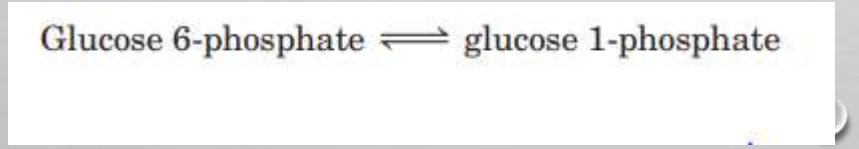
GLYCOGENESIS AND GLYCOGENOLYSIS

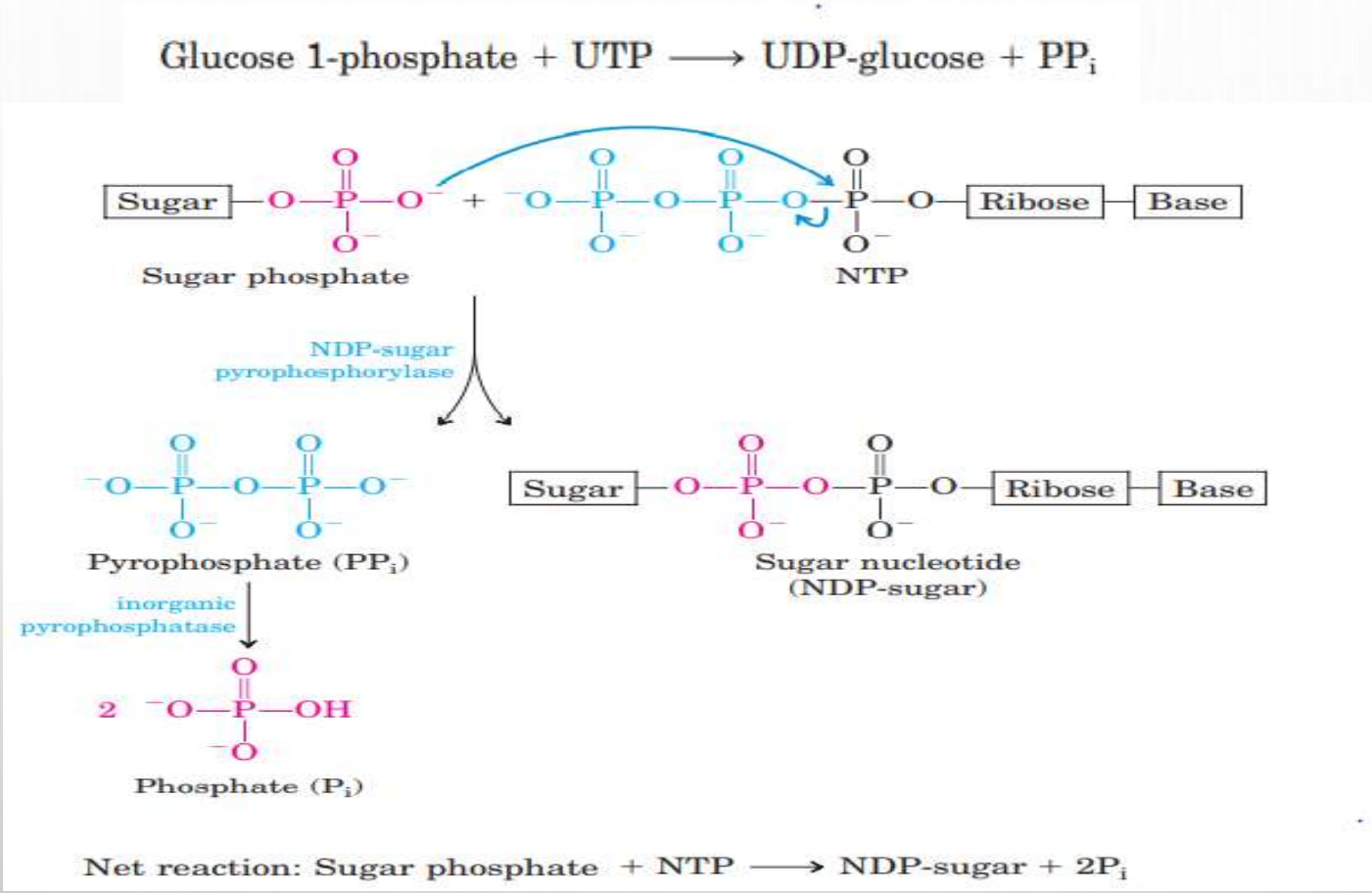
GLYCOGENESIS

- Glycogen synthesis takes place in virtually all animal tissues but is especially prominent in the liver and skeletal muscles.
- The starting point for synthesis of glycogen is glucose 6-phosphate.
- G-6-P can be derived from free glucose in a reaction catalyzed by the isozymes hexokinase I and hexokinase II in muscle and hexokinase IV (glucokinase) in liver.

- Some ingested glucose takes a more roundabout path to glycogen. It is first taken up by erythrocytes and converted to lactate glycolytically; the lactate is then taken up by the liver and converted to glucose 6-phosphate by gluconeogenesis.
- To initiate glycogen synthesis, the glucose 6-phosphate is converted to glucose 1-phosphate by phosphoglucomutase reaction.



- The product of this reaction is converted to UDP-glucose by the action of UDP-glucose pyrophosphorylase, in a key step of glycogen biosynthesis:



- UDP-glucose is the immediate donor of glucose residues in the reaction catalyzed by glycogen synthase, which promotes the transfer of the glucose residue from UDP-glucose to a nonreducing end of a branched glycogen molecule.

- Glycogen synthase cannot make the (1→6) bonds found at the branch points of glycogen; these are formed by the glycogen-branching enzyme, also called amylo (1 → 4) to (1 → 6) transglycosylase, or glycosyl-(4 → 6)-transferase.
- The glycogen-branching enzyme catalyzes transfer of a terminal fragment of 6 or 7 glucose residues from the nonreducing end of a glycogen branch having at least 11 residues to the C-6 hydroxyl group of a glucose residue at a more interior position of the same or another glycogen chain, thus creating a new branch.
- Further glucose residues may be added to the new branch by glycogen synthase.
- The biological effect of branching is to make the glycogen molecule more soluble and to increase the number of nonreducing ends. This increases the number of sites accessible to glycogen phosphorylase and glycogen synthase, both of which act only at nonreducing ends.

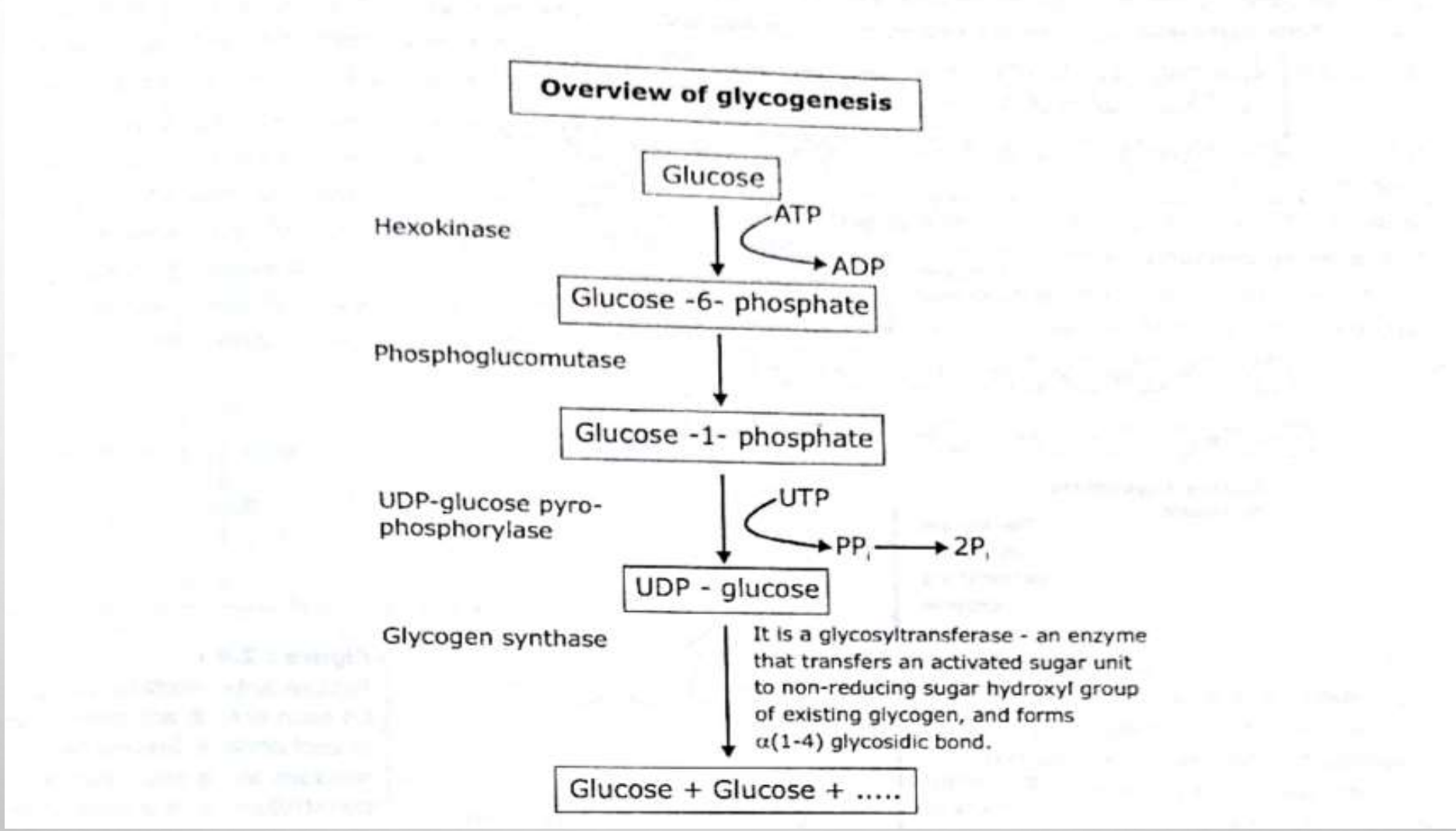


Figure: An overview of glycogen synthesis in which glucose is activated to UDP glucose that acts as precursor for glycogen

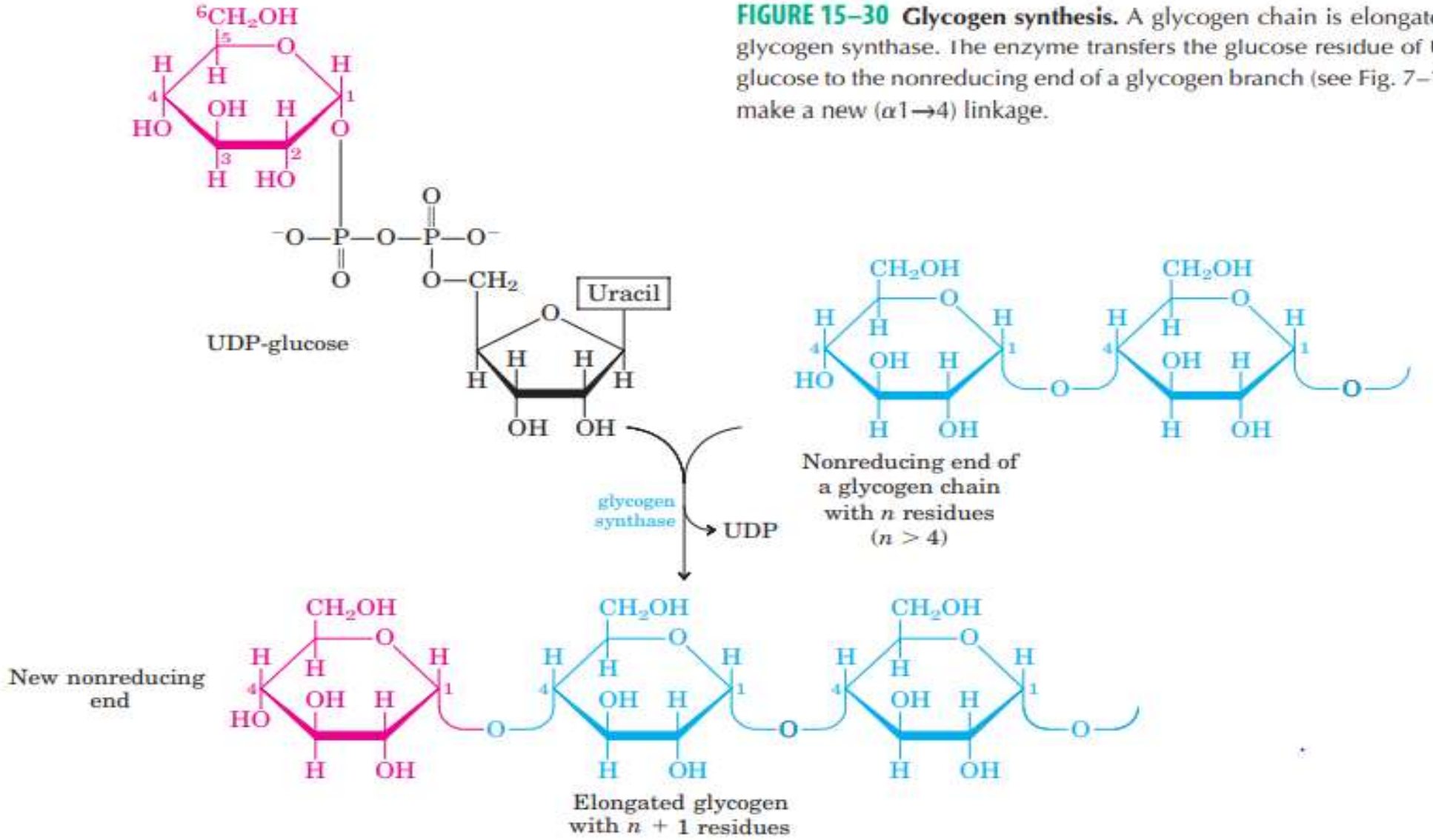


FIGURE 15–30 Glycogen synthesis. A glycogen chain is elongated by glycogen synthase. The enzyme transfers the glucose residue of UDP-glucose to the nonreducing end of a glycogen branch (see Fig. 7–14) to make a new ($\alpha 1 \rightarrow 4$) linkage.

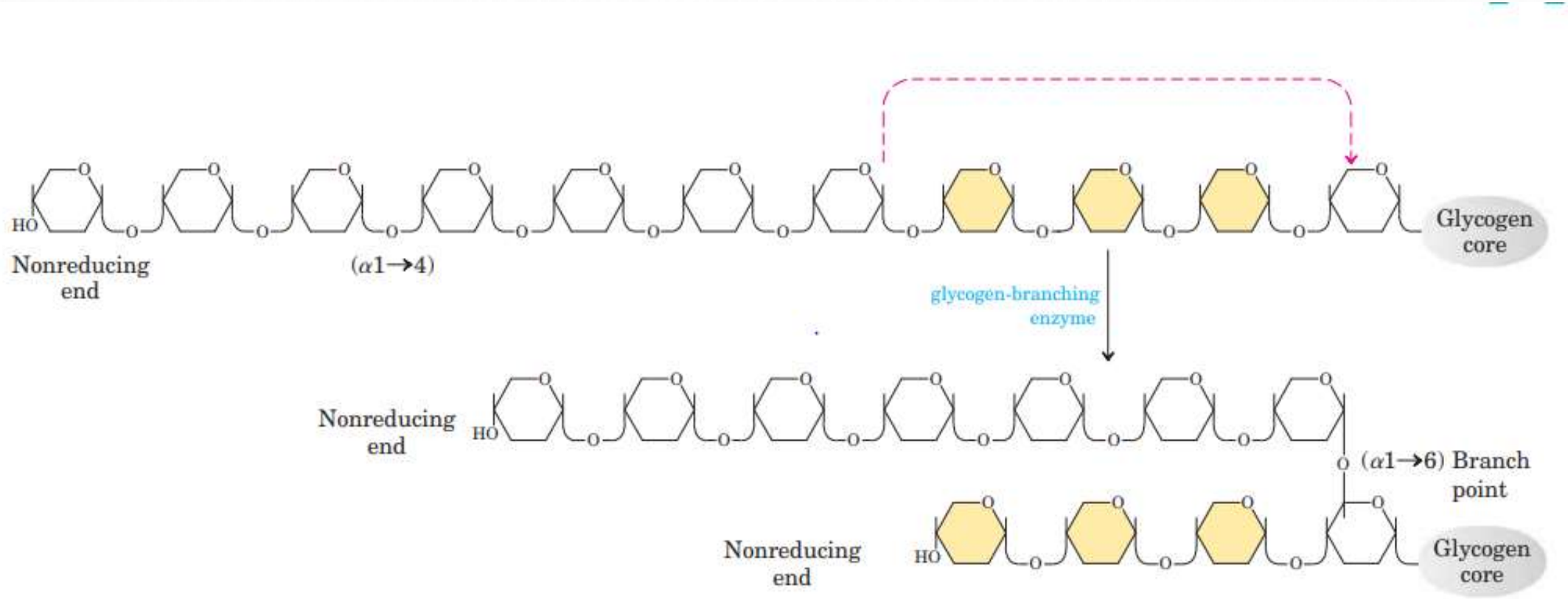


FIGURE 15–31 Branch synthesis in glycogen. The glycogen-branching enzyme (also called amylo (1→4) to (1→6) transglycosylase, or glycosyl-(4→6)-transferase) forms a new branch point during glycogen synthesis.

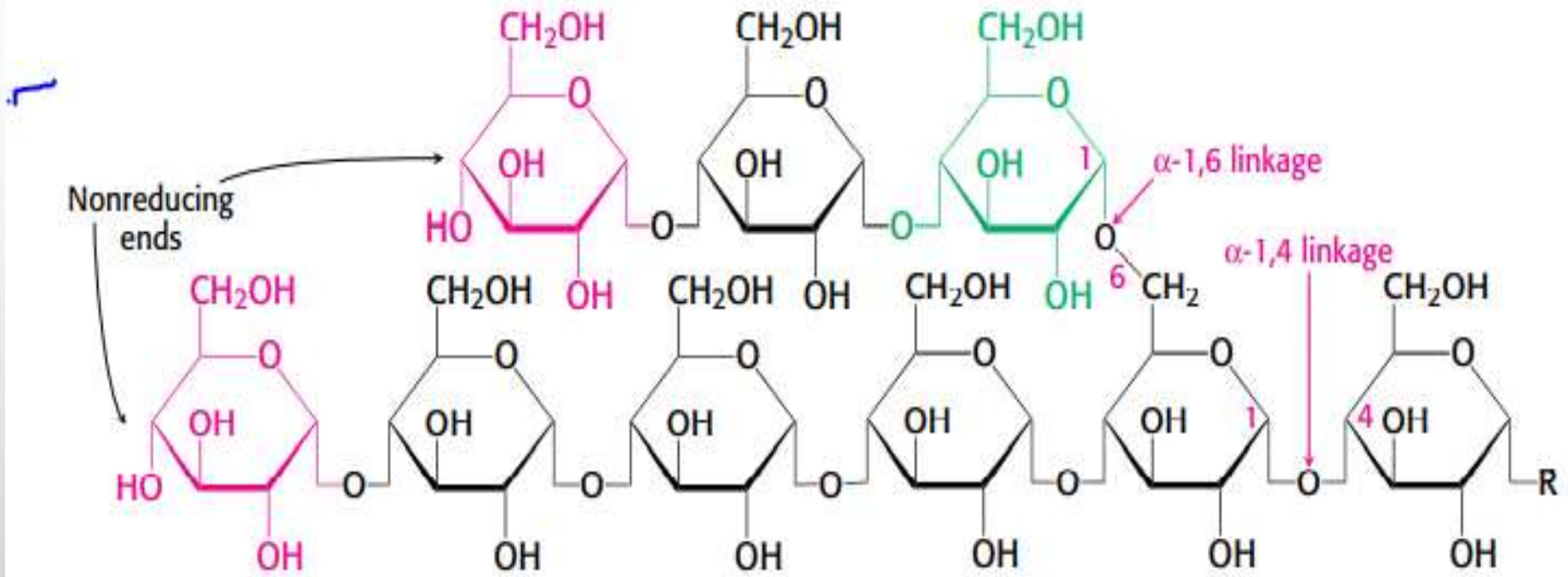
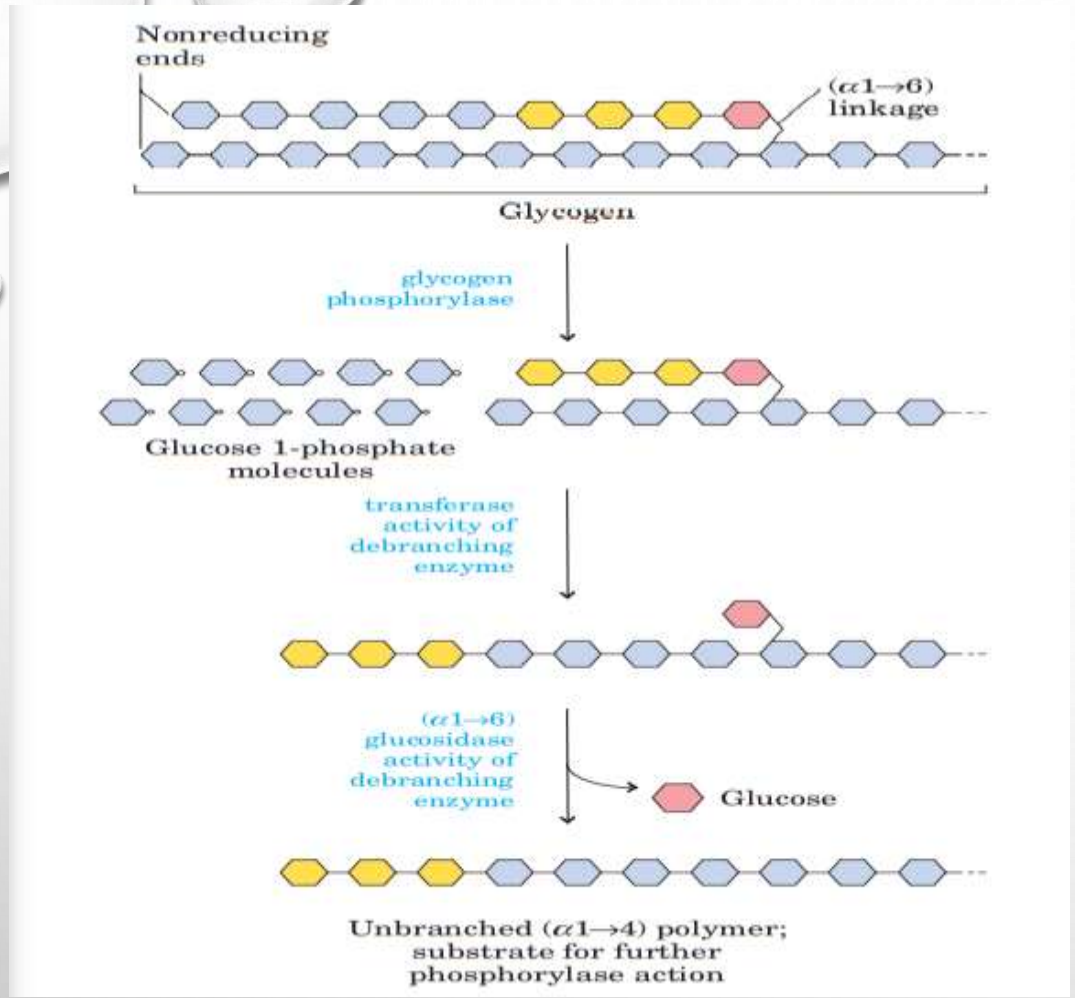
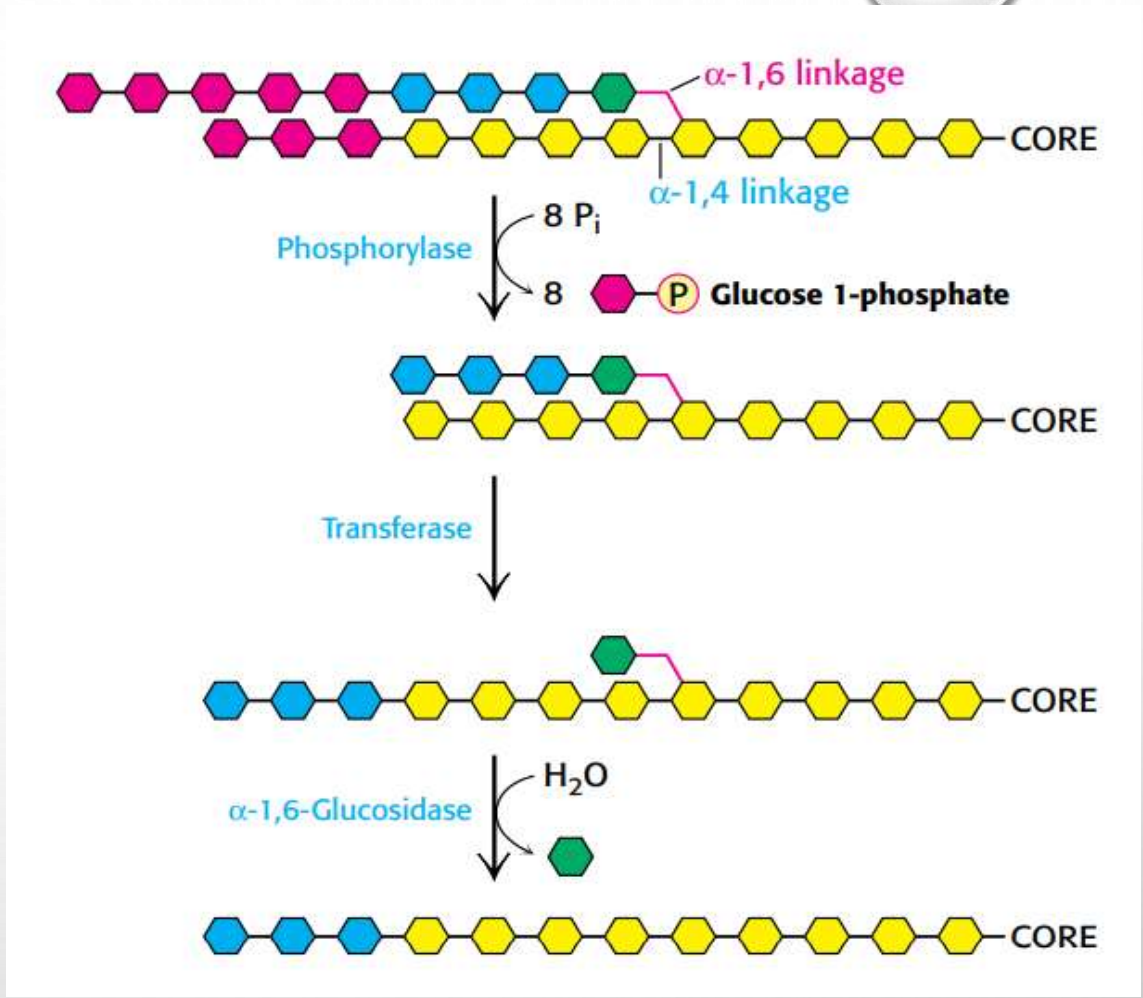


FIGURE 21.2 Glycogen structure. In this structure of two outer branches of a glycogen molecule, the residues at the nonreducing ends are shown in red and the residue that starts a branch is shown in green. The rest of the glycogen molecule is represented by R.

GLYCOGENOLYSIS

- In skeletal muscle and liver, the glucose units of the outer branches of glycogen enter the glycolytic pathway through the action of three enzymes: **glycogen phosphorylase, glycogen debranching enzyme**, and **phosphoglucomutase**.
- **Glycogen phosphorylase** catalyzes the reaction in which an (1 → 4) glycosidic linkage between two glucose residues at a nonreducing end of glycogen undergoes attack by inorganic phosphate (Pi), removing the terminal glucose residue as d-glucose-1-phosphate.
- **Glycogen phosphorylase** acts repetitively on the nonreducing ends of glycogen branches until it reaches a point four glucose residues away from an (1 → 6) branch point, where its action stops.
- Further degradation by **glycogen phosphorylase** can occur only after the debranching enzyme, catalyzes two successive reactions that transfer branches.
- Once these branches are transferred and the glucosyl residue at C-6 is hydrolyzed, glycogen phosphorylase activity can continue.





Gycogen breakdown near an (1→6) branch point. Following sequential removal of terminal glucose residues by glycogen phosphorylase), glucose residues near a branch are removed in a two-step process that requires a bifunctional debranching enzyme. First, the transferase activity of the enzyme shifts a block of three glucose residues from the branch to a nearby nonreducing end, to which they are reattached in (1 → 4) linkage. The single glucose residue remaining at the branch point, in (1 → 6) linkage, is then released as free glucose by the debranching enzyme's (1 → 6) glucosidase activity. The glucose residues are shown in shorthand form, which omits the –H, –OH, and –CH2OH groups from the pyranose ring.

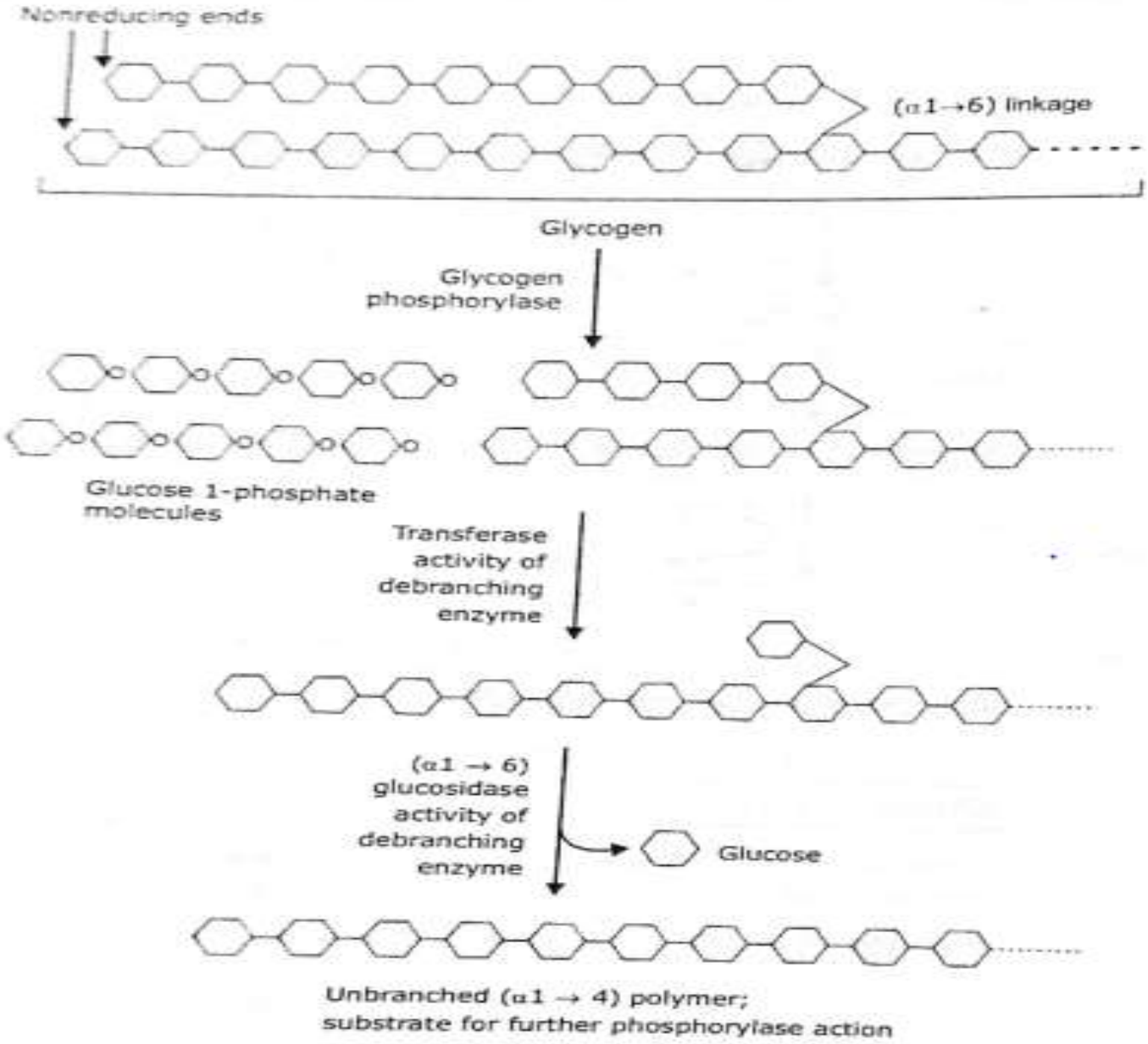


Figure : 2.46
First, α-1,4-glycosidic bonds on each branch are cleaved by phosphorylase, leaving four residues along each branch. The transferase shifts a block of three glycosyl residues from one outer branch to the other. The glucose residue is then removed by α-1,6-glucosidase, leaving a linear chain with all alpha-1,4 linkages, suitable for further cleavage by phosphorylase.

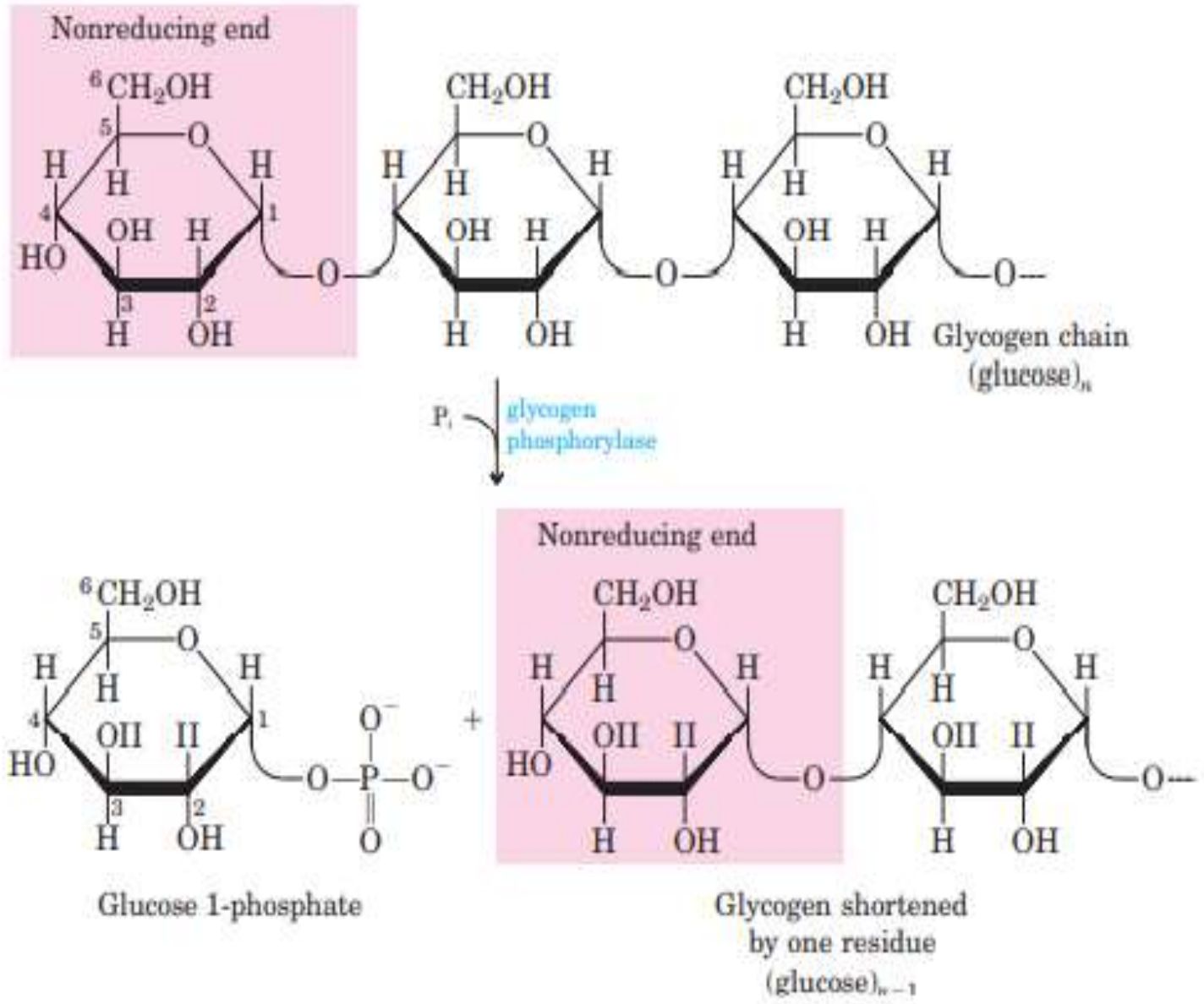


FIGURE 15–25 Removal of a glucose residue from the nonreducing end of a glycogen chain by glycogen phosphorylase. This process is repetitive; the enzyme removes successive glucose residues until it reaches the fourth glucose unit from a branch point (see Fig. 15–26).