

# Glycogen Synthesis

Chapter 25, Stryer Short Course

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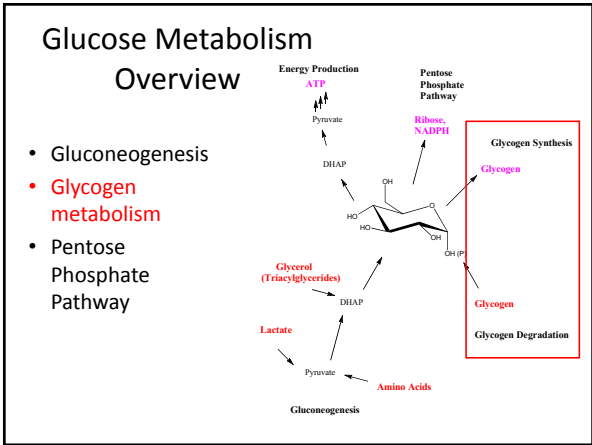
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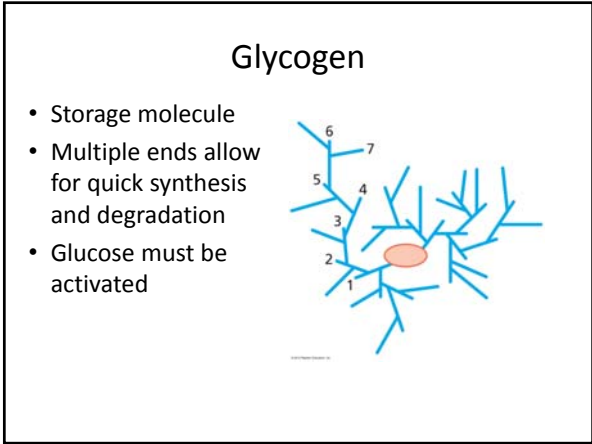
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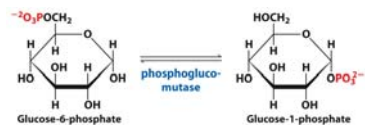
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### Chemistry of Synthesis

- Step 1



- Near equilibrium
- The link to glucose-6-phosphate, our central molecule

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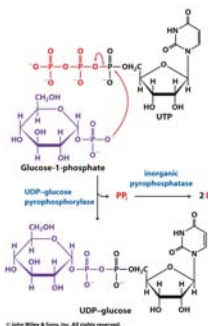
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### Chemistry of Synthesis

- Step 2
- Count high energy bonds
- Pyrophosphatase
  - Common motif
- UDP-glucose: activated for incorporation




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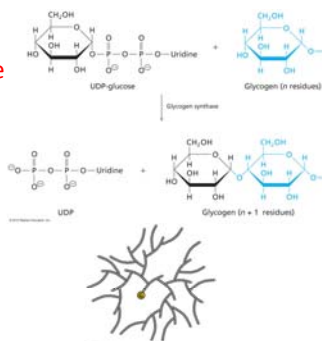
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### Chemistry of Synthesis

- Step 3
- Glycogen synthase
- Growing end is non-reducing
- Must be added to core
- UDP released




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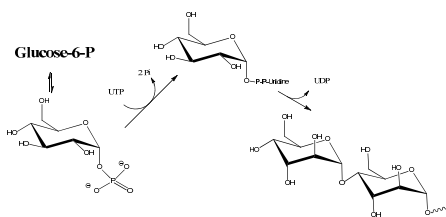
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### Energetics of Synthesis

- Total cost: one ATP equivalent from G-6-p




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### Step 4: Branching

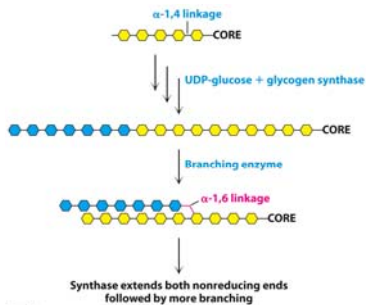


Figure 20.2  
Biochemistry of Plant Growth, Third Edition  
© 2010 Wiley-Blackwell

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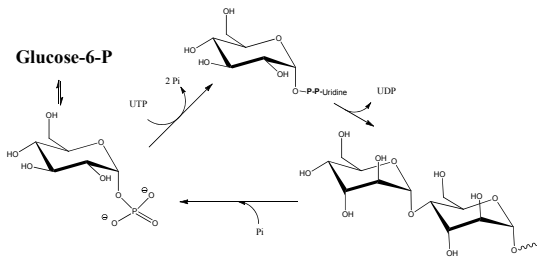
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### Overall Energetics



Glucose → glycogen costs 2 ATP per stored glucose

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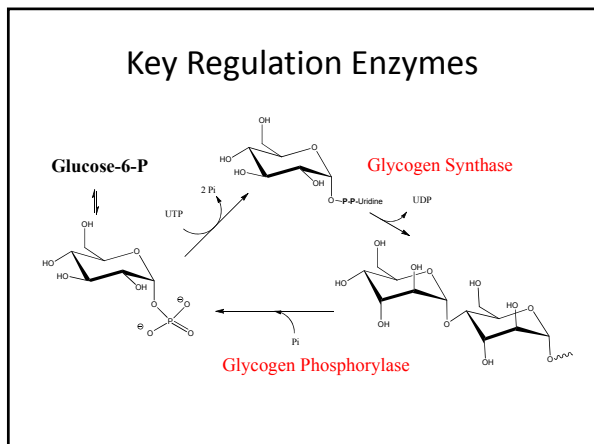
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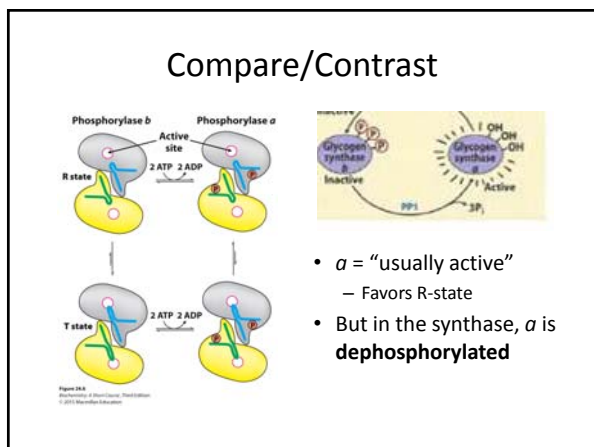
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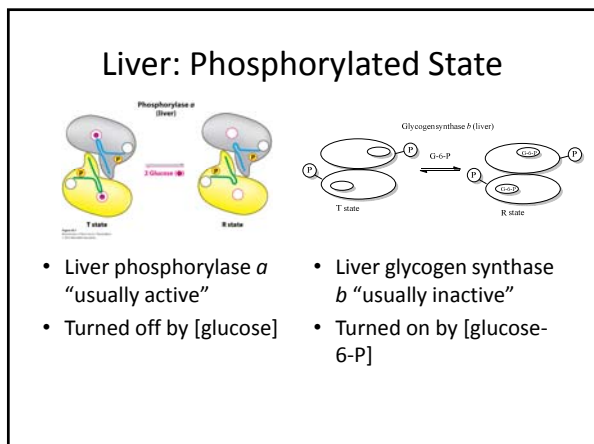
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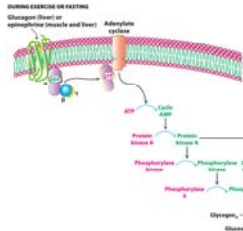
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## Reciprocal Regulation



- Epinephrine turns on phosphorylase
  - PKA phosphorylation
- Epinephrine turns off glycogen synthase
  - PKA phosphorylation

Figure 23.3  
Biochemistry of the Cell, 7th Edition  
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## Protein Phosphatase 1

- Opposite of PKA
  - Deactivates phosphorylase
  - Activates glycogen synthase
- Active in cell unless epinephrine signals PKA
  - PKA activates its inhibitors

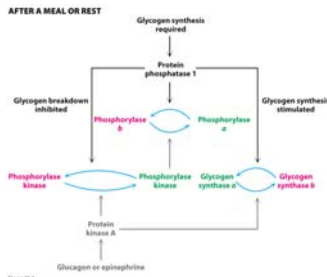


Figure 23.4  
Biochemistry of the Cell, 7th Edition  
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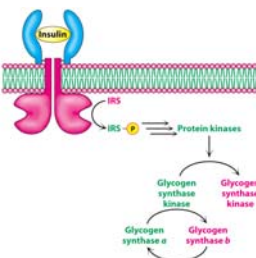
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## Insulin stimulates glycogen synthesis



- Insulin blocks the “turn off” switch for glycogen synthase
- Allows PP1 to “turn on” glycogen synthase

Figure 23.6  
Biochemistry of the Cell, 7th Edition  
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## Glucose stimulates glycogen synthesis

- Insulin is main stimulating signal
- Blood glucose level also controls glycogen
  - First, phosphorylase turned off
  - Then synthase turned on
  - No wasted overlap
  - Mechanism?

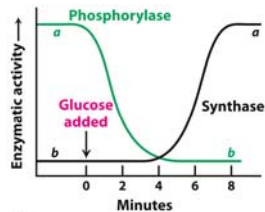


Figure 21-17 Molecular Biology of the Cell, 6th Edition © Garland Science 2015

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## Phosphorylase $\alpha$ is Glucose Sensor

- Phosphorylase  $\alpha$  (R state) binds and inactivates PP1
- When [glucose] up, PP1 is released and deactivates phosphorylase
- Only when all phosphorylase  $\alpha$  has been inactivated is PP1 available to activate glycogen synthase

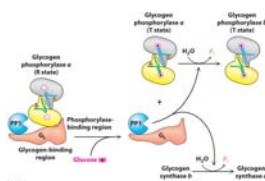


Figure 21-18 Molecular Biology of the Cell, 6th Edition © Garland Science 2015

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## Glycogen Storage Diseases

Table 23-1 Glycogen storage diseases

Type	Defective enzyme	Organ affected	Glycogen in the affected organ	Clinical features
I	von Gierke disease Glucose 6-phosphatase or transport system	Liver and kidney	Increased amount; normal structure	Muscle enlargement of the liver; failure to thrive; severe hypoglycemia; ketosis; hepatomegaly; hypophosphatemia.
II	Pompe disease $\alpha$ -1,4-glucosidase (lysosomal)	All organs	Muscle increase in amount; normal structure	Cardiorespiratory failure causes death, usually before age 2.
III	Cori disease $\alpha$ -1,6-glucosidase (branching enzyme)	Muscle and liver	Increased amount; short outer branches	Like type I, but milder course.
IV	Anderson disease Branching enzyme (or 1,4 $\alpha$ -D-glucanase)	Liver and spleen	Normal amount; very long outer branches	Progressive cirrhosis of the liver; liver failure causes death, usually before age 2.
V	McArdle disease Phosphorylase	Muscle	Moderately increased amount; normal structure	Limited ability to perform strenuous exercise because of painful muscle cramps. Diabetic patient is normal and well developed.
VI	Hers disease Phosphorylase	Liver	Increased amount	Like type I, but milder course.
VII	Phosphofruktokinase	Muscle	Increased amount; normal structure	Like type V.
VIII	Phosphorylase kinase	Liver	Increased amount; normal structure	Mild liver enlargement; mild hypoglycemia.

Note: Types I through VII are inherited as autosomal recessives; Type VIII is sex linked.

Table 23.1  
Biochemistry of the Cell, 3rd Edition  
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Many disrupt glycogen breakdown in muscle and/or liver (hypoglycemia, enlarged liver, muscle cramps...)

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