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 Pathway (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
E. coli Core Model


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
  - -> Ethanolamine
  - -> 1-C units
  - Glycine -> Purine nucleotides
  - Cysteine
- **Nicotinamide coenzymes**: Glyceral-3-phosphate -> Phospholipids
- **Sugar nucleotides**: Asparagine family, Aspartate family, Glutamate family
  - Asparagine
  - Threonine
  - Methionine -> Spermidine
  - Aspartate -> Nicotinamide coenzymes
  - Glutamate -> Hemes
- **Amino sugars**: Fatty Acids, Murein, Leucine
- **Fatty Acids**: Aspartate -> Nicotinamide coenzymes
- **Pyrimidine nucleotides**: Lysine
- **Purine nucleotides**: Folates, Riboflavin, Coenzyme A, Adenosylcobalamine, Nicotinamide
- **Phosphoribosyl pyrophosphate**: Tryptophan, Histidine
- **Vitamins and cofactors**: 2-Keto-3-deoxyoctanate, Heptose in Lipopolysaccharides (Endotoxin), Heme, Coenzyme A, Adenosylcobalamine, Nicotinamide, Folic acid, Riboflavin, Vitamins and cofactors
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  - -> 1-C units
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  - Fermentation
  - Nitrogen Metabolism
Glycolysis

E. coli Core Model


http://systemsbiology.ucsd.edu/Downloads/E_coli_Core
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 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.
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)
Metabolites & Reactions

Glycolysis

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Metabolite</th>
<th>Formula</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>dglc-D</td>
<td>D-Glucose</td>
<td>C₆H₁₂O₆</td>
<td>0</td>
</tr>
<tr>
<td>g6p</td>
<td>D-Glucose-6-phosphate</td>
<td>C₆H₁₁O₉P</td>
<td>-2</td>
</tr>
<tr>
<td>fru</td>
<td>D-Fructose</td>
<td>C₆H₁₂O₆</td>
<td>0</td>
</tr>
<tr>
<td>f6p</td>
<td>D-Fructose-6-phosphate</td>
<td>C₆H₁₁O₉P</td>
<td>-2</td>
</tr>
<tr>
<td>fdp</td>
<td>D-Fructose-1,6-bisphosphate</td>
<td>C₆H₁₀O₇P</td>
<td>-4</td>
</tr>
<tr>
<td>dhaP</td>
<td>Dihydroxyacetone-phosphate</td>
<td>C₃H₄O₆P</td>
<td>-2</td>
</tr>
<tr>
<td>g3p</td>
<td>Glyceroldehyde-3-phosphate</td>
<td>C₃H₂O₃P</td>
<td>-2</td>
</tr>
<tr>
<td>13dgp</td>
<td>3-Phospho-D-glycerol-1-phosphate</td>
<td>C₃H₄O₁₀P₂</td>
<td>-4</td>
</tr>
<tr>
<td>3pg</td>
<td>3-Phospho-D-glycerate</td>
<td>C₃H₄O₇P</td>
<td>-3</td>
</tr>
<tr>
<td>2pg</td>
<td>D-Glycerate-2-phosphate</td>
<td>C₃H₄O₇P</td>
<td>-3</td>
</tr>
<tr>
<td>pep</td>
<td>Phosphonolylpyruvate</td>
<td>C₃H₂O₄P</td>
<td>-3</td>
</tr>
<tr>
<td>pYr</td>
<td>Pyruvate</td>
<td>C₃H₃O₃</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)**
Aerobic Conditions
Carbon Source: Glucose

\[ \text{Glucose} \rightarrow \text{Glycolysis} \]

\[ \text{NADH} = \text{NADPH} = \text{ATP} = \]

\[ \text{O}_2 \]

\[ \text{AerobicGlucoseBioMass.m} \]
Anaerobic Conditions
Carbon Source: Glucose

Glucose $\downarrow$

ATP = ☀
NADPH = ⚪
NADH = ⚫

Glycolysis
Aerobic Conditions
Carbon Source: Fructose

Fructose → Glycolysis

O₂

AerobicFructoseBioMass.m

ATP = ☀️
NADPH = 🌟
NADH = ★
Anaerobic Conditions
Carbon Source: Fructose

Fructose → Glycolysis

ATP = ⭐
NADPH = ⭐
NADH = ⭐
**E. coli Core Model**

- Component Parts of the *E. coli* Core Model
- Glycolysis
- Pentose Phosphate Pathway
  - Tricarboxylic Acid (TCA) Cycle
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Pentose Phosphate Pathway

E.coli Core Model


http://systemsbiology.ucsd.edu/Downloads/E_coli_Core
Biosynthetic Precursors
(Pentose Phosphate Pathway)

Histidine
Purines (ATP, GTP, dATP, dGTP)
Pyrimidines (UTP, CTP, dCTP, dTTP)
Heptose in Lipopolysaccharides (Endotoxin)

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

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Metabolite</th>
<th>Formula</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>g6p</td>
<td>D-Glucose-6-phosphate</td>
<td>C₆H₁₁O₉P</td>
<td>-2</td>
</tr>
<tr>
<td>6pgl</td>
<td>6-phospho-D-glucono-1,5-lactone</td>
<td>C₆H₉O₉P</td>
<td>-2</td>
</tr>
<tr>
<td>6pgc</td>
<td>6-Phospho-D-gluconate</td>
<td>C₆H₁₀O₁₀P</td>
<td>-3</td>
</tr>
<tr>
<td>ru5p-D</td>
<td>D-Ribulose-5-phosphate</td>
<td>C₅H₉O₈P</td>
<td>-2</td>
</tr>
<tr>
<td>r5p</td>
<td>alpha-D-Ribose-5-phosphate</td>
<td>C₅H₉O₈P</td>
<td>-2</td>
</tr>
<tr>
<td>f6p</td>
<td>D-Fructose-6-phosphate</td>
<td>C₆H₁₁O₉P</td>
<td>-2</td>
</tr>
<tr>
<td>g3p</td>
<td>Glyceraldehyde-3-phosphate</td>
<td>C₃H₅O₆P</td>
<td>-2</td>
</tr>
<tr>
<td>xu5p-D</td>
<td>D-Xylulose-5-phosphate</td>
<td>C₅H₉O₈P</td>
<td>-2</td>
</tr>
<tr>
<td>s7p</td>
<td>Sedoheptulose-7-phosphate</td>
<td>C₇H₁₃O₁₀P</td>
<td>-2</td>
</tr>
<tr>
<td>e4p</td>
<td>D-Erythrose-4-phosphate</td>
<td>C₄H₇O₇P</td>
<td>-2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Reaction</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>G6PDH2r</td>
<td>glucose 6-phosphate dehydrogenase</td>
<td>g6p + nadp \rightarrow 6pgl + h + nadph</td>
</tr>
<tr>
<td>PGL</td>
<td>6-phosphogluconolactonase</td>
<td>6pgl + h₂o \rightarrow 6pgc + h</td>
</tr>
<tr>
<td>GND</td>
<td>phosphogluconate dehydrogenase</td>
<td>6pgc + nadp \rightarrow co₂ + nadph + ru5p-D</td>
</tr>
<tr>
<td>RPI</td>
<td>ribose-5-phosphate isomerase</td>
<td>r5p \rightarrow ru5p-D</td>
</tr>
<tr>
<td>TKT2</td>
<td>transketolase</td>
<td>e4p + xu5p-D \rightarrow f6p + g3p</td>
</tr>
<tr>
<td>TALA</td>
<td>transaldolase</td>
<td>g3p + s7p \rightarrow e4p + f6p</td>
</tr>
<tr>
<td>TKT1</td>
<td>transketolase</td>
<td>r5p + xu5p-D \rightarrow g3p + s7p</td>
</tr>
<tr>
<td>RPE</td>
<td>ribulose 5-phosphate 3-epimerase</td>
<td>ru5p-D \rightarrow xu5p-D</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)
Aerobic Conditions
Carbon Source: Glucose

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

Glucose

Non-oxidative Pathway

Glycolysis

ATP = 
NADPH = 
NADH = 

AnaerobicGlucoseBioMass.m
E. coli Core Model

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Tricarboxylic Acid Cycle (TCA)

E.coli Core Model


http://systemsbiology.ucsd.edu/Downloads/E_coli_Core
TCA Cycle

The tricarboxylic acid cycle (TCA 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 oxidization of acetate derived from carbohydrates, fats and proteins into carbon dioxide. In addition, the cycle provides precursors for certain amino acids as well as the reducing agent NADH.

http://en.wikipedia.org/wiki/TCA_cycle
Biosynthetic Precursors (TCA Cycle)

- Asparagine
- Aspartic acid
- Isoleucine
- Lysine
- Methionine
- Threonine
- Arginine
- Glutamine
- Glutamic acid
- Proline

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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.

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### 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>( \text{acoea} + \text{h}_2\text{o} + \text{oxa} \rightarrow \text{cit} + \text{coa} + \text{h} )</td>
</tr>
<tr>
<td>ACONTa</td>
<td>aconitase (half-reaction A, Citrate hydro-lyase)</td>
<td>( \text{cit} \Leftrightarrow \text{acon-C} + \text{h}_2\text{o} )</td>
</tr>
<tr>
<td>ACONTb</td>
<td>aconitase (half-reaction B, Isocitrate hydro-lyase)</td>
<td>( \text{acon-C} + \text{h}_2\text{o} \Leftrightarrow \text{icitr} )</td>
</tr>
<tr>
<td>ICDHyr</td>
<td>isocitrate dehydrogenase (NADP)</td>
<td>( \text{icitr} + \text{nad} \Leftrightarrow \text{akg} + \text{co2} + \text{nadph} )</td>
</tr>
<tr>
<td>AKGDH</td>
<td>2-Oxoglutarate dehydrogenase</td>
<td>( \text{akg} + \text{coa} + \text{nad} \rightarrow \text{co2} + \text{nad} + \text{succoa} )</td>
</tr>
<tr>
<td>SUCOAS</td>
<td>succinyl-CoA synthetase (ADP-forming)</td>
<td>( \text{atp} + \text{coa} + \text{succ} \rightarrow \text{atp} + \text{pi} + \text{succoa} )</td>
</tr>
<tr>
<td>FRD7</td>
<td>fumarate reductase</td>
<td>( \text{fum} + \text{q8h2} \rightarrow \text{q8} + \text{succ} )</td>
</tr>
<tr>
<td>SUCDi</td>
<td>succinate dehydrogenase (irreversible)</td>
<td>( \text{q8} + \text{succ} \rightarrow \text{fum} + \text{q8h2} )</td>
</tr>
<tr>
<td>FUM</td>
<td>fumarase</td>
<td>( \text{fum} + \text{h}_2\text{o} \Leftrightarrow \text{mal-L} )</td>
</tr>
<tr>
<td>MDH</td>
<td>malate dehydrogenase</td>
<td>( \text{mal-L} + \text{nad} \Leftrightarrow \text{h} + \text{nadlt} + \text{oxa} )</td>
</tr>
<tr>
<td>AKGt2r</td>
<td>2-oxoglutarate reversible transport via symport</td>
<td>( \text{akg[e]} + \text{h[e]} \Leftrightarrow \text{akg} + \text{h} )</td>
</tr>
<tr>
<td>SUCc2r</td>
<td>succinate transport out via proton antiport</td>
<td>( \text{h[e]} + \text{succ[e]} \rightarrow \text{h} + \text{succ[e]} )</td>
</tr>
<tr>
<td>SUCc2r 2</td>
<td>succinate transport via proton symport (2 H)</td>
<td>( 2 \text{h[e]} + \text{succ[e]} \rightarrow 2 \text{h} + \text{succ[e]} )</td>
</tr>
<tr>
<td>FUMt2 2</td>
<td>Fumarate transport via proton symport (2 H)</td>
<td>( \text{fum[e]} + 2 \text{h[e]} \rightarrow \text{fum} + 2 \text{h} )</td>
</tr>
<tr>
<td>MALt2 2</td>
<td>Malate transport via proton symport (2 H)</td>
<td>( 2 \text{h[e]} + \text{mal-L[e]} \rightarrow 2 \text{h} + \text{mal-L[e]} )</td>
</tr>
</tbody>
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Aerobic Conditions
Carbon Source: Glucose

Oxidative Pathway

ATP = ⭐
NADPH = ⭐
NADH = ⭐

Constraint-based Metabolic Reconstructions & Analysis

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

ATP = ☀️
NADPH = 🌟
NADH = 🌟
E. coli Core Model

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Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

**E. coli Core Model**

The glyoxylate 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 off for biosynthesis.

Glycoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

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 for Glyoxylate Cycle, Gluconeogenesis, and Anapleurotic Reactions

Cysteine
Glycine
Serine

Tyrosine
Tryptophan
Phenylalanine

Alanine
Leucine
Valine

Asparagine
Aspartic Acid
Isoleucine

Lysine
Methionine
Threonine

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

**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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Aerobic Conditions
Carbon Source: Pyruvate

Gluconeogenesis

Pyruvate

ATP = ☀️
NADPH = ⬷
NADH = ⬷
Aerobic Conditions
Carbon Source: Malate

ATP = ☀
NADPH = ⬜
NADH = ✖️
Aerobic Conditions
Carbon Source: Acetate

Gluconeogenesis

Acetate

\[ \text{ATP} = \star \]
\[ \text{NADPH} = \star \]
\[ \text{NADH} = \star \]
Aerobic Conditions
Carbon Source: Acetaldehyde
Aerobic Conditions
Carbon Source: Ethanol

Gluconeogenesis

ATP = 
NADPH = 
NADH = 

Ethanol
**E. coli Core Model**

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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.
Electron Transport Chain

Oxidative Phosphorylation and Transfer of Reducing Equivalents

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Metabolites & Reactions

<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_{49}H_{74}O_{4}</td>
<td>0</td>
</tr>
<tr>
<td>q8h2</td>
<td>Ubiquinol-8</td>
<td>C_{49}H_{76}O_{4}</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>nadp</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>nadph</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_{12}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>
</tr>
</tbody>
</table>

Oxidative Phosphorylation and Transfer of Reducing Equivalents

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

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

ATP = 🌟
NADPH = 🌟
NADH = 🌟

AerobicGlucoseBioMass.m
E. coli Core Model

• Component Parts of the E. coli Core Model
  • Glycolysis
  • Pentose Phosphate Pathway
  • Tricarbonoxylic 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

Constraint-based Metabolic Reconstructions & Analysis

Lesson: E.coli Metabolic Core

Fatty acids
Murein
Leucine

Alanine
Leucine
Valine

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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-LACt2</td>
<td>D-lactate transport via proton symport</td>
<td>h[e] + lac-D[e] ⇌ h + lac-D</td>
</tr>
<tr>
<td>PDH</td>
<td>pyruvate dehydrogenase</td>
<td>coa + nad + pyr → accoa + co2 + nadh</td>
</tr>
<tr>
<td>PFL</td>
<td>pyruvate formate lyase</td>
<td>coa + pyr → accoa + for</td>
</tr>
<tr>
<td>FORt1</td>
<td>formate transport via diffusion</td>
<td>for ⇌ for[e]</td>
</tr>
<tr>
<td>FORt2</td>
<td>formate transport via proton symport</td>
<td>for[e] + h[e] → for + h</td>
</tr>
<tr>
<td>PTA</td>
<td>phosphotransacetylase</td>
<td>accoa + pi ⇌ actp + coa</td>
</tr>
<tr>
<td>ACKr</td>
<td>acetate kinase</td>
<td>ac + atp ⇌ actp + adp</td>
</tr>
<tr>
<td>ACALD</td>
<td>acetaldehyde dehydrogenase (acetylating)</td>
<td>acald + coa + nad ⇌ accoa + h + nadh</td>
</tr>
<tr>
<td>ACLD2x</td>
<td>alcohol dehydrogenase (ethanol)</td>
<td>etoh + nad ⇌ acald + h + nadh</td>
</tr>
<tr>
<td>ACt2r</td>
<td>acetate reversible transport via proton symport</td>
<td>ac[e] + h[e] ⇌ ac + h</td>
</tr>
<tr>
<td>ACt2d</td>
<td>acetaldehyde reversible transport</td>
<td>acald[e] ⇌ acald</td>
</tr>
<tr>
<td>ETOH2r</td>
<td>ethanol reversible transport via proton symport</td>
<td>etoh[e] + h[e] ⇌ etoh + h</td>
</tr>
</tbody>
</table>

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Mixed Acid Fermentation

Anaerobic Conditions
Carbon Source: Glucose
E. coli Core Model

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- 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.


Nitrogen Metabolism
Biosynthetic Precursors
(Nitrogen Metabolism)

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Metabolites & Reactions

Nitrogen Metabolism

<table>
<thead>
<tr>
<th>Abbrev.</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>

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Reaction</th>
<th>Equation</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>GLU12r</td>
<td>L-glutamate transport via proton symport</td>
<td>glu-L[c] + b[e] ⇔ 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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