Biochemistry of Carbohydrates
Part I

Dr. Kevin Ahern
Biochemistry of Carbohydrates

Glucose
- 2 ATP
- 4 ATP
- 2 NAD⁺
- 2 NADH

2 Pyruvate

Aerobic Oxidation

Anaerobic Fermentation (Yeast/Bacteria)
- 2 NADH
- 2 NAD⁺
- 2 CO₂ + 2 Ethanol

Anaerobic Fermentation (Animals)
- 2 NADH
- 2 NAD⁺
- 2 Lactate

Citric Acid Cycle

Oxidative Phosphorylation
- 2 NADH + 6 O₂ + 30-38 ADP
- 2 NAD⁺ + 30-38 ATP

6 CO₂ + 6 H₂O
Glycolysis

• The Breakdown of Glucose
Glycolysis
• The Breakdown of Glucose

• Primary Energy Source of Cells
Glycolysis
• The Breakdown of Glucose

• Primary Energy Source of Cells
• Central Metabolic Pathway
Glycolysis
- The Breakdown of Glucose
- Primary Energy Source of Cells
- Central Metabolic Pathway
- All Reactions Occur in Cytoplasm
Glycolysis
- The Breakdown of Glucose

- Primary Energy Source of Cells
- Central Metabolic Pathway
- All Reactions Occur in Cytoplasm
- Two Phases

Phase 1
ATP Investment

1. **Glucose (GLU)**
   - ATP $\rightarrow$ ADP

2. **Glucose-6-phosphate (G6P)**
   - ATP $\rightarrow$ ADP

3. **Fructose-6-phosphate (F6P)**
   - ATP $\rightarrow$ ADP

4. **Dihydroxyacetone phosphate (DHAP)**

5. **Fructose-1,6-bisphosphate (F6P)**
   - ATP $\rightarrow$ ADP

6. **Glycereraldehyde-3-phosphate (GA3P)**

7. **1,3-bisphosphoglycerate (1,3BPG)**

8. **3-Phosphoglycerate (3-PG)**

9. **2-Phosphoglycerate (2-PG)**

10. **Phosphoenolpyruvate (PEP)**

11. **Pyruvate (PYR)**

- Two Phases
Glycolysis

- The Breakdown of Glucose

- Primary Energy Source of Cells
- Central Metabolic Pathway
- All Reactions Occur in Cytoplasm
- Two Phases

Phase 1
ATP Investment

Phase 2
Energy Production

Glycolysis

- ATP Investment
- Energy Production

Reactions:
- Glucose to Fructose-6-phosphate
- ATP Investment
- Energy Production
- Formation of NADH
- Formation of ATP
- Conversion of Pyruvate to Lactate

Chemical Equations:

1. Glucose (GLU) + 2 ADP → 2 ATP + 2 F6P
2. F6P + ADP → ATP + DHAP
3. DHAP + G6P → 2 GA3P
4. 2 GA3P + 2 NAD+ → 2 NADH + 2 1,3-BPG
5. 2 1,3-BPG + 2 ADP → 2 ATP + 2 3-PG
6. 2 3-PG → 2 2-PG
7. 2 2-PG → 2 PEP + 2 ADP
8. 2 PEP → 2 Pyruvate (PYR) + 2 ATP

Products:
- ATP
- NADH
- Pyruvate
**Glycolysis**
- The Breakdown of Glucose

- Primary Energy Source of Cells
- Central Metabolic Pathway
- All Reactions Occur in Cytoplasm
- Two Phases
- Produces 2 Pyruvates, 2 ATP, 2 NADH
Glycolysis

- Glucose
Glycolysis
• Glucose

• Stored in Polymers (Amylose/Amylopectin/Glycogen)
Glycolysis
• Glucose

• Stored in Polymers (Amylose/Amylopectin/Glycogen)
• Readily Released
Glycolysis
- Glucose

- Stored in Polymers (Amylose/Amylopectin/Glycogen)
- Readily Released
- Travels Easily in Blood
Glycolysis
• Glucose

• Stored in Polymers (Amylose/Amylopectin/Glycogen)
• Readily Released
• Travels Easily in Blood
• Made from Simple Precursors (Gluconeogenesis)
Glycolysis

• Phase 1

Glucose → Glucose-6-Phosphate (G6P)

Hexokinase

ATP → ADP + H+ with Mg++
Glycolysis

- Phase 1

Glucose → Glucose-6-Phosphate (G6P) via Hexokinase

Glucose + ATP → Glucose-6-Phosphate + ADP + H⁺
Glycolysis

• Phase 1

Glucose → Glucose-6-Phosphate (G6P)

Hexokinase

ATP

ADP + H⁺
Glycolysis

- Phase 1

- Regulated Step of Glycolysis

Glucose $\xrightarrow{\text{Hexokinase}}$ Glucose-6-Phosphate (G6P)
Glycolysis
• Phase 1

• Regulated Step of Glycolysis
• $\Delta G^\circ = -16.7 \text{ kJ/mol}$

Glucose $\rightarrow$ Glucose-6-Phosphate (G6P)

Hexokinase catalyzes the reaction, converting glucose to glucose-6-phosphate with the help of ATP and Mg$^{++}$. The reaction is regressed by the energy change $\Delta G^\circ = -16.7 \text{ kJ/mol}$. This step is crucial as it commits glucose to the glycolytic pathway and is regulated to control the flow of glucose into glycolysis.
Glycolysis
• Hexokinase
Glycolysis

- Hexokinase

- Found in Virtually All Cells
**Glycolysis**
- Hexokinase

- Found in Virtually All Cells
- Not Specific to Glucose
Glycolysis
• Hexokinase

- Found in Virtually All Cells
- Not Specific to Glucose
- Glucokinase - Higher $K_m$
Glycolysis

- Hexokinase

- Found in Virtually All Cells
- Not Specific to Glucose
- Glucokinase - Higher $K_m$
- Inhibited by G6P Product
Glycolysis

• Phase 1

Glucose-6-Phosphate (G6P)  \[ \overset{\text{Phosphoglucoisomerase}}{\leftrightarrow} \]  Fructose-6-Phosphate (F6P)

(G6P Isomerase)
Glycolysis
• Phase 1

Glucose-6-Phosphate (G6P)  \[ \text{Phosphoglucoisomerase} \]  Fructose-6-Phosphate (F6P)

Readily Reversible Reaction  \[ \Delta G^\circ = +1.7 \text{ kJ/mol} \]
Glycolysis

• Phase 1

Fructose-6-Phosphate (F6P) ➔ Fructose-1,6-Bisphosphate (F1,6BP)

Phosphofructokinase (PFK-1)

ATP \rightarrow ADP + H^+
**Glycolysis**

- Phase 1

Fructose-6-Phosphate (F6P) to Fructose-1,6-Bisphosphate (F1,6BP)

\[ \text{Fructose-6-Phosphate (F6P)} \xrightarrow{\text{Phosphofructokinase (PFK-1)}} \text{Fructose-1,6-Bisphosphate (F1,6BP)} \]

\[ \text{ATP} \xrightarrow{\text{Mg}^{2+}} \text{ADP} + \text{H}^+ \]
Glycolysis
• Phase 1

Fructose-6-Phosphate (F6P) → Phosphofructokinase → Fructose-1,6-Bisphosphate (F1,6BP)

Mechanism:
- Fructose-6-Phosphate (F6P) is converted to Fructose-1,6-Bisphosphate (F1,6BP) by the enzyme phosphofructokinase.
- The reaction requires ATP and is inhibited by high fructose-2,6-bisphosphate.

Chemical Structure: (Refer to the diagram for specific structures and reactions.)
**Glycolysis**
- Phase 1

- Important Regulatory Enzyme of Glycolysis

Fructose-6-Phosphate (F6P) \[ \text{Phosphofructokinase} \rightarrow \text{Fructose-1,6-Bisphosphate (F1,6BP)} \]

Fructose-6-Phosphate (F6P) \[ \text{ATP} \rightarrow \text{ADP} + \text{H}^+ \]
Glycolysis

- Phase 1

- Important Regulatory Enzyme of Glycolysis
- $\Delta G^\circ = -14.2 \text{ kJ/mol}$

Fructose-6-Phosphate (F6P)  Phosphofructokinase  Fructose-1,6-Bisphosphate (F1,6BP)
Glycolysis
- Phosphofructokinase
Glycolysis
• Phosphofructokinase

• AMP and Fructose 2,6 Bisphosphate Activate
Glycolysis

- Phosphofructokinase

- AMP and Fructose 2,6 Bisphosphate Activate
- ATP Inhibits
Glycolysis
- Phosphofructokinase

- AMP and Fructose 2,6 Bisphosphate Activate
- ATP Inhibits
- Two Binding Sites for ATP
**Glycolysis**
- Phase I

Fructose 1,6 Bisphosphate (F1,6 BP)

\[ \text{Aldolase} \]

Glyceraldehyde-3-Phosphate (GA3P)

Dihydroxyacetone Phosphate (DHAP)
**Glycolysis**
- Phase I

- $\Delta G^\circ = +23.9 \text{ kJ/mol}$

**Fructose 1,6 Bisphosphate (F1,6 BP)**

**Glyceraldehyde-3-Phosphate (GA3P)**

**Dihydroxyacetone Phosphate (DHAP)**

Diagram showing the aldolase-catalyzed reaction between Fructose 1,6 Bisphosphate and Glyceraldehyde-3-Phosphate to form Dihydroxyacetone Phosphate.
Glycolysis

• Aldolase Reaction

F1,6BP <=> GA3P + DHAP
**Glycolysis**
- Aldolase Reaction

**Energy Barrier**

\[ \Delta G = 23.9 + RT \ln \left( \frac{[\text{GA3P}][\text{DHAP}]}{[\text{F1,6BP}]} \right) \]
Glycolysis
• Aldolase Reaction

• Energy Barrier
• “Pushing”

\[ \Delta G = 23.9 + RT \ln \frac{[\text{GA3P}][\text{DHAP}]}{[\text{F1,6BP}]} \]

\[ \text{F1,6BP} \leftrightarrow \text{GA3P} + \text{DHAP} \]
Glycolysis

- Aldolase Reaction

- Energy Barrier
- “Pushing”
- “Pulling”

\[
\Delta G = 23.9 + RT \ln \left( \frac{[GA3P][DHAP]}{[F1,6BP]} \right)
\]

\[
\Delta G = 23.9 + RT \ln \left( \frac{[GA3P][DHAP]}{[F1,6BP]} \right)
\]

\[
\Delta G = 23.9 + RT \ln \left( \frac{[GA3P][DHAP]}{[F1,6BP]} \right)
\]

F1,6BP $\leftrightarrow$ GA3P + DHAP
Glycolysis

- Phase 2

Dihydroxyacetone Phosphate (DHAP) ➔ Glyceraldehyde-3-Phosphate (GA3P)
Glycolysis
• Phase 2

• Readily Reversible Reaction

Dihydroxyacetone Phosphate (DHAP)  Glyceraldehyde-3-Phosphate (GA3P)
Glycolysis

- Phase 2

- Readily Reversible Reaction
- \( \Delta G^\circ = 7.6 \text{ kJ/mol} \)

Dihydroxyacetone Phosphate (DHAP) → Glyceraldehyde-3-Phosphate (GA3P) via Triose Phosphate Isomerase
Glycolysis
• Phase 2

• Readily Reversible Reaction
• $\Delta G^{\circ'} = 7.6$ kJ/mol
• Diffusion-limited Enzyme

Dihydroxyacetone Phosphate (DHAP)  Glyceraldehyde-3-Phosphate (GA3P)
Glycolysis

- Phase 2

- Readily Reversible Reaction
- $\Delta G^\circ = 7.6$ kJ/mol
- Diffusion-limited Enzyme
- Perfect Enzyme

Dihydroxyacetone Phosphate (DHAP) \[ \overset{\text{CH}_2\text{OH}}{\overset{\text{O}}{\overset{\text{CH}_2}{\overset{\text{OPO}_3^{2-}}{}}} \]  \[ \overset{\text{O}}{\overset{\text{H}}{\overset{\text{CH}_2}{\overset{\text{OH}}{\overset{\text{OPO}_3^{2-}}{}}}}} \]  \[ \overset{\text{CH}_2}{\overset{\text{O}}{\overset{\text{H}}{\overset{\text{OH}}{\overset{\text{OPO}_3^{2-}}{}}}}} \]

Triose Phosphate Isomerase

Glyceraldehyde-3-Phosphate (GA3P)
Glycolysis

• Phase 2

Dihydroxyacetone phosphate

Enediol Intermediate?

Glyceraldehyde-3-phosphate
Glycolysis

• Phase 2

Glyceraldehyde-3-Phosphate Dehydrogenase (GA3PDH)

\[
\text{Glyceraldehyde-3-Phosphate (GA3P)} + \text{NAD}^+ + P_i \rightleftharpoons \text{1,3 Bisphosphoglycerate (1,3 BPG)} + \text{NADH} + H^+ 
\]
Glycolysis
• Phase 2

• Only Oxidation of Glycolysis

Glyceraldehyde-3-Phosphate Dehydrogenase (GA3PDH)

Glyceraldehyde-3-Phosphate (GA3P) + NAD⁺ + P_i ↔ 1,3 Bisphosphoglycerate (1,3 BPG) + NADH + H⁺
**Glycolysis**

- Phase 2

**Only Oxidation of Glycolysis**

\[
\text{Glyceraldehyde-3-Phosphate (GA3P)} + \text{NAD}^+ + \text{P}_i \rightleftharpoons \text{1,3 Bisphosphoglycerate (1,3 BPG)} + \text{NADH} + \text{H}^+ 
\]
**Glycolysis**
- Phase 2

- Only Oxidation of Glycolysis
- \( \Delta G^\circ = 6.3 \text{ kJ/mol} \)

Glyceraldehyde-3-Phosphate (GA3P) + NAD\(^+\) + P\(_i\) \rightleftharpoons 1,3 \text{ Bisphosphoglycerate (1,3 BPG)} + \text{NADH} + H^+
**Glycolysis**

- Phase 2

1,3 Bisphosphoglycerate (1,3 BPG) + ADP $\xrightarrow{\text{Phosphoglycerate Kinase}}$ 3 Phosphoglycerate (3-PG) + ATP
Glycolysis
  • Phase 2

  • Substrate Level Phosphorylation

\[
\begin{align*}
\text{1,3 Bisphosphoglycerate (1,3 BPG)} & \quad \text{Phosphoglycerate Kinase} \quad \text{3 Phosphoglycerate (3-PG)} \\
\end{align*}
\]
Glycolysis

- Phase 2

- Substrate Level Phosphorylation
- $\Delta G^\circ = -18.9 \text{ kJ/mol}$

\[
\text{1,3 Bisphosphoglycerate (1,3 BPG)} + \text{ADP} \xrightleftharpoons{\text{Phosphoglycerate Kinase}} \text{3 Phosphoglycerate (3-PG)} + \text{ATP}
\]
Glycolysis

Three means of making ATP
**Glycolysis**

Three means of making ATP

1. Substrate level phosphorylation - high energy molecule adds phosphate to ADP
Glycolysis

Three means of making ATP

1. Substrate level phosphorylation - high energy molecule adds phosphate to ADP
2. Oxidative phosphorylation - oxidative energy (electron movement) used in mitochondria to generate ATP
Glycolysis

Three means of making ATP

1. Substrate level phosphorylation - high energy molecule adds phosphate to ADP
2. Oxidative phosphorylation - oxidative energy (electron movement) used in mitochondria to generate ATP
3. Photophosphorylation - light energy captured in chloroplasts of plants to make ATP
Glycolysis

• Phase 2

3 Phosphoglycerate (3-PG) \rightarrow 2 Phosphoglycerate (2-PG)

Phosphoglycerate Mutase
Glycolysis
• Phase 2

• Minor Source of 2,3 BPG

3 Phosphoglycerate (3-PG)  2 Phosphoglycerate (2-PG)

Phosphoglycerate Mutase
Glycolysis
• Phase 2

• Minor Source of 2,3 BPG
• $\Delta G^\circ = 4.4$ kJ/mol

3 Phosphoglycerate (3-PG) \[\text{Phosphoglycerate Mutase}\] 2 Phosphoglycerate (2-PG)
Glycolysis
- 2,3 BPG and Glycolysis

1,3 BPG

- Released Freely in Erythrocytes and Placental Cells

2,3 BPG

- Released at a Low Level in All Cells

3-PG

- Phosphoglycerate Kinase

2-PG

- Phosphoglycerate Mutase

Phosphoglycerate Kinase

2,3 Bisphosphoglycerate Phosphatase

Phosphoglycerate Mutase

Bisphosphoglycerate Mutase

ADP

ATP

P_i

2,3 Bisphosphoglycerate
Glycolysis
• 2,3 BPG and Glycolysis

• 2,3 BPG Binds to Hemoglobin and Favors O₂ Release

1,3 BPG → 3-PG
Phosphoglycerate Kinase

3-PG → 2-PG
Phosphoglycerate Mutase

2-PG → 2,3 BPG
2,3 Bisphosphoglycerate Phosphatase

2,3 BPG → 2,3 BPG
Bisphosphoglycerate Mutase

Released Freely in Erythrocytes and Placental Cells

Released at a Low Level in All Cells
Glycolysis
- Phase 2

2 Phosphoglycerate (2-PG) $\rightleftharpoons$ Phosphoenolpyruvate (PEP)
Glycolysis
• Phase 2

• $\Delta G^\circ' = 1.8 \text{ kJ/mol}$

2 Phosphoglycerate (2-PG) \rightarrow \text{Enolase} \rightarrow \text{Phosphoenolpyruvate (PEP) + H}_2\text{O}
Glycolysis

• Phase 2

Phosphoenolpyruvate (PEP) → Pyruvate (Pyr)

Pyruvate Kinase

ADP + H⁺ \rightarrow ATP

Mg^{++}
**Glycolysis**

- Phase 2

- Substrate Level Phosphorylation

![Diagram](image)

- **Phosphoenolpyruvate (PEP)**
- **Pyruvate (Pyr)**
**Glycolysis**

- Phase 2

- Substrate Level Phosphorylation
- “Big Bang” of Glycolysis

\[
\text{ADP} + \text{H}^+ \rightarrow \text{ATP}
\]

Phosphoenolpyruvate (PEP) \[\rightarrow\] Pyruvate (Pyr)
Glycolysis
• Phase 2
• Substrate Level Phosphorylation
• “Big Bang” of Glycolysis
• $\Delta G^\circ = -31.7 \text{ kJ/mol}$

\[
\begin{align*}
\text{Phosphoenolpyruvate (PEP)} & \quad \xrightarrow{\text{Pyruvate Kinase}} \quad \text{Pyruvate (Pyr)} \\
\text{ADP} + \text{H}^+ & \quad \xrightarrow{\text{Mg}^{++}} \quad \text{ATP}
\end{align*}
\]
Glycolysis

- Phase 2

- Substrate Level Phosphorylation
- “Big Bang” of Glycolysis
- $\Delta G^\circ = -31.7 \text{ kJ/mol}$
- Essentially Irreversible

Phosphoenolpyruvate (PEP) $\xrightarrow{\text{Pyruvate Kinase}}$ Pyruvate (Pyr)

$\text{CH}_2\text{C(=O)OP(=O)O}^- \xrightarrow{\text{Pyruvate Kinase}} \text{CH}_3\text{C(=O)O}^-$

ADP $+ \text{H}^+$ $\xrightarrow{\text{Mg}^{++}}$ ATP
Glycolysis
• Pyruvate Kinase
Glycolysis

- Pyruvate Kinase

- Third Regulated Enzyme of Glycolysis
Glycolysis
- Pyruvate Kinase

- Third Regulated Enzyme of Glycolysis
- Inhibited by ATP, Alanine
**Glycolysis**
- Pyruvate Kinase

- Third Regulated Enzyme of Glycolysis
- Inhibited by ATP, Alanine
- Activated by F1,6BP
**Glycolysis**
- Pyruvate Kinase

- Third Regulated Enzyme of Glycolysis
- Inhibited by ATP, Alanine
- Activated by F1,6BP
- Inactivated by Phosphorylation
Glycolysis
• Pyruvate Kinase

• Third Regulated Enzyme of Glycolysis
• Inhibited by ATP, Alanine
• Activated by F1,6BP
• Inactivated by Phosphorylation
• Regulation Important for Gluconeogenesis
Glycolysis

- Pyruvate Kinase
Glycolysis

• Summary

Glucose + 2 ADP + 2P$_i$ + 2 NAD$^+$
Glycolysis

• Summary

Glucose + 2 ADP + 2P_i + 2 NAD^+

Yields
Glycolysis

• Summary

Glucose + 2 ADP + 2P_i + 2 NAD^+

Yields

2 Pyruvate + 2 ATP + 2 NADH + 2 H^+ + 2 H_2O
Metabolic Melody
The Sound of Glucose

(to the tune of "A Few of My Favorite Things")

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Metabolic Melody
Aldehyde sugars are always aldoses and
If there's a ketone we call them ketoses
Some will form structures in circular rings
Saccharides do some incredible things
Onto a glucose we add a 'P' to it
ATP energy ought to renew it
Quick rearranging creates F6P
Without requiring input energy

At a high rate
Add a phosphate
With PFK
F1,6BP is made up this way
So we can run and play

Aldolase breaks it and then it releases
DHAP and a few G3Pieces
These both turn in to 1,3 BPG
Adding electrons onto NAD
The Sound of Glucose
(to the tune of "A Few of My Favorite Things")
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Aldehyde sugars are always aldoses and
If there's a ketone we call them ketoses
Some will form structures in circular rings
Saccharides do some incredible things
Onto a glucose we add a 'P' to it
ATP energy ought to renew it
Quick rearranging creates F6P
Without requiring input energy

Phosphate plus ADP makes ATP
While giving cells what they need - en-er-gy
Making triphosphate's a situa-shun
Of substrate level phosphoryla-shun

At a high rate
Add a phosphate
With PFK
F1,6BP is made up this way
So we can run and play

3-B-P-G
2-B-P-G
Lose a water
PEP gets a high energy state
Just to make py-ru-vate

So all the glucose gets broken and bent
If there's no oxygen cells must ferment
Pyruvate / lactate our cells hit the wall
Some lucky yeast get to make ethanol

Aldolase breaks it and then it releases
DHAP and a few G3Pieces
These both turn in to 1,3 BPG
Adding electrons onto NAD

This is the end of your glucose's song
Unless you goof up and get it all wrong
Break it, don't make it to yield ATP
You'll save your cells from fu-til-i-ty
Metabolic Melody
Things You Should Remember
(to the tune of “In My Life”)
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Things You Should Remember
(to the tune of “In My Life”)
Copyright © Kevin Ahern

There are things you should remember
When you’re stud-y-ing for this exam
   All the pathways since September
   And the mol-e-cules comprising them

Though that is an awful lot of information
   I hope that you can retain it all
If you do you will avoid a grade deflation
When you-uuu study right, you will recall

   Now in all your preparation
There is soooome-thing you should regard
   How your brain stores information
So transcribe your notes onto a card
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I assure you it will up your recollection
Of enzymes and complex Haworth rings
It will drive performance to perfection
Simply from the act of writing things

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Of enzymes and complex Haworth rings
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So go-ooo forward now and write down things