Metabolism and Bioenergetics

Pratt and Cornely, Chapter 12

Fuel and Digestion

• Breakdown of food biomolecules to monomers
• Absorption of monomers
  – Storage
  – metabolism
Carbohydrates

- Amylase in mouth, intestine
  - Amylose
  - Amylopectin
- Transported through intestine to portal, vein
  - liver/bloodstream
- Storage
  - Muscle
  - Liver
  - Converted to fat

Proteins

- Breakdown of peptide bond
  - Gastric proteases
  - Pancreatic proteases
- Amino acids transported through intestine to blood/liver
  - Incorporated into proteins (if needed)
  - Broken down to carbs and fats (storage)
Lipids

- Digestion
  - Pancreatic lipases
  - Bile salts
- Transported through intestinal cell (diffusion or transport)
- Re-packaged
- Circulated as chylomicrons and lipoproteins
- Stored in adipose

Mobilization of Glycogen

- Required for brain
- Highly branched; release of energy
- Phosphorolysis
- Muscle: Energy conservation
- Liver: phosphate hydrolysis before entering blood
Mobilization of Lipids

- Primary energy for heart
- Compact energy form
- Lipases release from adipose
- Circulate as protein complexes
- Major basal energy source

Protein Processing

- Proteins not a storage form
- But do need constantly degrade (diet or outside source)
- Lysozyme
  - Membrane and extracellular
  - pH 5 optimum
- Proteasome
  - Barrel shaped
  - Ubiquitin tag
Problem 25

- Check the box of each pathway in which this intermediate is a reactant or product

<table>
<thead>
<tr>
<th></th>
<th>Glycolysis</th>
<th>Citric Acid Cycle</th>
<th>Fatty Acid metabolism</th>
<th>TAG synthesis</th>
<th>Transamination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl-CoA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glyceraldehyde-3-P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyruvate</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Redox Reactions

- Catabolism  
  - Oxidation

- Anabolism  
  - Reduction

Redox Cofactors

- 2 electron transfer  
  - NAD⁺/NADH (catabolism)
  - NADP⁺/NADPH (anabolism)

- 1 or 2 electron transfer  
  - FAD/FADH₂

- 1 electron transfer  
  - Ubiquinone, metals
  - membrane

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Catalytic Cofactors

- Electron transport chain
- Purpose of breathing oxygen

Essential Nutrients

<table>
<thead>
<tr>
<th>TABLE 12-1</th>
<th>Some Essential Substances for Humans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino Acids</td>
<td>Fatty Acids</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>Linoleate</td>
</tr>
<tr>
<td>Leucine</td>
<td>Linolenate</td>
</tr>
<tr>
<td>Lysine</td>
<td>Linolenate</td>
</tr>
<tr>
<td>Methionine</td>
<td>Linolenate</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>Linolenate</td>
</tr>
<tr>
<td>Threonine</td>
<td>Linolenate</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>Linolenate</td>
</tr>
<tr>
<td>Valine</td>
<td>Linolenate</td>
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</tbody>
</table>

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Vitamins

TABLE 12.2 Vitamins and Their Roles

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Coenzyme Product</th>
<th>Biochemical Reaction</th>
<th>Human Deficiency Disease</th>
<th>Text Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water-Soluble</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascorbic acid (C)</td>
<td>Ascorbate</td>
<td>Collagen for hydroxylation of collagen</td>
<td>Scurvy</td>
<td>Box 5-D</td>
</tr>
<tr>
<td>Thiamin (B1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cobalamin (B12)</td>
<td>Cobalamin coenzymes</td>
<td>Folic acid for aliphatic reactions</td>
<td>Anemia</td>
<td>Section 17-1</td>
</tr>
<tr>
<td>Follic acid</td>
<td>Tetrahydrofolate</td>
<td>Follic acid for one-carbon transfer reactions</td>
<td>Anemia</td>
<td>Section 16-1</td>
</tr>
<tr>
<td>Lipoic acid</td>
<td>Lipopeptide</td>
<td>Lipoic acid for acetyl transfer reactions</td>
<td>*</td>
<td>Section 16-1</td>
</tr>
<tr>
<td>Niacinamide (nicacin, B3)</td>
<td>Niacinamide coenzymes (NAD+**, NADP+*)</td>
<td>Niacinamide for oxidation-reduction reactions</td>
<td>Pellagra</td>
<td>Fig. 9-3, Section 12-2</td>
</tr>
<tr>
<td>Pantothentic acid (B5)</td>
<td>Coenzyme-A</td>
<td>Coenzyme-A for acetyl transfer reactions</td>
<td>*</td>
<td>Fig. 3-3, Section 12-3</td>
</tr>
<tr>
<td>Pyridoxine (B6)</td>
<td>Pyridoxal phosphate</td>
<td>Pyridoxal phosphate for amino-group transfer reactions</td>
<td>*</td>
<td>Section 18-1</td>
</tr>
<tr>
<td>Riboflavin (B2)</td>
<td>Flavin coenzymes (FAD, FMN)</td>
<td>Riboflavin for oxidation-reduction reactions</td>
<td>*</td>
<td>Fig. 3-3</td>
</tr>
<tr>
<td>Thiamine (B3)</td>
<td>Thiamine: pyrophosphate</td>
<td>Thiamine for alpha-keto acid transfer reactions</td>
<td>Beriberi</td>
<td>Sections 12-2, 14-1</td>
</tr>
<tr>
<td>Folic-Soluble</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin A (retinal)</td>
<td></td>
<td>Light-absorbing pigment</td>
<td>Blindness</td>
<td>Box 8-B</td>
</tr>
<tr>
<td>Vitamin D</td>
<td></td>
<td>Hormone that promotes Ca2+ absorption</td>
<td>Rickets</td>
<td>Box 8-B</td>
</tr>
<tr>
<td>Vitamin E (tocopherol)</td>
<td></td>
<td>Antioxidant</td>
<td>*</td>
<td>Box 8-B</td>
</tr>
<tr>
<td>Vitamin K</td>
<td></td>
<td>Co-factor for carboxylation of blood coagulation proteins</td>
<td>Blood</td>
<td>Box 8-B</td>
</tr>
</tbody>
</table>

*Deficiency in humans is rare or unknown.
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Problem 33

- Refer to table 12.2 to identify the vitamin necessary for these reactions:

\[
\begin{align*}
\text{IN: } & \quad \text{COO}^- + \text{ATP} + \text{HCO}_3^- \\
\text{CH}_3

\text{II: } & \quad \text{COO}^- + \text{ADP} + \text{P}_i \\
\text{CH}_3

\text{III: } & \quad \text{H}_2\text{N} - \text{CH} \quad \text{COO}^- \\
\text{CH}_3

\text{IV: } & \quad \text{COO}^- + \text{CaA} - \text{DH} \\
\text{CH}_3

\text{V: } & \quad \text{H}_2\text{C} - \text{C} - \text{S} - \text{CaA} + \text{CO}_2
\end{align*}

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Vitamin Chemistry

• We will build throughout semester
• Introduction to fundamental chemistry of decarboxylation

![Thiamine (vitamin B₁)](image)

Pyridoxyl Phosphate (PLP)
Vitamin B₆

Qualitative Energetics

• ATP: High energy bonds—inhherent chemistry
  – Electrostatic repulsion
  – Solvation of products
  – Resonance
• Rxn goes to “completion”
Energy Currency

Anaerobic systems

- high jump
- power lift
- shot put
- tennis serve

Aerobic systems

- sprints
- football line play

- Glycolysis
  - 200 – 400 m race
  - 100 m swim

- Oxidative phosphorylation
  - race beyond 500 m

Duration of activity

- 4 s
- 10 s
- 1.5 min
- 3 min

phosphoanhydride bonds

Adenosine

AMP

ADP

ATP
Formal Metabolism

Nutrient $\rightarrow$ ADP + $P_i$ $\rightarrow$ Product

catabolism $\rightarrow$ ATP $\rightarrow$ anabolism

Waste product $\rightarrow$ ATP $\rightarrow$ Precursor

Uphill or Downhill?

Glucose $\rightarrow$ Glucose-6-phosphate $\rightarrow$ Phosphocreatine

Glucose-1-phosphate $\rightarrow$ Glucose-6-phosphate $\rightarrow$ Acetyl-CoA

Creative
Qualitative Predictions

• Inherently favorable, unfavorable, or near equilibrium?

\[
\begin{align*}
\text{GMP} + \text{ATP} & \iff \text{GDP} + \text{ADP} \\
\text{GDP} + \text{ATP} & \iff \text{GTP} + \text{ADP} \\
\text{AMP} + \text{ATP} & \iff 2 \text{ ADP} \\
\text{AMP} + \text{ATP} + 2 \text{ P_i} & \iff 2 \text{ ATP} + 2 \text{ H_2O}
\end{align*}
\]

Thermodynamics: A metaphor
Common Misconceptions

- Is this reaction at equilibrium or not?
- If not, in which direction does the equilibrium lie?

Standard Free Energy vs. Free Energy

If, in this example, $\Delta G^\circ$ is negative, then $\Delta G$ is negative.

Once it reaches equilibrium, $\Delta G^\circ$ is still negative, but $\Delta G$ is zero.
Standard Free Energy vs. Free Energy

\[
\text{ATP} \leftrightarrow \text{ADP} + P \quad \Delta G^\circ \text{ is } -32 \text{ kJ}
\]
\[
\Delta G \text{ is } -32 \text{ kJ}
\]

\[
\text{ADP} \leftrightarrow \text{ATP} + P \quad \Delta G^\circ \text{ is } -32 \text{ kJ}
\]
\[
\Delta G \text{ is zero}
\]

Quantitative

- Inherent component
- Concentration component

\[
\Delta G_{\text{reaction}} = \Delta G^\circ_{\text{reaction}} + RT \ln \left( \frac{[\text{products}]}{[\text{reactants}]} \right)
\]
Equilibrium

• Equilibrium = DEAD!
• What is \([\text{product}] / [\text{rxt}]\) ratio of ATP hydrolysis to ADP at equilibrium? \((\Delta G = 0)\)

\[
\Delta G_{\text{reaction}} = \Delta G^\circ_{\text{reaction}} + RT \ln \left( \frac{[\text{products}]}{[\text{reactants}]} \right)
\]

• \([\text{ADP}][\text{Pi}] / [\text{ATP}] = 4.1 \times 10^5 = K_{eq}\)

Free Energy of ATP hydrolysis

• Actual cellular concentrations don’t vary much from \([\text{P},] = [\text{ATP}] = 5 \text{ mmol and } [\text{ADP}] = 1 \text{ mmol}\)
• Problem 43: What is the actual free energy of ATP hydrolysis in the cell? More or less than -32 kJ?

\[
\Delta G_{\text{reaction}} = \Delta G^\circ_{\text{reaction}} + RT \ln \left( \frac{[\text{products}]}{[\text{reactants}]} \right)
\]
Two Types of Reactions

• Near-equilibrium reactions
  – Actual [pdt] / [rxt] ratio near the equilibrium concentrations
  – $\Delta G$ close to zero (regardless of $\Delta G^\circ$)
  – Not regulated—part of overall flux of metabolism

• Metabolically irreversible reactions
  – $\Delta G$ far from zero
  – Can only be overcome by energy input
  – regulated
ATP in Metabolism

• Overcoming a barrier...
  – Can’t change concentrations (ammonia is toxic!)
  – Couple the reaction to a spontaneous reaction!

\[ \text{Glutamate} + \text{NH}_4^+ \iff \text{glutamine} + \text{H}_2\text{O} \]
\[ \Delta G^{\circ}\text{reaction} = +14 \text{ kJ mol}^{-1} \]

– Problem 59: Write an equation to couple this reaction to ATP hydrolysis.

Mechanism of Coupling

\[ \text{Glutamate} \xrightarrow{\text{ATP}} \gamma\text{-Glutamyl phosphate} \xrightarrow{\text{ADP}} \text{Glutamine} \]
Another Type of Coupling

• Problem 50: The standard free energy of formation of UDP-glucose from G-1-P and UTP is about zero. Yet the production of UDP-glucose is highly favorable. Explain.

Glucose-1-phosphate + UTP $\leftrightarrow$ UDP-glucose + PP$_i$

Phosphoryl Transfer in Energetic Intermediates

**Phosphoryl group transfer potential**

$$\text{PPi} \rightarrow 2 \text{ Pi} = -29 \text{ kJ/mol}$$
Problem 42

• Calculate the biological standard free energy for the isomerization of G-1-P to G-6-P. Is it spontaneous under standard conditions? Is it spontaneous when [G-6-P] is 5 mM and [G-1-P] = 0.1 mM?

<table>
<thead>
<tr>
<th>Compound</th>
<th>ΔG°° (kJ · mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphoenolpyruvate</td>
<td>-61.9</td>
</tr>
<tr>
<td>1,3-Bisphosphoglycerate</td>
<td>-49.4</td>
</tr>
<tr>
<td>ATP → AMP + PP</td>
<td>-45.6</td>
</tr>
<tr>
<td>Phosphocreatine</td>
<td>-43.1</td>
</tr>
<tr>
<td>ATP → ADP + P</td>
<td>-30.5</td>
</tr>
<tr>
<td>Glucose-1-phosphate</td>
<td>-20.9</td>
</tr>
<tr>
<td>PP → 2 P</td>
<td>-19.2</td>
</tr>
<tr>
<td>Glucose-6-phosphate</td>
<td>-13.8</td>
</tr>
<tr>
<td>Glycerol-3-phosphate</td>
<td>-9.2</td>
</tr>
</tbody>
</table>

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