2.5.2 Glycogen metabolism

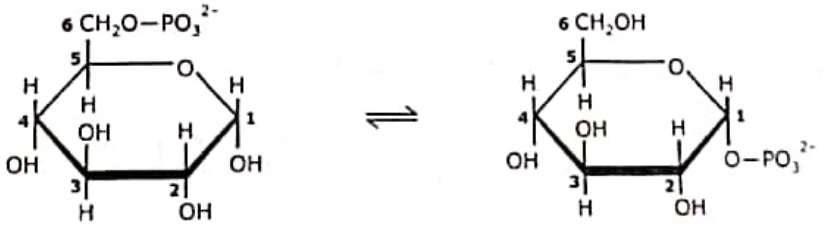
Glycogen structure and storage

Glycogen is a highly branched, very large polymer of glucose molecules linked along its main line by α-1, 4-glycosidic linkages; branches arise by α-1,6-glycosidic bonds at about every tenth residue. Glycogen occurs in the cytosol as granules, which also contain the enzymes that catalyze its formation and use.

Muscle and liver are the major sites for the storage of glycogen, and although its concentration in the liver is higher, the much greater mass of skeletal muscle stores a greater total amount of glycogen. Liver can mobilize its glycogen for the release of glucose to the rest of the body, but muscle can only use its glycogen for its own energy needs.

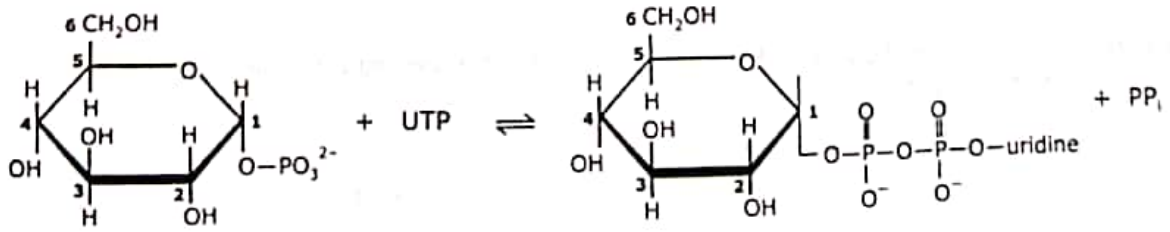
Glycogen synthesis (Glycogenesis)

Glycogen is synthesized from glucose 6-phosphate (G6P) mainly in the muscle and liver and stored within these tissues as glycogen granules. The first step in glycogen synthesis is the formation of glucose 1-phosphate (G1P), catalyzed by *phosphoglucomutase*. G6P is isomerized to glucose 1-phosphate.



Glucose 6-phosphate ⇌ Glucose 1-phosphate

The glucose 1-phosphate is then activated to enable its incorporation into glycogen. The activated form is uridine diphosphate glucose (UDP-glucose). UDP-glucose acts as a precursor of glycogen and is formed from glucose 1-phosphate and uridine triphosphate (UTP).

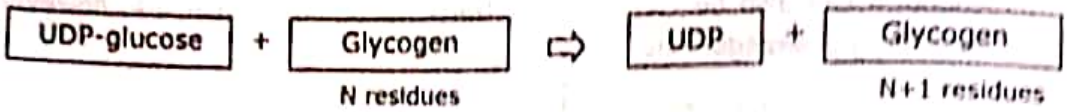


Glucose 1-phosphate + UTP ⇌ Uridine diphosphate glucose + PP_i

The reaction is catalyzed by *UDP-glucose pyrophosphorylase*. The C-1 carbon of the glucosyl unit being esterified to the diphosphate moiety of UDP.

Action of glycogen synthase

New glucosyl units are added to the non-reducing terminal residues of glycogen. The activated glucosyl unit, UDP-glucose is transferred to the hydroxyl group at a C-4 terminus of glycogen to form an α-1,4-glycosidic linkage. In the process of elongation, UDP is displaced by the terminal hydroxyl group of the growing glycogen molecule. This reaction is catalyzed by **glycogen synthase**, the key regulatory enzyme in glycogen synthesis.



Glycogen synthase can add glucosyl residues only if the polysaccharide chain already contains more than four residues. Thus, glycogen synthesis requires a *primer*. This priming function is carried out by **glycogenin**, a protein composed of two identical subunits, each bearing an oligosaccharide made up of few glucose units linked by α-1,4 glycosidic linkage. Carbon 1 of the first unit of this chain, the reducing end, is covalently attached to the specific tyrosine in each glycogenin subunit. How is this primer formed? Each subunit of glycogenin catalyzes the addition of few glucose units to its partner in the glycogenin dimer. UDP-glucose is the donor in this autoglycosylation. After the synthesis of oligosaccharide (a primer), glycogen synthase takes over to extend the glycogen molecule.

Formation of branch chains

Glycogen synthase catalyzes only α-1,4 glycosidic bond formation to yield α-amylose. Branching is accomplished by a separate enzyme called *branching enzyme*. Branching enzyme (also known as amylo-1,4 → 1,6 transglycosylase) moves a 7-unit segment of α-1,4 residues from a glycogen chain to a C-6 hydroxyl group of a glucosyl residue, that is four residues away from an existing branch.

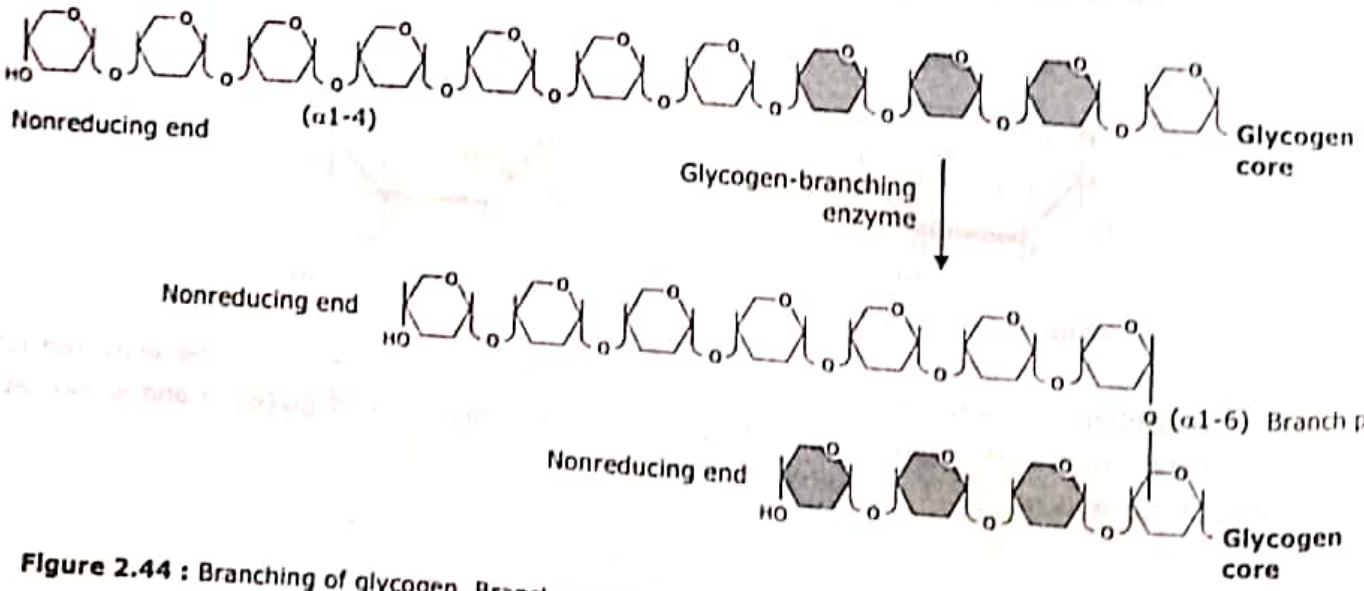


Figure 2.44 : Branching of glycogen. Branches are formed by transferring a 7-residue terminal segment from an α-1,4 linked glucan chain to the C6—OH group of a glucose residue on the same or another chain.

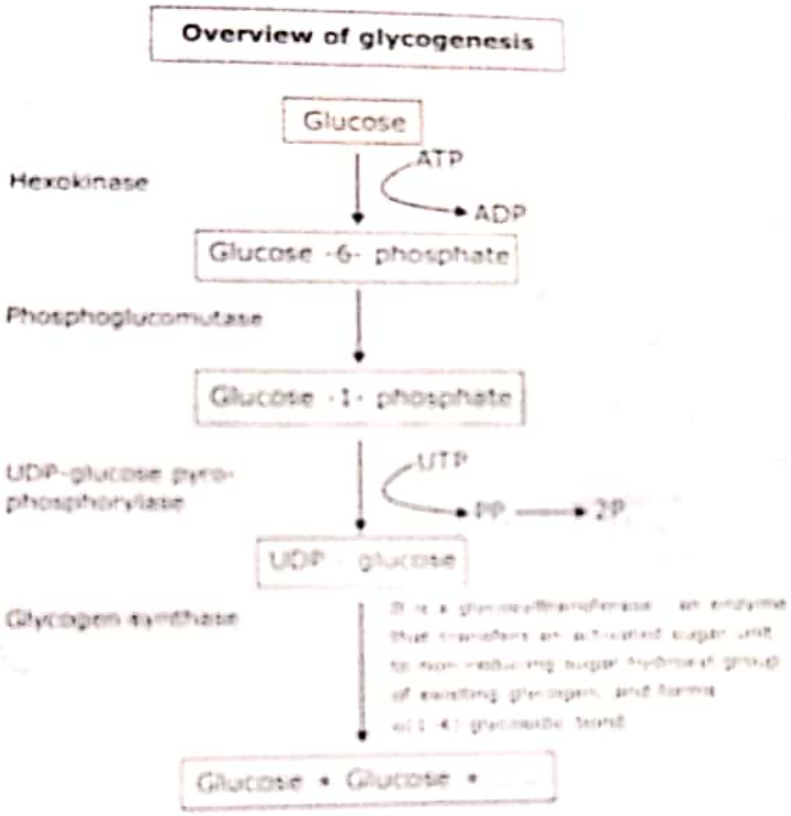


Figure 2.45 : An overview of glycogen synthesis in which glucose is activated to UDP glucose that acts as precursor for glycogen.