GLYCOGENESIS AND GLYCOGENOLYSIS

Glycogen

- Storage form of glucose in animals.
- Stored in the liver (6-8%) & muscle (1-2%).
- Quantity more in the muscle(~250g) than liver(75g) due to higher muscle mass.
- Stored as granules in the cytosol.

Glycogen vs. Fat as source of energy:-

- Fat cannot be rapidly metabolised like glycogen.
- Fat cannot generate energy in the absence of oxygen.
- Brain requires a continuous supply of glucose, which come from glycogen.
- Fat cannot produce glucose.

Glycogenesis

- The glycogen synthesis occurs by a pathway distinctly different from the reversal of glycogen breakdown.
- It is the intracellular synthesis of glycogen from glucose.

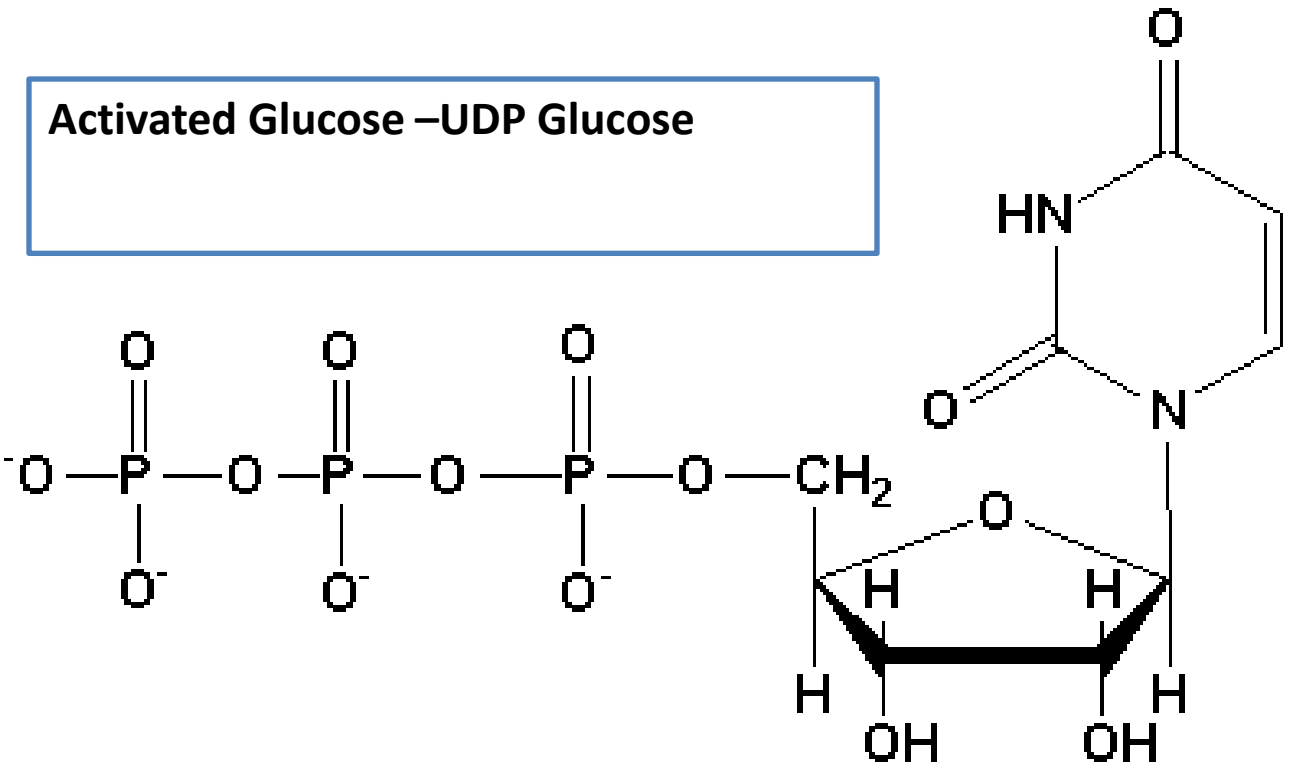
Site and steps:

- The main site is the cytosol of liver and muscle cells. In the liver it forms 8-10% of its wet weight and in muscle it forms 1-2% of its wet weight. Most other cells may store minute amounts.

Glycogenesis :- Synthesis of glycogen from glucose.

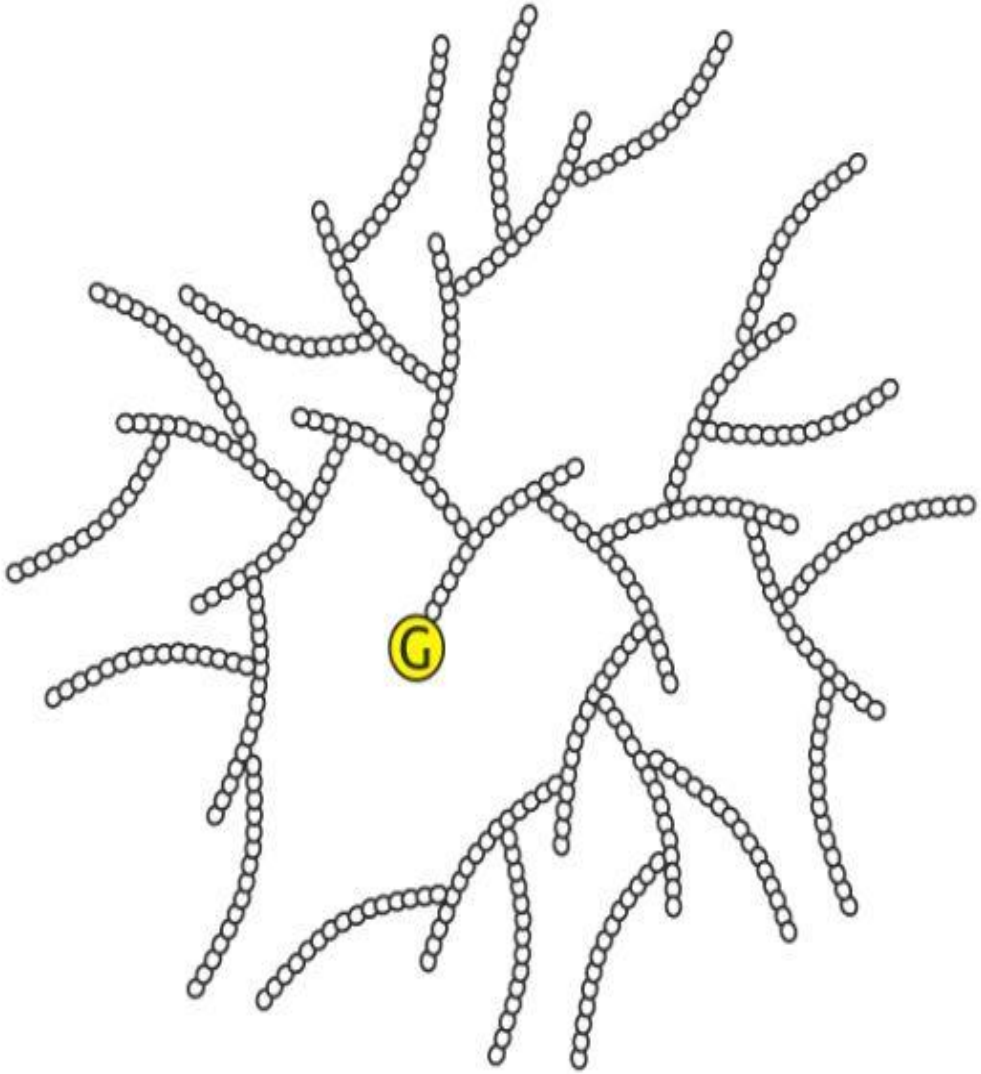
Site :- Cytosol

Activated Glucose –UDP Glucose

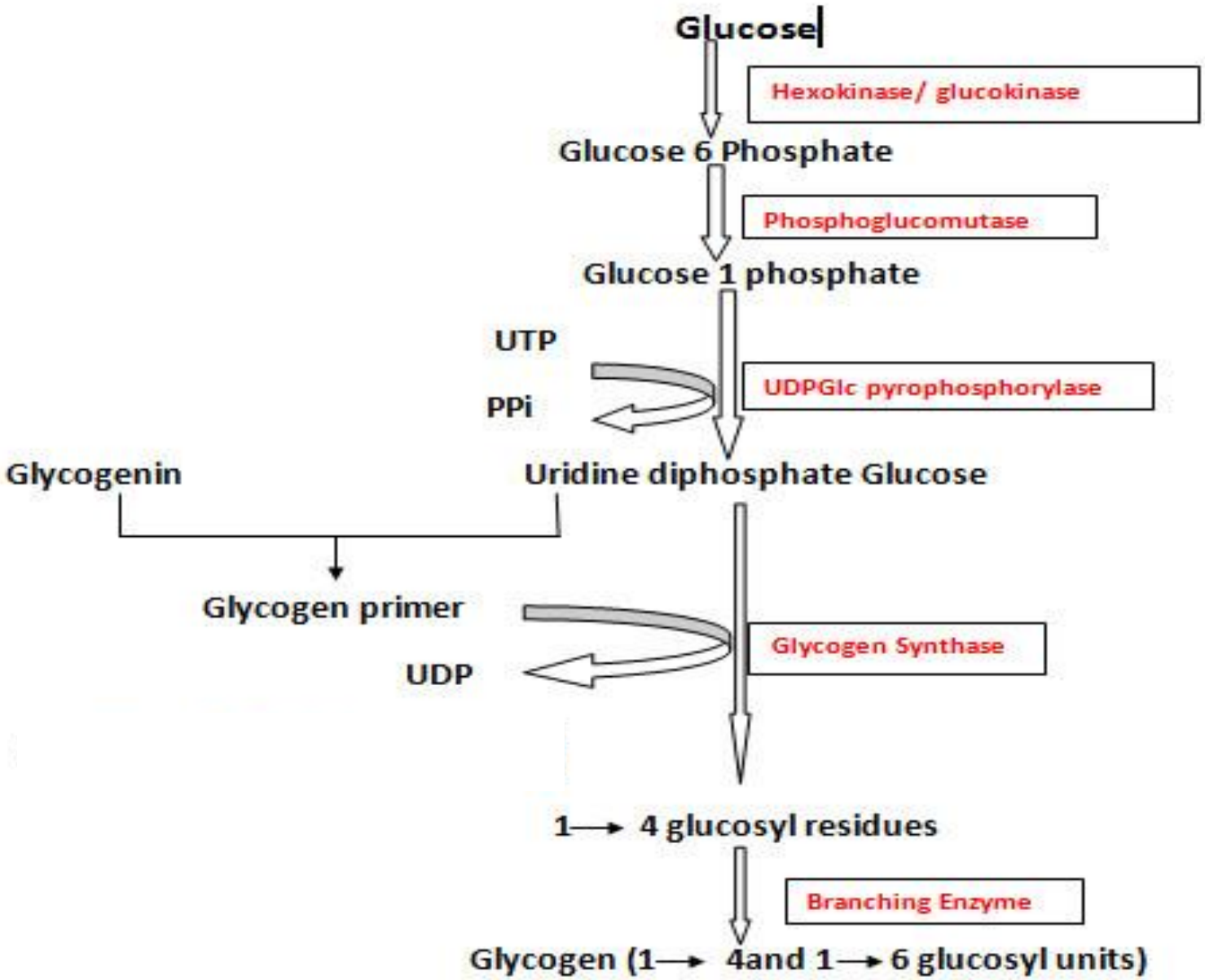


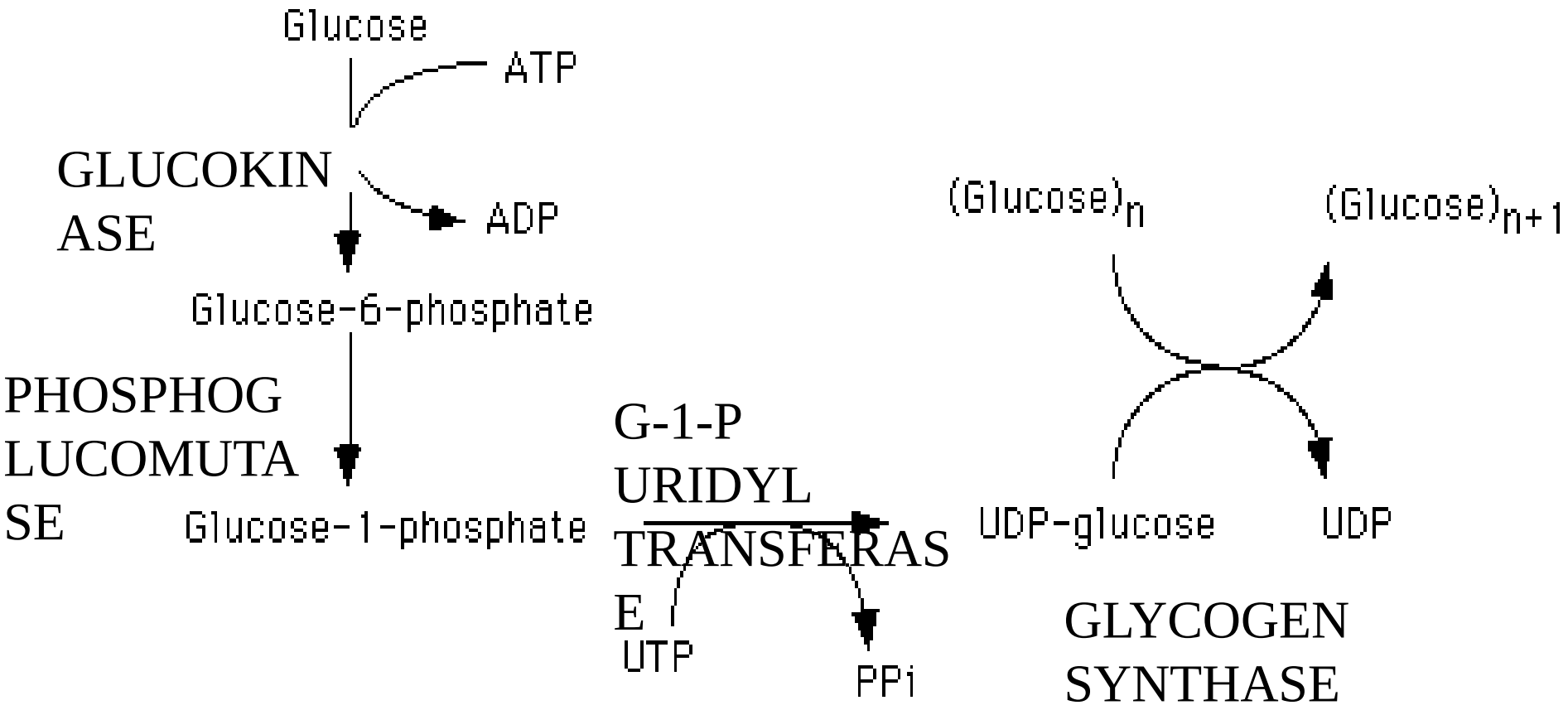
Uridine Triphosphate (UTP)

Structure of Glycogen

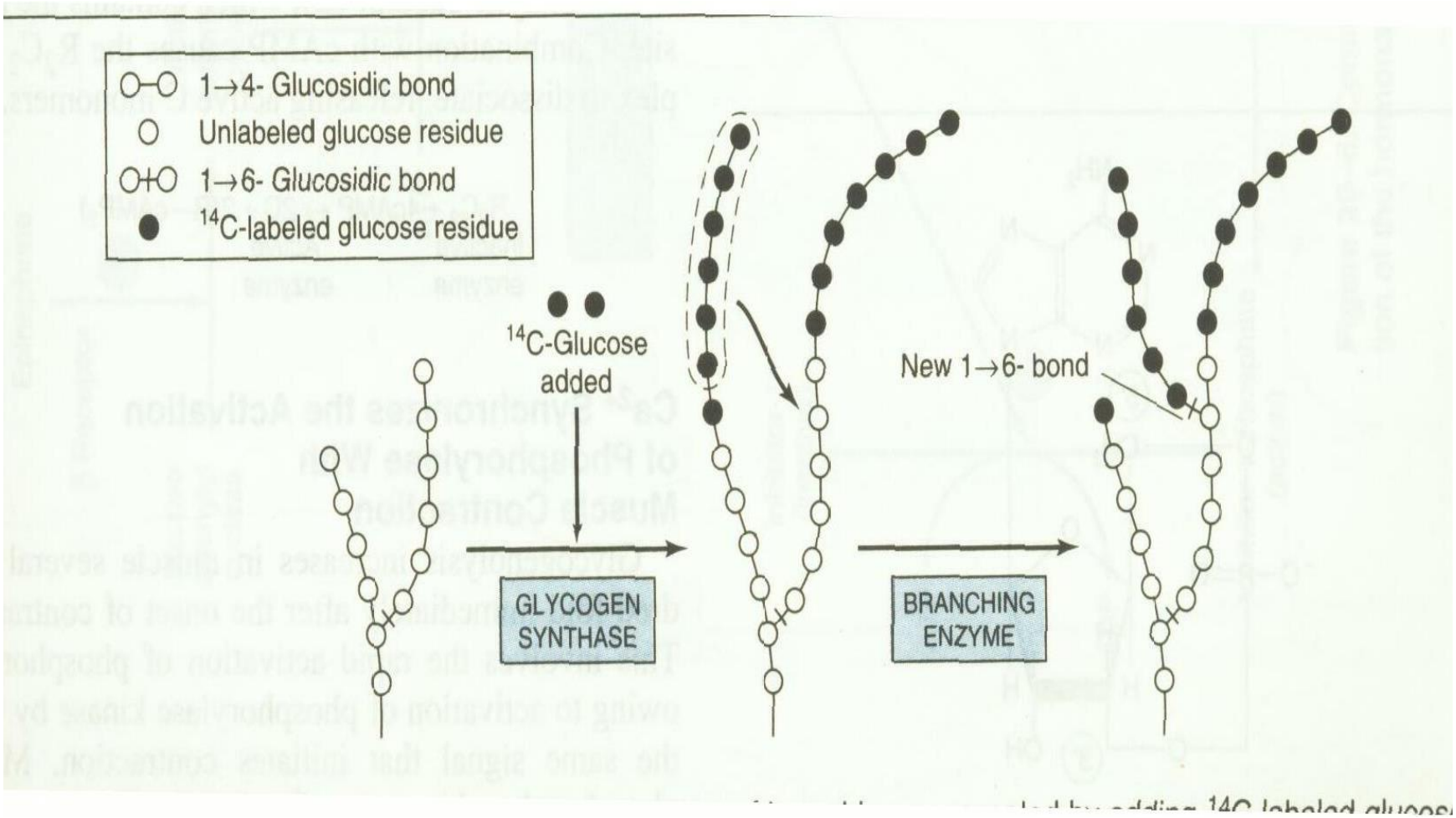


Glycogenesis steps





Glycogen primer or Glycogenin required to initiate Glycogenesis



Glycogen Synthase transfers Glucose from UDP-Glucose to the non-reducing end of the Glycogen to form α-1,4 linkages.

Branching enzyme :- Amylo α-1,4 →1,6 transglucosidase (Glucosyl α-4-6 transferase)

Overall Reaction of Glycogenesis :-

$(Glucose)_n$ + Glucose + 2 ATP ⟶

$(Glucose)_{n+1}$ + 2 ADP + Pi

Glycogen Degradation
(Glycogenolysis)

- ✓ **Definition:** It is the degradation of glycogen to glucose 6-phosphate & glucose in muscle & liver respectively.
- ✓ **Substrate:** Glycogen
- ✓ **Site:** Liver, Skeletal Muscles
- ✓ **Subcellular site:** Cytosol.
- ✓ **Steps:**

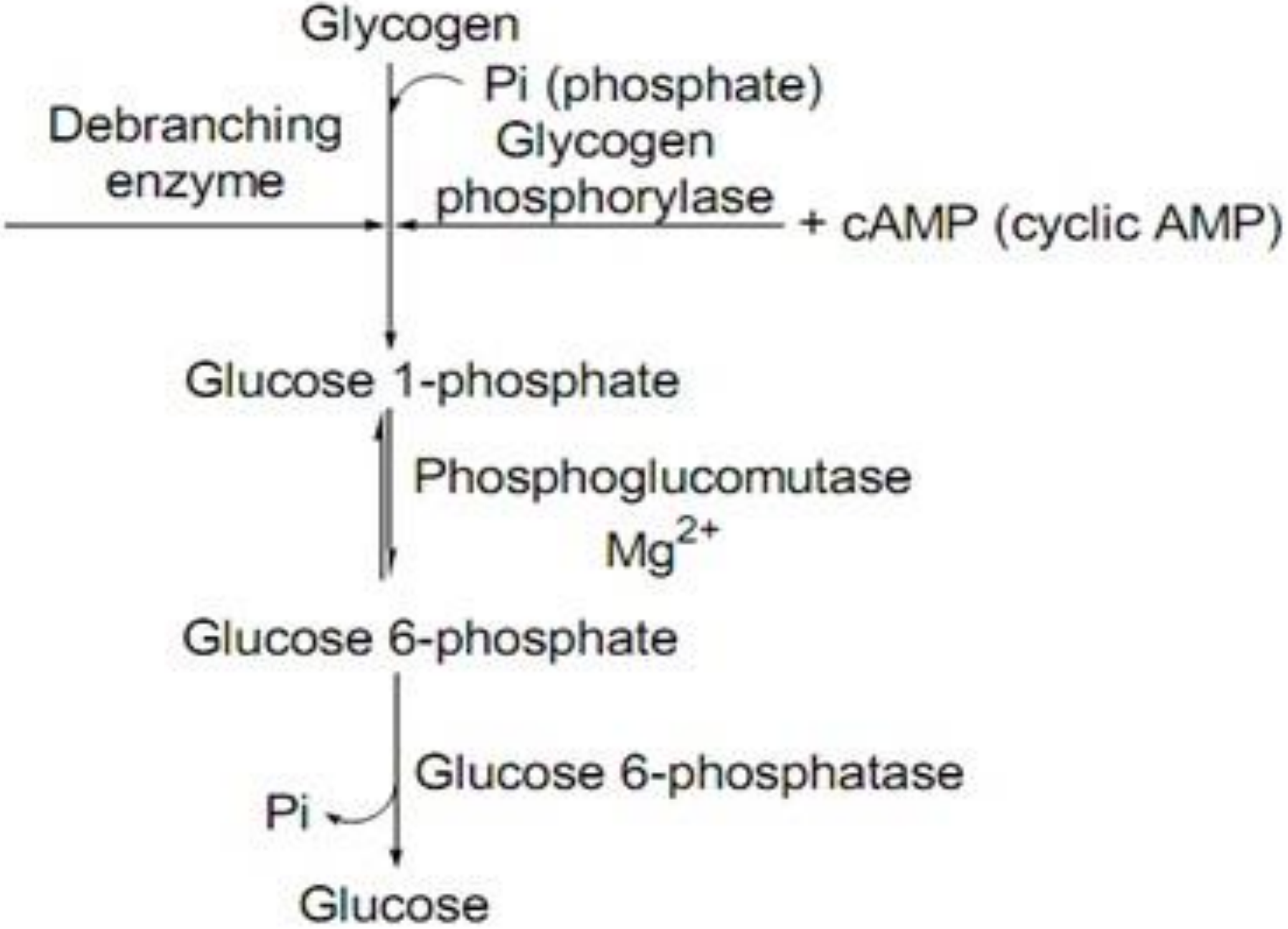
1. Action of GLYCOGEN PHOSPHORYLASE
2. Action of Debranching Enzyme
3. Formation of Glucose.

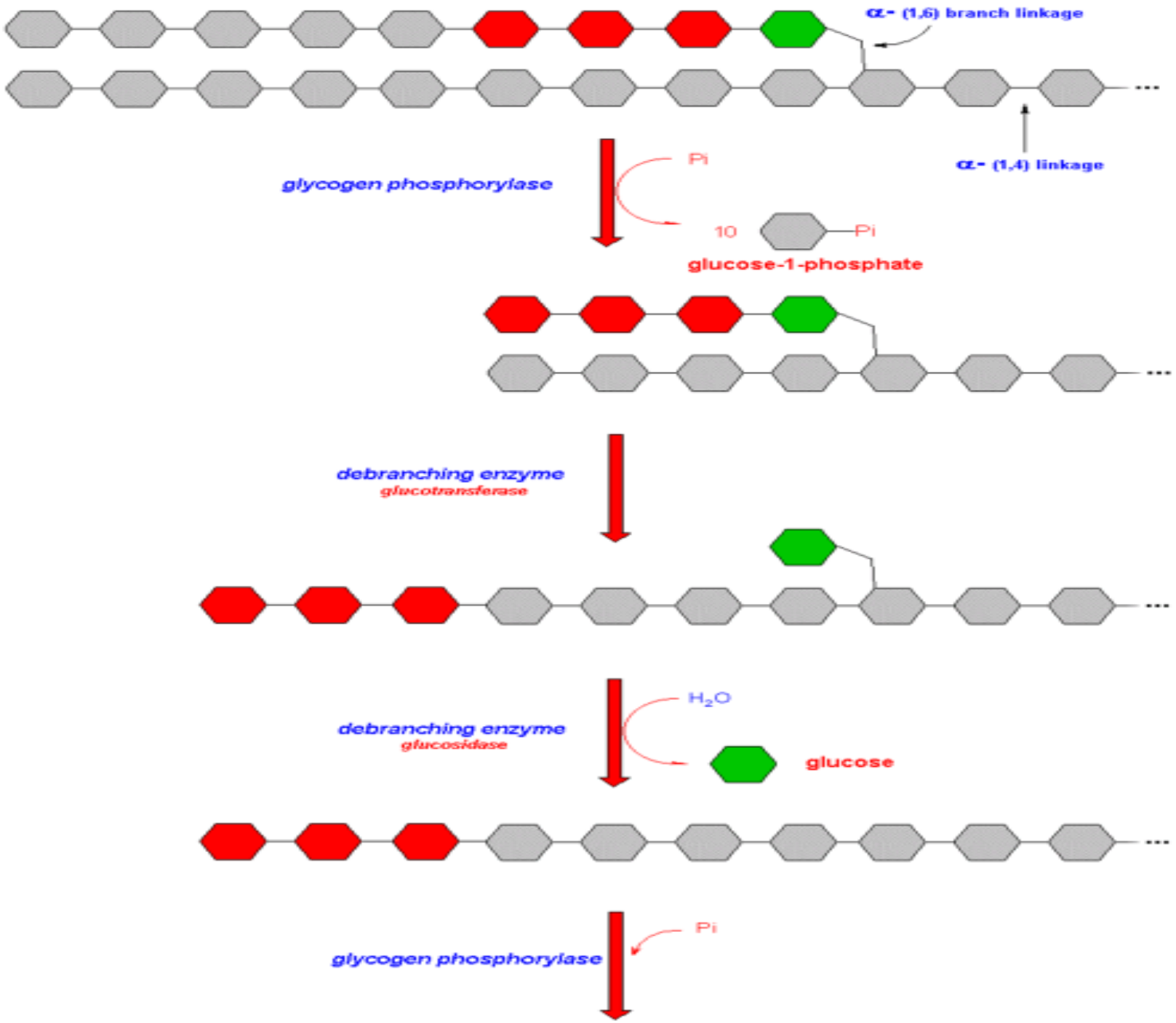
Enzymes of Glycogenolysis :-

1. Glycogen Phosphorylase.
2. Debranching enzyme :

α-1 :4 Transferase, α-1,6 and α-1,4 glucosidase

3. Glucose - 6- phosphatase


Glycogen
Pi (phosphate)
Debranching enzyme
Glycogen phosphorylase
+ cAMP (cyclic AMP)
Glucose 1-phosphate
Phosphoglucomutase
Mg^{2+}
Glucose 6-phosphate
Glucose 6-phosphatase
Pi
Glucose


α- (1,6) branch linkage
α- (1,4) linkage
glycogen phosphorylase
Pi
10
Pi
glucose-1-phosphate
debranching enzyme
glucotransferase
debranching enzyme
glucosidase
H_2O
glucose
glycogen phosphorylase
Pi

- **GLUCOSE-6-PHOSPHATASE ABSENT IN MUSCLES**

- **LYSOSOMAL DEGRADATION**
  - **Alpha 1,4 glucosidase.**
    (acid maltase)

Regulation of glycogenesis & Glycogenolysis

Key enzyme of Glycogenesis- Glycogen Synthase

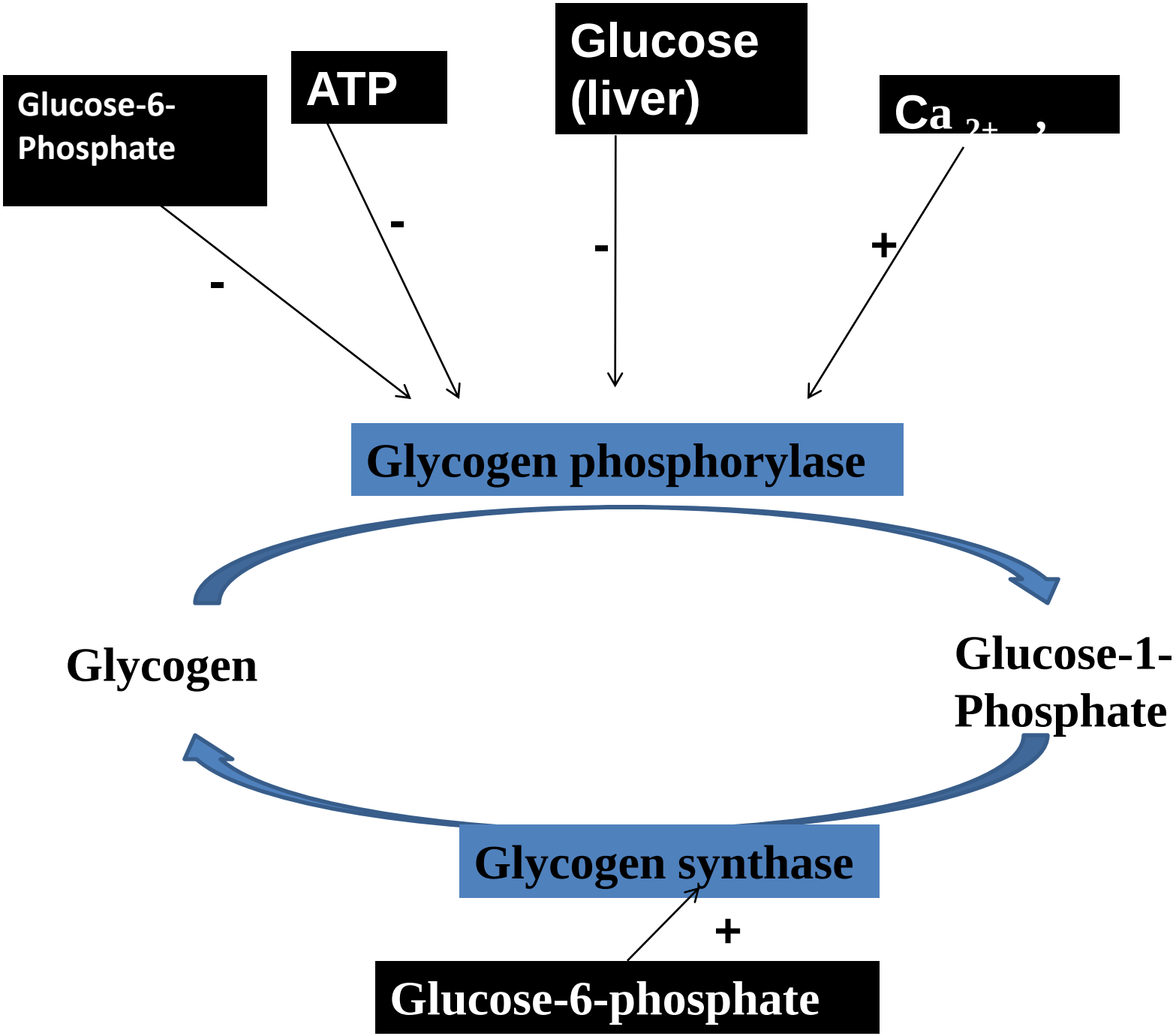
Key enzyme of Glycogenolysis- Glycogen Phosphorylase

Three Regulatory Mechanisms

1. **Allosteric Regulation.**
2. **Hormonal Regulation.**
3. **Influence of Calcium.**

Allosteric Regulation of Glycogen Metabolism :-

- When substrate availability & energy level is high, Glycogen synthesis is increased.
- When glucose concentration is low & energy level low, Glycogen breakdown is enhanced.
- In well-fed state, Glucose-6-P allosterically activates Glycogen Synthase. At the same time, allosterically inhibits Glycogen Phosphorylase.
- Free Glucose in the liver is also a allosteric inhibitor of Glycogen Phosphorylase.


Glucose-6-Phosphate
ATP
Glucose (liver)
Ca 2+ ,
-
-
-
+
Glycogen phosphorylase
Glycogen
Glucose-1-Phosphate
Glycogen synthase
+
Glucose-6-phosphate

Hormonal Regulation of Glycogen Metabolism :-

- Hormones control Glycogen synthesis & degradation by covalent modification ie., phosphorylation & Dephosphorylation.
- cAMP acts as second messenger.
- cAMP activates Protein Kinase.
- Protein Kinase causes phosphorylation of enzymes, either activating or deactivating them.

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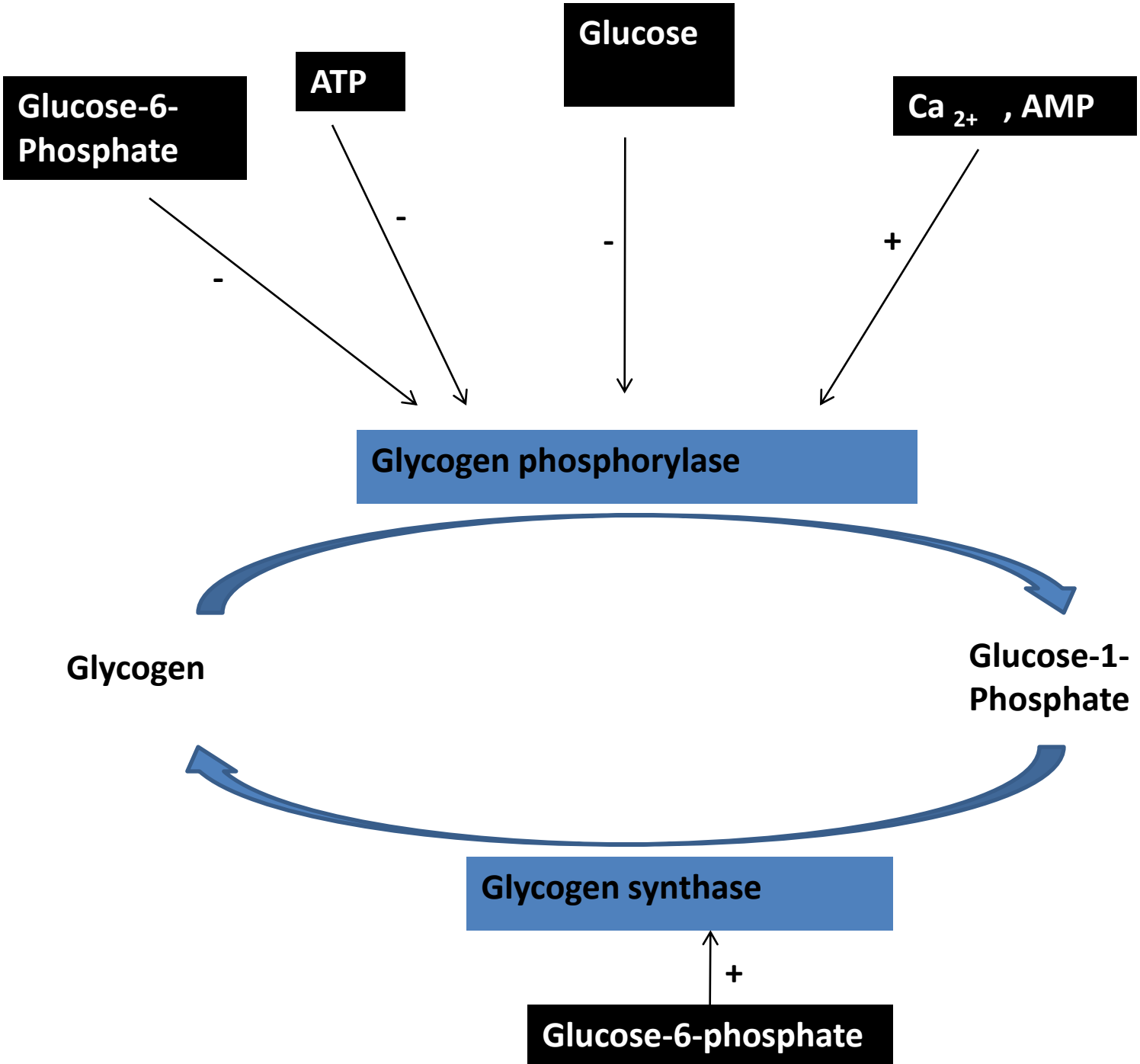
Glucose
ATP
Glucose-6-Phosphate
Ca 2+ , AMP
-
-
-
+
Glycogen phosphorylase
Glycogen
Glucose-1-Phosphate
Glycogen synthase
+
Glucose-6-phosphate

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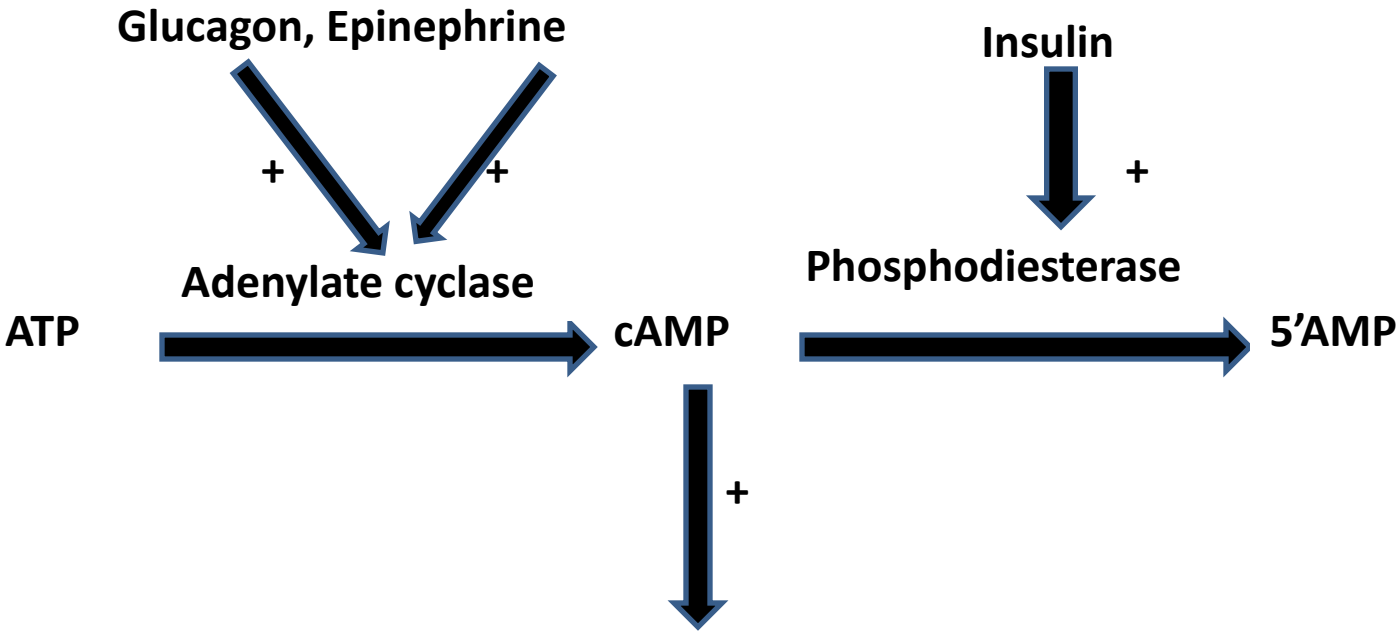

- Inactive Glycogen synthase
- Active Glycogen Phosphorylase

Effect of Calcium :-

muscle contracts

Ca^{2+} ions released from sarcoplasmic reticulum of muscle

Ca^{2+} ions bind to calmodulin (calcium binding protein)

Calcium calmodulin complex directly activates Protein Kinase without the involvement of cAMP.

Glycogen Storage Diseases

Type I: VON GIERKE'S DISEASE (G-6-phosphatase)

Commonest

- **Fasting Hypoglycemia.**
- **Adrenaline has no effect.**
- **Lactic Acidosis.**
- **Hyperuricemia.**
- **Liver Enlargement – Cirrhosis.**

- **TYPE II (POMPE'S): Lysosomal Maltase (α-1,4 glucosidase).**
- **TYPE III (CORI'S / LIMIT DEXTRINOSIS): Debranching Enzyme**
- **TYPE IV (AMYLOPECTINOSIS / ANDERSON'S) : Branching Enzyme.**
- **TYPE V (McARDLE'S) : Muscle Phosphorylase**
- **TYPE VI (HER'S) : Liver Phosphorylase**
- **TYPE VII (TARUI'S) : Phosphofructokinase**
- **TYPE VIII (PHOSPHORYLASE KINASE)**
- **TYPE IX (GLYCOGEN SYNTHASE)**

QUESTIONS ????

1) What is Glycogen ?
2) Monosaccharide B) Disaccharide
C) Homopolysaccahride D) Heteropolysaccahride
2) It is a Storage form of
A) Carbohydrate B) Protein C) Lipid D) All of above
3) Key enzyme of Glycogenesis-
A) Hexokinase B) Glucose - 6- phosphatase
C) Glycogen Phosphorylase D) Glycogen Synthase
4) Key enzyme of Glycogenolysis
A) Glucose - 6- phosphatase B) Glycogen Phosphorylase
C) Glycogen Synthase D) None of Above
5) Site of Glycogenesis
A) Mitochondria B) Cytosol C) Lysosome D) Nucleus

ANSWERS

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