E.coli CORE MODEL:
METABOLIC CORE
LEARNING OBJECTIVES

Each student should be able to:

- Describe the glycolysis pathway in the core model.
- Describe the TCA cycle in the core model.
- Explain gluconeogenesis.
- Describe the pentose phosphate pathway in the core model.
- Describe the glyoxylate cycle and anapleurotic pathways in the core model.
- Describe the oxidative phosphorylation and electron transport chain pathways in the core model.
- Describe the fermentation pathways in the core model.
- Describe the nitrogen metabolism pathways in the core model.
E. coli Core Model

- Component Parts of the E. coli Core Model
- Glycolysis
- Pentose Phosphate Shunt
- Tricarbonoxylic Acid (TCA) Cycle
- Glycoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism
Component Parts of the *E. coli* Core Model

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)

http://systemsbiology.ucsd.edu/Downloads/E_coli_Core
**E. coli Precursor Metabolites**

- **Pyruvate family**
  - Alanine
  - Valine
  - Leucine
  - Isoleucine
  - Isoprenoids

- **Aromatic Family**
  - Tyrosine
  - Tryptophan
  - Phenylalanine

- **Chorismate**

- **Serine Family**
  - Serine -> Tryptophan
  - Serine -> Ethanolamine
  - Serine -> 1-C units
  - Glycine -> Purine nucleotides
  - Cysteine

- **Nicotinamide coenzymes**
  - Glyceral-3-phosphate -> Phospholipids

- **Aspartate family**
  - Asparagine
  - Threonine
  - Methionine -> Spermidine
  - Aspartate -> Nicotinamide coenzymes
  - Aspartate -> Pyrimidine nucleotides

- **Amino sugars**
  - Murein
  - Leucine

- **Lysine**

- **Fatty Acids**
  - Murein
  - Leucine

- **Aspartate family**
  - Glutamine
  - Arginine -> Polyamines
  - Proline

- **Glutamate family**
  - Glutamate -> Hemes
  - Glutamine
  - Arginine -> Spermidine

- **Vitamins and cofactors**
  - Folic acid
  - Riboflavin
  - Coenzyme A
  - Adenosylcobalamine
  - Nicotinamide

- **Phosphoribosyl pyrophosphate**

- **Tryptophan**

- **Histidine**

- **2-Keto-3-deoxyoctanate**

- **Heptose in Lipopolysaccharides (Endotoxin)**

- **Heme**

- **Purine nucleotides**

- **Pyrimidine nucleotides**
E. coli Core Model

- Component Parts of the E. coli Core Model
  - Glycolysis
    - Pentose Phosphate Shunt
    - Tricarboxylic Acid (TCA) Cycle
    - Glycoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
    - Oxidative Phosphorylation and Transfer of Reducing Equivalents
    - Fermentation
    - Nitrogen Metabolism
Glycolysis

E. coli Core Model


http://systemsbiology.ucsd.edu/Downloads/E_coli_CoreAnaTCAOxP
Glycolysis is the metabolic pathway that converts glucose into pyruvate. The free energy released in this process is used to form the high-energy compounds of ATP and NADH.

http://en.wikipedia.org/wiki/Glycolysis
Glycolysis

Glycolysis is the metabolic pathway that converts glucose or fructose into a series of precursors for biosynthesis terminating with pyruvate. The free energy released in this process is used to form the high-energy compounds of ATP and NADH.
Metabolites & Reactions

Glycolysis

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Metabolite</th>
<th>Formula</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>&amp;k{glc-D}</td>
<td>D-Glucose</td>
<td>C_6H_{12}O_6</td>
<td>0</td>
</tr>
<tr>
<td>&amp;k{g6p}</td>
<td>D-Glucose-6-phosphate</td>
<td>C_6H_{11}O_9P</td>
<td>-2</td>
</tr>
<tr>
<td>&amp;k{fru}</td>
<td>D-Fructose</td>
<td>C_6H_{12}O_6</td>
<td>0</td>
</tr>
<tr>
<td>&amp;k{f6p}</td>
<td>D-Fructose-6-phosphate</td>
<td>C_6H_{11}O_9P</td>
<td>-2</td>
</tr>
<tr>
<td>&amp;k{f6p-2}</td>
<td>D-Fructose-1,6-bisphosphate</td>
<td>C_6H_{10}O_7P_2</td>
<td>-4</td>
</tr>
<tr>
<td>&amp;k{dihap}</td>
<td>Dihydroxyacetone-phosphate</td>
<td>C_3H_{6}O_5P</td>
<td>-2</td>
</tr>
<tr>
<td>&amp;k{g3p}</td>
<td>Glyceroldehyde-3-phosphate</td>
<td>C_3H_{2}O_5P</td>
<td>-2</td>
</tr>
<tr>
<td>&amp;k{13dpg}</td>
<td>3-Phospho-D-glyceroyl-phosphate</td>
<td>C_3H_{4}O_{10}P_2</td>
<td>-4</td>
</tr>
<tr>
<td>&amp;k{3pg}</td>
<td>3-Phospho-D-glycerate</td>
<td>C_3H_{4}O_7P</td>
<td>-3</td>
</tr>
<tr>
<td>&amp;k{2pg}</td>
<td>D-Glycerate-2-phosphate</td>
<td>C_3H_{4}O_7P</td>
<td>-3</td>
</tr>
<tr>
<td>&amp;k{pep}</td>
<td>Phosphoenolpyruvate</td>
<td>C_3H_{2}O_5P</td>
<td>-3</td>
</tr>
<tr>
<td>&amp;k{pyr}</td>
<td>Pyruvate</td>
<td>C_3H_{3}O_3</td>
<td>-1</td>
</tr>
</tbody>
</table>

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
Biosynthetic Precursors (Glycolysis)

- Sugar Nucleotides
- Amino Sugars
- Phospholipids
- Cysteine
- Glycine
- Serine
- Tyrosine
- Tryptophan
- Phenylalanine
- Alanine
- Leucine
- Valine

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
Constraint-based Metabolic Reconstructions & Analysis

Lesson: E.coli Metabolic Core

Aerobic Conditions
Carbon Source: Glucose

Glucose → Glycolysis

AerobicGlucoseBioMass.m
Anaerobic Conditions
Carbon Source: Glucose

Glucose $\rightarrow$ Glycolysis

ATP = ☀️
NADPH = 🍊
NADH = 🍊
**Aerobic Conditions**
**Carbon Source: Fructose**

Fructose $\rightarrow$ Glycolysis $\rightarrow$ 

Aerobic Glucose BioMass.m
Constraint-based Metabolic Reconstructions & Analysis

Lesson: E. coli Metabolic Core

Aerobic Glucose BioMass.m

Anaerobic Conditions
Carbon Source: Fructose

Fructose → Glycolysis

ATP = ☀️
NADPH = 🌟
NADH = 🌟
Aerobic Conditions
Carbon Source: Pyruvate

Does not grow in Anaerobic Conditions

Gluconeogenesis

Pyruvate → ATP
NADH = ▲
NADPH = ▼

AerobicGlucoseBioMass.m
E. coli Core Model

- Component Parts of the E. coli Core Model
- Glycolysis
- Pentose Phosphate Shunt
- Tricarbonoxylic Acid (TCA) Cycle
- Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism
Pentose Phosphate Shunt

E. coli Core Model

Pentose Phosphate Shunt (Pentose Phosphate Pathway)

The pentose phosphate pathway generates NADPH and provides the 5-carbon (alpha-D-ribose-5-phosphate, “r5p”), 4-carbon biosynthetic precursors (D-erythrose-4-phosphate, “e4p”), and the 7-carbon, sedoheptulose-7-phosphate.

There are two distinct phases in the pathway. The first is the oxidative phase, in which NADPH is generated, and the second is the non-oxidative synthesis of 5-carbon and 4-carbon precursors.
<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Reaction</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>g6p</td>
<td>glucose 6-phosphate dehydrogenase</td>
<td>g6p + nadp $\rightleftharpoons$ 6pgl + h + nadph</td>
</tr>
<tr>
<td>6pgl</td>
<td>6-phospho-D-glucono-1,5-lactone</td>
<td>6pgl + h2o $\rightarrow$ 6pgc + h</td>
</tr>
<tr>
<td>6pgc</td>
<td>6-Phospho-D-gluconate</td>
<td>6pgc + nadp $\rightarrow$ co2 + nadp + ru5p-D</td>
</tr>
<tr>
<td>ru5p-D</td>
<td>D-Ribulose-5-phosphate</td>
<td>r5p $\rightleftharpoons$ ru5p-D</td>
</tr>
<tr>
<td>r5p</td>
<td>alpha-D-Ribose-5-phosphate</td>
<td></td>
</tr>
<tr>
<td>f6p</td>
<td>D-Fructose-6-phosphate</td>
<td>C6H11O9P -2</td>
</tr>
<tr>
<td>g3p</td>
<td>Glyceraldehyde-3-phosphate</td>
<td>C3H5O6P -2</td>
</tr>
<tr>
<td>xu5p-D</td>
<td>D-Xylose-5-phosphate</td>
<td>C5H9O8P -2</td>
</tr>
<tr>
<td>s7p</td>
<td>Sedoheptulose-7-phosphate</td>
<td>C7H13O10P -2</td>
</tr>
<tr>
<td>e4p</td>
<td>D-Erythrose-4-phosphate</td>
<td>C4H7O7P -2</td>
</tr>
</tbody>
</table>

Metabolites & Reactions
Pentose Phosphate Pathway

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Constraint-based Metabolic Reconstructions & Analysis

Biosynthetic Precursors
(Pentose Phosphate Pathway)

Histidine
Purines (ATP, GTP, dATP, dGTP)
Pyrimidines (UTP, CTP, dCTp, dTTP)

Heptose in Lipopolysaccharides (Endotoxin)

Tryptophan
Tyrosine
Phenylalanine

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
Aerobic Conditions
Carbon Source: Glucose

Glucose \downarrow
Glycolysis

Oxidative Pathway

AerobicGlucoseBioMass.m
**Anaerobic Conditions**

**Carbon Source: Glucose**

- Glucose → Non-oxidative Pathway → Glycolysis → ATP, NADH, NADPH

**Equations:**

- **ATP:**
- **NADPH:**
- **NADH:**
E. coli Core Model

- Component Parts of the E. coli Core Model
  - Glycolysis
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  - Tricarbonoxylic Acid (TCA) Cycle
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  - Fermentation
  - Nitrogen Metabolism
Tricarboxylic Acid Cycle (TCA)

E. coli Core Model

TCA Cycle

The tricarboxylic acid cycle (TCA cycle), citric acid cycle — also known as the citric acid cycle, the Krebs cycle — is a series of chemical reactions used by all aerobic organisms to generate energy through the oxidation of acetate derived from carbohydrates, fats and proteins into carbon dioxide. In addition, the cycle provides precursors including certain amino acids as well as the reducing agent NADH.

http://en.wikipedia.org/wiki/TCA_cycle
TCA Cycle

The oxidative pathway of the TCA cycle runs counterclockwise in the lower part of the cycle, from oxaloacetate, oaa, through 2-oxoglutarate, akg. Continuing counterclockwise from 2-oxoglutarate, the full tricarboxylic acid cycle can totally oxidize acetyl-CoA, but is only functional during aerobic growth on acetate or fatty acids.

Under anaerobic conditions, the TCA cycle functions not as a cycle, but as two separate pathways. The oxidative pathway, the counterclockwise lower part of the cycle, still forms the precursor 2-oxoglutarate. The reductive pathway, the clockwise upper part of the cycle, forms the precursor succinyl-CoA.
Metabolites & Reactions

TCA Cycle

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Reaction</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS</td>
<td>citrate synthase</td>
<td>acceu + h2o + oxa -&gt; cit + coa + h</td>
</tr>
<tr>
<td>ACONTa</td>
<td>aconitase (half-reaction A, Citrate hydro-lyase)</td>
<td>cit &lt;=&gt; acou-C + h2o</td>
</tr>
<tr>
<td>ACONTb</td>
<td>aconitase (half-reaction B, Isocitrate hydro-lyase)</td>
<td>acou-C + h2o = icit</td>
</tr>
<tr>
<td>ICDHy</td>
<td>isocitrate dehydrogenase (NADP)</td>
<td>icit + nadp = akg + co2 + nadph</td>
</tr>
<tr>
<td>AKDH</td>
<td>2-Oxoglutarate dehydrogenase</td>
<td>akg + coa + nad = co2 + nad + succoa</td>
</tr>
<tr>
<td>SUCOAS</td>
<td>succinyl-CoA synthetase (ADP-forming)</td>
<td>atp + coa + succ -&gt; adp + pi + succoa</td>
</tr>
<tr>
<td>FAD7</td>
<td>fumarate reductase</td>
<td>fum + q8h2 = q8 + succ</td>
</tr>
<tr>
<td>SUCDi</td>
<td>succinate dehydrogenase (irreversible)</td>
<td>q8 + succ -&gt; fum + q8h2</td>
</tr>
<tr>
<td>FUM</td>
<td>fumarase</td>
<td>fum + h2o = mal-L</td>
</tr>
<tr>
<td>MDH</td>
<td>malate dehydrogenase</td>
<td>mal-L + nad = h + nadh + oxa</td>
</tr>
<tr>
<td>AKGt2r</td>
<td>2-oxoglutarate reversible transport via symport</td>
<td>akg[e] + h[e] -&gt; akg + h</td>
</tr>
<tr>
<td>SUCt3</td>
<td>succinate transport out via proton antiport</td>
<td>h[e] + succ -&gt; h + succ[e]</td>
</tr>
<tr>
<td>SUCt2</td>
<td>succinate transport via proton symport (2 H)</td>
<td>2 h[e] + succ[e] -&gt; 2 h + succ</td>
</tr>
<tr>
<td>FUMt2</td>
<td>Fumarate transport via proton symport (2 H)</td>
<td>fum[e] + 2 h[e] -&gt; fum + 2 h</td>
</tr>
<tr>
<td>MALt2</td>
<td>Malate transport via proton symport (2 H)</td>
<td>2 h[e] + mal-L[e] -&gt; 2 h + mal-L</td>
</tr>
</tbody>
</table>

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
Biosynthetic Precursors
(TCA Cycle)

Asparagine
Aspartic acid
Isoleucine
Lysine
Methionine
Threonine

Arginine
Glutamine
Glutamic acid
Proline

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Aerobic Conditions
Carbon Source: Glucose

ATP = ☀
NADPH = ⚫
NADH = ⚫
Anaerobic Conditions
Carbon Source: Glucose

ATP =  sun
NADPH =  blue
NADH =  red

Oxidative Pathway
E. coli Core Model

• Component Parts of the E. coli Core Model
  • Glycolysis
  • Pentose Phosphate Shunt
  • Tricarboxylic Acid (TCA) Cycle
  • Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
  • Oxidative Phosphorylation and Transfer of Reducing Equivalents
  • Fermentation
  • Nitrogen Metabolism
Glycoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

**E. coli Core Model**

The glycoxylate cycle and gluconeogenic reactions allow *E. coli* to grow on 3-carbon (pyruvate) and 4-carbon compounds (malate, fumarate, succinate) by avoiding the loss of carbon to carbon dioxide from the TCA cycle, providing a pathway for generation of glycolytic intermediates from TCA intermediates, and reversing the carbon flux through glycolysis to produce essential precursors for biosynthesis.

Anapleurotic reactions replenish TCA intermediates drained of for biosynthesis.

Glycoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
Metabolites & Reactions
Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Metabolite</th>
<th>Formula</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>glx</td>
<td>Glyoxylate</td>
<td>C₂H₂O₂</td>
<td>-1</td>
</tr>
</tbody>
</table>

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Biosynthetic Precursors for Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

- Cysteine
- Glycine
- Serine
- Tyrosine
- Tryptophan
- Phenylalanine
- Alanine
- Leucine
- Valine
- Asparagine
- Aspartic Acid
- Isoleucine
- Lysine
- Methionine
- Threonine
Aerobic Conditions
Carbon Source: Acetate

Gluconeogenesis

Acetate

O₂

ATP =☀
NADPH =球星
NADH =球星
Aerobic Conditions
Carbon Source: Acetaldehyde

ATP = ☀️
NADPH = 🌟
NADH = 🌟

Gluconeogenesis

Acetaldehyde

O₂
Aerobic Conditions
Carbon Source: Ethanol

ATP = ☀️
NADPH = 🍦
NADH = ⚫
E. coli Core Model

- Component Parts of the E. coli Core Model
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- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism
Oxidative Phosphorylation and Transfer of Reducing Equivalents

**E. coli Core Model**


http://systemsbiology.ucsd.edu/Downloads/E coli_Core
Oxidative Phosphorylation and Transfer of Reducing Equivalents

- Energy is required to drive endergonic processes such as biosynthesis, polymerization, active transport of substrate into the cell against concentration gradients, maintaining internal pH, and motility. There are two main mechanisms for the production of energy, **substrate level phosphorylation**, and the **electron transport chain**.

- Substrate level phosphorylation is where ATP is formed by a reaction between ADP and a phosphorylated intermediate of a fueling pathway. Examples include: phosphoglycerate kinase, PGK, and pyruvate kinase, PYK, in glycolysis, and succinyl-CoA synthetase, SUCOAS, in the tricarboxylic acid cycle. Each molecule of glucose can potentially lead to the net generation of four molecules of ATP.

- The electron transport chain which produces the bulk of the cell’s ATP under aerobic conditions. Mitchell’s chemiosmotic theory describes the mechanism by which electron transport is coupled to the generation of ATP. The electron transport chain translocates protons, $H^+$, from the cytoplasm, across the cytoplasmic membrane into the periplasmic space. Since the cytoplasmic membrane is effectively impermeable to protons and hydroxyl ions, $OH^-$, this establishes a difference in concentration of protons, and a difference in electrical charge, across the cytoplasmic membrane. This thermodynamic potential difference gives rise to a **proton motive force** which can be utilized to drive a myriad of endergonic reactions, such as synthesis of high energy currency metabolites, such as ATP.
Oxidative Phosphorylation and Transfer of Reducing Equivalents

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## Metabolites & Reactions

### Oxidative Phosphorylation and Transfer of Reducing Equivalents

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Name</th>
<th>Formula</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>q8</td>
<td>Ubiquinone-8</td>
<td>C_{40}H_{74}O_{14}</td>
<td>0</td>
</tr>
<tr>
<td>q8h2</td>
<td>Ubiquinol-8</td>
<td>C_{40}H_{76}O_{14}</td>
<td>0</td>
</tr>
<tr>
<td>nad</td>
<td>Nicotinamide-adenine-dinucleotide (NAD(^+))</td>
<td>C_{21}H_{26}N_{7}O_{14}P_{2}</td>
<td>-1</td>
</tr>
<tr>
<td>nadh</td>
<td>Nicotinamide-adenine-dinucleotide-reduced</td>
<td>C_{21}H_{27}N_{7}O_{14}P_{2}</td>
<td>-2</td>
</tr>
<tr>
<td>napd</td>
<td>Nicotinamide-adenine-dinucleotide-phosphate</td>
<td>C_{21}H_{26}N_{7}O_{17}P_{3}</td>
<td>-3</td>
</tr>
<tr>
<td>napdh</td>
<td>Nicotinamide-adenine-dinucleotide-phosphate-reduced</td>
<td>C_{21}H_{26}N_{7}O_{17}P_{3}</td>
<td>-4</td>
</tr>
<tr>
<td>atp</td>
<td>Adenosine-5'-triphosphate</td>
<td>C_{10}H_{19}N_{5}O_{13}P_{3}</td>
<td>-4</td>
</tr>
<tr>
<td>adp</td>
<td>Adenosine diphosphate</td>
<td>C_{10}H_{12}N_{5}O_{10}P_{2}</td>
<td>-3</td>
</tr>
<tr>
<td>amp</td>
<td>Adenosine monophosphate</td>
<td>C_{10}H_{12}N_{5}O_{7}P</td>
<td>-2</td>
</tr>
<tr>
<td>h</td>
<td>Proton</td>
<td>H</td>
<td>+1</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Name</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>NADH16</td>
<td>NADH dehydrogenase (ubiquinone-8 &amp; 3 protons)</td>
<td>(4 \text{ h} + \text{nadh} + q8 \rightarrow 3 \text{ h[e]} + \text{nad} + q8h2)</td>
</tr>
<tr>
<td>CYTRB</td>
<td>cytochrome oxidase bd (ubiquinol-8: 2 protons)</td>
<td>(2 \text{ h} + \frac{1}{2} \text{o2} + q8h2 \rightarrow \text{h2o} + 2 \text{ h[e]} + q8)</td>
</tr>
<tr>
<td>O2t</td>
<td>O2 transport via diffusion</td>
<td>(\text{o2[e]} \rightleftharpoons \text{o2})</td>
</tr>
<tr>
<td>ATPS1r</td>
<td>ATP synthase (four protons for one ATP)</td>
<td>(\text{adp} + 4 \text{ h[e]} + \text{pi} \rightleftharpoons \text{atp} + \text{h2o} + 3 \text{ h})</td>
</tr>
<tr>
<td>ATPM</td>
<td>ATP maintenance requirement</td>
<td>(\text{atp} + \text{h2o} \rightleftharpoons \text{adp} + \text{h} + \text{pi})</td>
</tr>
<tr>
<td>ADK1</td>
<td>adenylate kinase</td>
<td>(\text{amp} + \text{atp} \rightleftharpoons 2 \text{ adp})</td>
</tr>
<tr>
<td>THD2</td>
<td>NAD(P) transhydrogenase</td>
<td>(2 \text{ h[e]} + \text{nadh} + \text{nadph} \rightarrow 2 \text{ h} + \text{nad} + \text{nadph})</td>
</tr>
<tr>
<td>NADTRHD</td>
<td>NAD transhydrogenase</td>
<td>(\text{nad} + \text{nadph} \rightleftharpoons \text{nadh} + \text{nadph})</td>
</tr>
</tbody>
</table>

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Aerobic Conditions
Carbon Source: Glucose

- ATP = ☀
- NADPH = 🔴
- NADH = 🌟

Constraint-based Metabolic Reconstructions & Analysis

2016 H. Scott Hinton

Lesson: E. coli Metabolic Core
Anaerobic Conditions
Carbon Source: Glucose

Glucose →

ATP = ✈
NADPH = ✭
NADH = ✭
E. coli Core Model

- Component Parts of the E. coli Core Model
- Glycolysis
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- Tricarboxylic Acid (TCA) Cycle
- Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
- Oxidative Phosphorylation and Transfer of Reducing Equivalents
- Fermentation
- Nitrogen Metabolism
Fermentation

*E. coli* Core Model

Fermentation is the process of extracting energy from the oxidation of organic compounds, such as carbohydrates, using an endogenous electron acceptor (not oxygen), which is usually an organic compound.

Glycolysis results in the net production of 2 ATP per glucose by substrate level phosphorylation, but this is low compared to 17.5 ATP per glucose for aerobic respiration. The substrates of fermentation are typically sugars, so during fermentative growth, each cell must maintain a large magnitude flux through glycolysis to generate sufficient ATP to drive the constitutive biosynthesis, polymerization, and assembly reactions required for growth. This necessitates a large magnitude efflux of fermentative end products since there is insufficient ATP to assimilate all carbon as biomass. Approximately 10% of carbon substrate is assimilated due to the poor energy yield of fermentation.


http://systemsbiology.ucsd.edu/Downloads/E_coli_Core
Fermentation

Alanine
Leucine
Valine

Fatty acids
Murein
Leucine

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
Metabolites & Reactions

Fermentation

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Reaction</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDH</td>
<td>D-lactate dehydrogenase</td>
<td>lac-D + nad ⇔ h + nadh + pyr</td>
</tr>
<tr>
<td>D</td>
<td>LACT2</td>
<td>D-lactate transport via proton symport</td>
</tr>
<tr>
<td></td>
<td>PDH</td>
<td>pyruvate dehydrogenase</td>
</tr>
<tr>
<td></td>
<td>PFL</td>
<td>pyruvate formate lyase</td>
</tr>
<tr>
<td></td>
<td>FORt1</td>
<td>formate transport via diffusion</td>
</tr>
<tr>
<td></td>
<td>FORt2</td>
<td>formate transport via proton symport</td>
</tr>
<tr>
<td></td>
<td>PTAr</td>
<td>phosphotransacylase</td>
</tr>
<tr>
<td></td>
<td>ACKr</td>
<td>acetate kinase</td>
</tr>
<tr>
<td></td>
<td>ACALD</td>
<td>acetaldehyde dehydrogenase (acetylating)</td>
</tr>
<tr>
<td></td>
<td>ALCD2x</td>
<td>alcohol dehydrogenase (ethanol)</td>
</tr>
<tr>
<td></td>
<td>ACt2r</td>
<td>acetate reversible transport via proton symport</td>
</tr>
<tr>
<td></td>
<td>ACALD4</td>
<td>acetaldehyde reversible transport</td>
</tr>
<tr>
<td></td>
<td>ETOH2r</td>
<td>ethanol reversible transport via proton symport</td>
</tr>
</tbody>
</table>

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
Mixed Acid Fermentation

Anaerobic Conditions
Carbon Source: Glucose

AerobicGlucoseBioMass.m
E. coli Core Model

- Component Parts of the E. coli Core Model
  - Glycolysis
  - Pentose Phosphate Shunt
  - Tricarboxylic Acid (TCA) Cycle
  - Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions
  - Oxidative Phosphorylation and Transfer of Reducing Equivalents
  - Fermentation
  - Nitrogen Metabolism
Nitrogen Metabolism

*E. coli* Core Model

Nitrogen is the fourth most abundant atom in *E. coli* and enters the cell either by ammonium ion uptake, NH4+, or as a moiety within organic molecules, such as glutamine or glutamate.

The *E. coli* core model covers the pathways between 2-oxoglutarate, L-glutamate, and L-glutamine.


http://systemsbiology.ucsd.edu/Downloads/E_coli_Core
Constraint-based Metabolic Reconstructions & Analysis

Nitrogen Metabolism

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
Biosynthetic Precursors (Nitrogen Metabolism)

Reconstruction and Use of Microbial Metabolic Networks: the Core Escherichia coli Metabolic Model as an Educational Guide by Orth, Fleming, and Palsson (2010)
# Metabolites & Reactions

## Nitrogen Metabolism

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Metabolite</th>
<th>Formula</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>glu-L</td>
<td>L-Glutamate</td>
<td>C₅H₈NO₄</td>
<td>-1</td>
</tr>
<tr>
<td>glu-L</td>
<td>L-Glutamine</td>
<td>C₅H₁₀N₂O₃</td>
<td>0</td>
</tr>
<tr>
<td>nh₄</td>
<td>Ammonium</td>
<td>H₄N</td>
<td>+1</td>
</tr>
</tbody>
</table>

### Abbreviation | Reaction                                           | Equation                                           |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>GLNabc</td>
<td>L-glutamine transport via ABC system</td>
<td>atp + glu-L[c] + h₂o → adp + glu-L + h + pi</td>
</tr>
<tr>
<td>GLU2r</td>
<td>L-glutamate transport via proton symport</td>
<td>glu-L[c] + h[c] ⇔ glu-L + h</td>
</tr>
<tr>
<td>GLUDy</td>
<td>glutamate dehydrogenase (NADP)</td>
<td>glu-L + h₂o + nadp ⇔ akg + h + nadph + nh₄</td>
</tr>
<tr>
<td>GLNS</td>
<td>glutamine synthetase</td>
<td>atp + glu-L + nh₄ → adp + glu-L + h + pi</td>
</tr>
<tr>
<td>GLUSy</td>
<td>glutamate synthase (NADPH)</td>
<td>akg + glu-L + h + nadph → 2 glu-L + nadp</td>
</tr>
<tr>
<td>GLUN</td>
<td>glutaminase</td>
<td>glu-L + h₂o → glu-L + nh₄</td>
</tr>
</tbody>
</table>

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Aerobic Conditions

Carbon Source: Glucose

Glucose $\rightarrow$ ATP = $\bigcirc$
NADPH = $\blacklozenge$
NADH = $\blacklozenge$

O$_2$
E. coli Core Model

- Component Parts of the E. coli Core Model
- Glycolysis
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