Glycogen metabolism

ANSC/FSTC 607
Physiology and Biochemistry of Muscle as a Food
GLYCOGEN METABOLISM

I. Distribution of glycogen

A. Liver
   1. Contains up to 6% glycogen.
   2. Provides glucose for systemic metabolism.

B. Muscle
   1. Rarely exceeds 1% (very consistent).
   2. Because of muscle mass, muscle contains three to four times as much glycogen as liver.

II. Overview of glycogen metabolism

![Diagram of glycogen metabolism]
III. Glycogen synthesis

A. Reactions

\[
\begin{align*}
G-6-P & \xrightarrow{\text{phosphoglucomutase}} G-1-P \\
G-1-P + UTP & \xrightarrow{\text{G-1-P uridyltransferase}} \text{UDP-glucose + PP}_i \\
\text{UDP-glucose + glycogen} & \xrightarrow{\text{glycogen synthase}} \text{UDP + glycogen}_{n+1}
\end{align*}
\]

B. Glycogen branching

1. Structure of glycogen
   a. Backbone consists of \(\alpha-1,4\) glycosidic linkages.
   b. Branchpoints consist of \(\alpha-1,6\) glycosidic linkages.
2. Mechanism of branching
   a. 11 α-1,4 glycoside residues are added to a chain.
   b. The terminal six residues are transferred to an adjacent chain in a α-1,6 glycosidic linkage.

![Diagram of glycogen metabolism](image1.png)

**Figure 20-3.** The biosynthesis of glycogen. The mechanism of branching as revealed by adding $^{14}C$-labeled glucose to the diet in the living animal and examining the liver glycogen at further intervals.

![Diagram of glycogen structure](image2.png)

**Figure 11.3**
Branched structure of glycogen, showing α-1,4 and α-1,6 linkages.
C. Regulation of glycogen synthesis

1. Phosphorylation of glycogen synthase via epinephrine
   a. GSK\(_1\) (cAMP-dependent protein kinase) phosphorylates serine residues.
   b. GSK\(_2\) (phosphorylase kinase) phosphorylates serine residues.
   c. GSK\(_3\) (glycogen synthase-specific kinase) phosphorylates serine residues.

2. Action of insulin
   a. Stimulates phosphatases.
   b. Provides G-6-P, which provides substrate.
D. Role of glycogenin

1. Binds glucose residues
2. Serves as primer for glycogen synthesis.
3. Catalyzes synthesis of initial glycogen polymer: 8 residues are condensed, after which glycogen synthase extends the molecule.
4. Forms the core of the β-particle (55,000 glucose residues).
5. Cross-sectional view of glycogen
V. Glycogen degradation

A. cAMP binds with regulatory subunit of protein kinase, frees catalytic subunit.

B. Catalytic subunits (protein kinase A) phosphorylate phosphorylase kinase.

C. Phosphorylase kinase phosphorylates glycogen phosphorylase.

D. Glycogen phosphorylase adds phosphate groups to the 1-carbon of glucosyl residues of glycogen, producing G1P.

E. This reaction also produces free glucose at branch points.
IV. Regulation of glycogen degradation

A. Phosphorylase$_b$ activity modulated by:
   1. P$_i$, AMP/IMP activate
   2. ATP, G6P inhibit

B. Phosphorylase$_a$ activity modulated by glucose (inhibits).

C. Phosphorylase kinase activity regulated by calcium.
   1. Concentration required for activation of phosphorylase kinase is lower for the phosphorylated form.
   2. Concentration of calcium required for activation of phosphorylase kinase is that which yields half-maximal stimulation of myosin ATPase.
**Glycogen metabolism**

**In muscle:** Epinephrine binds to surface receptor.

**In liver:** Glucagon binds to surface receptor.

ATP $\xrightarrow{\text{adenylate cyclase}}$ cAMP + PP$_i$

CH$_3$OH

Phosphorylase $b$ kinase (inactive)

ATP $\xrightarrow{\text{CAMP-dependent protein kinase}}$ ADP

CH$_3$O

Phosphorylase $b$ kinase (active)

OH

CH$_2$

2ATP $\xrightarrow{\text{phosphorylase b kinase}}$ 2ADP

CH$_2$

Phosphorylase $b$ (less active)

OH

CH$_2$

 Increased glycogen breakdown provides fuel (glucose-1-phosphate)

**In muscle:** Glucose enters the glycolytic pathway.

**In liver:** Glucose is released into blood.