B.SC-4TH SEM
UNIT-2 (CC-410)

GLYCOGENESIS

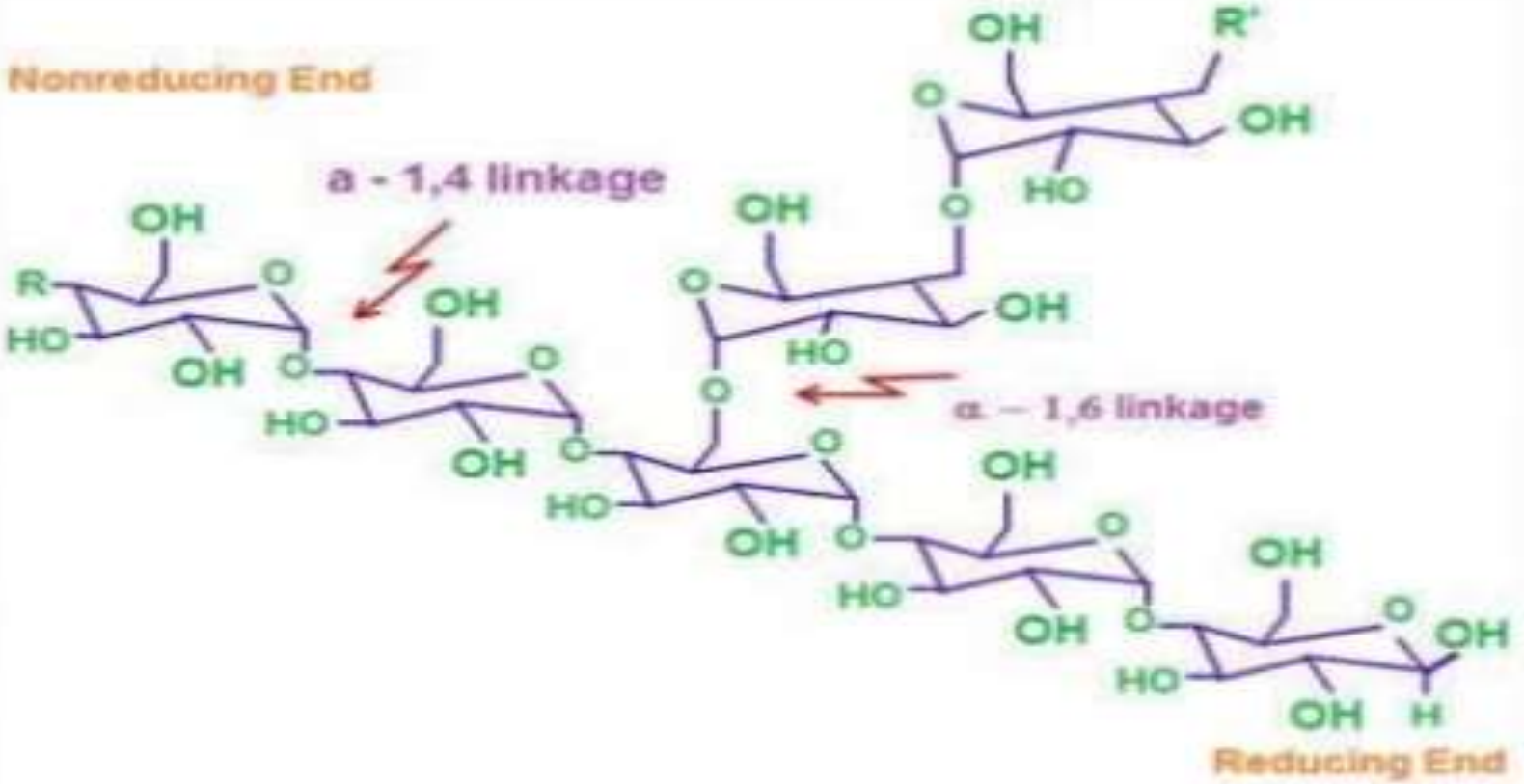
BY

DR. AMRESH KUMAR

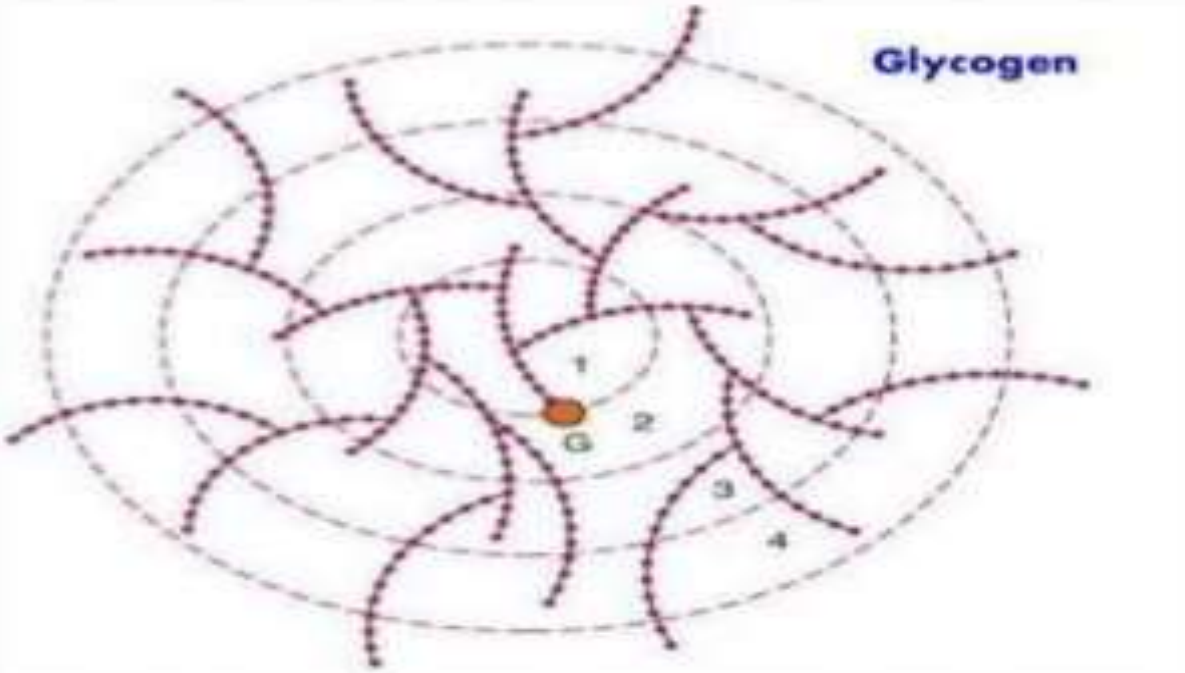
DEPT. OF ZOOLOGY, PWC, PATNA-01

WHAT IS GLYCOGEN ???

Glycogen is a homo-polymer made up of repeated units of α D glucose and each molecule is linked to each other by 1→4 glycosidic bond which is a link connecting the 1st C atom of the active glucose residue to the 6th C atom of the approaching glucose molecule.



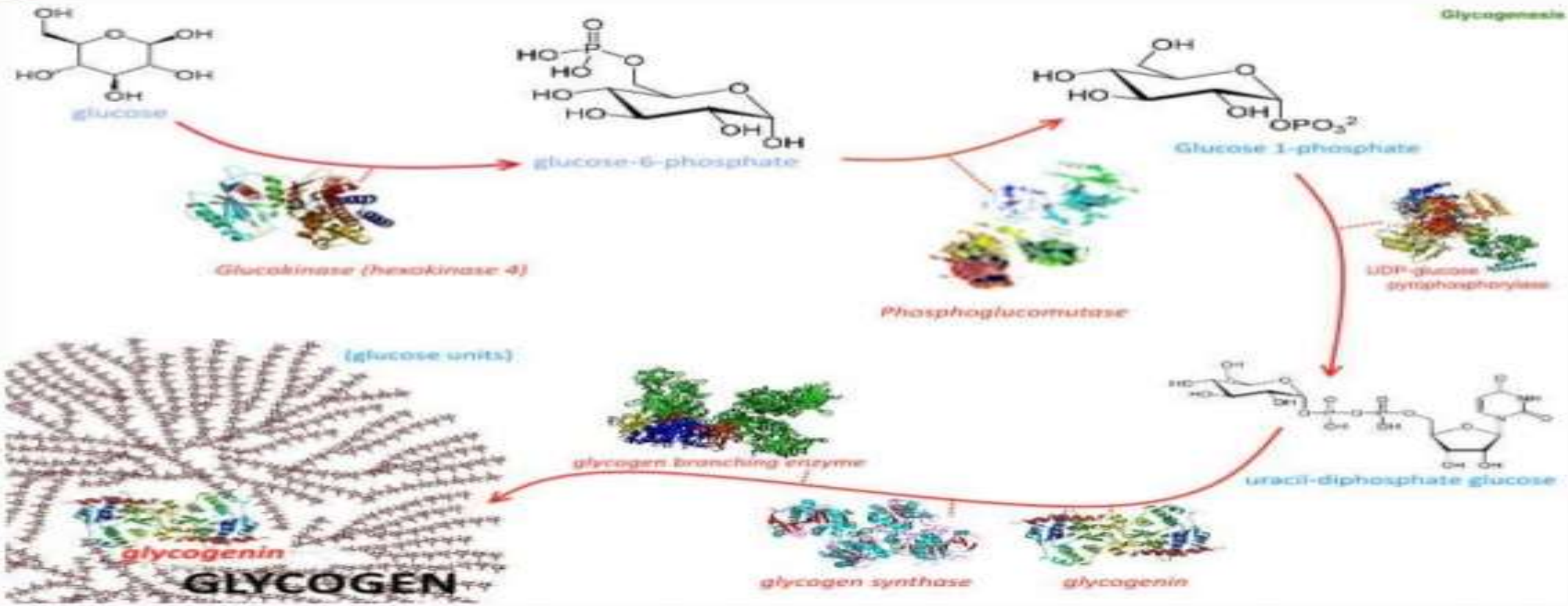
- Once there is a chain consisting of 8 to 10 glycosidic residues in the glycogen fragment, branching begins by 1 – 6 linkages.
- Liver glycogen is synthesized in the well fed states.
- Muscle glycogen is synthesized when the muscle glucose get depleted in intense physical exercise.



GLYCOGENESIS

- Glycogenesis is the biosynthesis of glycogen, the major storage form of carbohydrates in animals similar to starch in plants.
- Sites of storage – liver and muscles.
- Sub cellular site – cytosol.
-
- Stores excess carbohydrates we consume, in the form of glycogen which could be broken down to glucose when needed (glycogenolysis)
- Muscle glycogen provides a readily glucose for glycolysis within the muscle itself
- Liver glycogen functions to store and export glucose to maintain blood glucose between meals.

GLYCOGENESIS PATHWAY



STEPS

- Glucose phosphorylation
- Glu 6 P to Glu 1 P conversion
- UDP Glucose – synthesis of the carrier molecule
- Glycogen primer
- Elongation of glycogen chain
- Branching in glycogen

Glucose phosphorylation

Reaction catalyzed by hexokinase in muscles and glucokinase in liver

Glucose + ATP ⟶ Glucose 6 phosphate +ADP + Pi

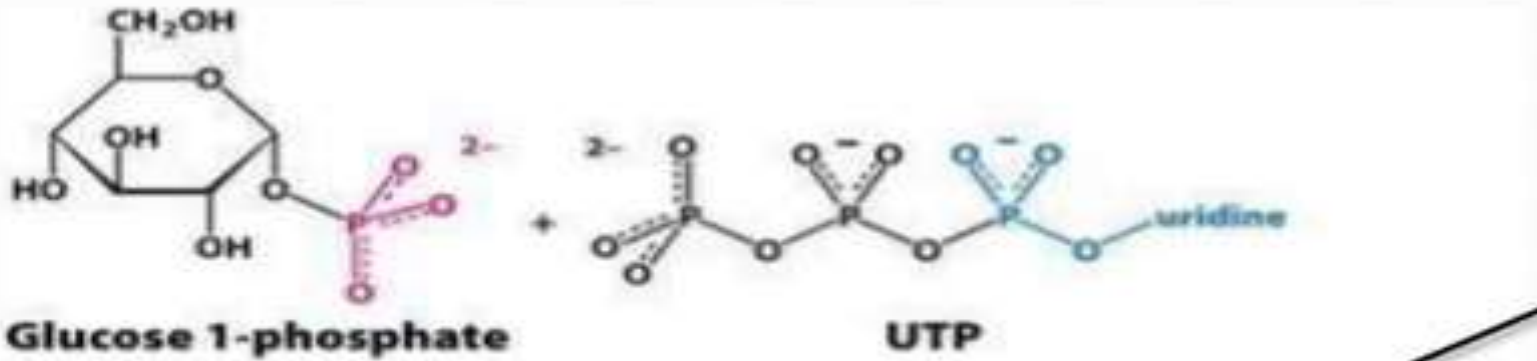
Glu 6 P to Glu 1 P conversion

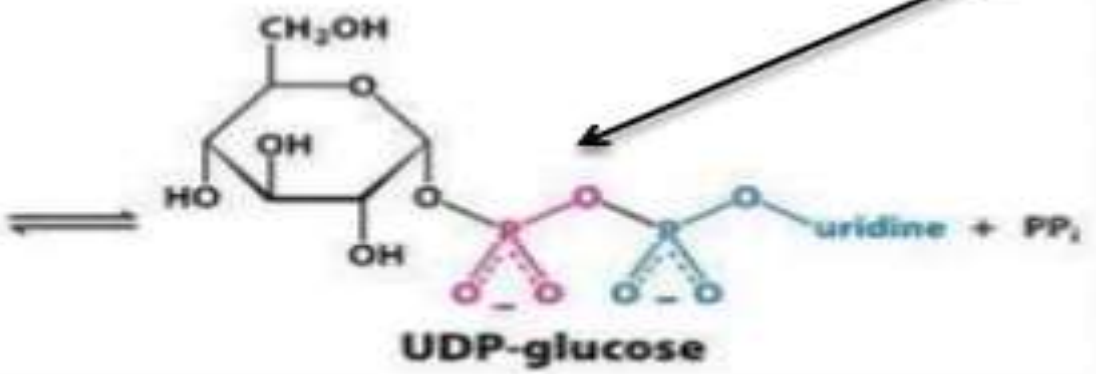
Glucose 6 phosphate is converted to glucose 1 phosphate in a reaction catalyzed by the enzyme phosphoglucomutase

Glu 6 P + Enz-P ⟷ Glu 1.6 bis P + Enz ⟷ Glu P + Enz-P

UDP Glucose – Synthesis of the carrier molecule

ENZYME – **UDP glucose pyrophosphorylase**





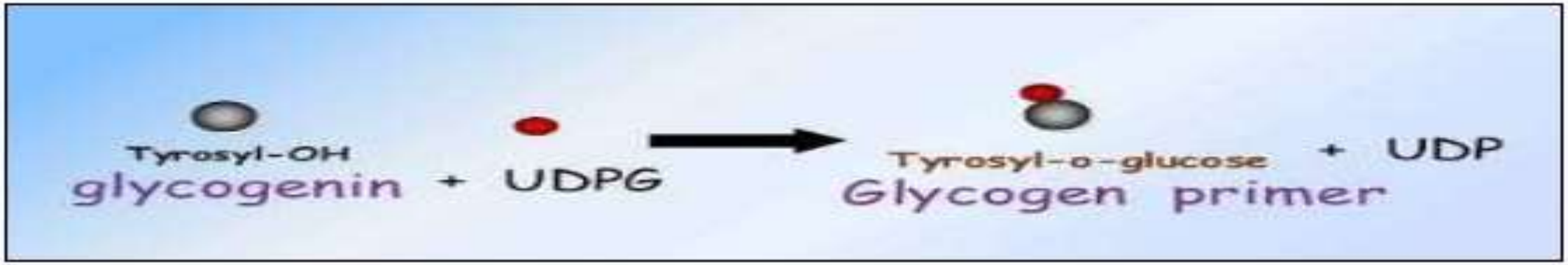
acts as a vehicle that carries the glucose molecule which is to be added to the budding glycogen molecule

Glycogen Primer

- A small fragment of pre-existing glycogen must act as a 'primer ' to initiate glycogen synthesis.

- In glycogen depleted condition, a protein primer called glycogenin acts as the flooring to which the glucose molecules from UDP glucose are added like blocks
- The hydroxyl (OH) of the amino acid tyrosine of glycogenin is the site at which the initial glucose unit is attached

- The enzyme glycogen initiator synthase transfers the first molecule of glucose to glycogenin.

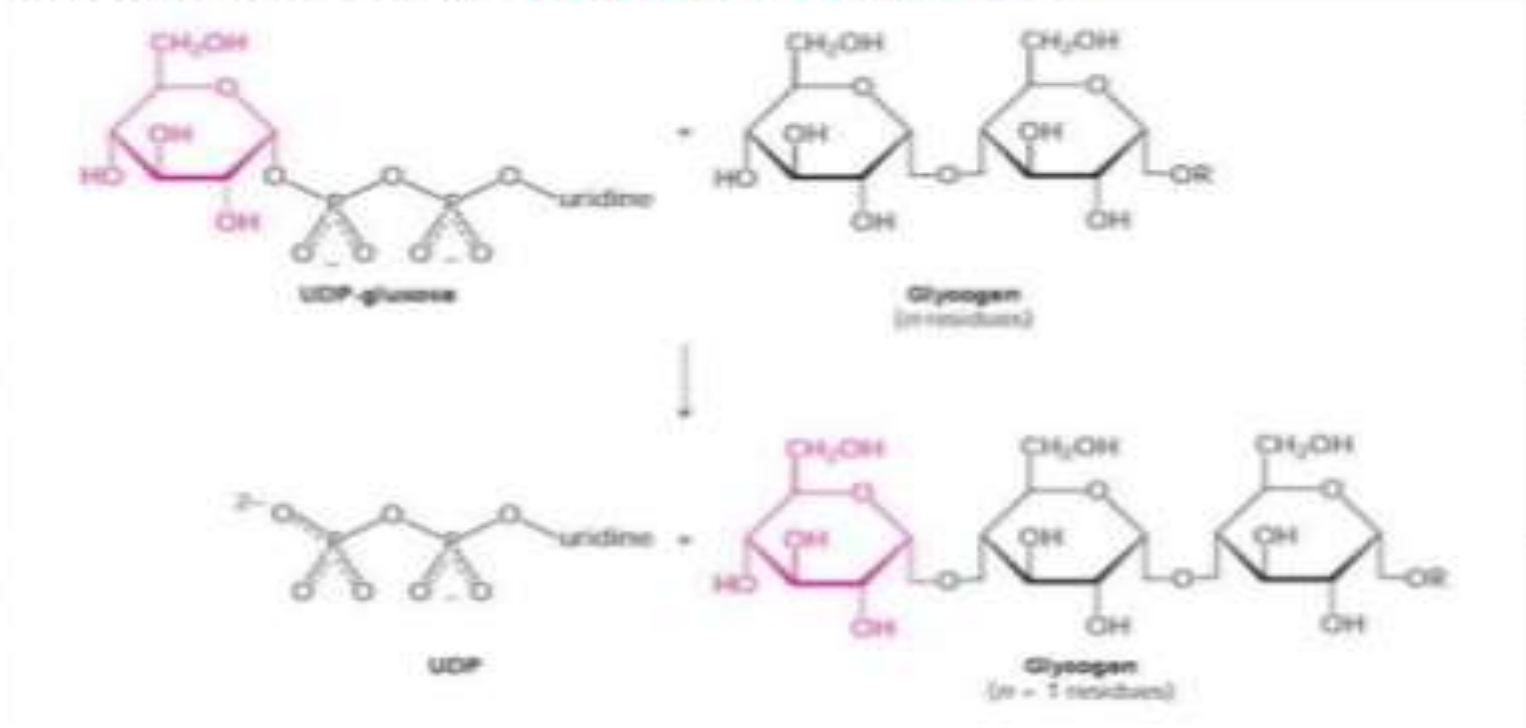


- Then glycogenin itself takes up few glucose residues to form a fragment of primer which serves as an acceptor for the rest of the glucose molecules
- During initial additions of glucose glycogenin acts as auto catalyst and forms the glycogen fragment on which further glucose residues are added by 1-4 linkage by the enzyme glycogen synthase

Elongation of Glycogen Chain

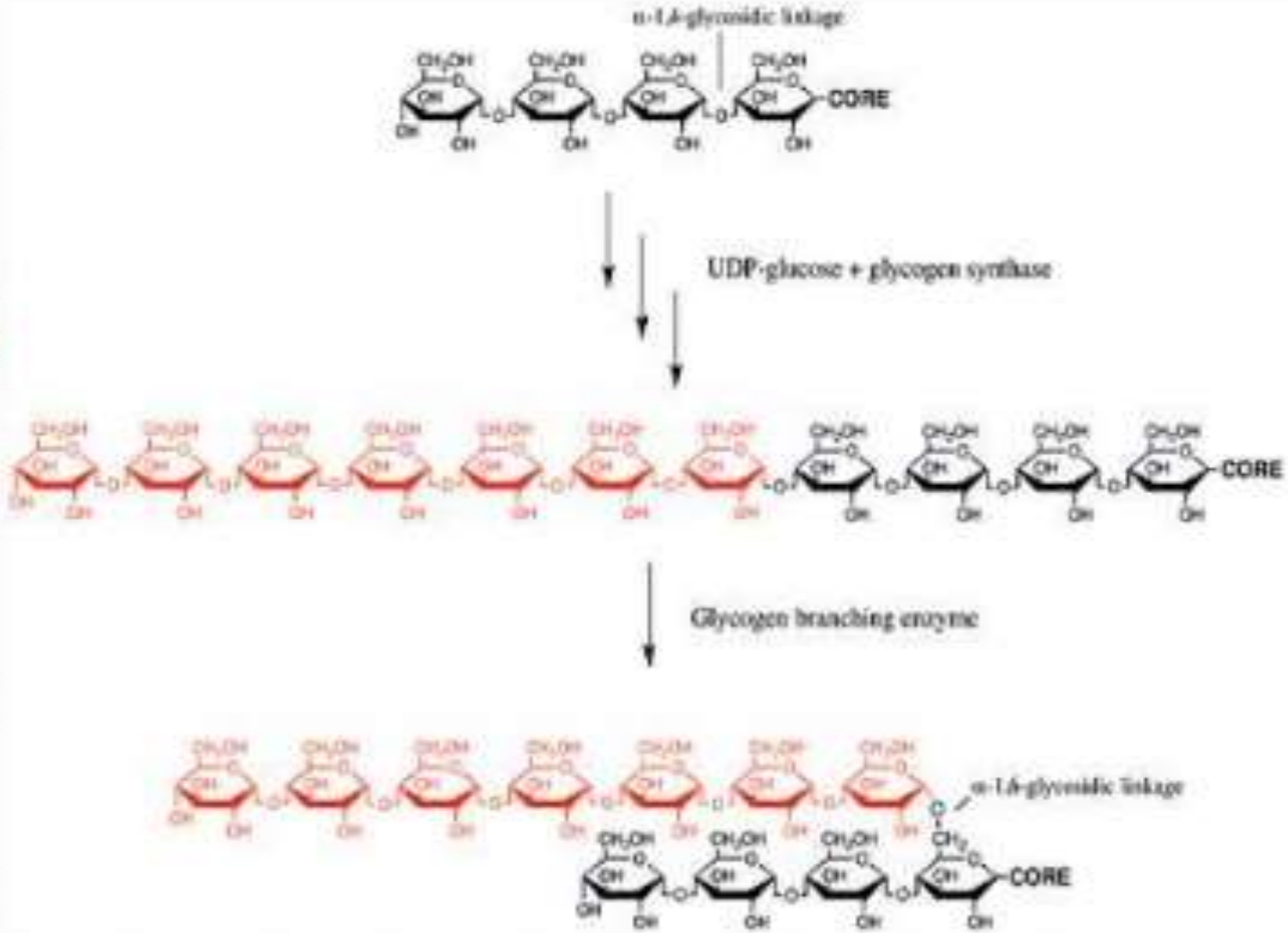
Link is formed between the 1st C atom of the standing glucose residue on the end point of the fragment and 4th C of the glucose residue that is being added to fragment → 1-4 glycosidic bond

Enzyme catalyzing this step is glycogen synthase



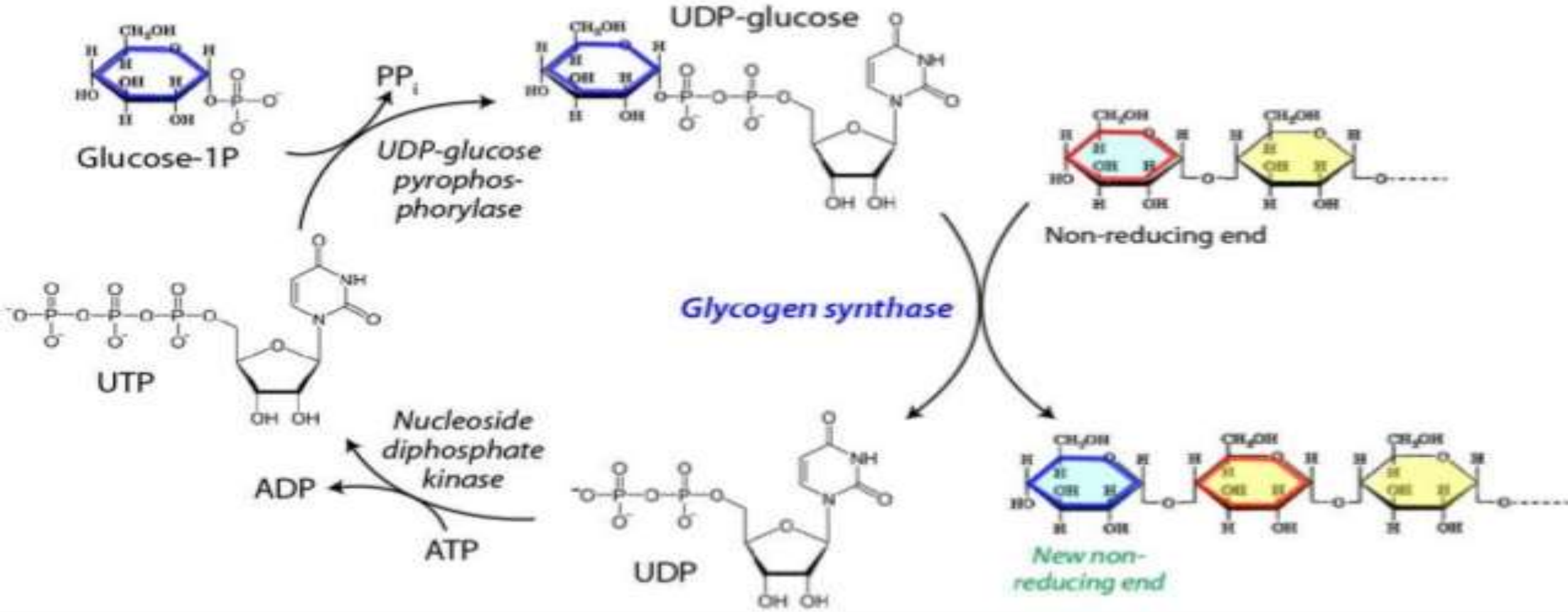
Branching in glycogen

- Glycogen is a branched tree-like structure.
- Branching enzyme – amylo-(1 →4)→(1→6) transglucosylase
- α-(1→6) linkages, which occurs every 8-12 residues
- Transfers 6-7 residue segment from the nonreducing end
- Newly created branch further glucose units are added by α(1→4)linkage by glycogen synthase



- The branching result in more number of end points for UDP glucose to add further glucose residues to it. Thus branching enzyme results in extensively branched large glycogen molecule.
- Defective branching enzyme → Anderson disease
- **2 ATP** used in this process .
  1 for the phosphorylation of glucose to glucose 6 phosphate
  another for the conversion of UDP to UTP

Glycogen synthesis is strictly monitored to regulate the blood glucose level. It is activated in well fed state and suppressed in fasting.


Glucose-1P
PPi
UDP-glucose pyrophos-phorylase
UDP-glucose
UTP
Glycogen synthase
Non-reducing end
Nucleoside diphosphate kinase
ADP
ATP
UDP
New non-reducing end

- When two metabolic pathways runs in opposite direction at the same time
- No overall net effect, no net production of ATP.
- In fact, ATP is used up in generating heat.
- Used in hibernation animals to produce heat, in brown adipose tissues of young animals & to regulate metabolic pathways

Under physiological conditions , the reaction catalyzed by PFK:

$$F6P + ATP \rightarrow FBP + ADP + Pi$$

Is highly exergonic. Consequently the back reaction has a negligible rate compared to the forward reaction. Fructose 1,6bisphosphatase (FBPase), however which is present in many mammalian tissues (and which is essential enzyme in gluconeogenesis) catalyzes the exergonic hydrolysis of FBP

$$FBP + H_2O \rightarrow F6P + Pi$$

Note that the combined reactions catalyzed by PFK and FBPase result in net ATP hydrolysis:

$$ATP + H_2O \longleftrightarrow ADP + Pi$$

Such a set of opposing reactions is known as a **substrate cycle** because it cycles a substrate to an intermediate and back again. When this set of reactions was discovered, it was referred to as a **futile cycle** since its net result seemed to be the useless consumption of ATP.

- The synthesis of glycogen from glucose is called as glycogenesis.
- Glycogenesis takes place in the cytosol & requires ATP and UTP, besides glucose.
- Steps:
- Synthesis of UDP-glucose:
- The enzymes hexokinase (in muscle) & glucokinase (in liver) convert glucose to glucose 6-phosphate

- **Phosphoglucomutase** catalyses the conversion of **glucose 6-phosphate to glucose 1-phosphate.**
- **Uridine diphosphate glucose (UDP-glucose) is synthesized from glucose 1-phosphate & UTP** by UDP-glucose pyrophosphorylase.

Requirement of primer to initiate glycogenesis

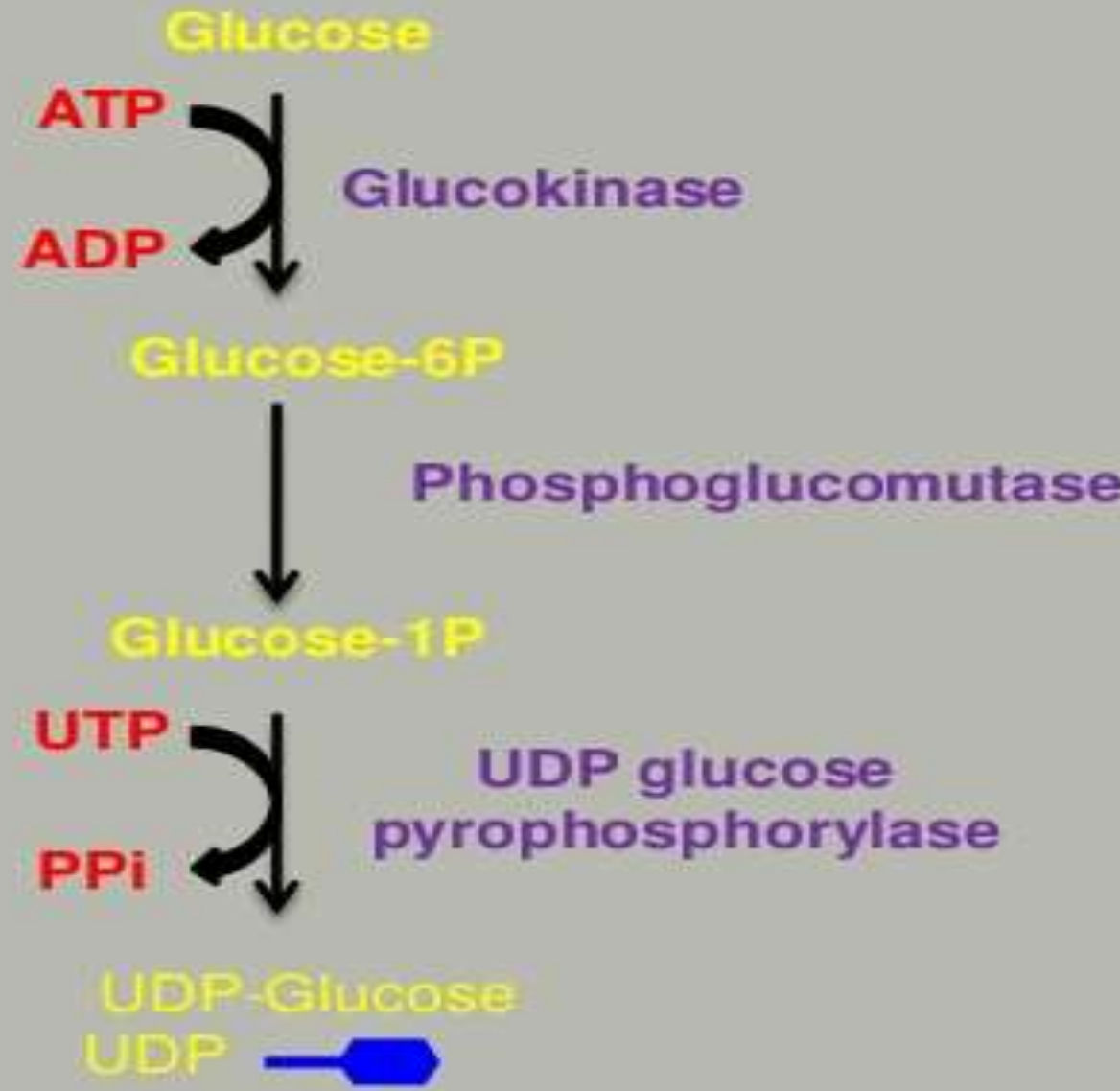
- A small fragment of pre-existing glycogen must act as a 'primer' to initiate glycogen synthesis.
- A specific protein 'glycogenin' can accept glucose from UDP Glucose.
- The hydroxyl group (OH) of the amino acid tyrosine of glycogenin is the site at which the initial glucose unit is attached.

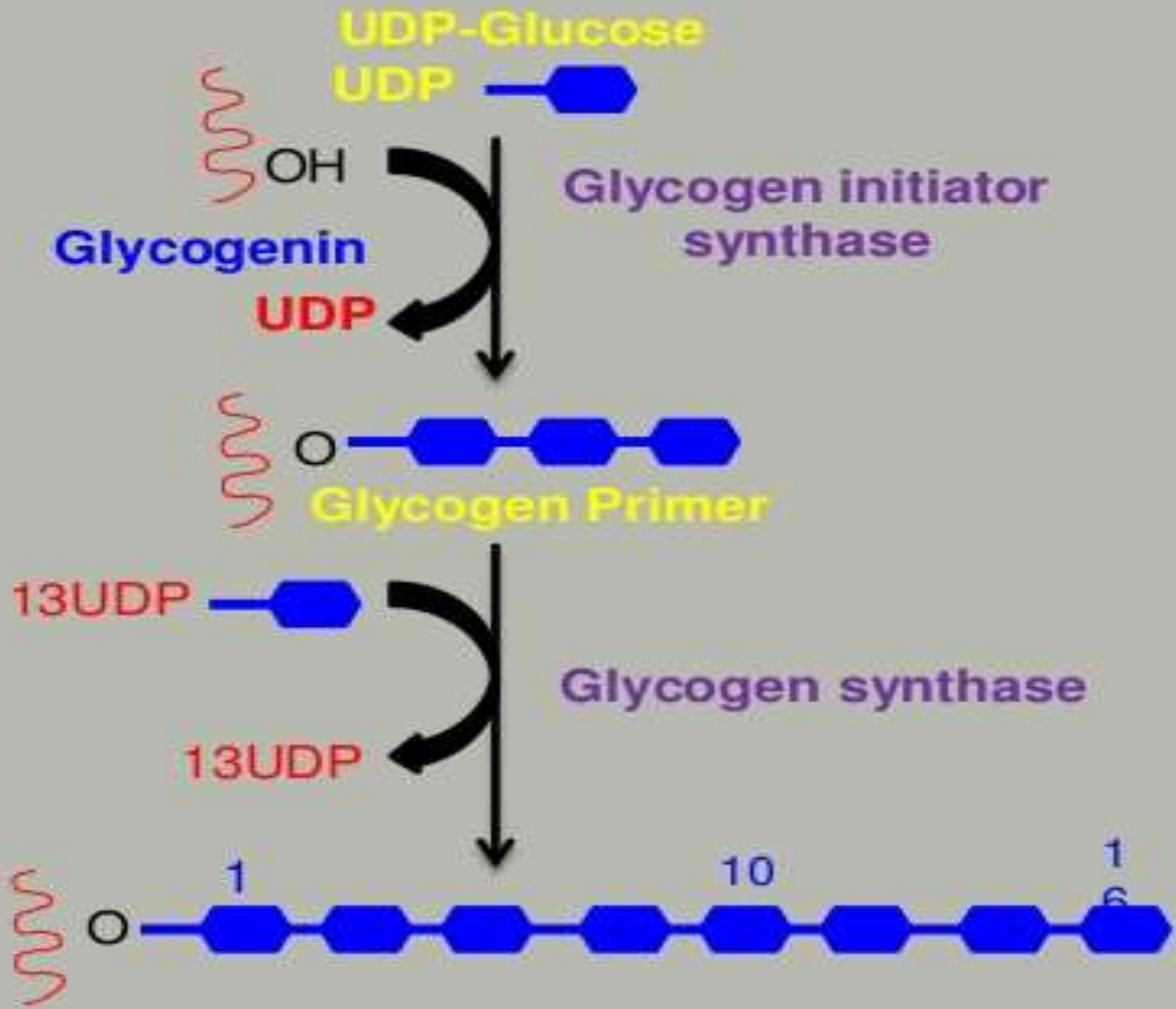
- The enzyme glycogen initiator synthase transfers the first molecule of glucose to glycogenin.
- Then glycogenin itself takes up a few glucose residues to form a fragment of primer which serves as an acceptor for the rest of the glucose molecules.

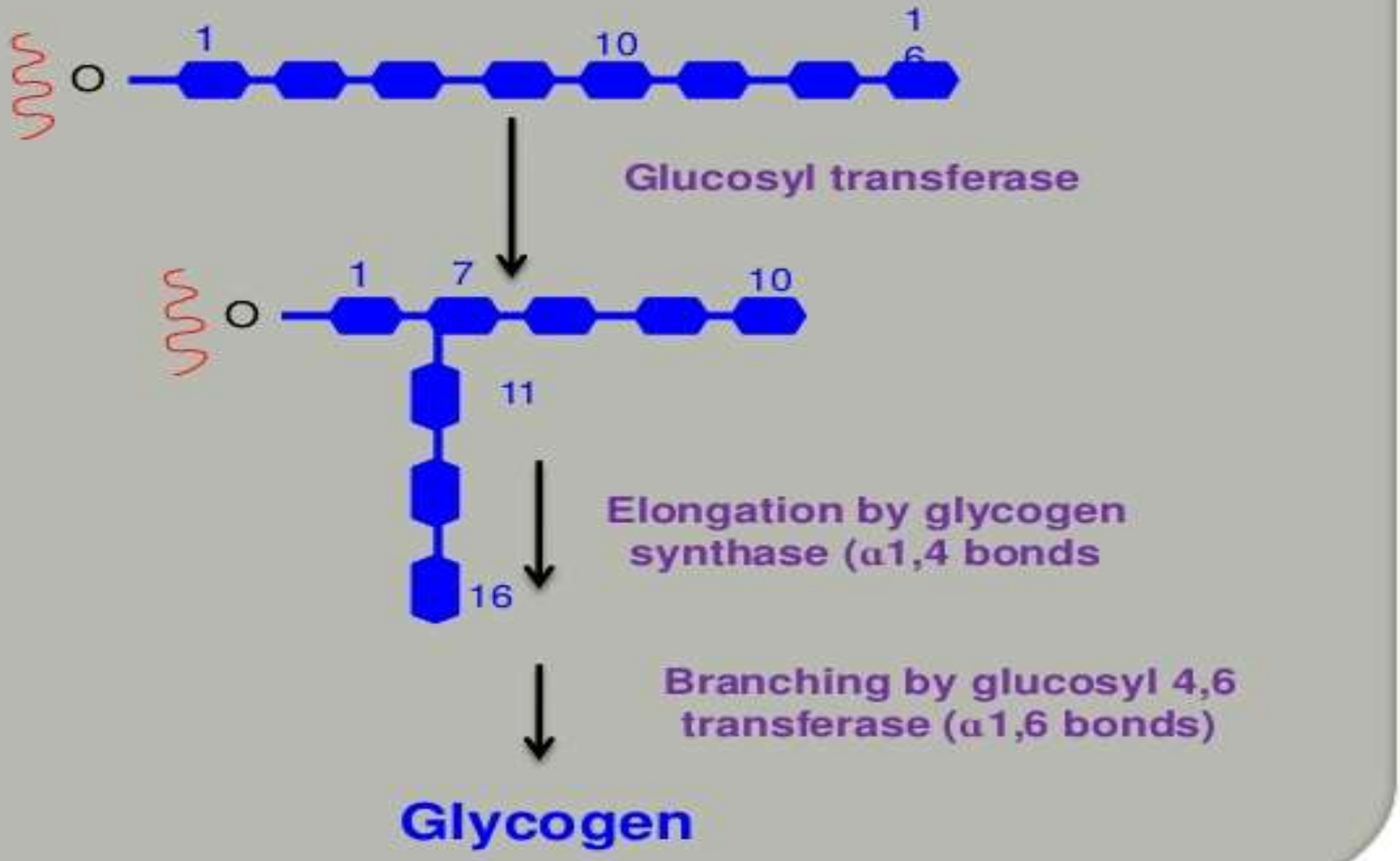
Glycogen synthesis by glycogen synthase

- Glycogen synthase is responsible for the formation of 1,4-glycosidic linkages.
- This enzyme transfers the glucose from UDP-glucose to the non-reducing end of glycogen to form α- 1,4 linkages.

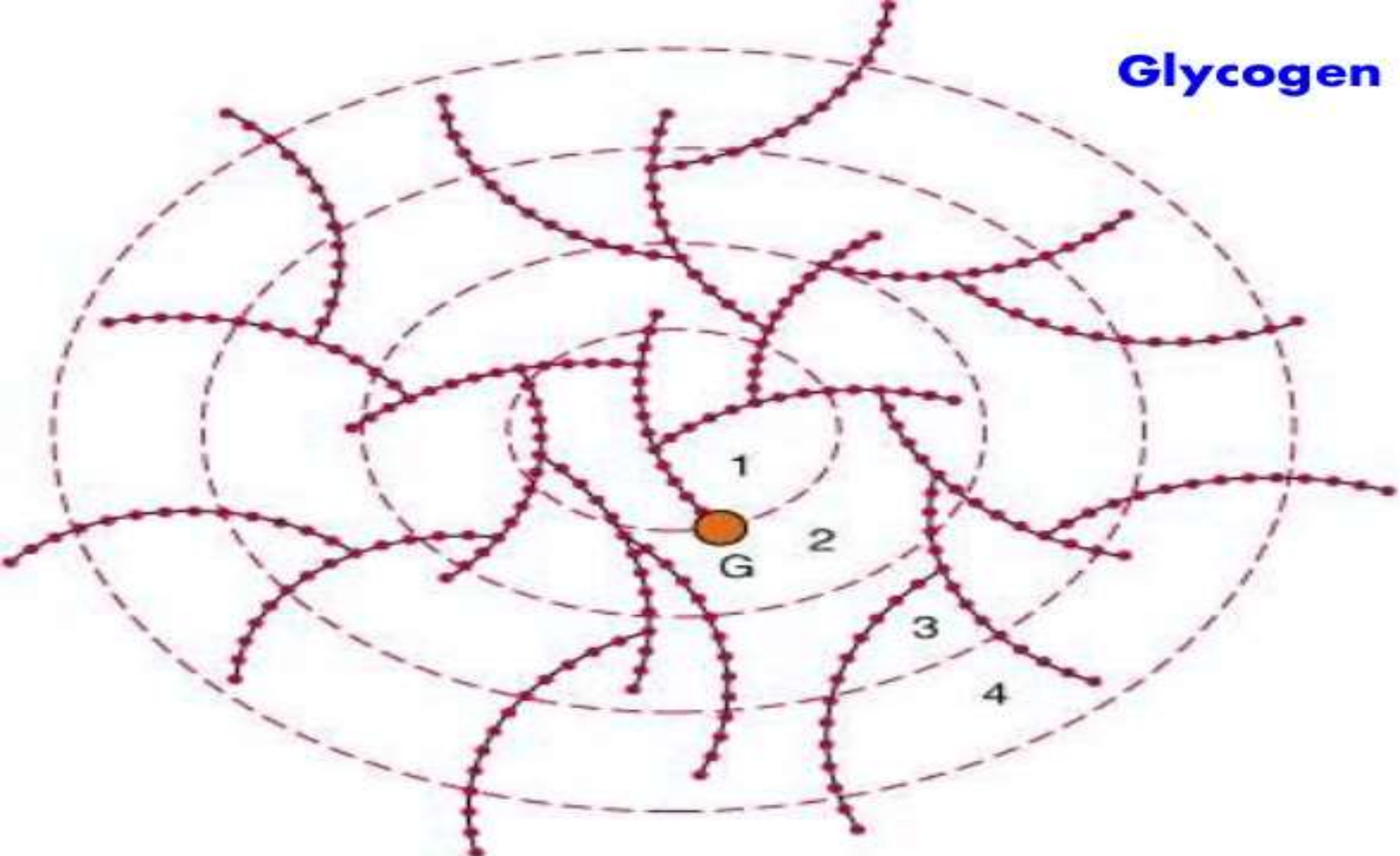
- This enzyme transfers a small fragment of 5 to 8 glucose residues from the non-reducing end of glycogen chain (by breaking α-1,4 linkages) to another glucose residue where it is linked by α-1,6 bond.
- This leads to the formation of a new non-reducing end, besides the existing one.
- Glycogen is further elongated & branched, by the enzymes glycogen synthase & glucosyl 4-6 transferase.


Glucose
ATP
ADP
Glucokinase
Glucose-6P
Phosphoglucomutase
Glucose-1P
UTP
PPi
UDP glucose
pyrophosphorylase
UDP-Glucose
UDP


UDP-Glucose
UDP
OH
Glycogenin
UDP
Glycogen initiator synthase
O
Glycogen Primer
13UDP
13UDP
Glycogen synthase
O
1
10
1
6


1
10
1
6
Glucosyl transferase
1
7
10
11
16
Elongation by glycogen synthase (α1,4 bonds
Branching by glucosyl 4,6 transferase (α1,6 bonds)
Glycogen

Glycogen



Thank you