Glycogen Metabolism

With some notes!

The biochemistry team

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Objectives:

- Why do we need to store carbohydrates in muscle?
- Why carbohydrates are stored as glycogen?
- Overview of glycogen synthesis (Glycogenesis)
- Overview of glycogen breakdown (Glycogenolysis)
- Key elements in regulation of both Glycogenesis and Glycogenolysis

Note!
Anything in green is something I added from taking notes in class and from the book… I hope you find it helpful.

The significance of glycogen branching

- The branching makes glycogen more soluble, it increases the speed of glycogen degradation and synthesis… as a result, glycogen can be readily used when needed…
- The ends are non-reducing, they are the point of addition and removal…
- Glycogenesis is anabolic, UTP is consumed…
- glycogen (the storage form of glucose) cannot be released into the bloodstream. It will be used as a source of ATP by muscles

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)

In muscles, glucose 6-P enters glycolysis directly… no need for converting it to glucose…… glucose 6-phosphatase is absent in muscles.

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

in liver, glucose 6-P is converted to glucose which will help maintain blood glucose levels.

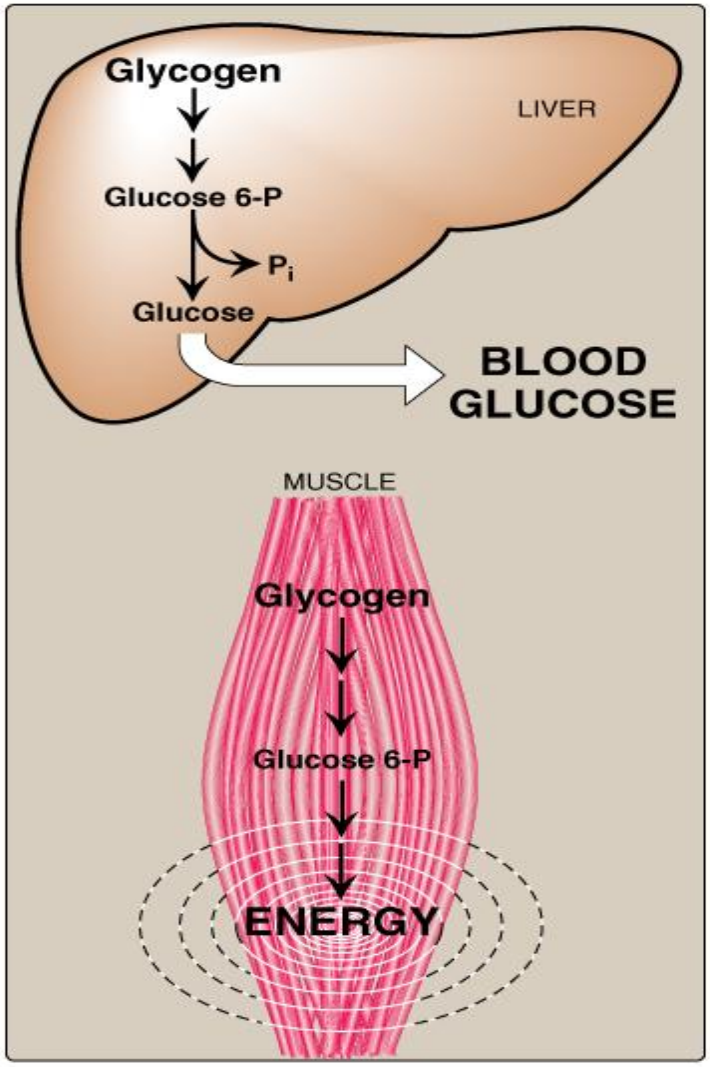


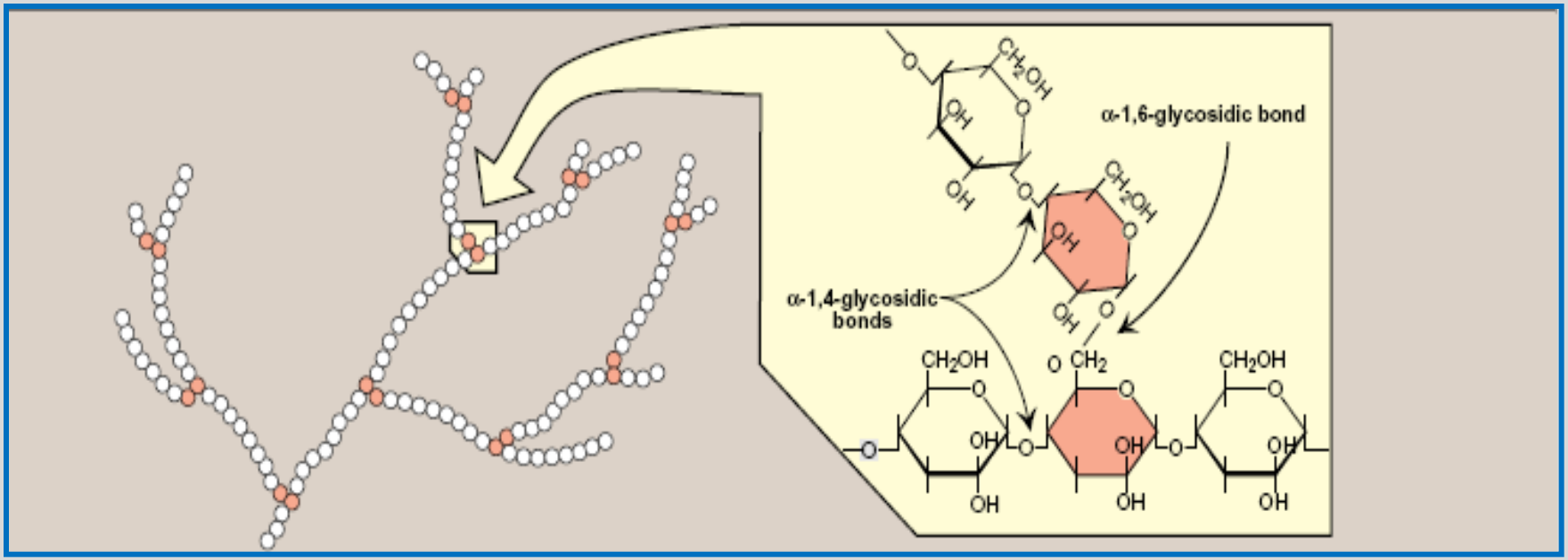
Figure 11.2

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

"uridine diphosphate " makes glucose metabolically active

2- Initiation of synthesis:

Elongation of pre-existing glycogen fragment

OR

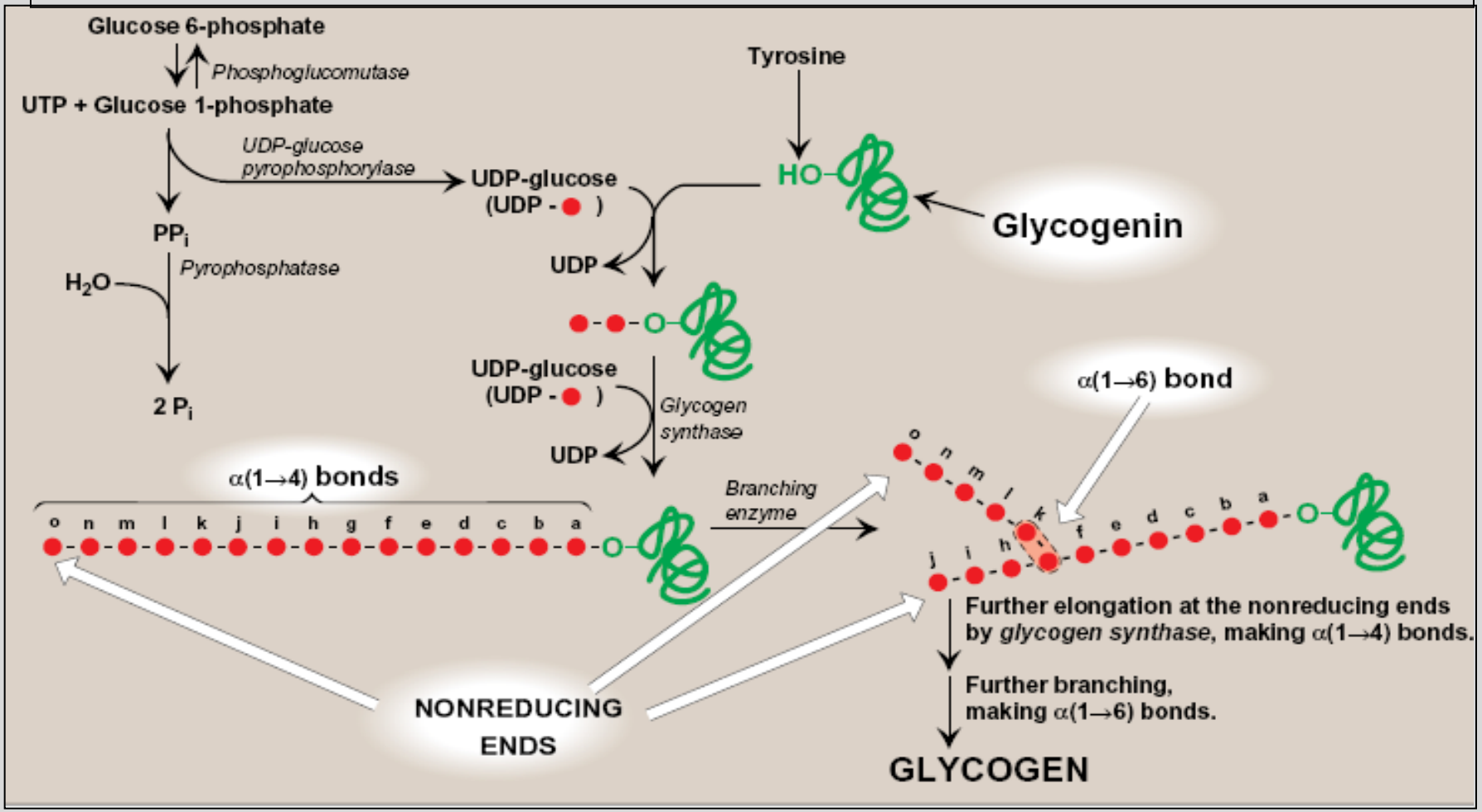
The use of glycogen primer (glycogenin, is auto-catalytic, it can add few glucose molecules then the process will continue by glycogenesis)

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



The diagram is for clarification… try to understand the process of glycogenesis… It will give you a clear idea about what you are reading now…

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)
"pyridoxal phosphate is required as a co-enzyme"

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

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

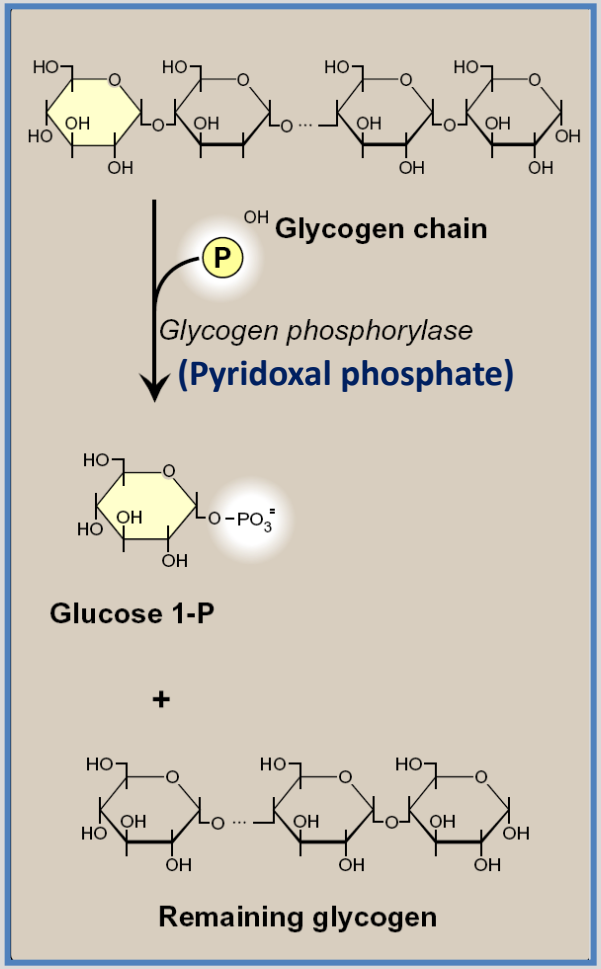
Overall product:
8 glucose 6-P and 1 glucose are produced
8 ----------> 1

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

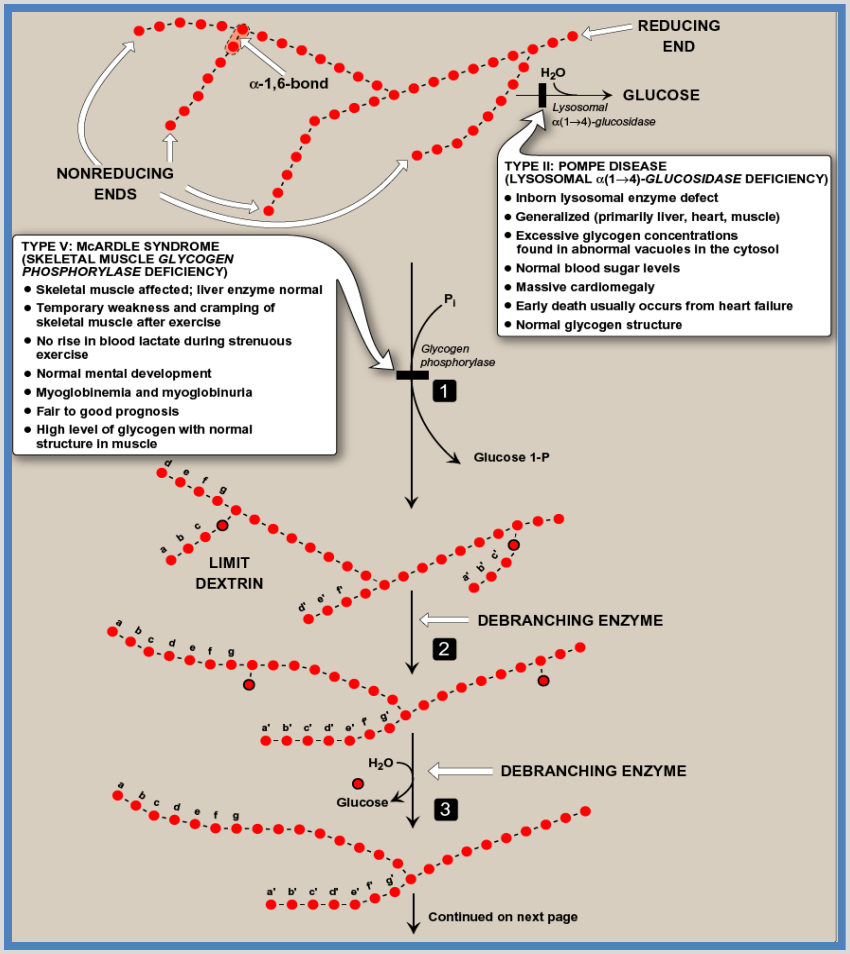
- G-6-P is ***not*** converted to free glucose "in muscles"

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

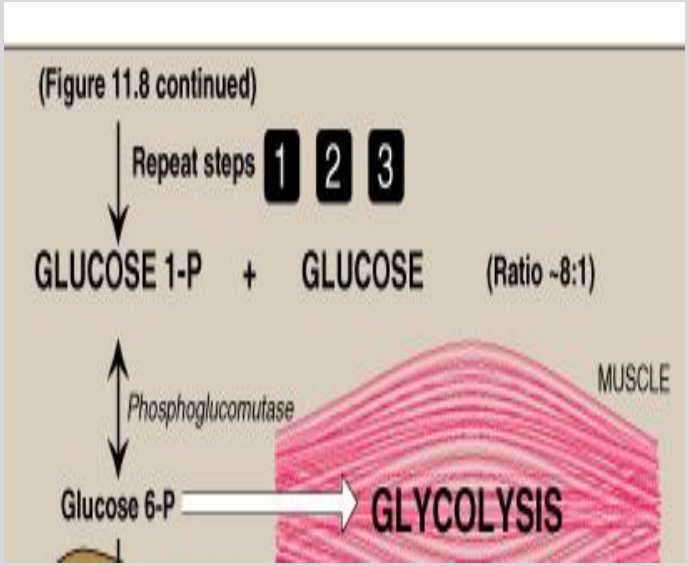
Glycogenolysis



Glycogenolysis



You can find this figure in the book, page 128.



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**

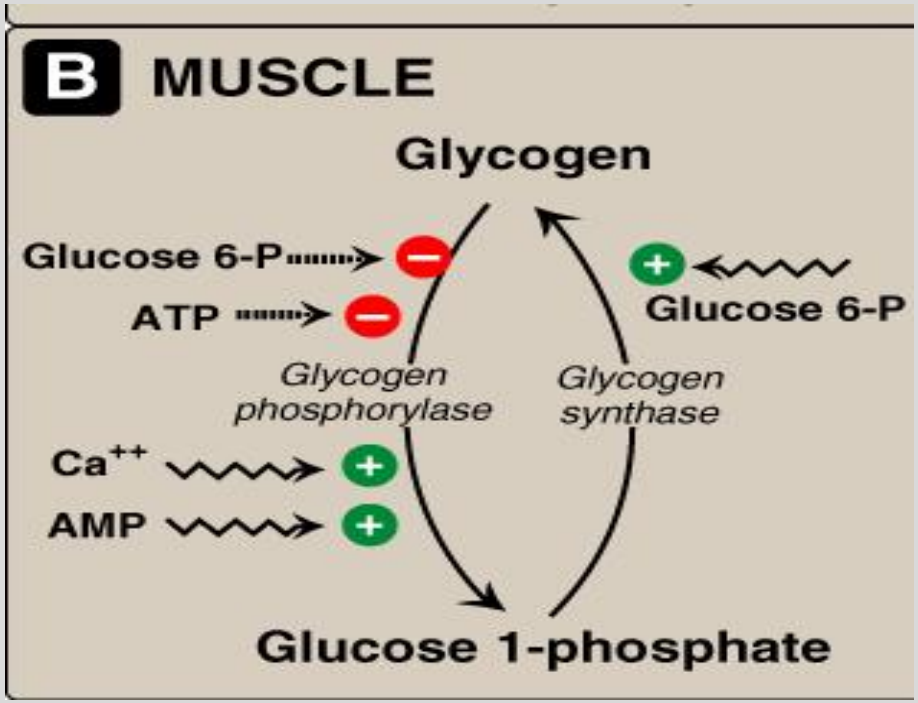
- **Regulation occurs by 2 mechanisms:**

  1- Allosteric regulation

  2- Hormonal regulation (Covalent modification)

Regulation of Glycogen Metabolism
1. Allosteric Regulation

very important !
Make sure you memorize all the inhibitors and activators.



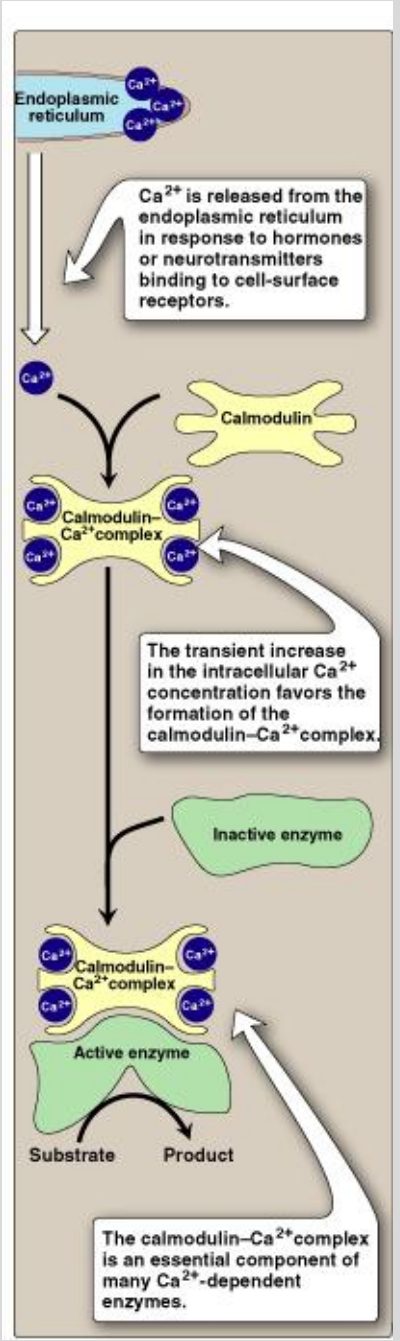
Glycogen synthase does NOT have
Allosteric sites for Ca++ , AMP & ATP

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



important !

Regulation of Glycogen Metabolism:
2. Hormonal Regulation by Epinephrine

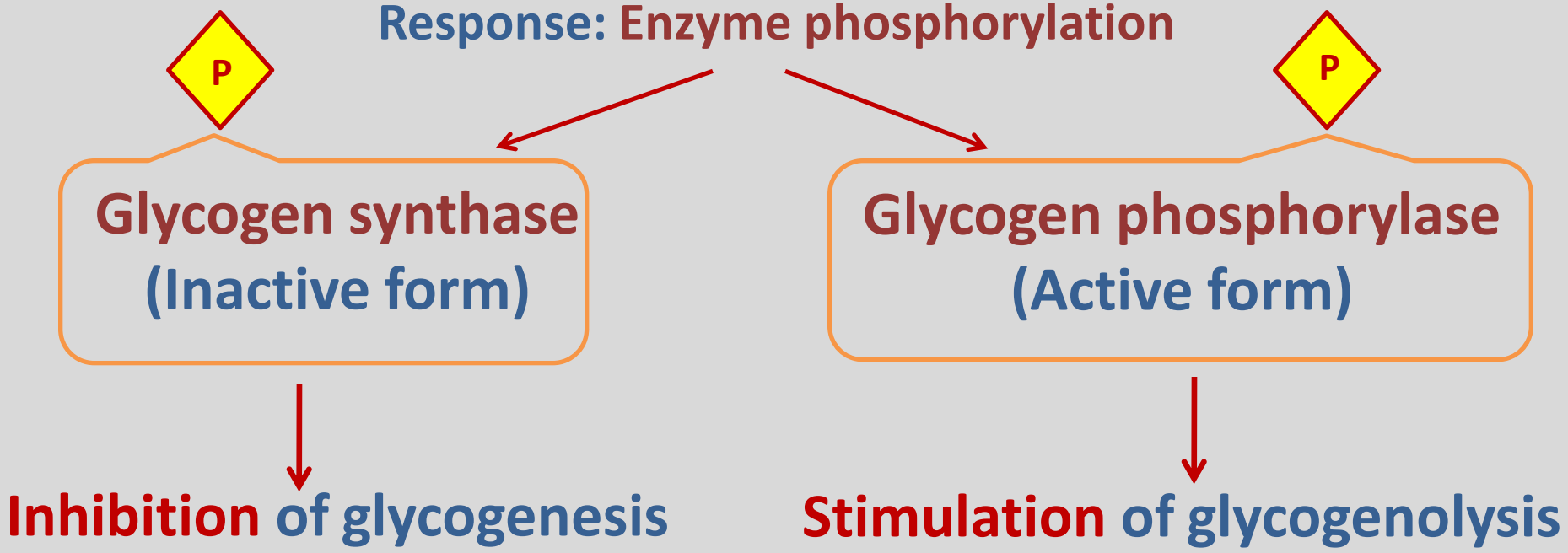
Muscle contraction

Epinephrine release

Skeletal muscle: Epinephrin/receptor binding

Second messenger: cAMP

Response: Enzyme phosphorylation



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 "McArdle syndrome"

Glycogen Storage Diseases
GSD Type V (Mc Ardle Syndrome)

- **Deficiency of skeletal muscle glycogen phosphorylase**

• excessive accumulation of normal glycogen structure inside skeletal muscles.

•weakness of muscles, and cramps.

•No rise in blood lactate during hard exercise.

•Normal mental development.

•Myoglobinemia and myoglobinuria. **"you will find a simple definition for these terms at the end"**

• fair to good prognosis.

• fasting blood glucose level is normal.

Note: we will only be asked about Mc Ardle syndrome. I removed the picture, and mentioned all the symptoms here, the last one is not on the book, it was mentioned in the lectuer… if you want to look at the two other diseases, they are found in the book, page 128,129.

Important facts

- **When glycolysis starts with glucose 6-phosphate the net ATP produced is 9 ”in case of glycolysis of glycogen derived glucose in muscles”.**
- **The rate limiting enzyme in glycogenesis is Glycogen Synthase.**
- **The rate limiting enzyme in glycogenolysis is Glycogen Phosphorylase.**

Definitions

- Myoglobinemia : when myoglobin (which is found in muscles) leaks into the blood circulation, the condition is described as myoglobinemia. our blood will eventually be filtered in the kidneys. There, the kidney will extract the myoglobin, and myoglobin will be present in the urine, and that is myoglobinuria.

“note: I made up this definition to simplify the idea, if you don’t like it, look it up!”