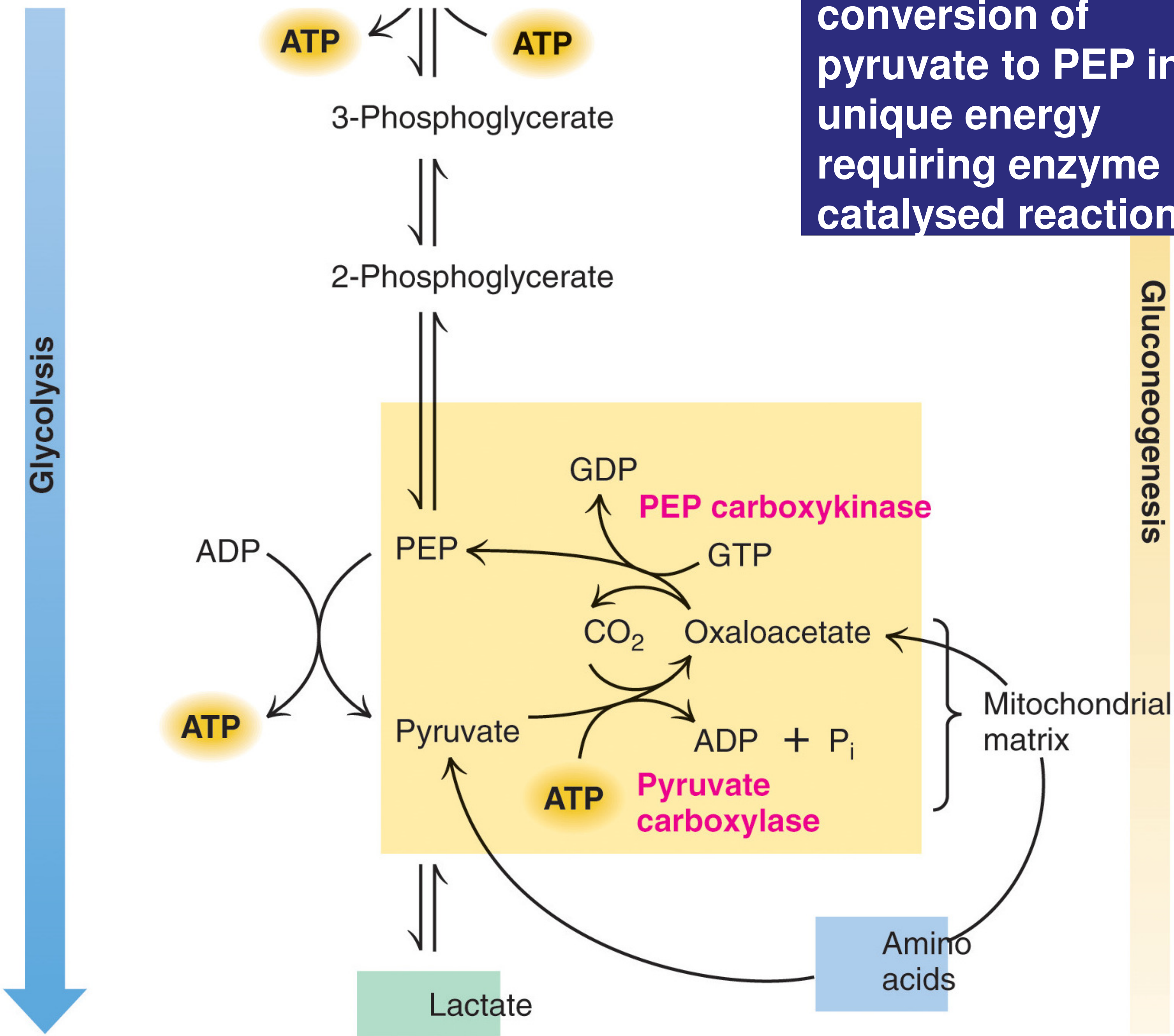
Pyruvate carboxylase

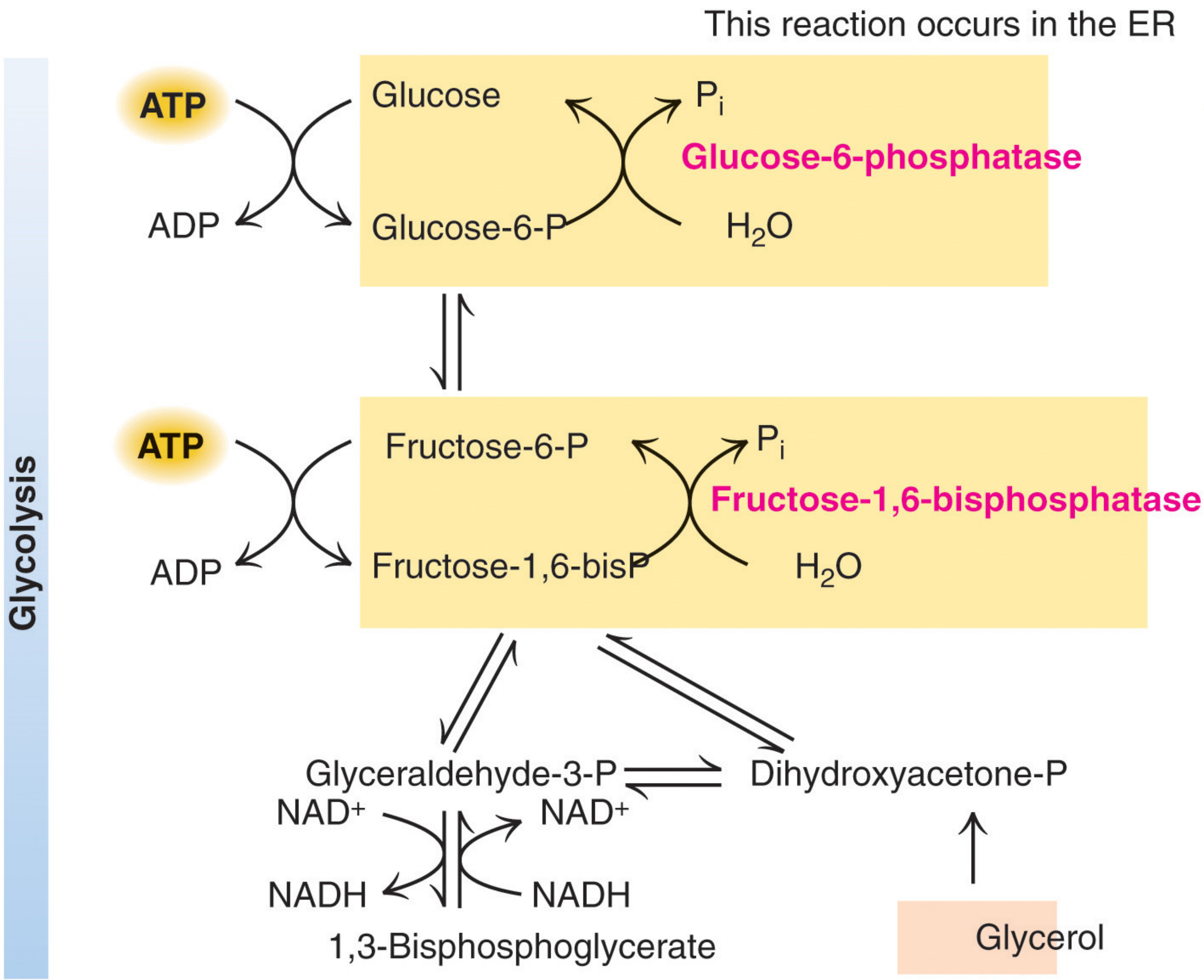
Fructose-1,6-bisphosphatase

PEP carboxykinase

Glucose-6-phosphatase

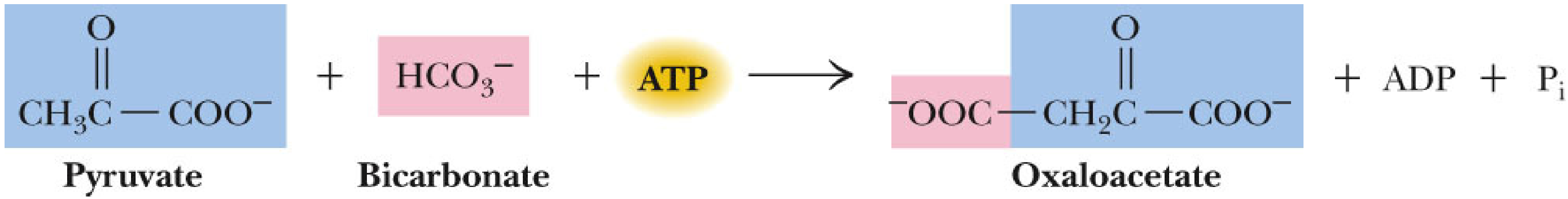
conversion of pyruvate to PEP in 2 unique energy requiring enzyme catalysed reactions



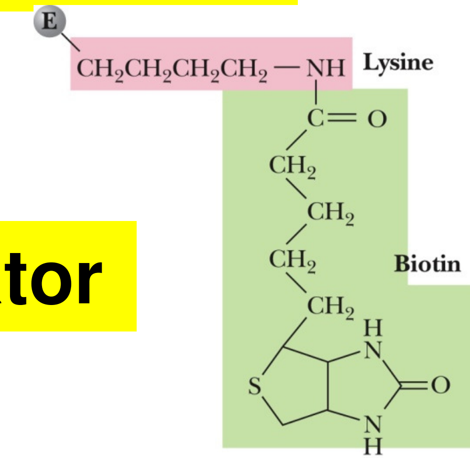


This reaction occurs in the ER
ATP
Glucose
P_i
Glucose-6-phosphatase
ADP
Glucose-6-P
H_2O
ATP
Fructose-6-P
P_i
Fructose-1,6-bisphosphatase
ADP
Fructose-1,6-bisP
H_2O
Glycolysis
Gluconeogenesis
Glyceraldehyde-3-P
Dihydroxyacetone-P
NAD^+
NAD^+
NADH
NADH
1,3-Bisphosphoglycerate
Glycerol

1. Pyruvate carboxylase

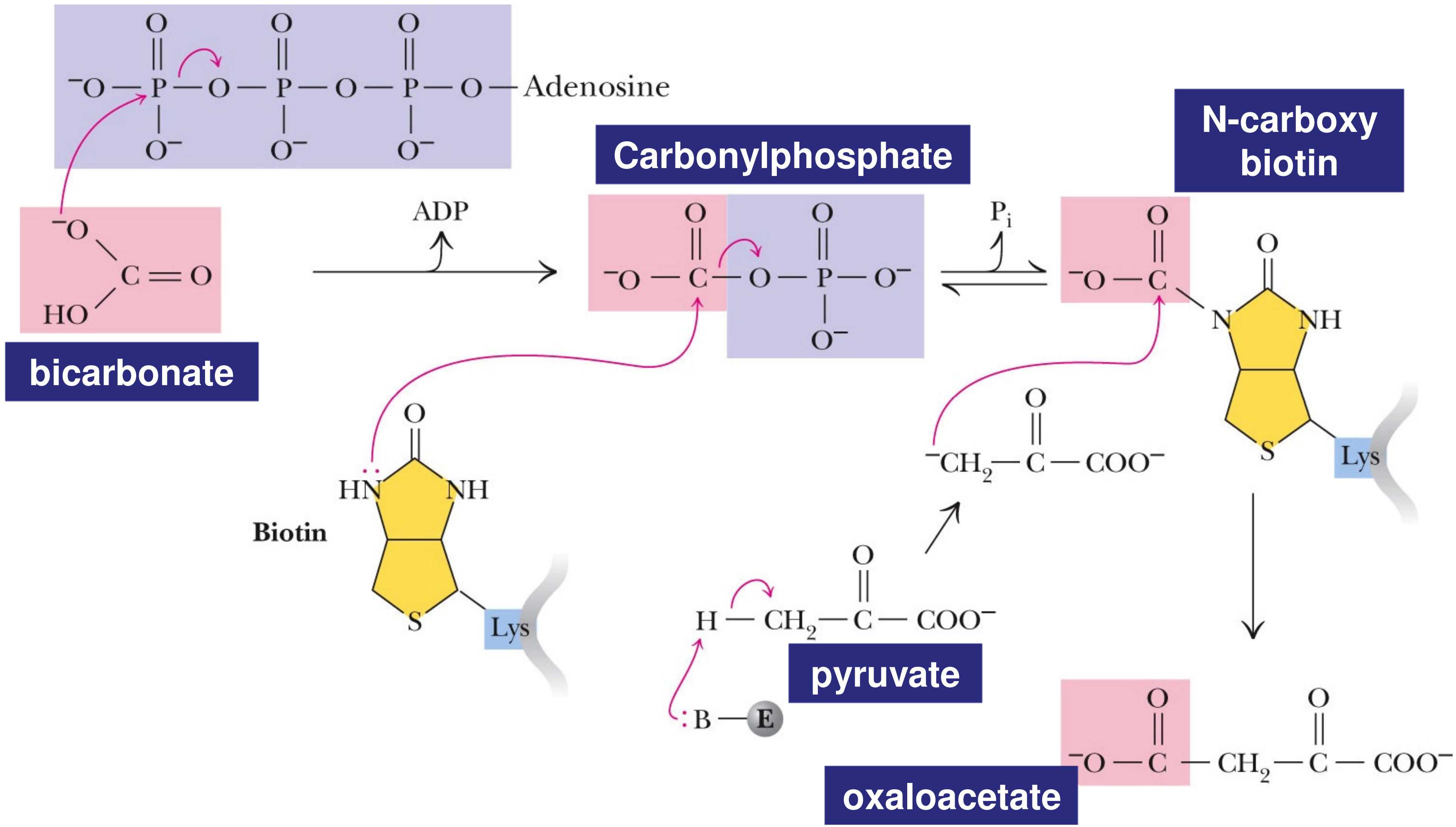


Enzyme is dependent on biotin (coenzyme)



Acetyl Co-A is an allosteric activator

Reaction mechanism of pyruvate carboxylase

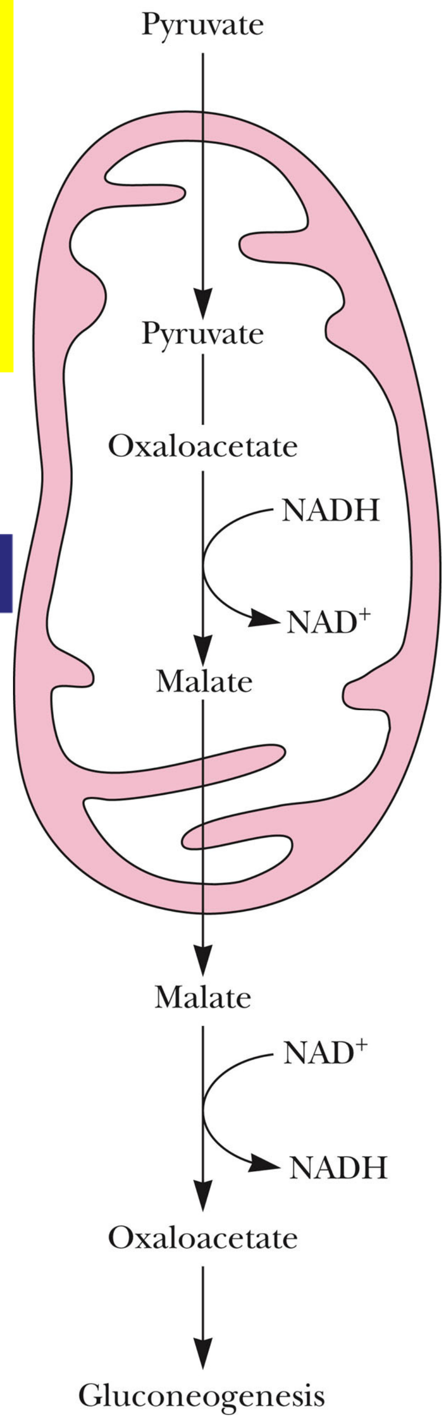


Write down why acetyl co A would be an activator of pyruvate carboxylase

Pyruvate transported into mitochondrion

Acetyl –co A

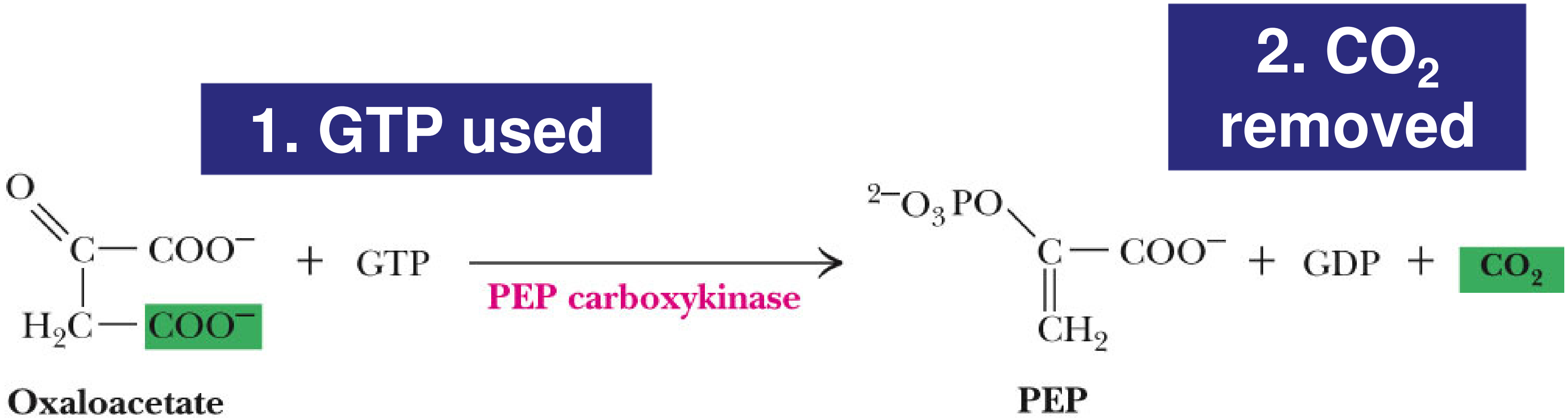
oxaloacetate



Pyruvate carboxylase in matrix

PEP carboxykinase in matrix and cytosol

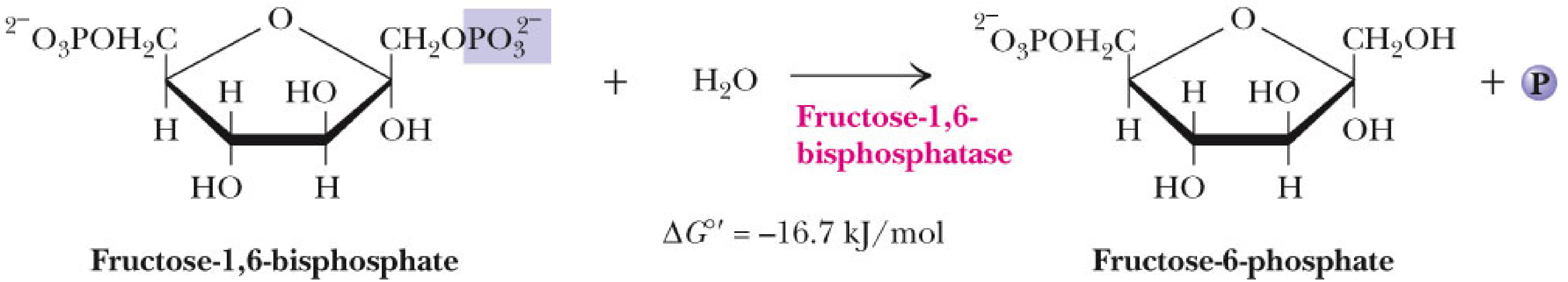
2. PEP carboxykinase



Pyruvate carboxylase is a priming reaction

3. Fructose-1,6-bisphosphatase

Allosteric regulation

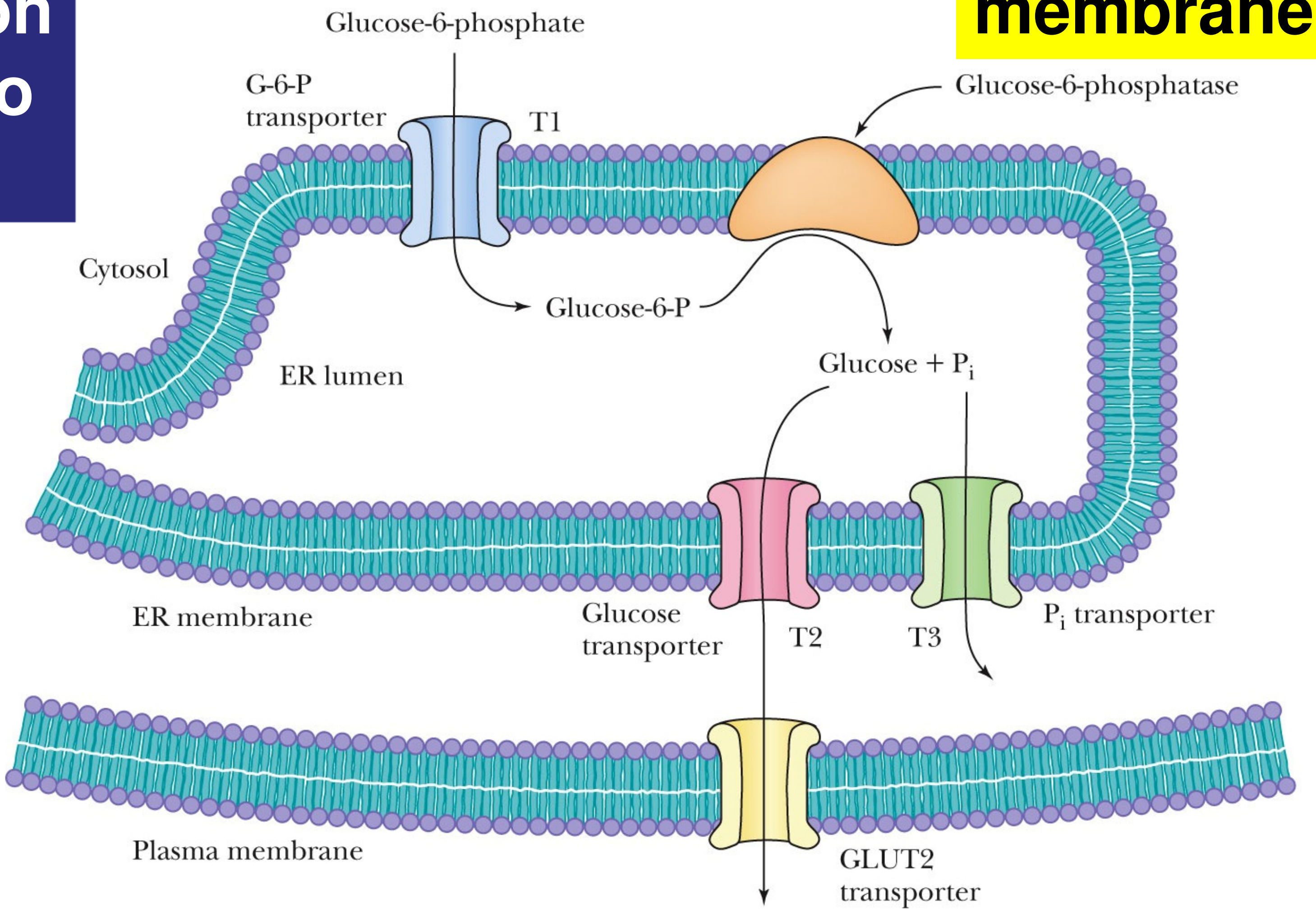


Hydrolysis of phosphoester bond therefore thermodynamically favourable

4. Glucose-6-phosphatase

Final step: conversion of G-6P to glucose

ER membrane



Net reaction for gluconeogenesis:

2 pyruvate + 4 ATP + 2 GTP + 2 NADH + 2 H^+ + 6 H_2O → glucose + 4 ADP + 2 GDP + 6 Pi + 2 NAD^+

ΔG = -75.7 kJ/mol

Net reaction for reverse of glycolysis

2 pyruvate + 2 ATP + 2 NADH + 2 H^+ + 2 H_2O → glucose + 2 ADP + 2 Pi + 2 NAD^+

ΔG = 75.7 kJ/mol

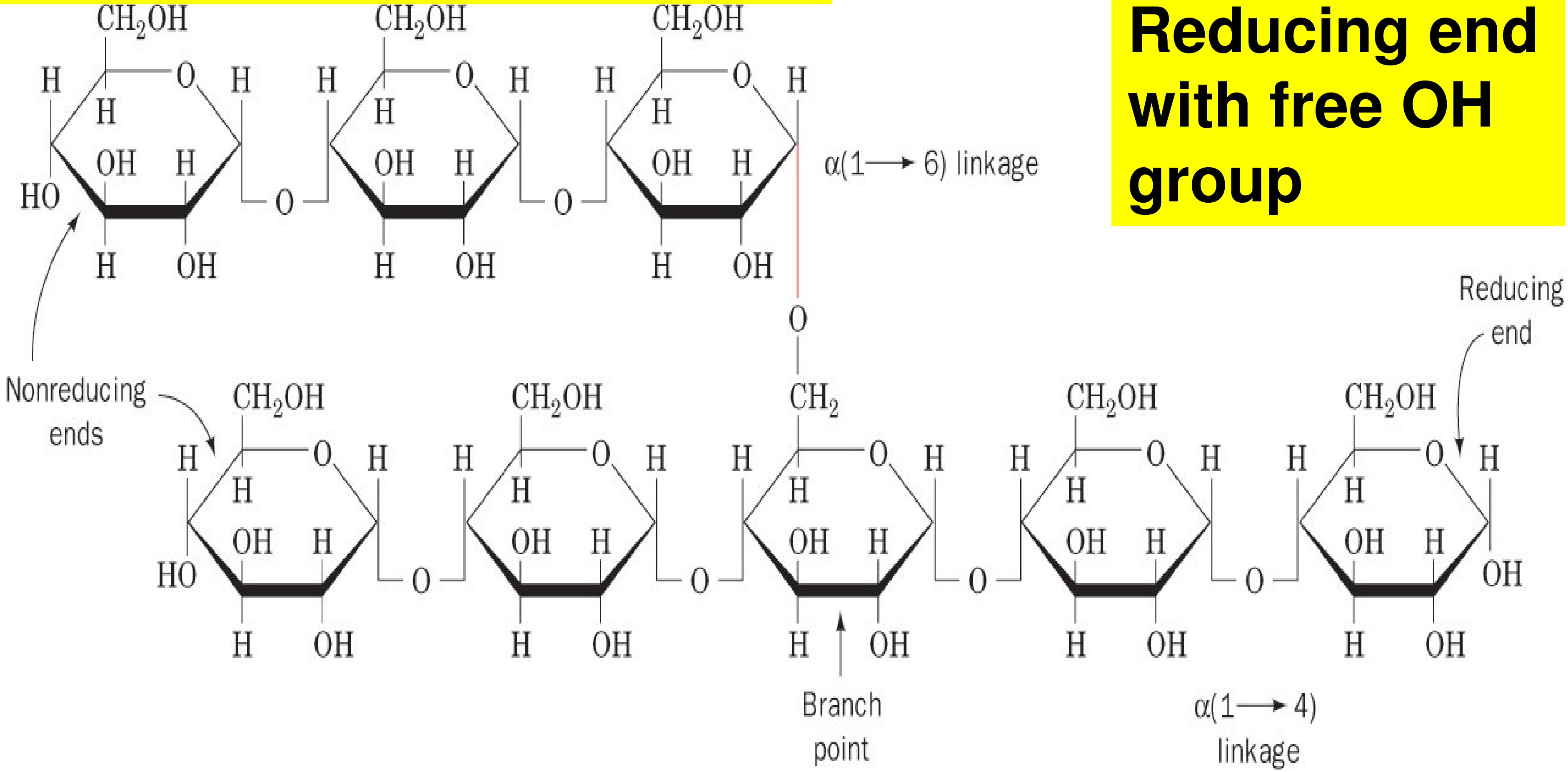
Comment on the differences between these processes

Gluconeogenesis summary

Structure of glycogen

Branch points separated by 8-12 glucosyl units

Reducing end with free OH group



Catabolism of starch and glycogen

exoglycosidase

- α-Amylase

Digestion of starch

- Endoglycosidase

Hydrolyses $\alpha 1 \rightarrow 4$ glycosidic linkages at random positions

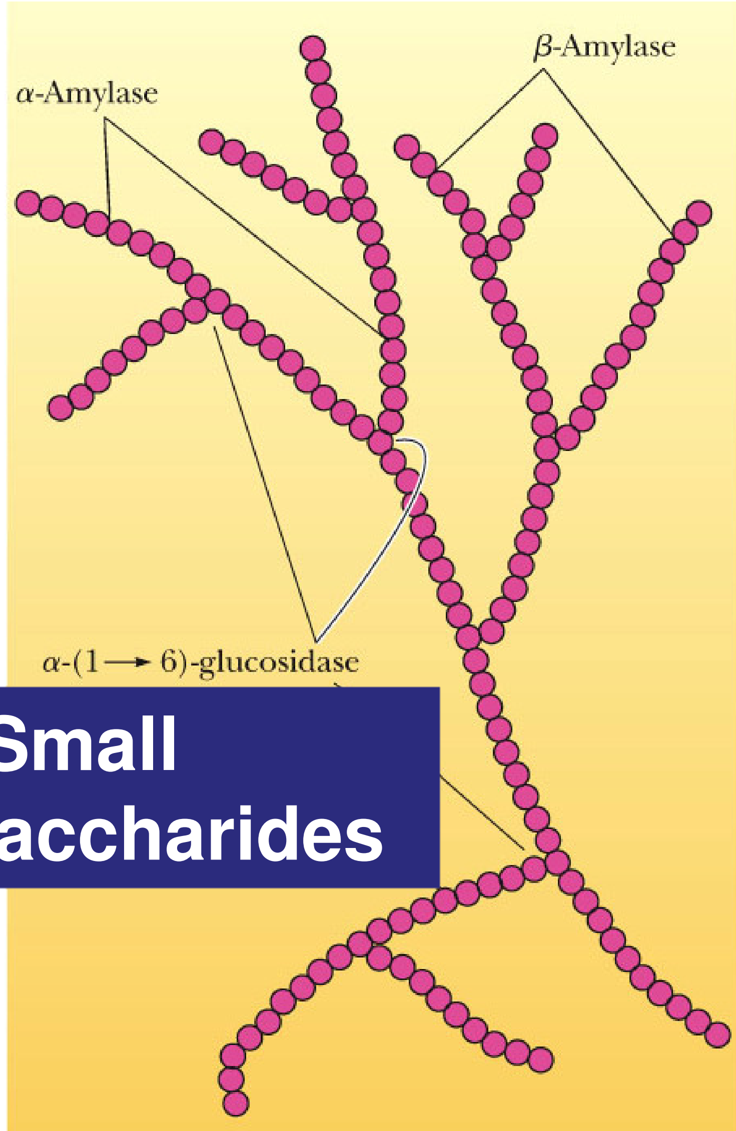
maltose

maltotriose

Small oligosaccharides

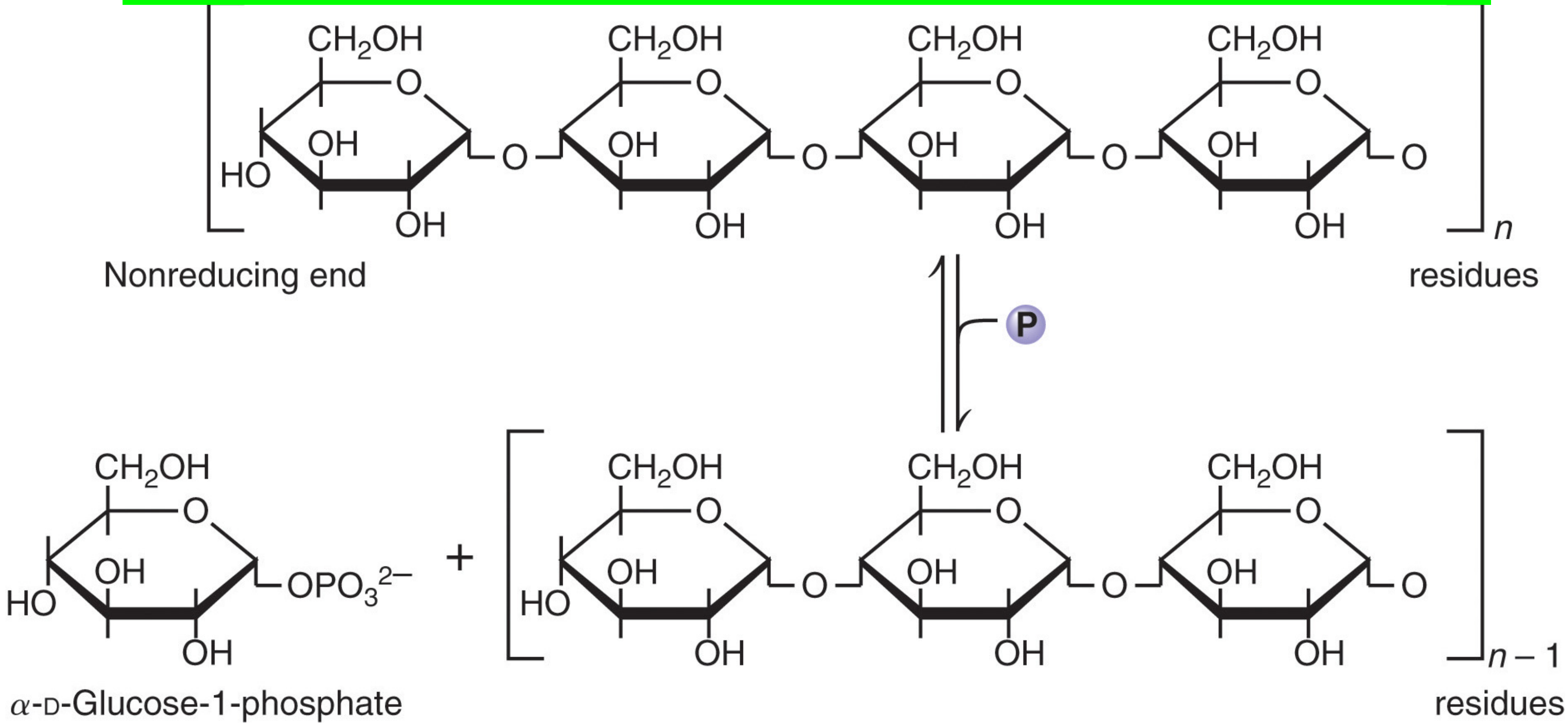
- Branches?

Limit dextrins



Reaction catalysed by glycogen phosphorylase

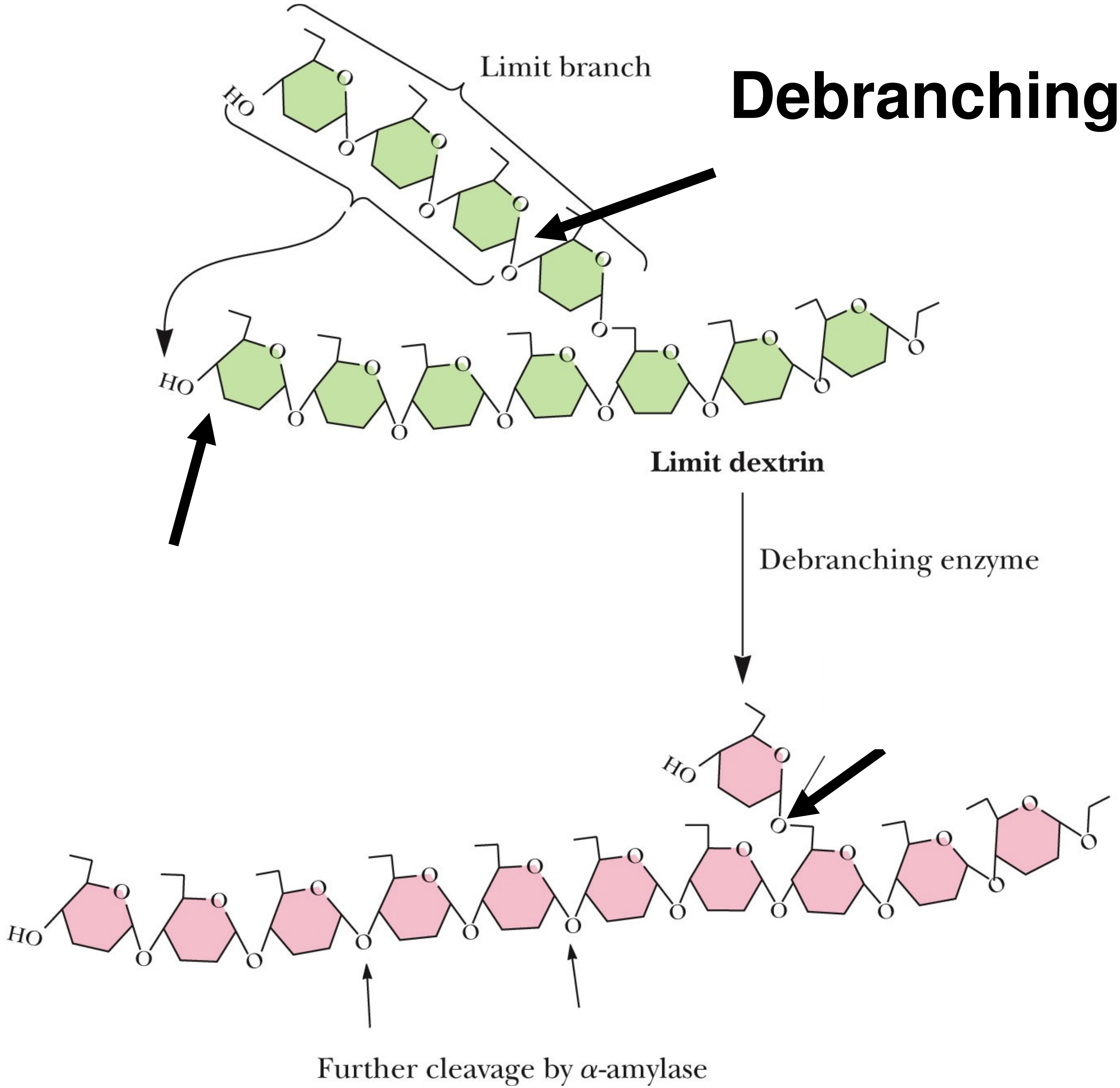
Glycogen (n-residues) + Pi → glycogen (n - 1 residues) + G1P



Debranching

- Glycogen phosphorylase and α-amylase can only cleave 5 units away from a branch point
- Can only cleave $\alpha(1\rightarrow4)$ glycosidic links
- The end products of cleavage via these enzymes are **limit dextrins**

Debranching enzyme



Why break glycogen down for energy rather than fats?

- mobilise fat
- metabolised anaerobically
- maintain blood glucose levels

Fatty Acid Catabolism: β-oxidation

Chapter 23

Fatty acids

- Obtained from diet

phospholipids **triacylglycerols**