Cellular Respiration
Stage 1: Glycolysis
What's the point?

The point is to make ATP!
Glycolysis

- Breaking down glucose
  - “glyco – lysis” (splitting sugar)
    - glucose → → → → → pyruvate
      - 6C → 2x 3C
    - ancient pathway which harvests energy
      - where energy transfer first evolved
      - transfer energy from organic molecules to ATP
      - still is starting point for **ALL** cellular respiration
    - but it’s inefficient
      - generate only **2 ATP** for every **1 glucose**
  - occurs in cytosol

In the cytosol? Why does that make evolutionary sense?

That’s not enough ATP for me!
Evolutionary perspective

- **Prokaryotes**
  - first cells had no organelles

- **Anaerobic atmosphere**
  - life on Earth first evolved *without free oxygen* \((O_2)\) in atmosphere
  - energy had to be captured from organic molecules in absence of \(O_2\)

- **Prokaryotes** that evolved glycolysis are ancestors of all modern life
  - **ALL** cells still utilize glycolysis

Enzymes of glycolysis are “well-conserved”

You mean we’re related? Do I have to invite them over for the holidays?
Overview

10 reactions

- Convert glucose (6C) to 2 pyruvate (3C)
- Produces: 4 ATP & 2 NADH
- Consumes: 2 ATP
- Net yield: 2 ATP & 2 NADH

DHAP = dihydroxyacetone phosphate
G3P = glyceraldehyde-3-phosphate
Glycolysis summary

**ENERGY INVESTMENT**

Glucose → 2 ADP (Discharged)

2 ADP → 2 ATP

**ENERGY PAYOFF**

2 NAD^+ (Charged) → 2 NADH

4 ADP (Charged) → 4 ATP

**NET YIELD**

Glucose → 2 Pyruvate + 2H_2O

2 ADP + 2P_i → 2 ATP

2 NAD^+ → 2 NADH + 2H^+

**endergonic**

invest some ATP

**exergonic**

harvest a little ATP & a little NADH

**net yield**

✓ 2 ATP

✓ 2 NADH
1st half of glycolysis (5 reactions)

Glucose “priming”

- get glucose ready to split
  - phosphorylate glucose
  - molecular rearrangement
- split destabilized glucose

1. Glucose
   - ATP
   - hexokinase
   \[ \text{Glucose} + \text{ATP} \rightarrow \text{Glucose 6-phosphate} + \text{ADP} \]

2. Glucose 6-phosphate
   - phosphoglucone isomerase
   \[ \text{Glucose 6-phosphate} \rightarrow \text{Fructose 6-phosphate} \]

3. Fructose 6-phosphate
   - ATP
   - phosphofructokinase
   \[ \text{Fructose 6-phosphate} + \text{ATP} \rightarrow \text{Fructose 1,6-bisphosphate} + \text{ADP} \]

4. Fructose 1,6-bisphosphate
   - aldolase
   \[ \text{Fructose 1,6-bisphosphate} \rightarrow \text{Dihydroxyacetone phosphate} + \text{Glyceraldehyde 3-phosphate (G3P)} \]

5. Glyceraldehyde 3-phosphate (G3P)
   - glyceraldehyde 3-phosphate dehydrogenase
   \[ \text{Glyceraldehyde 3-phosphate (G3P)} + \text{NAD}^+ \rightarrow \text{Glyceraldehyde 3-phosphate (G3P)} + \text{NADH} \]

6. 1,3-Bisphosphoglycerate (BPG)
   - 1,3-Bisphosphoglycerate (BPG)
   \[ \text{1,3-Bisphosphoglycerate (BPG)} + \text{P}_i + \text{NAD}^+ \rightarrow \text{1,3-Bisphosphoglycerate (BPG)} + \text{NADH} \]
2nd half of glycolysis (5 reactions)

**Energy Harvest**

- **NADH production**
  - G3P donates H
  - oxidizes the sugar
  - reduces NAD⁺
  - NAD⁺ → NADH

- **ATP production**
  - G3P → → → pyruvate
  - PEP sugar donates P
    - “substrate level phosphorylation”
  - ADP → ATP

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**Payola! Finally some ATP!**
Substrate-level Phosphorylation

- In the last steps of glycolysis, where did the P come from to make ATP?
  - the sugar substrate (PEP)

P is transferred from PEP to ADP

- kinase enzyme
- ADP → ATP

I get it!
The P_i came directly from the substrate!
Energy accounting of glycolysis

- **Net gain** = 2 ATP + 2 NADH
  - some energy investment (-2 ATP)
  - small energy return (4 ATP + 2 NADH)
- **1 6C sugar → 2 3C sugars**

2 ATP  
2 ADP

glucose → → → → pyruvate

6C

2 NAD^+  
2 NADH

4 ADP  
4 ATP

2x 3C

All that work! And that's all I get?

But glucose has so much more to give!
Is that all there is?

- Not a lot of energy...
  - for 1 billion years+ this is how life on Earth survived
    - no $O_2$ = slow growth, slow reproduction
    - only harvest 3.5% of energy stored in glucose
      - more carbons to strip off = more energy to harvest

$glucose \rightarrow \rightarrow \rightarrow \rightarrow pyruvate$

Hard way to make a living!
But can’t stop there!

raw materials → products

Glycolysis

\[
glucose + 2\text{ADP} + 2\text{P}_i + 2\text{NAD}^+ \rightarrow 2 \text{pyruvate} + 2\text{ATP} + 2\text{NADH}
\]

Going to run out of \text{NAD}^+

- without regenerating \text{NAD}^+, energy production would stop!
- another molecule must accept H from \text{NADH}
  - so \text{NAD}^+ is freed up for another round
How is NADH recycled to NAD$^+$?

Another molecule must accept H from NADH.

- With oxygen:
  - Aerobic respiration
  - NAD$^+$ is recycled via the Krebs cycle.

- Without oxygen (anaerobic respiration or fermentation):
  - Lactic acid fermentation
  - Alcohol fermentation

Which path you use depends on who you are...
Glycolysis- The Movie!

http://www.youtube.com/watch?v=ub1zTkZL5sE&feature=related
Fermentation (anaerobic)

- **Bacteria, yeast**
  
  \[
  \text{pyruvate} \rightarrow \text{ethanol} + \text{CO}_2
  \]
  
  daughter cell + energy
  
  - beer, wine, bread

- **Animals, some fungi**
  
  \[
  \text{pyruvate} \rightarrow \text{lactic acid}
  \]
  
  daughter cell + energy
  
  - cheese, anaerobic exercise (no O\textsubscript{2})
**Alcohol Fermentation**

\[\text{pyruvate} \rightarrow \text{ethanol} + \text{CO}_2\]

- **3C**
- **2C**
- **1C**

- **NADH**
- **NAD**

**Dead end process**

- at ~12% ethanol, kills yeast
- can’t reverse the reaction

**Count the carbons!**
Lactic Acid Fermentation

- Reversible process
  - once $O_2$ is available, lactate is converted back to pyruvate by the liver

\[
\text{pyruvate} \leftrightarrow \text{lactic acid} \quad O_2
\]

\[
\begin{align*}
3C & \quad \text{NADH} \\
3C & \quad \text{NAD}^+ \\
\end{align*}
\]

Count the carbons!

Recycle NADH

Animals, some fungi

2 ADP + 2 $P_i$ → 2 ATP

Glucose → GLYCOLYSIS

2 NAD$^+$ → 2 NADH + 2 H$^+$

2 Pyruvate → 2 Lactate
Pyruvate is a branching point.

**Pyruvate**

- **Fermentation**
- **Anaerobic respiration**
- **Mitochondria**
- **Krebs cycle**
- **Aerobic respiration**
What's the point?

The point is to make ATP!
And how do we do that?

- **ATP synthase**
  - set up a $H^+$ gradient
  - allow $H^+$ to flow through ATP synthase
  - powers bonding of $P_i$ to ADP

$$ADP + P_i \rightarrow ATP$$

But... Have we done that yet?
NO!
There’s still *more*
to my story!
Any Questions?