Introduction to metabolism
Problem: note the diversity of chemicals in the cell

- amino acids (20+)
- sugars (?)
- nucleotides (5+)
- lipids (?)
- “secondary” compounds

Cells need to have mechanisms for synthesis (anabolism) and degradation (catabolism)

Note variations, connected to ecology:

<table>
<thead>
<tr>
<th>Class</th>
<th>Energy source</th>
<th>C source</th>
</tr>
</thead>
<tbody>
<tr>
<td>photoautotrophs</td>
<td>light</td>
<td>CO₂</td>
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Concentrate on chemoheterotrophs (animals) [but we will also talk about photosynthesis]
Oxidation has a dual role: building blocks and energy

In our high O\textsubscript{2} environment: reduced compounds seem more energetic
e.g., C:
most reduced: \begin{align*}
&\text{CH}_4 & \text{Highly negative } \Delta G^o' \text{ for oxidation} \\
&\text{-CH}_2-\text{CH}_3 \\
&\text{-CH}_2-\text{CH}_2-\text{OH} \\
&\text{-CH}_2-\text{CH}=\text{O} \\
&\text{-CH}_2-\text{COOH}
\end{align*}

most oxidized \begin{align*}
&\text{O}=\text{C}=\text{O} & \text{Positive/zero } \Delta G^o' \text{ for oxidation}
\end{align*}

• An intermediate level of oxidation is required for C skeletons
• Obtaining a proper redox state and focusing it on the manipulation of covalent bonds is a major objective of metabolism
• Oxidation can provide a source of energy, $\Delta G^o'$, to force reactions forward through coupled reactions
A metabolic map
A metabolic map

Each step represents an individual reaction catalyzed by one of these types of enzymes:

1. Oxidoreductases (oxidation-reduction reactions)
2. Transferases (transfer of functional groups)
3. Hydrolases (hydrolysis reactions)
4. Lyases (addition to double bonds)
5. Isomerases (isomerization reactions)
6. Ligases (formation of bonds with ATP cleavage)
Mycoplasma pneumoniae has a simple structure and reduced metabolism.

Proteome Organization in a Genome-Reduced Bacterium
The biochemistry of *M. pneumoniae* is much simpler than that shown earlier.
We will focus on a subset of the pathways in *M. pneumoniae*, but also add oxidative energy metabolism (citric acid cycle, electron transport system), photosynthesis and a little bit of amino acid metabolism.
Metabolism (often) consists of enzyme-catalyzed reactions transferring $\Delta G$ (energy, Pi), redox state (electrons), and/or 1-C or 2-C units through “coenzymes”

- ADP/ATP
- NAD$^+$/NADH
- FAD/FADH$_2$
- CoASH/Acetyl-SCoA
ATP provides energy and phosphate

ATP + H₂O --> ADP + Pᵢ  \( \Delta G^o' = -30.5 \) kJ/mol

Why is \( \Delta G^o' \) negative? Resonance makes the product Pi more stable.

Uses: transfer of \( \Delta G \) and/or charge (as Pi)
  - e.g., motile proteins: charge changes tertiary structure
  - e.g., transient –P- or AMP- conjugation
    “activates” a compound in a pathway
  Glucose + ATP --> glucose-6-P + ADP
NADH (nicotinamide adenine dinucleotide) carries electrons (reducing power) and energy

\[
\text{NADH} + \text{H}^+ \rightarrow \text{NAD}^+ + 2 \text{H}^+ + 2 \text{e}^-
\]

\[
\Delta G^o' = -62 \text{ kJ/mol}
\]

(Reversed, NAD\(^+\) is a useful oxidizing agent, e.g., alcohols -C-OH to aldehydes -CH=O)
Flavin (FAD – flavin adenine dinucleotide, FMN – flavin mononucleotide) also carries electrons (1 or 2) and energy

\[ \text{FADH}_2 \rightarrow \text{FAD} + 2 \text{H}^+ + 2 \text{e}^- \]

\[ \Delta G^o' = -0.6 \text{ to } -17 \text{ kJ/mol} \]

(FAD is another useful oxidizing agent e.g., -CH\_2-CH\_2- \rightarrow -CH=CH-)

![Diagram of Flavin structures]
Coenzyme A (CoA, CoA-SH) carries 2-carbon units

\[ \text{CH}_3\text{-C-S-CoA} + \text{HR} \]
Since animals cannot synthesize most coenzymes, the coenzymes (or their precursors) are vitamins (that is, must be obtained in the diet).

Coenzyme A  FAD, FMN  NAD  pyridoxal phosphate
Deficiencies of vitamins and their coenzymes are pathological

Deficiency causes:

- Hypertension
- Cheliosis
- Pellagra:
  - photophobia
  - dermatitis
  - diarrhea
  - insanity
- Depression
- confusion
- convulsions
Summary

• The diverse chemicals in the cell are linked by synthetic and degradative reactions arranged in pathways.

• Redox reactions are essential for synthesis and for applying energy ($\Delta G$).

• Various coenzymes are mediators of energy, electron, and carbon-unit transfers in metabolism (you need to know the essential structures and reactions of ATP, NAD$^+$/NADH, FAD/FADH$_2$, and CoA).