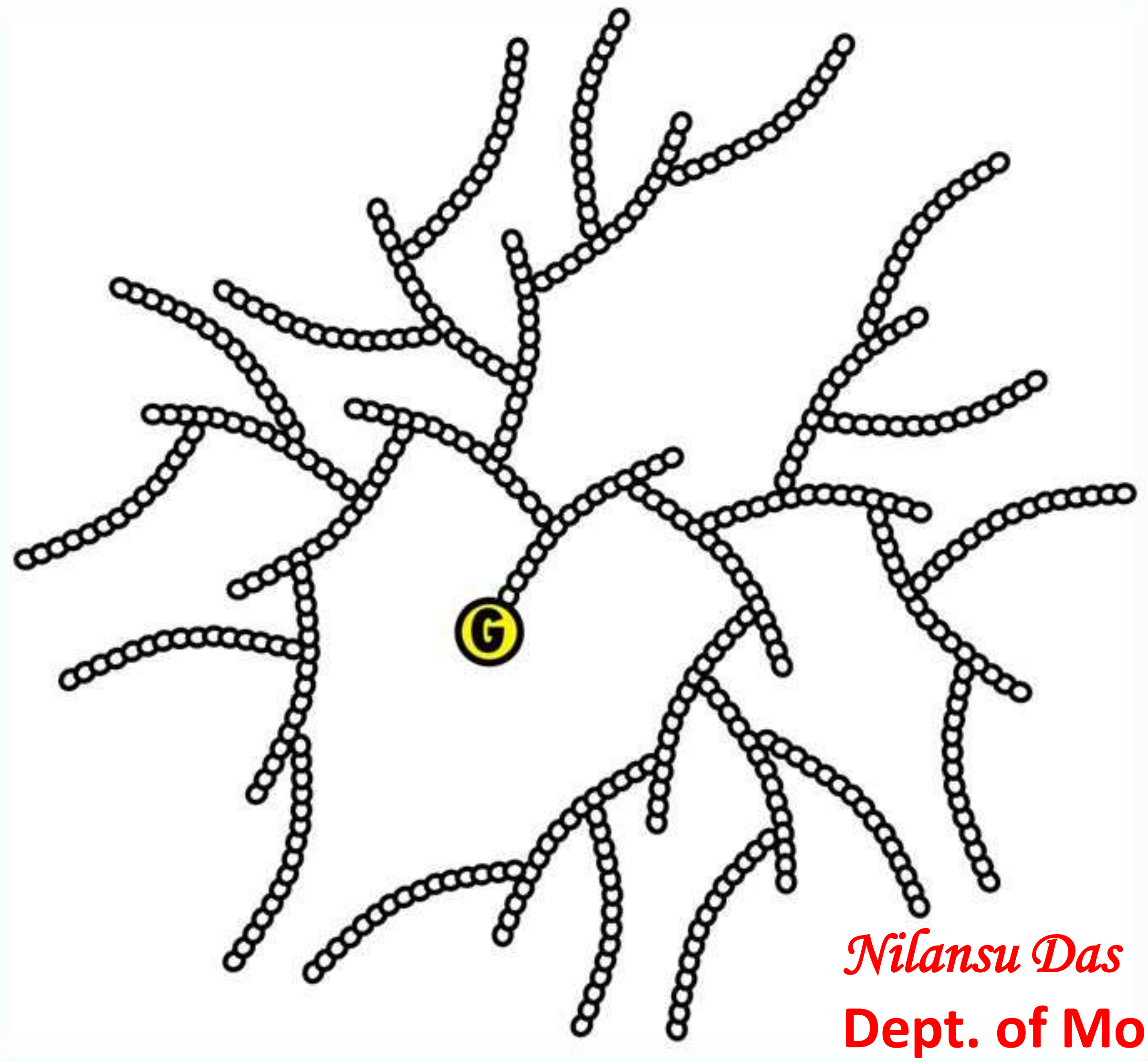
# Glycogen Metabolism




*Nilansu Das*
**Dept. of Molecular Biology**
**Surendranath College**

# Glycogen Metabolism

**Glycogen Metabolism comprises of synthesis of glycogen from glucose….. Glycogenesis**

**and**

**Breaking down of Glycogen to glucose to elevate the blood sugar level…. Glycogenolysis**

# Glycogenesis

**Glycogenesis is the process of glycogen synthesis, in which glucose molecules are added to chains of glycogen for storage.**

**This process is activated during rest periods following the Cori cycle, in the liver, and also activated by insulin in response to high glucose levels.**

# Steps of Glycogenesis

**Glucose is converted into glucose 6-phosphate by the action of glucokinase or hexokinase with conversion of ATP to ADP.**

**Glucose-6-phosphate is converted into glucose-1-phosphate by the action of phosphoglucomutase, passing through the obligatory intermediate glucose-1,6-bisphosphate.**

**Glucose-1-phosphate is converted into UDP-glucose by the action of the enzyme UDP-glucose pyrophosphorylase.**

**Pyrophosphate is formed, which is later hydrolysed by pyrophosphatase into two phosphate molecules.**

# Steps of Glycogenesis … contd

The enzyme glycogenin is needed to create initial short glycogen chains, which are then lengthened and branched by the other enzymes of glycogenesis.

Glycogenin, a homodimer, has a tyrosine residue on each subunit that serves as the anchor for the reducing end of glycogen.

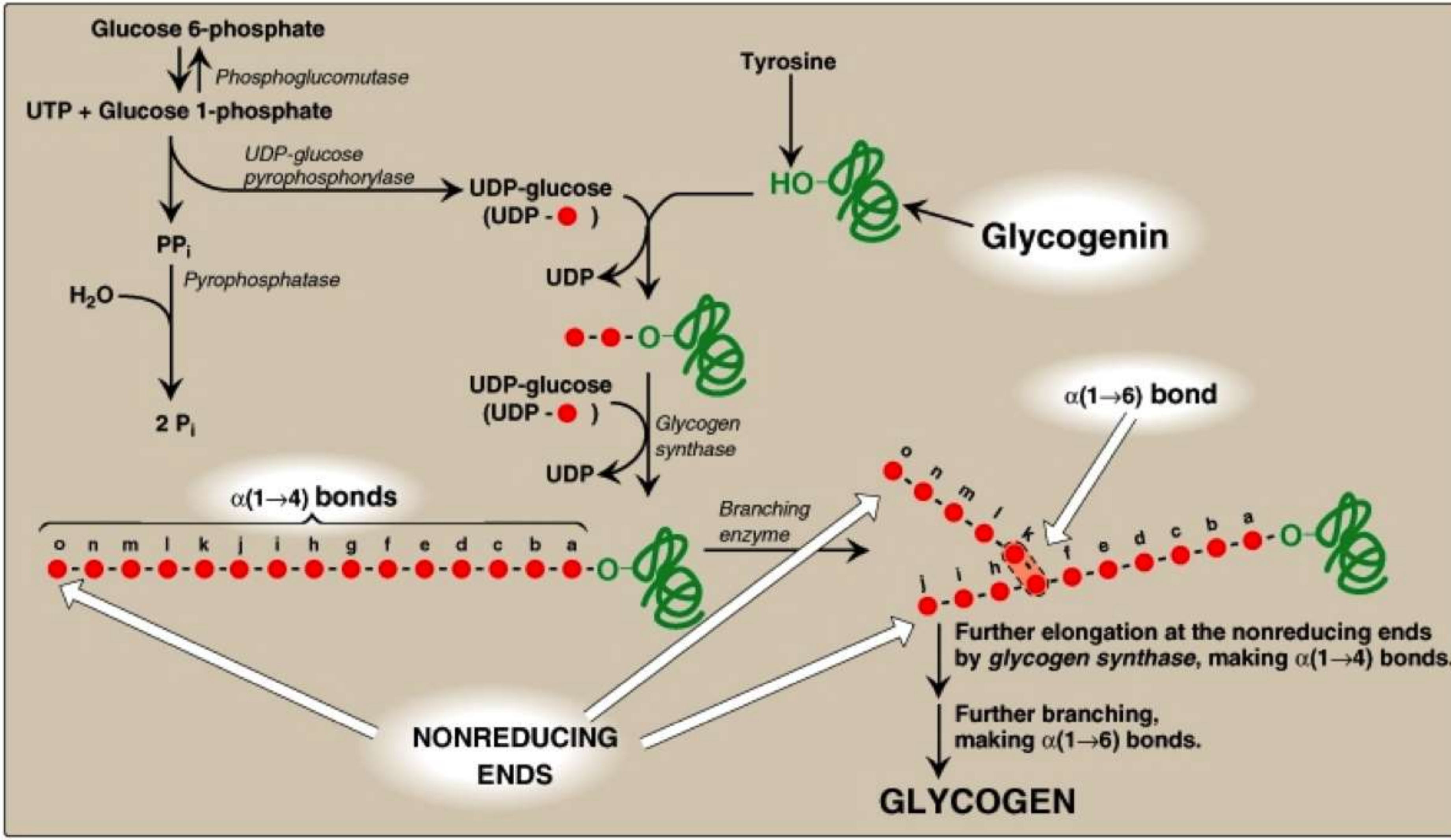
Initially, about eight UDP-glucose molecules are added to each tyrosine residue by glycogenin, forming α(1→4) bonds.

# Steps of Glycogenesis ... contd

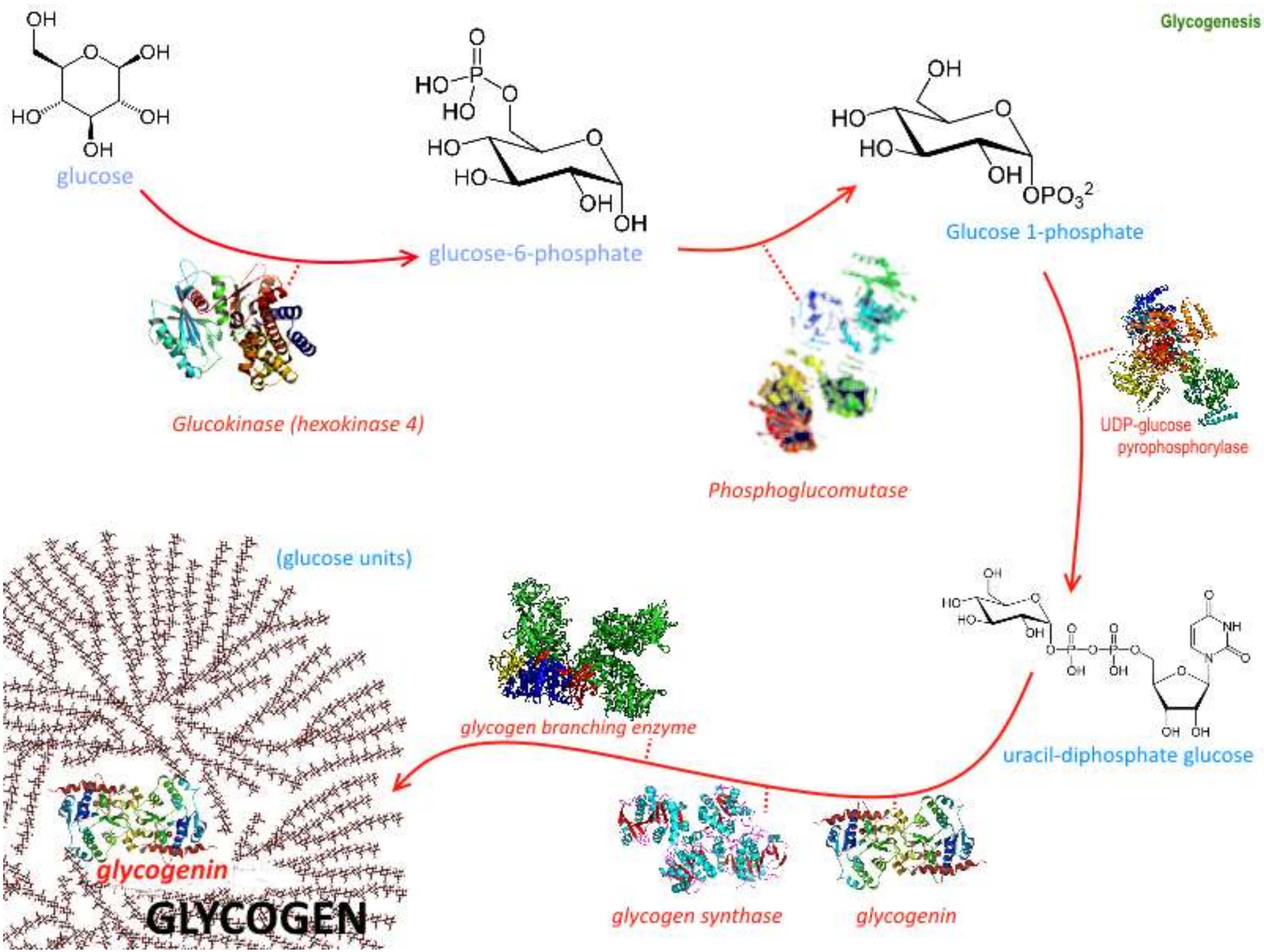
**Once a chain of eight glucose monomers is formed, glycogen synthase binds to the growing glycogen chain and adds UDP-glucose to the 4-hydroxyl group of the glucosyl residue on the non-reducing end of the glycogen chain, forming more α(1→4) glycosidic linkages in the process.**

**Branches are made by glycogen branching enzyme (also known as amylo-α(1:4)→α(1:6)transglycosylase), which transfers the end of the chain onto an earlier part via α-1:6 glycosidic bond, forming branches, which further grow by addition of more α-1:4 glycosidic units**

# Glycogen Synthesis



# Glycogen Synthesis



# Control and regulations Glycogenesis

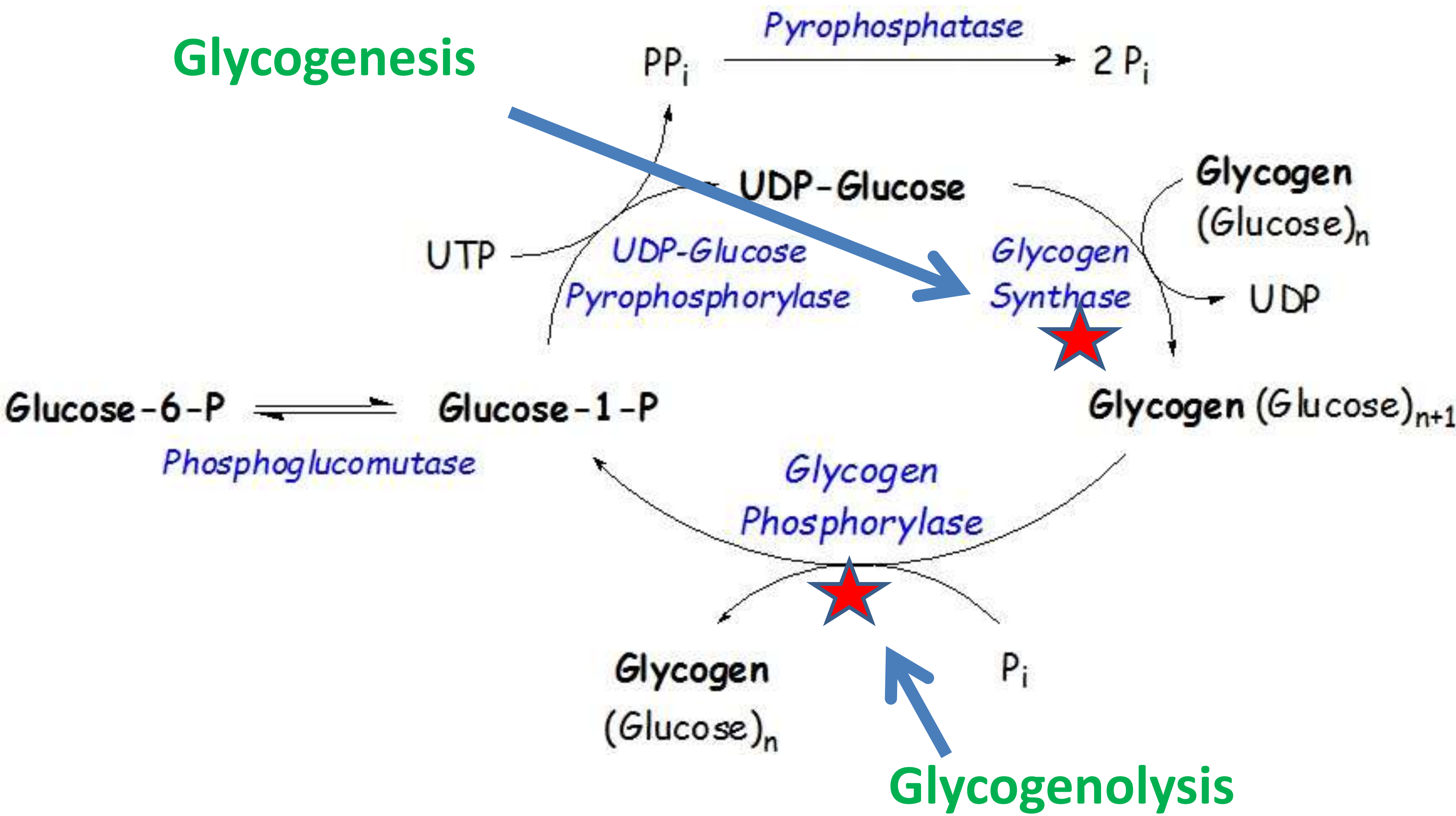
Glycogenesis responds to hormonal control.

One of the main forms of control is the varied phosphorylation of glycogen synthase and glycogen phosphorylase.

This is regulated by enzymes under the control of hormonal activity, which is in turn regulated by many factors.

As such, there are many different possible effectors when compared to allosteric systems of regulation.

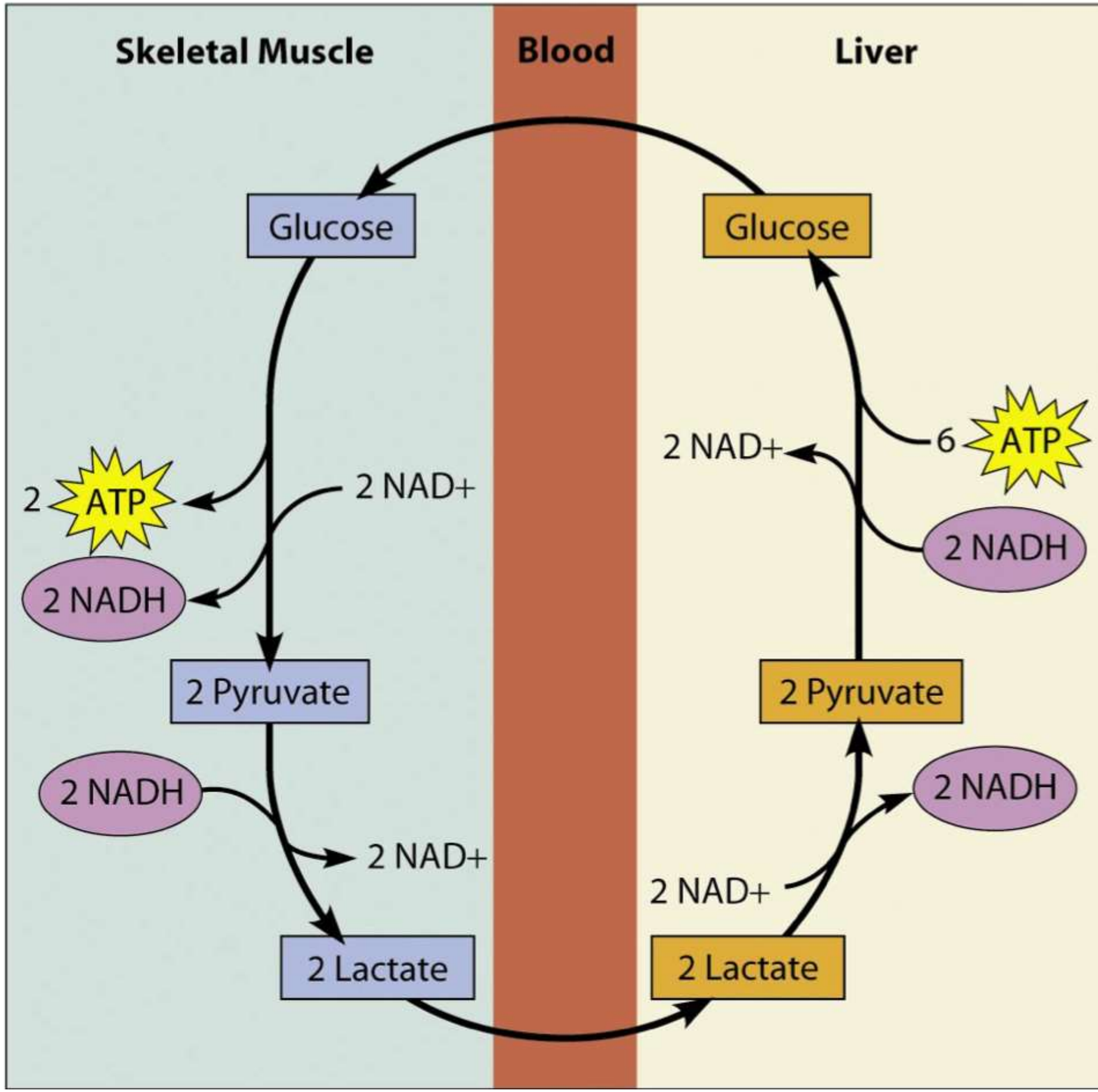
# Control and regulations  Glycogenesis



# The Cori Cycle

The Cori cycle (also known as the Lactic acid cycle), refers to the metabolic pathway in which lactate produced by anaerobic glycolysis in the muscles moves to the liver and is converted to glucose, which then returns to the muscles and is cyclically metabolized back to lactate

If muscle activity has stopped, the glucose is used to replenish the supplies of glycogen through glycogenesis.



# Control and regulations Glycogenesis

## Epinephrine (adrenaline)

**Glycogen phosphorylase is activated by phosphorylation, whereas glycogen synthase is inhibited.**

**Glycogen phosphorylase is converted from its less active "b" form to an active "a" form by the enzyme phosphorylase kinase.**

**This latter enzyme is itself activated by protein kinase A and deactivated by phosphoprotein phosphatase-1.**

# Epinephrine (adrenaline)

**Protein kinase A itself is activated by the hormone adrenaline.**

**Epinephrine binds to a receptor protein that activates adenylate cyclase.**

**The latter enzyme causes the formation of cyclic AMP from ATP; two molecules of cyclic AMP bind to the regulatory subunit of protein kinase A, which activates it allowing the catalytic subunit of protein kinase A to dissociate from the assembly and to phosphorylate other proteins.**

# Epinephrine (adrenaline)

.

**The less active "b" form glycogen phosphorylase, can itself be activated without the conformational change.**

**5'AMP acts as an allosteric activator, whereas ATP is an inhibitor, as already seen with phosphofructokinase control, helping to change the rate of flux in response to energy demand.**

**Epinephrine not only activates glycogen phosphorylase but also inhibits glycogen synthase.**

**This amplifies the effect of activating glycogen phosphorylase. This inhibition is achieved by a similar mechanism, as protein kinase A acts to phosphorylate the enzyme, which lowers activity.**

**This is known as co-ordinate reciprocal control.**

# Calcium ions

**Calcium ions or cyclic AMP (cAMP) act as secondary messengers.**

**This is an example of negative control.**

**The calcium ions activate phosphorylase kinase.**

**This activates glycogen phosphorylase and inhibits glycogen synthase.**

# Glycogenolysis

**Glycogenolysis is the breakdown of glycogen (n) to glucose-1-phosphate and glycogen (n-1). Glycogen branches are catabolized by the sequential removal of glucose monomers via phosphorolysis, by the enzyme glycogen phosphorylase.**

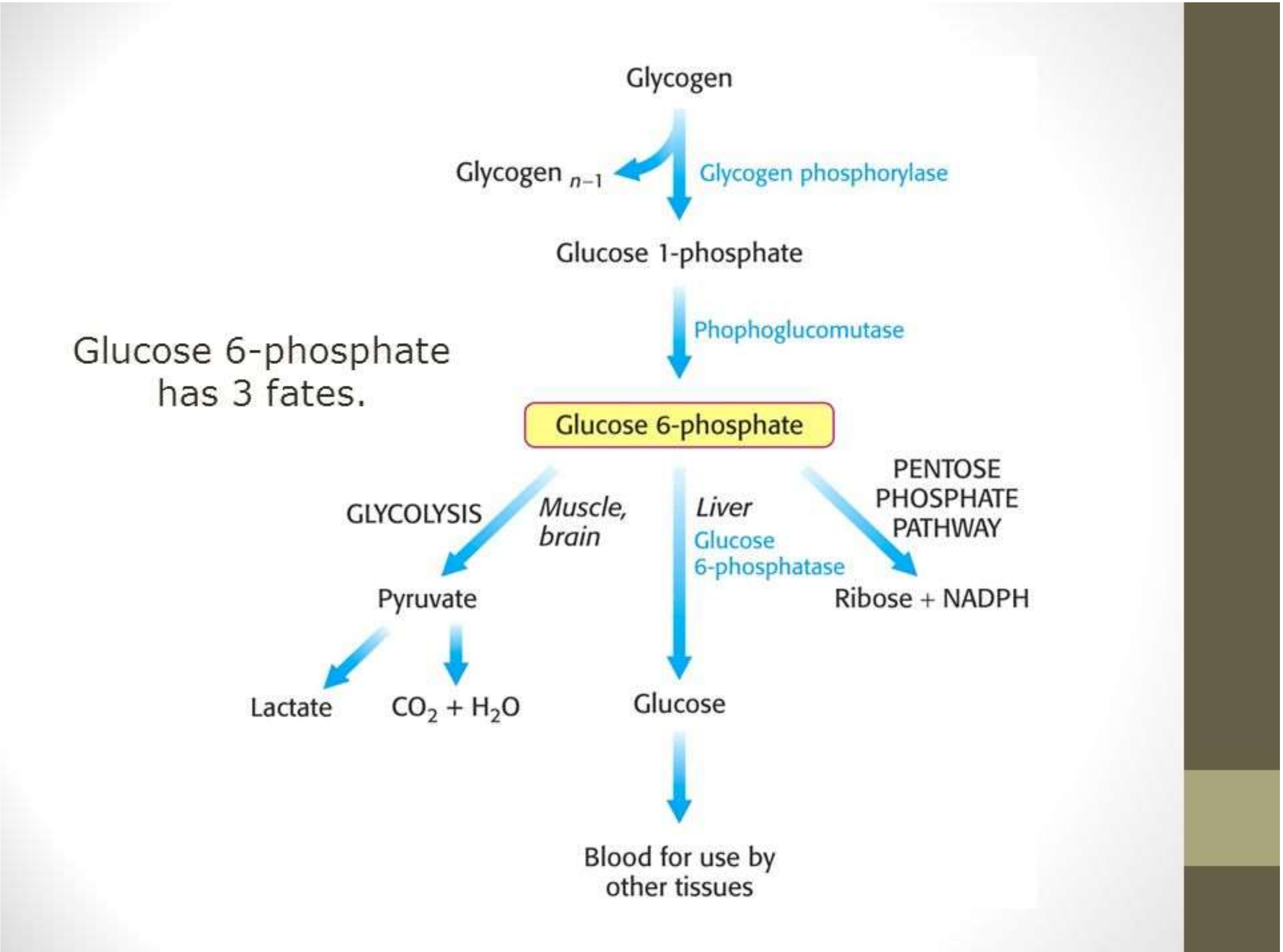
**The overall reaction for the breakdown of glycogen to glucose-1-phosphate is:**

$$\text{glycogen}_{(n\ \text{residues})} + P_i \rightleftharpoons \text{glycogen}_{(n-1\ \text{residues})} + \text{glucose-1-phosphate}$$

**Here, glycogen phosphorylase cleaves the bond linking a terminal glucose residue to a glycogen branch by substitution of a phosphoryl group for the α[1→4] linkage.**

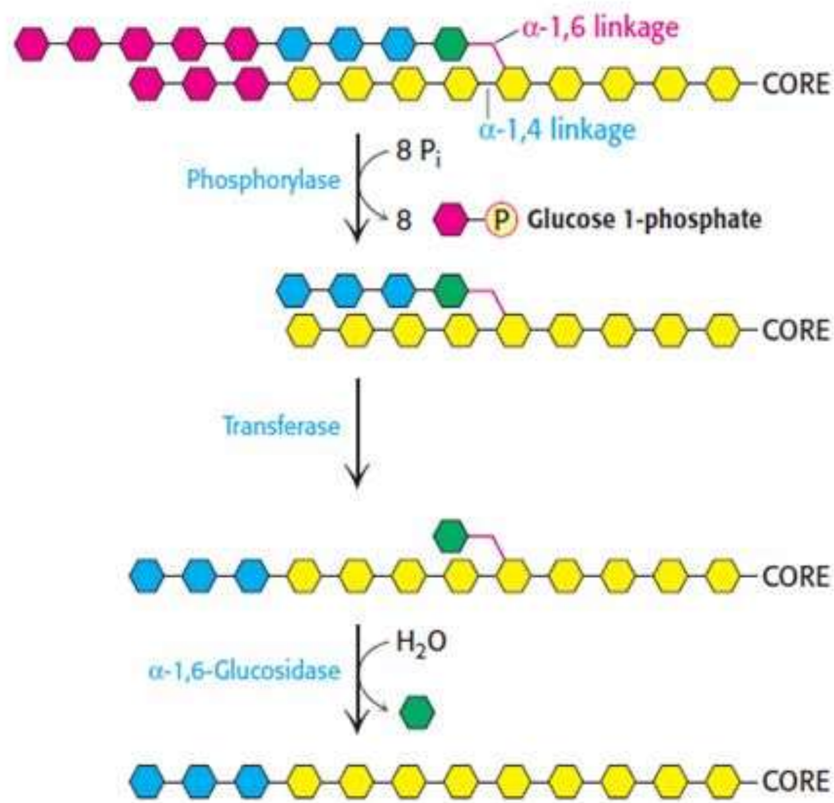
**Glucose-1-phosphate is converted to glucose-6-phosphate (an intermediate of glycolysis) by the enzyme phosphoglucomutase.**

# Three fates of Glucose 6-Phosphate

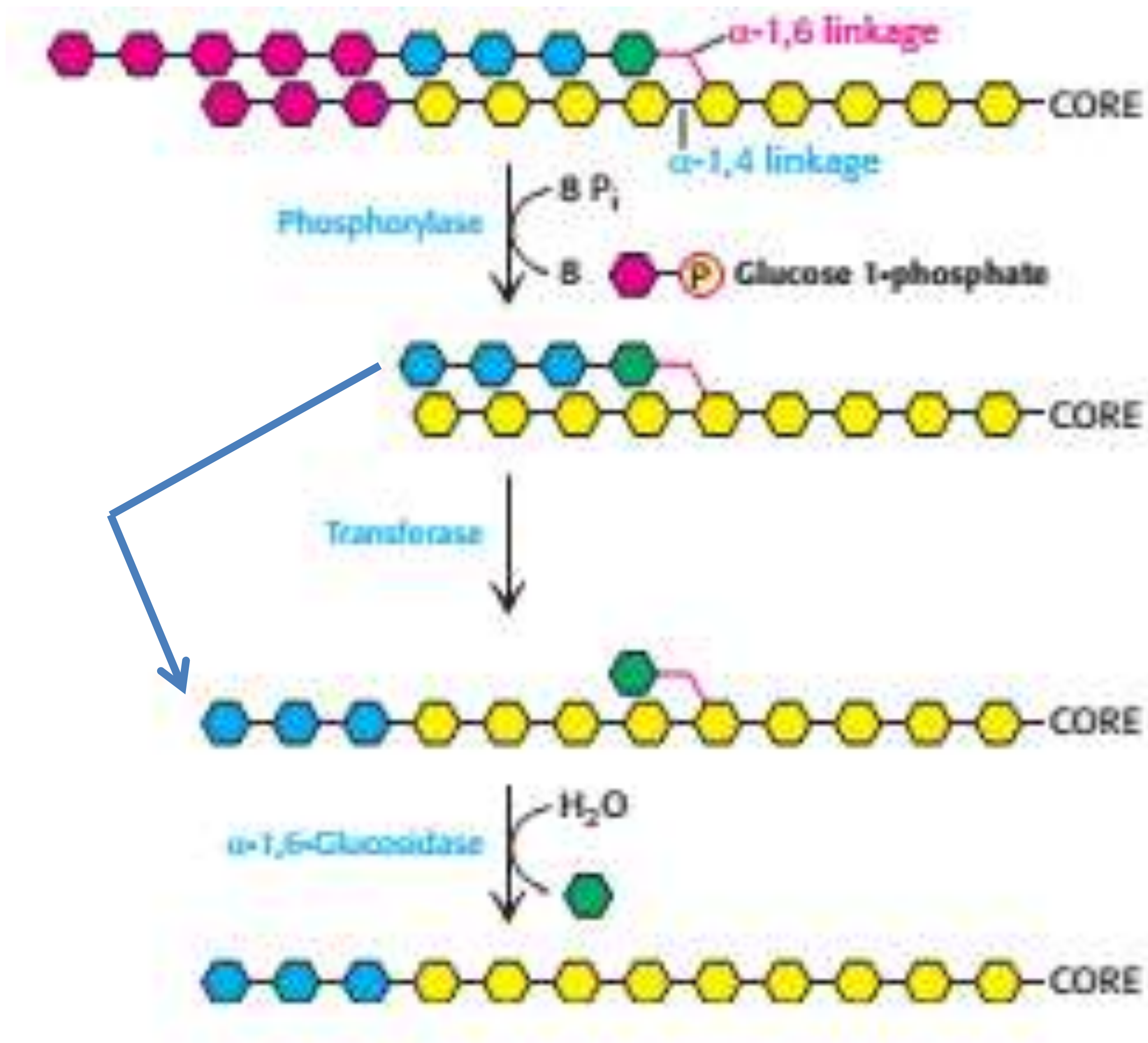


# Catabolism - Glycogenolysis

- **Glycogen phosphorylase** removes glucosyl unit from non-reducing end by phosphorylysis (releases glucose-1-phosphate)
- **Debranching enzyme** (transferase activity) moves 3 glucose units to another branch; hydrolyzes α-1,6 linkage with glucosidase function (same polypeptide chain for eukaryotes)



# Steps of Glycogenolysis



# Regulations  Glycogenolysis

Glycogenolysis is regulated hormonally in response to blood sugar levels by glucagon and insulin, and stimulated by epinephrine .

In myocytes, glycogen degradation may also be stimulated by neural signals.

Insulin lowers blood sugar level whereas glucagon and other hormones elevate  it.

# Limit Dextrin

**The highly branched core that remains( limiting) after exhaustive treatment of amylopectin or glycogen with *α*- and/or *β*-amylases.**

**It is formed because these enzymes cannot hydrolyse the (1→6) glycosidic linkages present.**

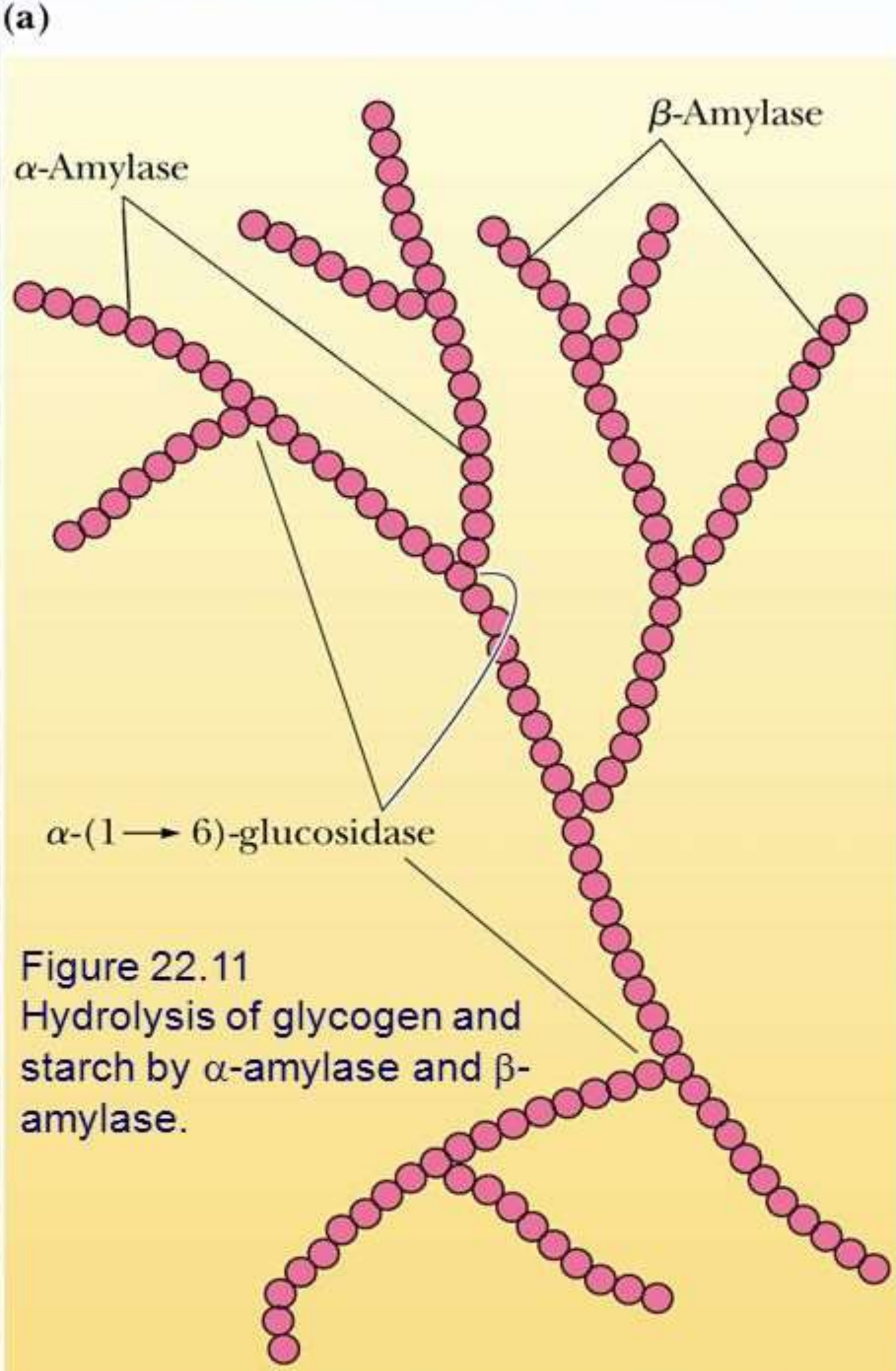



Figure 22.11
Hydrolysis of glycogen and starch by α-amylase and β-amylase.

- α-Amylase can cleave on either side of a branch point
- But activity is reduced near the branch points and stops four residues from any branch point
- limit dextrins

# Thank You

*Nilansu Das*

**Dept. of Molecular Biology**

**Surendranath College**