Glycogenesis

Dr. Garima Hore,
SA.C.T-I,
Department of Zoology,
Dr. Kanailal Bhattacharyya College.

Objectives

- To understand the synthesis of glycogen.
- Role of glycogenin in glycogen synthesis.
- Glycogen branching.
- Hormonal regulation of glycogenesis.

Introduction

- **Glycogenesis** is the **formation of glycogen**, a multibranched polysaccharide of glucose that serves as a form of energy storage in animals.
- Site : Cytosol of all cells particularly liver and muscles.
- Glycogen is a **highly branched**, large polymer of glucose molecules linked along its main line by **α-1, 4 glycosidic linkages**; branches arise by **α-1,6 glycosidic bond** at about every tenth residues.
- It occurs in the **cytoplasm** as granules. Granules also contain the enzymes and regulatory proteins which is required for its synthesis and degradation.
- It acts as an important energy reserve for the body.
- It is **stored in the liver and skeletal muscle**. Glycogen stored in the muscles will be utilized for the energy requirement of muscles only, while glycogen stored in the liver will be used for the energy requirement of the rest of the body.
- Glycogen metabolism is very important because it **facilitates the blood glucose level** to be maintained between meals (liver glycogen) and also act as an energy reserve for muscular activity. The maintenance of blood glucose is essential in order to supply energy to tissues.
- Blood is closely monitored and regulated by hormones. If blood glucose level rises, our body hormones came into action to reduce the excess sugar. This is done by increasing the process of glycogenesis. It means synthesis and storage of glycogen. The suffix 'genesis' means creation; so, glycogenesis is the creation of glycogen.

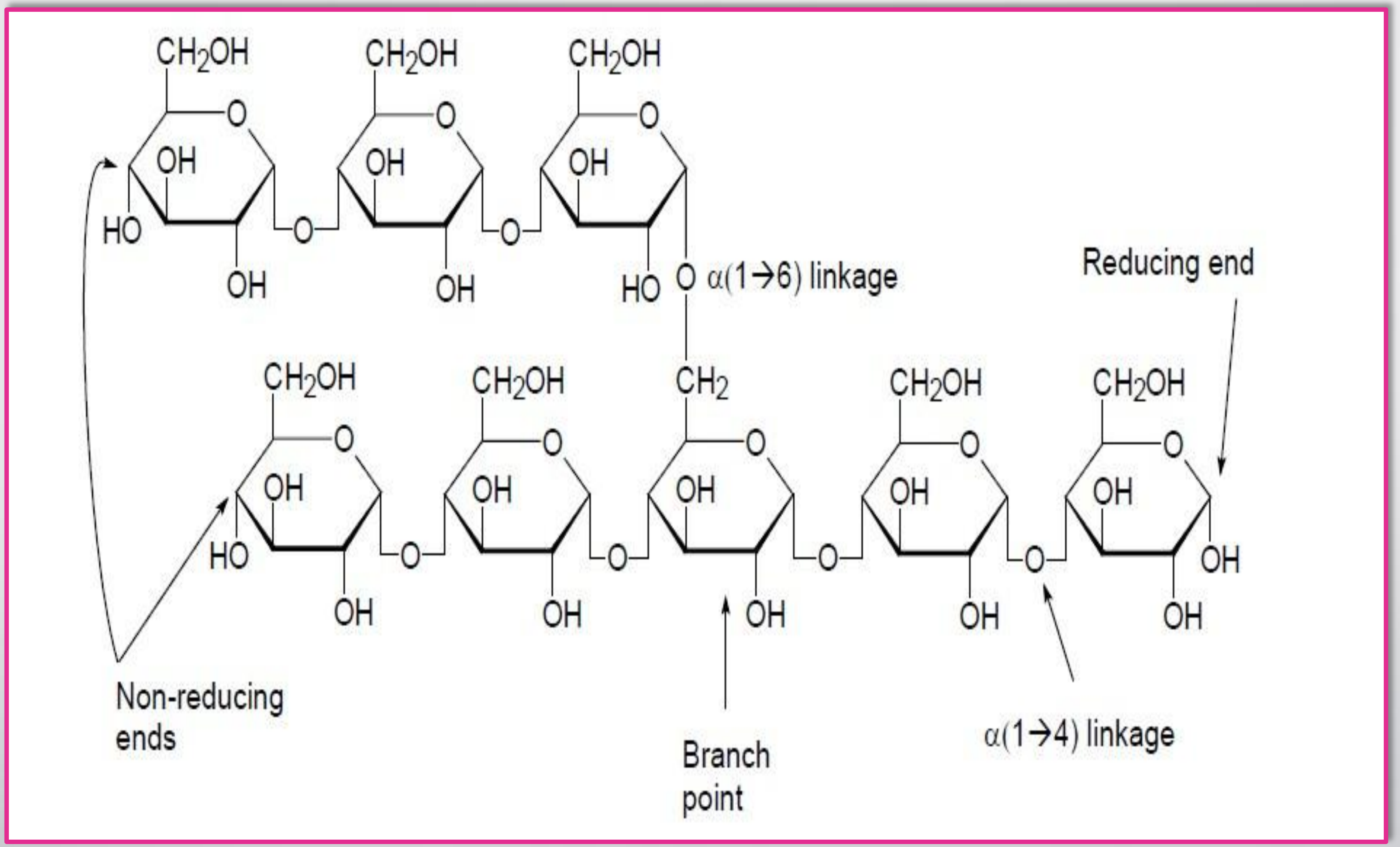

Fig. 1: Structure of Glycogen

STEPS OF GLYCOGENESIS

- UDP-glucose formation by UDP-glucose pyrophosphorylase.
- Glycogen synthesis by glycogen synthase.
- Glycogen Branching.

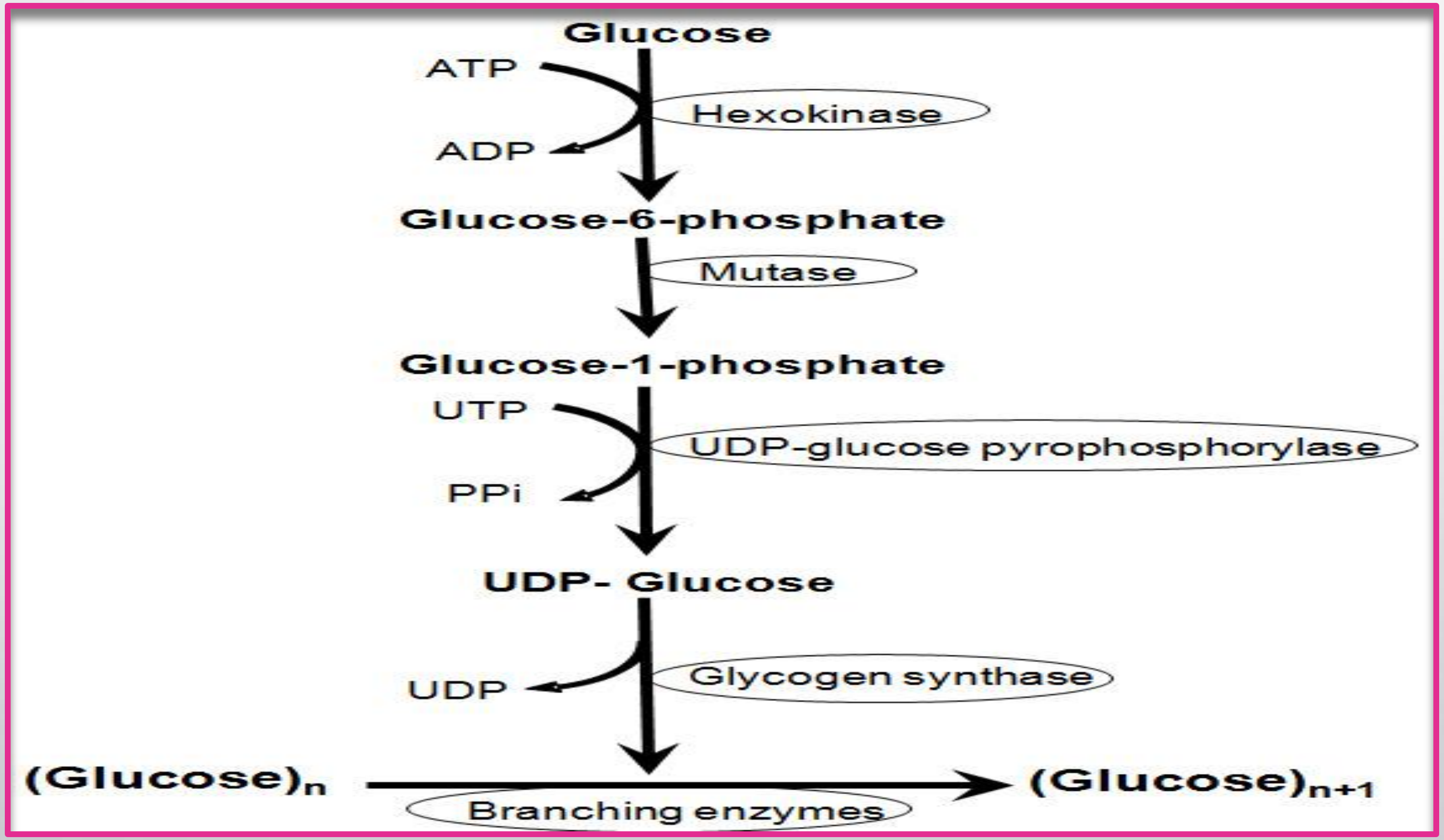

Fig. 2: Overview of Glycogenesis.

UDP-glucose formation by UDP-glucose pyrophosphorylase:

- Glucose is activated before polymerisation in to glycogen. **Hexokinase** enzyme (In muscles) or **glucokinase** enzyme (in liver) catalyzes the **phosphorylation of glucose to glucose-6- phosphate.**
- For further anabolic polymerisation reaction, it is converted in to **glucose-1-phosphate** by the reversible action of **Phosphoglucomutase**.
- **Glucose-1- phosphate** is then attached to UTP by the action of **UDP-Glucose.**
- Pyrophosphorylase form UDP-Glucose and pyrophosphate. The C-1 carbon of the glucosyl unit is esterified to the diphosphate group of UDP. The ΔG° of this reaction is very less . Pyrophosphates (PPi) formed is hydrolyzed to 2 Pi (orthophosphate). This reaction is highly exergonic reaction. Conversion of PPi to orthophosphate is catalysed by Inorganic pyrophosphatase.
- **UDP-glucose** is the activated form of glucose used for metabolism of galactose and biosynthesis. It is a high energy compound. It can donate glucose units to the growing glycogen chain. No further energy is required for synthesis of glycogen.

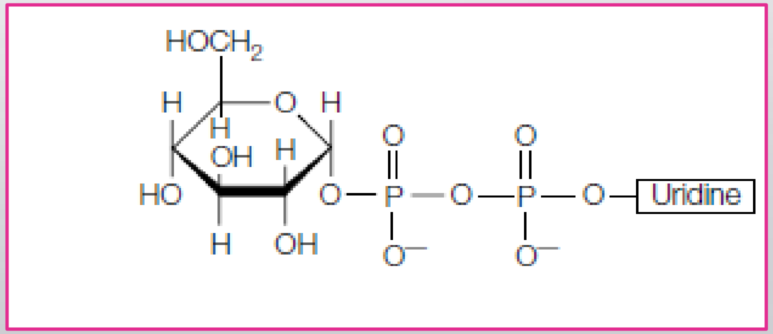

Fig. 3: Structure of UDP-glucose

Glycogen synthesis by glycogen synthase

- Glycogen synthase transfers the **glucosyl residue** from UDP-glucose to the **non reducing terminal** residues of glycogen. It is transferred to **hydroxyl terminal** of **C4** end of glycogen to form an **α-1–4 glycosidic bond**.
- This reaction is catalysed by **glycogen synthase**. Glycogen synthase is the **regulatory enzyme** in synthesis of glycogen.

$$\text{UDP-glucose} + (\text{glycogen})_{n\ \text{residues}} \longrightarrow \text{UDP} + (\text{glycogen})_{n+1\ \text{residues}}$$

- Glycogen synthesis requires a primer. It can add glucosyl residues to the glycogen chain if it contains more than four residues. It means that glycogen synthase can only extend an existing chain. Priming function is carried out by **glycogenin**.

Glycogenin

- It is a primer for glycogen synthesis. It is a protein which composed of two identical subunits. It is a **37 kDa protein** that is **glycosylated** on a specific **tyrosine** residue. Glycogenin contains **eight** glucose units linked by **α- 1–4 linkages**. These glucose molecules are added to the protein by **autocatalysis**.
- Formation of glycogenin primer: The first glucose molecule is attached to the hydroxyl group on Tyr-194 of glycogenin, which is catalysed by the subunit of glycogenin. Then it is auto catalytically extends the glucose chain by up to seven residues long. This glucose molecule is donated by UDPG. In this form, glycogenin can act as a primer.

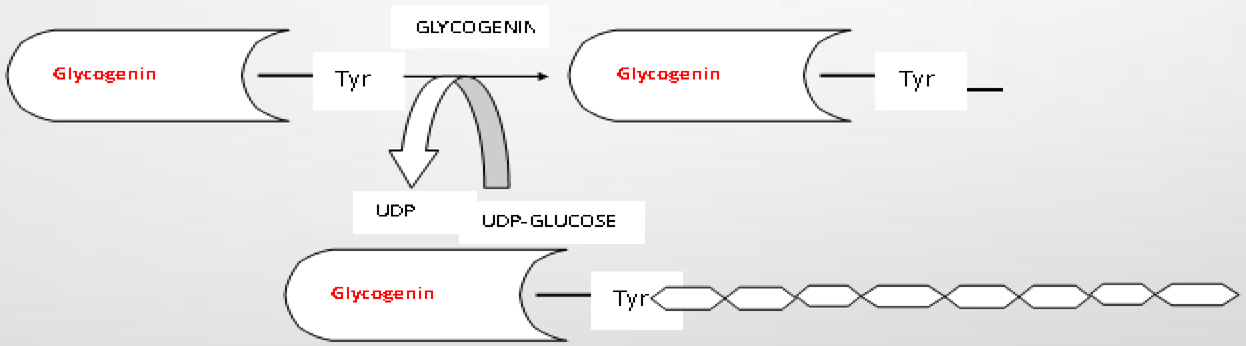

Fig. 4: Formation of glycogenin primer.

- New glucose residue is attached to the primer by Glycogen synthase. Glycogen Synthase catalyzes the transfer of glucose from UDP-glucose. New glucose molecule will transfer to the C-4 hydroxyl group at the non reducing end of the growing glycogen molecule.

Glycogen Branching

- Glycogen synthase catalyzes only α- 1–4 glycosidic bonds. It results in to the formation of α- amylose.
- **Branching** is catalysed by separate enzyme called **Branching enzyme**.
- It is also known as **amylo-(1–4→1–6) transglycosylase.**
- After a number of glucose units have been linked as a straight chain with α1–4 linkages, branching enzyme breaks α 1–4 bonds.
- It breaks a **7 unit segment** of **α 1–4 residues** from a glycogen chain and transfers to a **C-6 hydroxyl** group of a glucosyl residue that is **four** residues **away from an existing branch**. Reattachment is done by creating an **α1–6 bond**.
- Branches are very important in a growing chain of glycogen. Enzymes involved in glycogen synthesis (glycogen synthase) and degradation (glycogen phosphorylase) works only at the ends of the glycogen molecules. More terminal ends increases the rate of synthesis and degradation of glycogen.

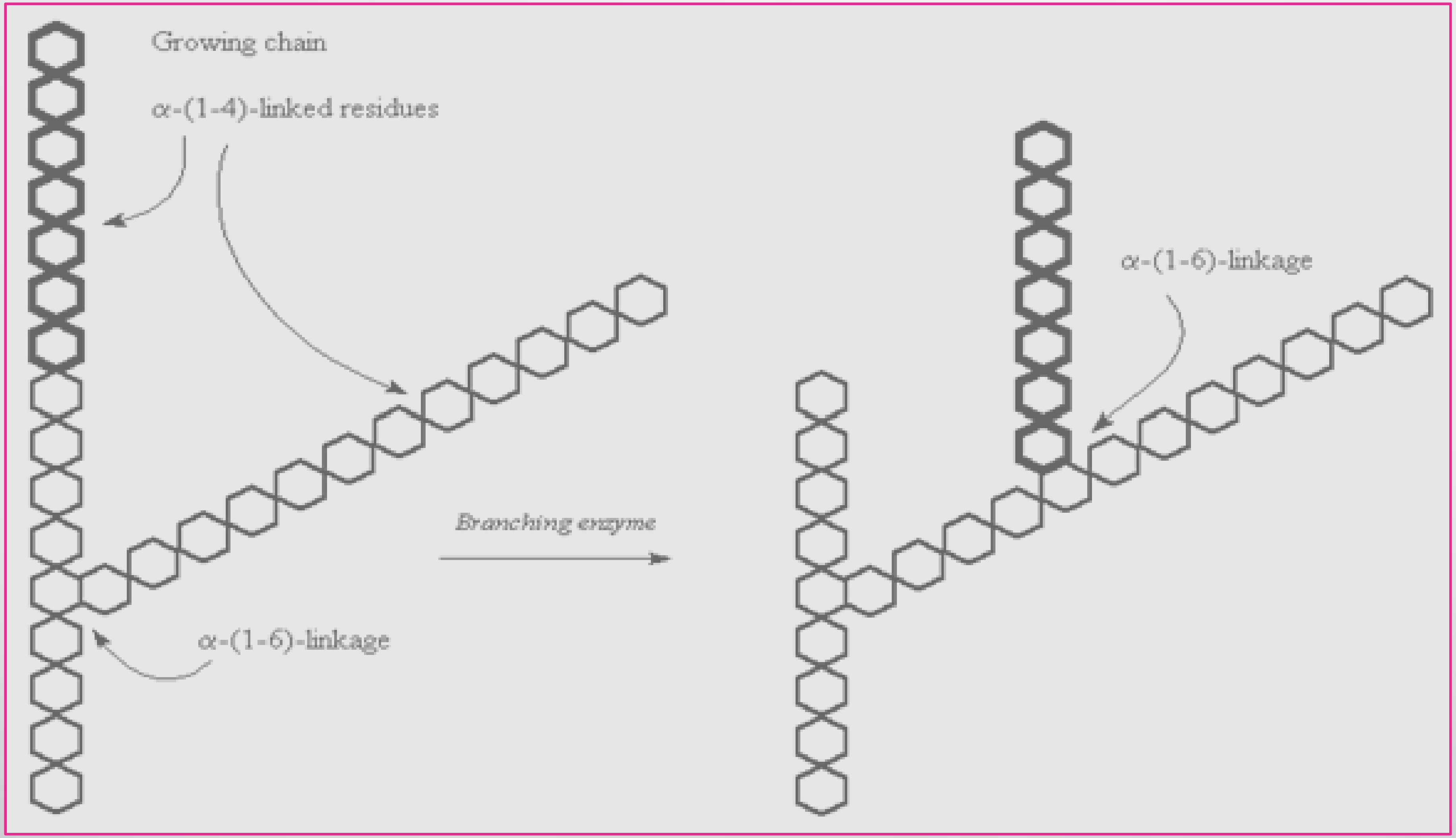

Fig. 5: Glycogen Branching

Hormonal regulation of glycogenesis

- Glycogen synthase, the key enzyme of Glycogenesis exists in activate (dephosphorylated) and inactive (phosphorylated) form. Hormones like **glucagon and epinephrine** are diabetogenic i.e. they **increase the blood glucose level**. Thus they **antagonize glycogen synthesis** which is an effective way of reducing blood glucose level and storing it for further use.

- **Insulin** is an anti diabetic hormone. It **lowers the blood glucose level** by **stimulating** the **uptake of glucose** by muscle cells and **Glycogenesis** in liver and muscle.

Thank You!