BIOCHEMISTY

Course No.-DTC-111, Credit Hours – 2 (1+1)

GLYCOGEN
DEGRADATION AND SYNTHESIS

BINITA RANI
ASSOCIATE PROFESSOR (DAIRY CHEMISTRY)
FACULTY OF DAIRY TECHNOLOGY
S.G.I.D.T., BVC CAMPUS,
P.O.- BVC, DIST.-PATNA-800014

• **Glycogen** => polymer of **glucose** linked => **α 1-4** glycosidic bonds with branches every 10 residues or so => **α 1-6** glycosidic bonds => **energy reserve** => the body.

• Two main **storage sites** => **liver** and **muscle** => stored as granules in **cytosol**. **Granules** => glycogen , enzymes and regulatory proteins => required for **glycogen degradation and synthesis**.

• **Glycogen metabolism** => important => **blood glucose** level => maintained between meals (via glycogen stores in liver) & provides an energy reserve => **muscular** activity.

•Maintenance of blood glucose => essential => **brain** => uses only glucose.

Glycogen Degradation

- **Two enzymes** : **Glycogen phosphorylase** & **Glycogen debranching enzyme**.
- **1.Glycogen phosphorylase** => **α1-4** branches => **remove=>** glucose resides => > 5**residues** from a **branchpoint**.

Glycogen **phosphorylase**

- **Glycogen & inorganic phosphate** (Pi) ==========➔ **glucose 1-phosphate**.
- The (**reversible**) reaction is as follows:

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

- 2. **Glycogen-debranching enzyme** => **α1-6** branches

phosphoglucomutase

- **Glucose 1-phosphate** ==========> **Glucose 6-phosphate**

$$glucose\ 1-phosphate \rightleftharpoons glucose\ 6-phosphate$$

- Fate of the **glucose 6-phosphate** depends on the **tissue**.
  - **Liver**

glucose 6-phosphatase

  - **glucose 6-phosphate** ==========> **glucose** => diffuses out => bloodstream => maintain => blood glucose concentration:

$$glucose\ 6-phosphate + H_2O \rightarrow glucose + P_i$$

  - **Muscle**
  - Glucose 6-phosphate => **glycolysis** => produce **energy quickly**

  - **Doesn't contain** glucose 6-phosphatase.

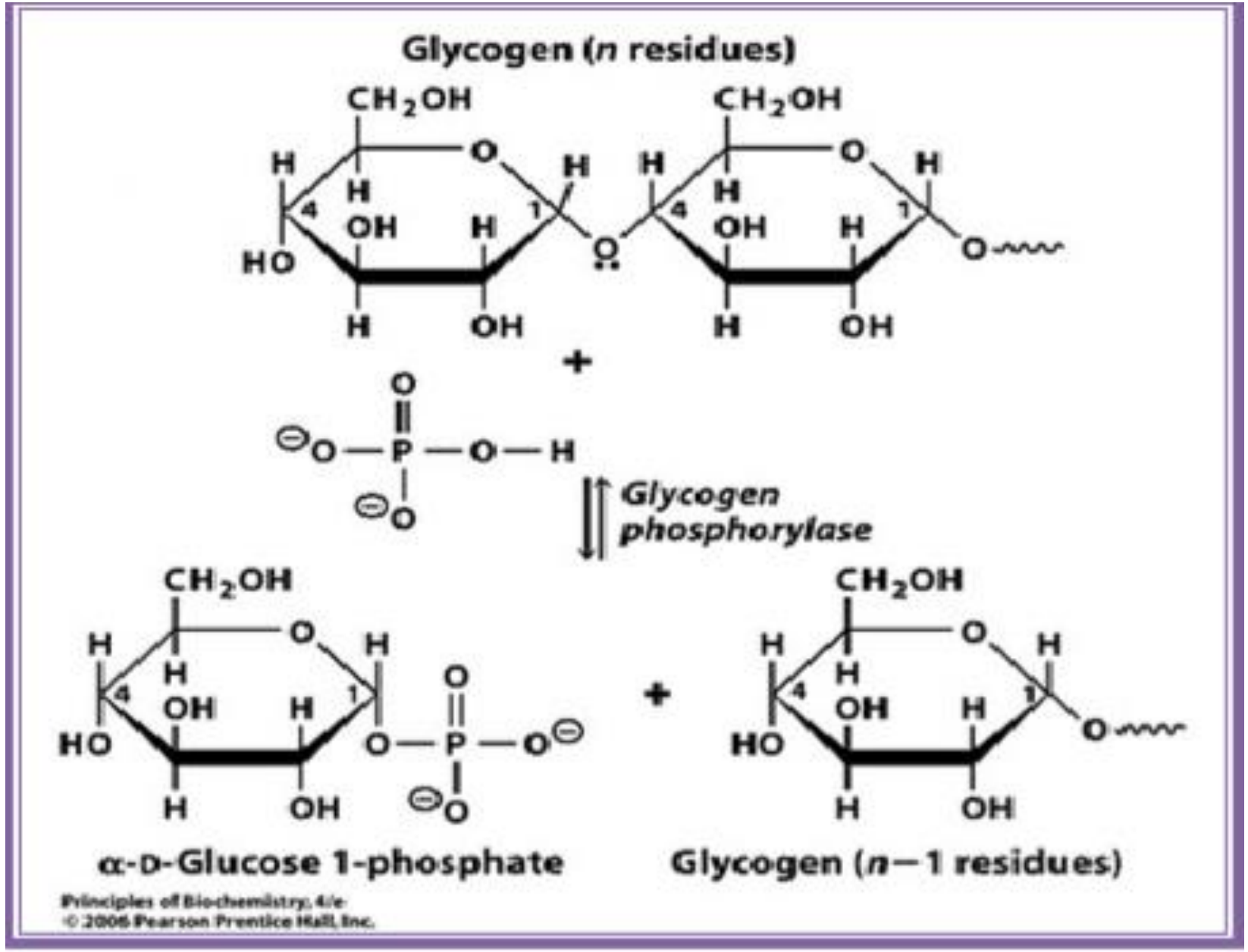
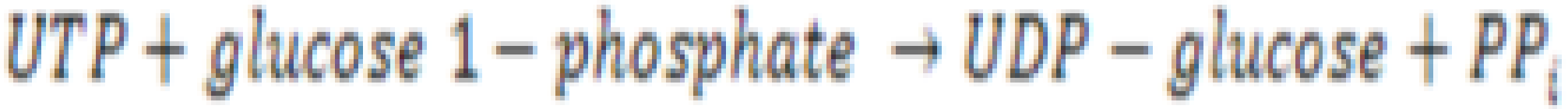


Fig. 19.1 Glycogen degradation

Glycogen Synthesis

Three enzymes are needed to synthesize glycogen:

1. **UDP –glucose pyrophosphorylase** => synthesis of **UDP-glucose** from UTP and glucose 1phosphate:



Pyrophosphate (PPi) => hydrolyzed by inorganic **pyrophosphatase** => releasing energy .

Overall reaction => highly exergonic & essentially irreversible.

2. Glycogen synthase

Transfers => glycosyl residue => UDP-glucose to => **C4 OH** group -- at nonreducing end of glycogen molecule => forming an **α1-4 glycosidic bond**.

- Only **extend** => existing chain => needs a **primer** (protein) called **glycogenin** => contains **eight glucosyl units** linked via **α1-4** linkages => added to protein by itself (i.e. autocatalysis) => **It is this molecule that glycogen synthase => extends**.
- **Each glycogen granule** contains => only **a single glycogenin molecule** at its core.
- Glycogen synthase is **fully active** => only when in contact with glycogenin .

3. **Branching enzyme [amylo-(1-4→1-6) transglycosylase**

After formation of a long straight chain (α1-4 linkages) => branching enzyme => breaks one of the α1-4 bonds => transfers a block of residues (**about seven**) => **a more interior site =>** in the glycogen molecule => **reattaching** these by creating an **α1-6 bond**.

- Branches are important => because enzymes => degrade and synthesize glycogen => only at the ends of the molecule.

- **Existence of many termini =>** allows rapid rate of synthesis and degradation

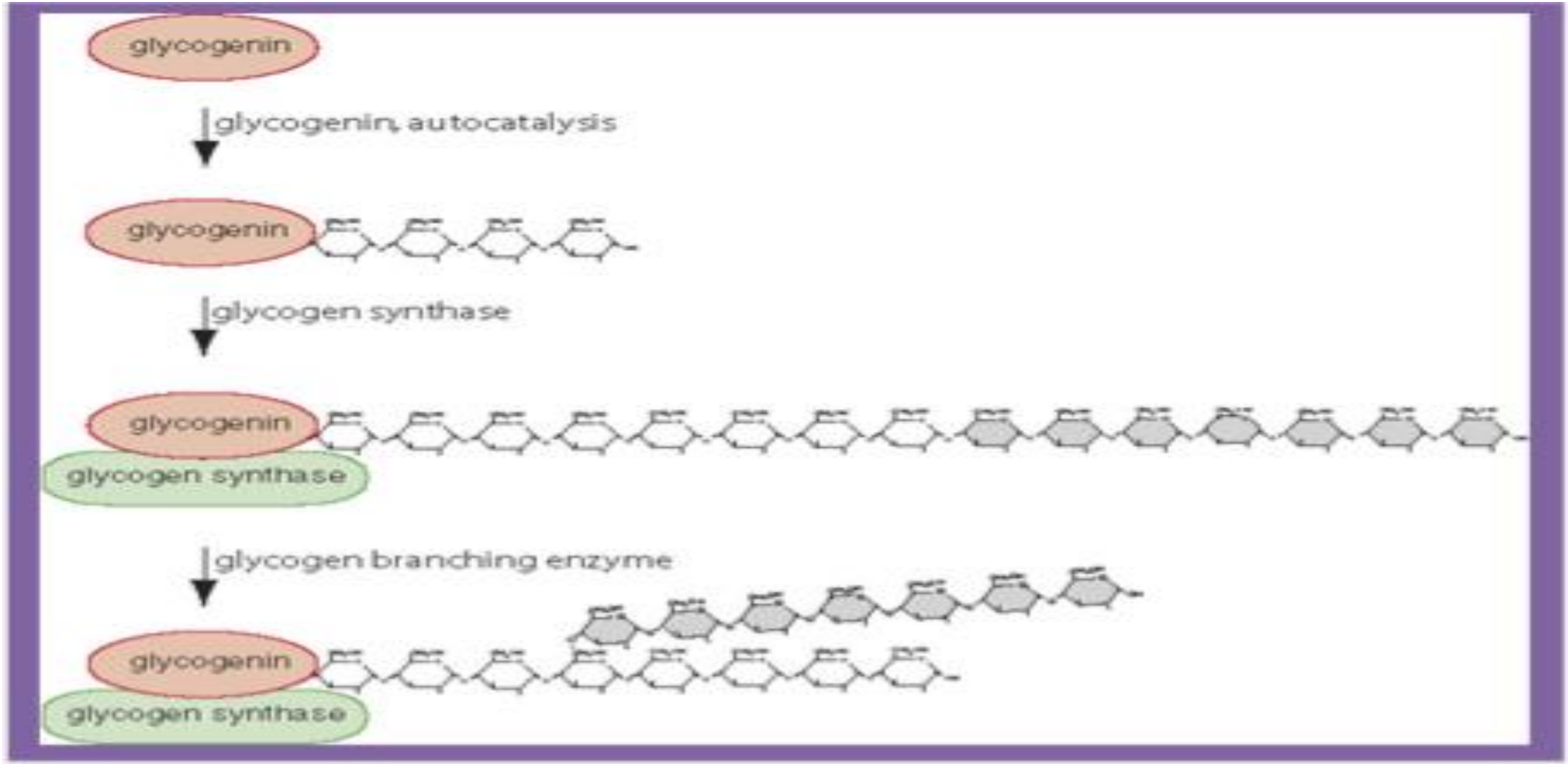


Fig. 19.2 Glycogen Synthesis

Control of Glycogen Metabolism

Glycogen degradation and glycogen synthesis => controlled both by **allosteric regulation** , **covalent** and by **hormonal control.**

Allosteric control and covalent modification

• **Phosphorylase** exists in phosphorylated **active a form** & dephosphorylated normally **inactive b form** => **interconverted** by **phosphorylase kinase** and **protein phosphatase I**.

• **muscle** : phosphorylase b is **activated** <= **high concentrations of AMP** generated <= exercise and => **degrades glycogen**, **but** AMP stimulation is **opposed** by **high concentrations of ATP & glucose 6-phosphate** so, enzyme => **inactive** in resting muscle.

• **liver** : **phosphorylase b** is not responsive to AMP but

phosphorylase a is **deactivated** by **glucose .**

➢ **Only when glucose levels are low => Glucose production from glycogen occurs**.

• Conversely to **phosphorylase** , **glycogen synthase** exists as => **phosphorylated inactive b form** & **dephosphorylated active a form**.

Hormonal control by epinephrine and glucagon

•**Epinephrine** (adrenaline) stimulates **glycogen degradation** in **muscle**.
• **Epinephrine and glucagon** stimulate **glycogen degradation** in **liver**.
•Hormone binds => plasma membrane receptor => activates **adenylate cyclase** via a G protein => synthesizes cAMP from ATP => activates **protein kinase A** => phosphorylates => **phosphorylase kinase** => convert **inactive phosphorylase b => active phosphorylase a**

•Same active **protein kinase A inactivates glycogen synthase** by phosphorylation, converting **active glycogen synthase a** => **glycogen synthase b**.

• **When hormone levels fall, stimulation of glycogen degradation is turned off by**
degradation of cAMP to 5'AMP => by phosphodiesterase and
dephosphorylation of phosphorylated forms of phosphorylase and synthase by
proteinphosphatase I.

Insulin

- Released => bloodstream when blood glucose concentration is **high** => stimulates **glycogen synthesis**.

- It binds & activates a receptor **protein kinase** in the plasma membrane of target cells => activation of an insulin-responsive **protein kinase** => activates **protein phosphatase I** by phosphorylation => ensures that **phosphorylase and glycogen synthase** are dephosphorylated => **inhibiting glycogen degradation** and **activating glycogen synthesis.**