Glycogen Metabolism

By

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Objectives:

- Storage of carbohydrates in liver & muscle
- Carbohydrates storage as glycogen
- Overview of glycogen synthesis (Glycogenesis)
- Overview of glycogen breakdown (Glycogenolysis)
- Key elements in regulation of both Glycogenesis and Glycogenolysis

Location & Functions of Glycogen

- **Location of glycogen in the body**

  skeletal muscle & liver

  400 g in muscles (1-2% of resting muscles weight)
  100 g in liver (~ 10% of well-fed liver)

- **Functions of glycogen:**

  Function of muscle glycogen: fuel reserve (ATP) (during muscular exercise)

  Function of liver glycogen: a source for blood glucose (especially during early stages of fasting)

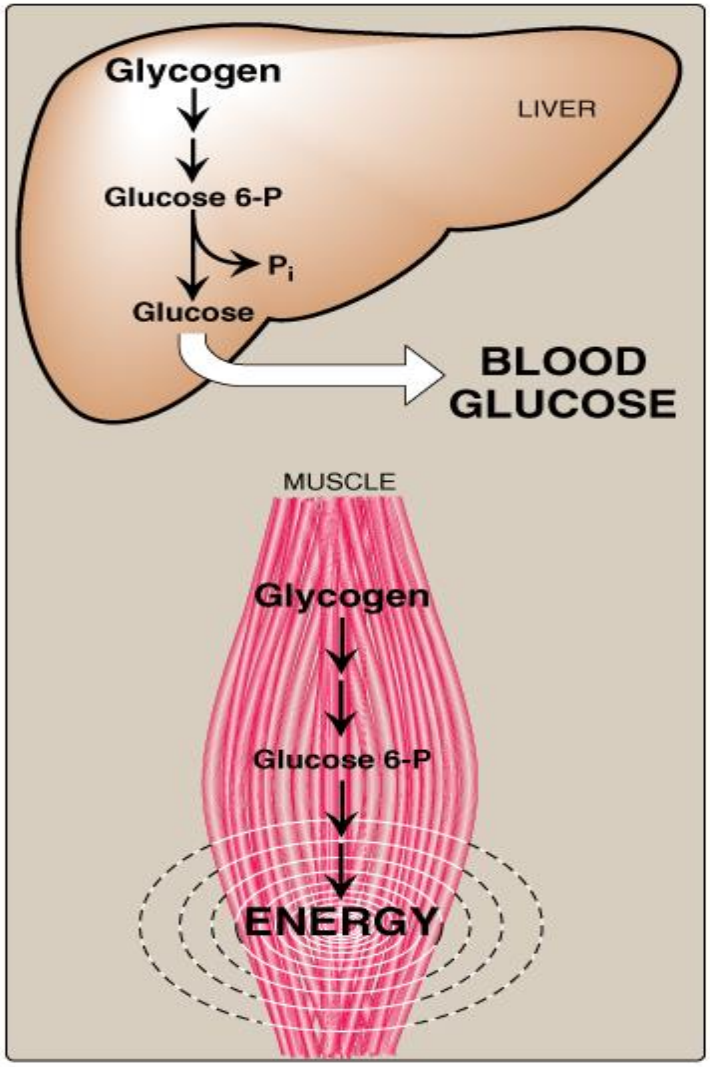


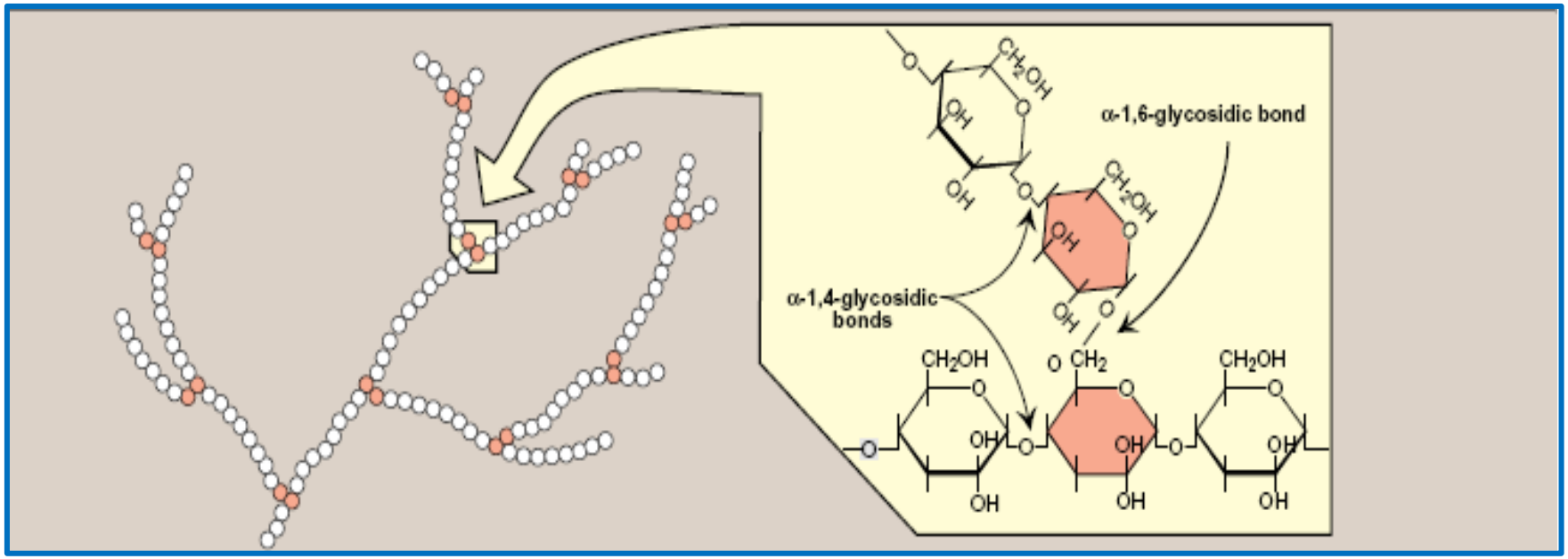
Figure 11.2

Functions of muscle and liver glycogen.

Structure of Glycogen

- **Glycogen is a branched-chain homopolysaccharide made exclusively from α- D-glucose**
- **Glucose residues are bound by α(1 - 4) glucosidic linkage**
- **Branches (every 8-10 residue) are linked by α(1-6) glucosidic linkage**
- Glycogen is present in the **cytoplasm** in the form of granules which contain most of the enzymes necessary for glycogen synthesis & degradation

Structure of Glycogen



Metabolism of Glycogen in Skeletal Muscle

Glycogenesis:

Synthesis of Glycogen from Glucose

Glycogenolysis:

Breakdown of Glycogen to Glucose-6-phosphate

GLYCOGENESIS

(*Synthesis* of Glycogen in Skeletal Muscles)

1- Building blocks: UDP-GLUCOSE

2- Initiation of synthesis:

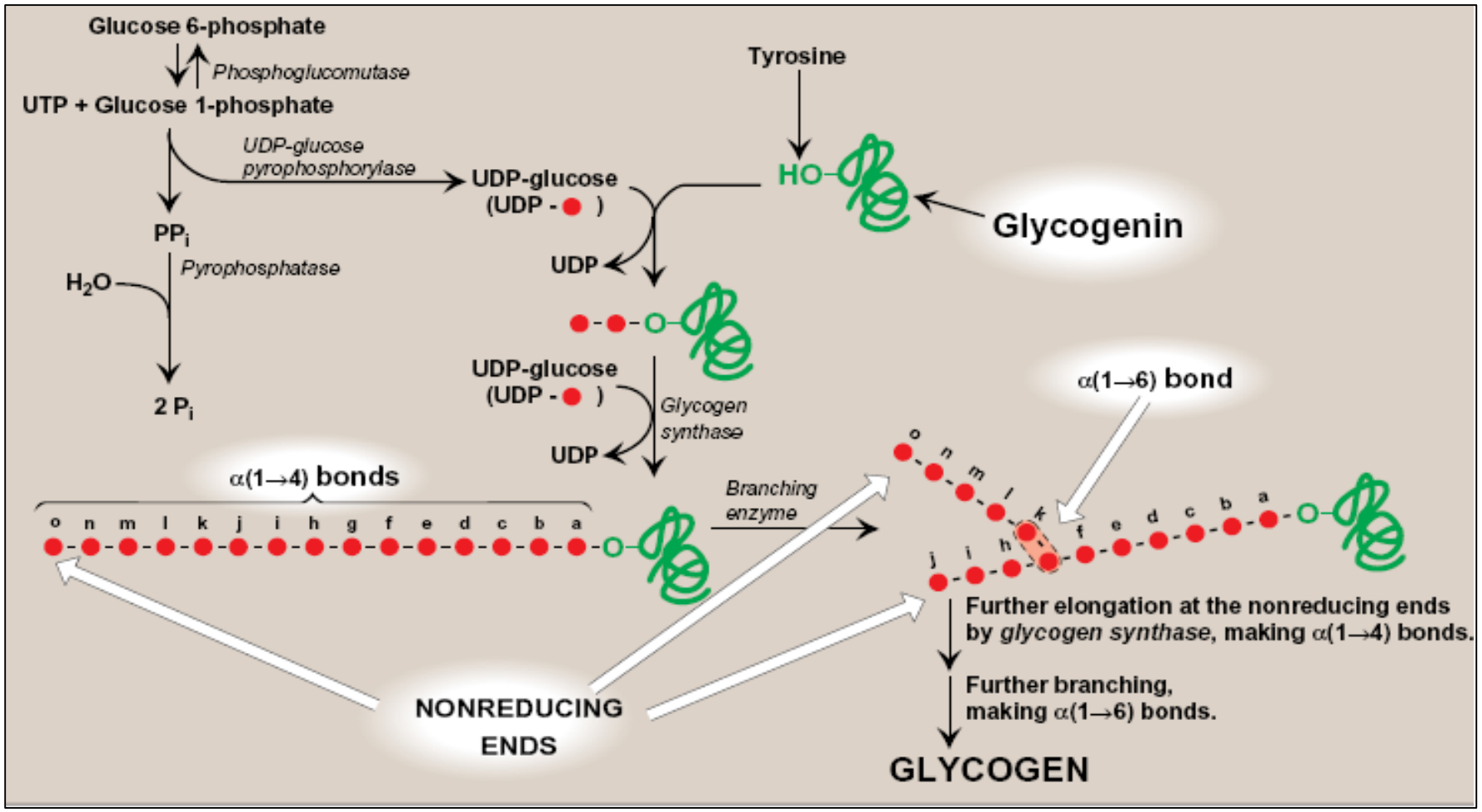
Elongation of pre-existing glycogen fragment
OR
The use of glycogen primer (glycogenin)

3- ELONGATION: Glycogen synthase (for α1-4 linkages)

Glycogen synthase **cannot** initiate synthesis but only elongates pre-existing glycogen fragment or glycogen primer (glycogenin)

4- BRANCHING: Branching enzyme (for α1-6 linkages)

Synthesis of Glycogen



Glycogenolysis

(Breakdown of glycogen in skeletal muscles)

1- **Shortening of glycogen chain:** by **glycogen phosphorylase**

Cleaving of α(1-4) bonds of the glycogen chain producing glucose 1-phosphate
Glucose 1-phosphate is converted to **glucose 6-phosphate** (by mutase enzyme)

2- Removal of branches : by **debranching enzymes**

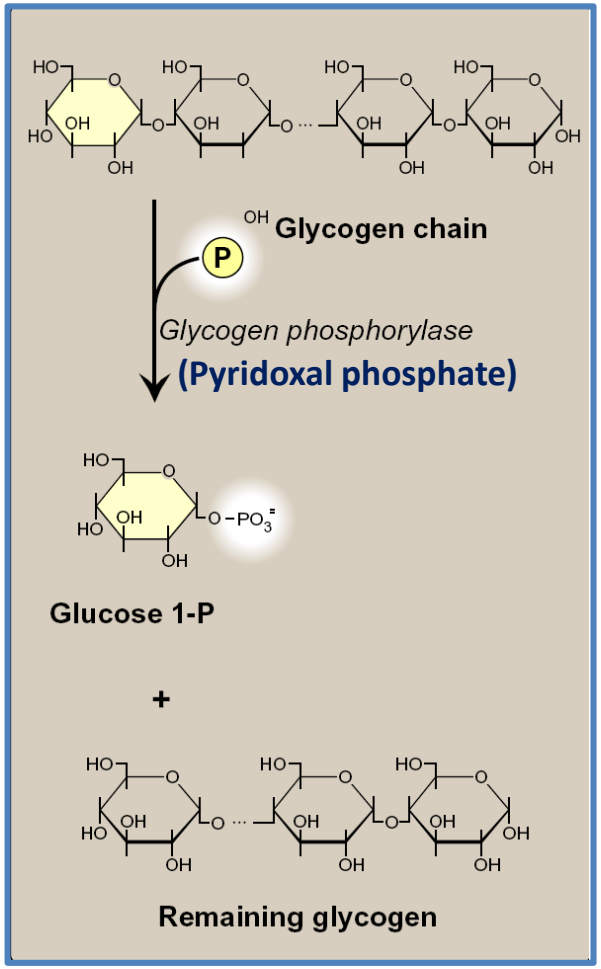
Cleaving of α(1-6) bonds of the glycogen chain producing **free glucose (few)**

3- Fate of glucose 6-phosphate (G-6-P):

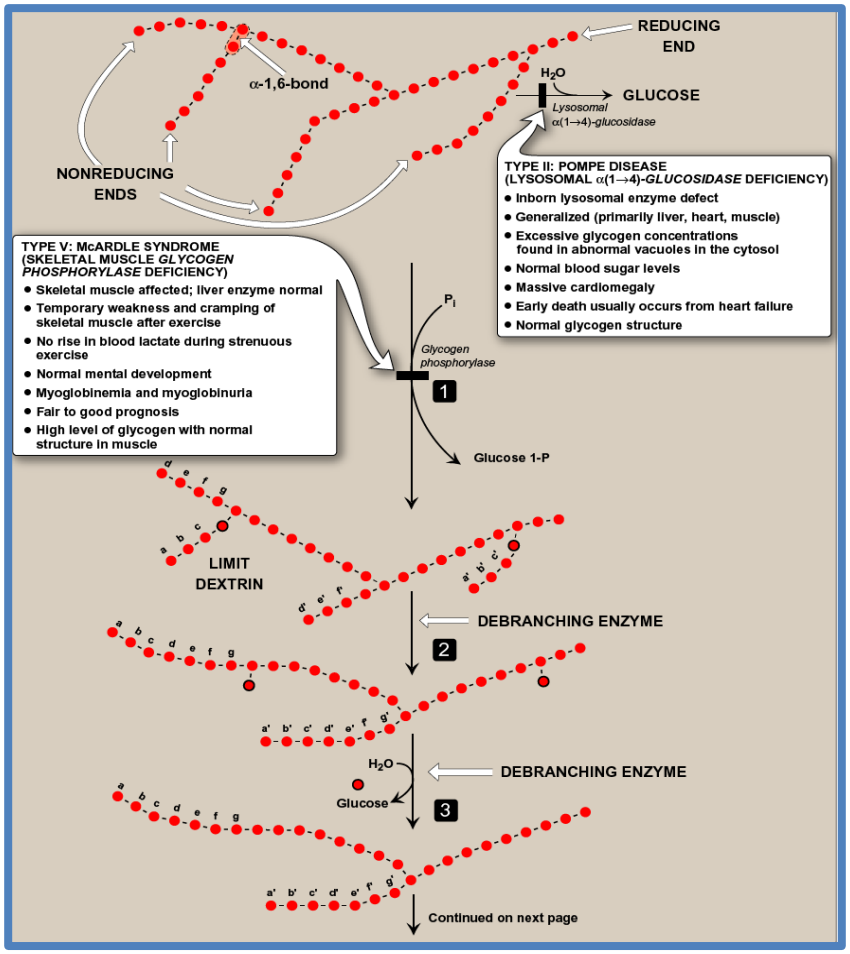
- G-6-P is ***not*** converted to free glucose

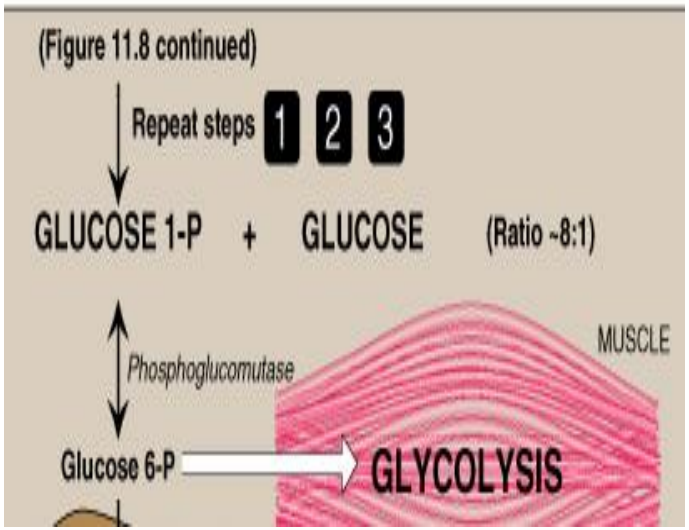
- It is used as a source of energy for skeletal muscles during muscular exercise (by anaerobic glycolysis starting from G-6-P step)

Glycogenolysis



Glycogenolysis





Regulation of Glycogen Metabolism

Synthesis & degradation of glycogen are tightly regulated

In Skeletal Muscles:

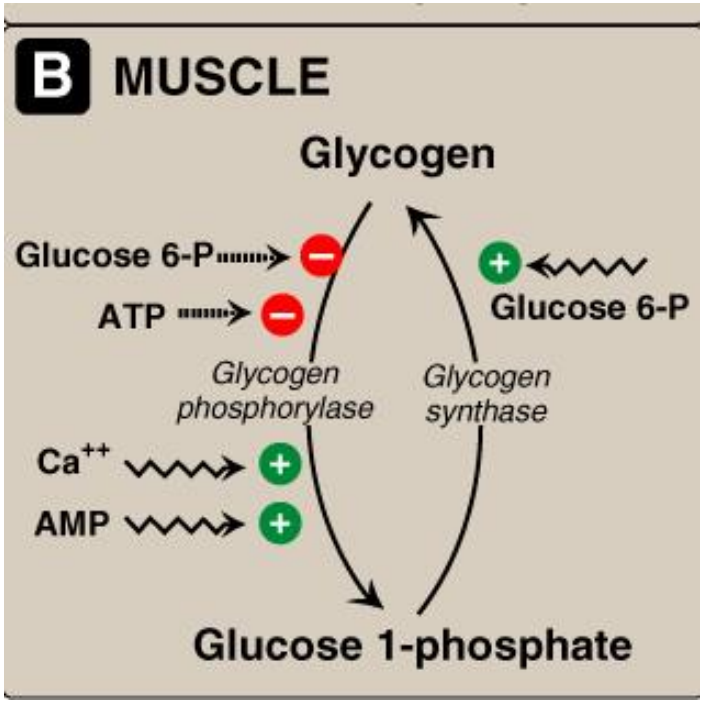
- Glycogen **degradation** occurs during **active exercise**
- Glycogen **synthesis** begins when the **muscle is at rest**

- **Regulation occurs by 2 mechanisms:**

  1- Allosteric regulation

  2- Hormonal regulation (Covalent modification)

Regulation of Glycogen Metabolism
1. Allosteric Regulation

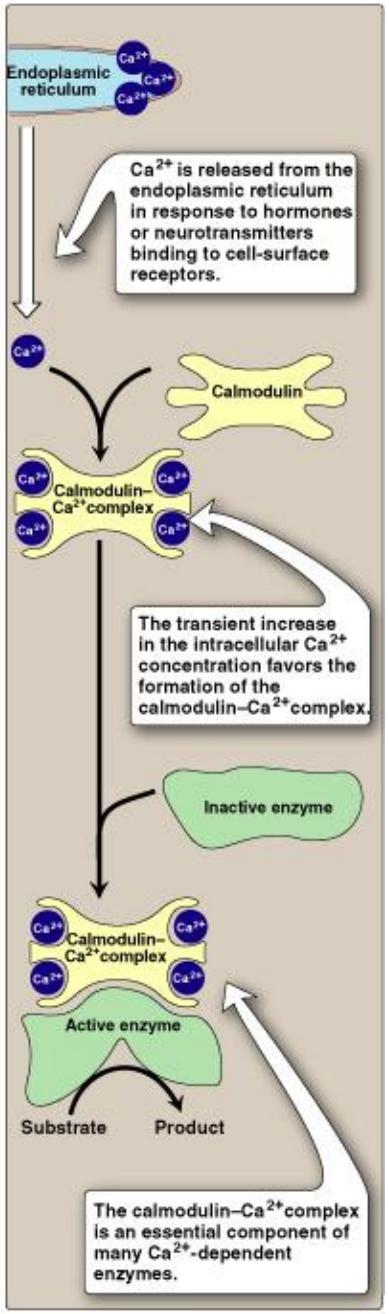


Regulation of Glycogen Metabolism

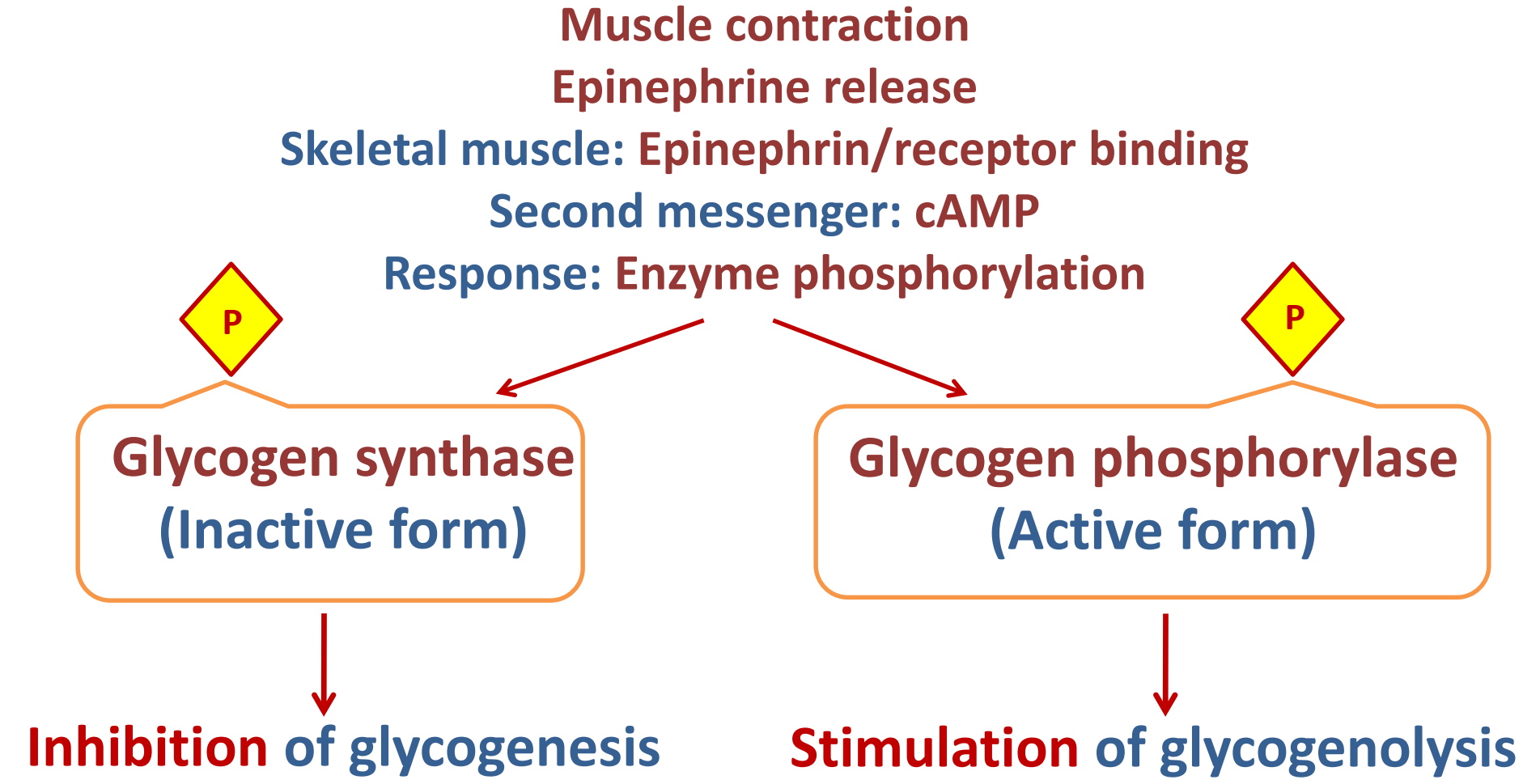
Increase of calcium during muscle contraction

Formation of Ca^{2+} -calmodulin complex

Activation of Ca^{2+} -dependent enzymes, e.g., glycogen phosphorylase



Regulation of Glycogen Metabolism: 2. Hormonal Regulation by Epinephrine



Glycogen Storage Diseases

A group of genetic diseases that result from a defect in an enzyme required for glycogen synthesis or degradation

They result in:

Formation of abnormal glycogen structure

OR

Excessive accumulation of normal glycogen in a specific tissue

Glycogen Storage Diseases
GSD Type V (Mc Ardle Syndrome)

- **Deficiency of skeletal muscle glycogen phosphorylase**