Intermolecular Forces
1) Electrostatic Interactions - +/- attractions
2) Hydrogen Bonding – a super strong dipole-dipole force
   -must have hydrogen bound to S, O, N (S-H, O-H, or N-H bond)
3) Dipole-Dipole Forces – interaction between molecules having permanent dipole moments
   -the larger the dipole moment, the larger the force
4) Dipole-Induced Dipole Forces - interaction between a polar molecule and a nonpolar molecule; the polar
   molecule induces a dipole in the nonpolar molecule
5) London Dispersion Forces – due to induced dipoles
   -all molecules have these
   -the larger the molecule, the larger the force
6) Hydrophobic Interactions – tendency of nonpolar molecules to coalesce in an aqueous environment
   -hydrophobic (”water-fearing”) vs hydrophilic (”water loving”) vs amphipathic

Hydrogen bonding in H₂O results in high M.P. and B.P., high enthalpies of fusion and vaporization, high heat
capacity, high surface tension

Acids and Bases
Acid – Proton donor
Base – Proton Acceptor

\[
pH = -\log[H^+] \quad \text{and} \quad [H^+] = 10^{-pH}
\]

\[
[pOH] = -\log[OH^-] \quad \text{and} \quad [OH^-] = 10^{-pOH}
\]

Auto-ionization of H₂O: \( H_2O \ce{<=>} H^+ + OH^- \)

\[
K_a = [H^+] [OH^-] = 1 \times 10^{-14}
\]

Acid dissociation in water: \( HA + H_2O \ce{<=>} H_3O^+ + A^- \)

\[
K_a = \frac{[H_3O^+] [A^-]}{[HA]}
\]

Base dissociation in water: \( A^- + H_2O \ce{<=>} HA + OH^- \)

\[
K_b = \frac{[OH^-] [HA]}{[A^-]}
\]

What is the pH of 0.01M HCl?

What is the pH of a 0.1M solution of acetic acid (pKₐ = 4.75)?
Titration Curves
- For monoprotic acids and bases
- For polyprotic acids and bases

**Buffers**
Buffer – A solution that resists changes in pH. It is composed of a weak acid and its conjugate base or a weak base and its conjugate acid.

Buffer Range – pH = pKa ± 1

**Maximum Buffering Capacity**
1) pH ~ pKa
2) High concentrations of HA/A⁻

**Calculations with buffers**

\[
pH = pK_a + \log \left( \frac{[A^-]}{[HA]} \right) \quad \frac{[A^-]}{[HA]} = 10^{(pH - pKa)} \quad [A^-] + HA = \text{total_buffer_conc.}
\]

Show how to make 1L of a 1M acetate buffer solution of pH 5.35 using the appropriate concentrations of acetic acid (pKa = 4.75) and sodium acetate.

Show how to make 1L of a 1M acetate buffer solution of pH 5.35 using acetic acid and 2M NaOH.

Show how to make 1L of a 1M acetate buffer solution of pH 5.35 using sodium acetate and 2M HCl.

How much would the pH change if we added 10mL of 1M HCl to the above acetate buffer at pH 5.35?
**Amino Acids**

- D vs. L-amino acids
  - L-amino acids have the S configuration

- Polar (hydrophilic) vs Non-polar (hydrophobic) side chains

- Acidic vs. Basic Side Chains

- Planar geometry around peptide bonds

<table>
<thead>
<tr>
<th>AA</th>
<th>pKa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asp</td>
<td>3.86</td>
</tr>
<tr>
<td>Glu</td>
<td>4.25</td>
</tr>
<tr>
<td>Cys</td>
<td>8.33</td>
</tr>
<tr>
<td>Tyr</td>
<td>10.07</td>
</tr>
<tr>
<td>Lys</td>
<td>10.53</td>
</tr>
<tr>
<td>Arg</td>
<td>12.48</td>
</tr>
<tr>
<td>His</td>
<td>6.0</td>
</tr>
</tbody>
</table>
Protein Structure

Primary Structure
Amino Acid Sequence (N→C)
Determines 3D shape of peptide

Secondary Structure (Held together by H-bonding in the backbone)
Alpha-helix (3.6 residues per turn; 5.4Å per turn)
Beta-sheet (parallel and anti-parallel)

Tertiary Structure (due to interactions of the AA side chains)
3D folding of a single peptide; involved are hydrophobic interactions, electrostatic interactions, hydrogen bonding and covalent bonding (Disulfide bridges between cysteine residues)

Quaternary Structure (same interactions involved as in tertiary structure)
Interaction of multiple subunits (separate peptide chains) as in hemoglobin -Cooperativity

Classes of Proteins
1) Globular Proteins
Hydrophobic residues are sequestered in the interior of the protein while hydrophylic residues are on the outer surface.

2) Membrane Proteins
Hydrophobic residues face outwards to interact with the lipids in the cell membrane while hydrophilic residues face inwards.

3) Fibrous Proteins
Usually hydrophobic and have a highly repetitive amino acid sequence (ex. collagen)

Protein Denaturation
Unfolding of a protein due to changes in pH, temperature, salt concentration or heavy metal ions; also due to the addition of organic solvents or detergents, reducing agents or to mechanical stress

Myoglobin vs Hemoglobin
H⁺, CO₂, and decrease the affinity of Hemoglobin for O₂ (Bohr Effect)
BPG also decreases the affinity of Hemoglobin for O₂
   -Adult vs fetal hemoglobin
**Enzymes**

Rates and Rate Laws
rate = $k[A]^x[B]^y$

- orders have to be determined experimentally or from a mechanism

**Enzyme Kinetics**

Lock and Key vs. Induced Fit Model

Michaelis-Menton Kinetics (non-allosteric enzymes)

Standard Plot of velocity vs [S]

\[
V = \frac{V_{\text{max}}[S]}{K_m + [S]}
\]

Lineweaver-Burke Plot (Double Reciprocal plot) of $1/v$ vs $1/[S]$

Competitive Inhibition

- Inhibitor binds to the active site
- Changes $K_m$ but not $V_{\text{max}}$
Non-competitive Inhibition
-Inhibitor binds somewhere other than the active site
-Changes $V_{\text{max}}$ not $K_m$

Allosteric Enzymes
-Ex. ATCase
-Exhibit Cooperativity
-Feedback Inhibition
-homotropic vs. heterotropic effectors

K Systems – Inhibitor/Activator affects the $K_{0.5}$ but not $V_{\text{max}}$
V Systems - Inhibitor/Activator affects the $V_{\text{max}}$ but not $K_{0.5}$

Concerted Model
-Enzyme has tense and relaxed states
-Tense state has low affinity for substrate
-Relaxed state has high affinity for substrate
-Effectors stabilize 1 of the 2 states and all subunits switch concertedly (together)

Sequential Model
-Enzyme has tense and relaxed states
-Tense state has low affinity for substrate
-Relaxed state has high affinity for substrate
-A change in a single subunit makes it easier for a change in another subunit

Regulation by Phosphorylation
-Ser, Thr, and Tyr residues can be phosphorylated by kinases (usually uses ATP)
-Phosphorylation can either activate or inhibit an enzyme depending upon the enzyme
-Na+/K+ ATPase
-Glycogen phosphorylase

Zymogens – inactive precursors that become active upon modification

Cofactors – can be metal ions (act as lewis acids) or organic molecules (coenzymes)

Catalysis
1) Proximity Effects
2) Strain Effects
3) Electrostatic Effects
4) Acid-Base Effects
5) Covalent Catalysis
College Biochemistry Chapter 5 - Bioenergetics

Bioenergetics

\[ \Delta G = \Delta G^\circ + RT \ln Q \] (Free energy under non-standard conditions)

\[ \Delta G^\circ = -RT \ln K_{eq} \]

<table>
<thead>
<tr>
<th>(\Delta G^\circ)</th>
<th>Exergonic (Spontaneous)</th>
<th>Endergonic (Nonspontaneous)</th>
<th>At equilibrium</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>= 0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Free Energy Changes for Select Metabolic Processes

<table>
<thead>
<tr>
<th>Reaction</th>
<th>(\Delta G^\circ) (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP + H2O → ADP + Pi</td>
<td>-30.5</td>
</tr>
<tr>
<td>ATP + H2O → AMP + PPi</td>
<td>-32.2</td>
</tr>
<tr>
<td>PPi + H2O → 2 Pi</td>
<td>-33.5</td>
</tr>
<tr>
<td>Gluc-6-P + H2O → glucose + Pi</td>
<td>-12.5</td>
</tr>
</tbody>
</table>

Metabolism

Catabolism vs Anabolism

Glucose as fuel:

\[ C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O \]

NAD+/NADH – 2 e⁻ redox agent involved in catabolism

NADP+/NADPH - 2 e⁻ redox agent involved in anabolism

FAD/ FADH₂ & FMN/FMNH₂ – 1 or 2 e⁻ redox agents
College Biochemistry Chapter 6 - Carbohydrates

**Carbohydrates**

D vs. L-sugars

Aldose vs. Ketose

Triose, Tetrose, Pentose, Hexose

Furanose vs Pyranose

Hemi-acetals (hemi-ketals) and Acetals (ketals)

Alpha vs. Beta (anomeric carbon)

Mutarotation

**Reducing sugars**

All open chain aldoses and most ketoses and hemi-acetals/hemi-ketals are reducing

All acetals and ketals are non-reducing sugars

**Glycosidic Linkages**

Sucrose – glucose-fructose with an $\alpha,\beta(1,2)$ linkage

Monosaccharides – glucose, fructose, galactose, etc.

Oligosaccharides – sucrose (glucose-fructose) and lactose (glucose-galactose) are disaccharides

Polysaccharides – amylose (linear glucose polysaccharide with $\alpha$-1,4 linkages)

- amylopectin (branched glucose polysaccharide with $\alpha$-1,4 and $\alpha$-1,6 linkages)
- glycogen (branched glucose polysaccharide with $\alpha$-1,4 and $\alpha$-1,6 linkages)
- cellulose (linear glucose polysaccharide with $\beta$-1,4 linkages)
Glycolysis

Time didn’t allow for thorough coverage of everything. I’ve tried to note (both in the video and in this outline) subjects that you’ll want to look at in more detail than we had time for.

1. Glucose
   - Hexokinase: ATP → ADP
2. Glucose-6-Phosphate (G-6-P)
   - Glucose-Phosphate Isomerase
3. Fructose-6-Phosphate (F-6-P)
   - PFK-1: ATP → ADP
4. Fructose-1,6-Bisphosphate (FBP)
   - Aldolase
   - Dihydroxyacetone phosphate (DHAP)
     - Triosephosphate Isomerase
     - Glyceraldehyde-3-Phosphate (G-3-P)
5. Glyceraldehyde-3-Phosphate (G-3-P)
   - Glyceraldehyde-3-Phosphate Dehydrogenase: NAD⁺ → NADH
6. 1,3-bisphosphoglycerate (BPG)
   - Phosphoglycerate Kinase
7. 3-Phosphoglycerate (3-PG)
   - Phosphoglycerate Mutase
   - Enolase
   - Phosphoenolpyruvate (PEP)
   - Pyruvate Kinase
8. Pyruvate

MAJOR REGULATORY STEP
Glycolysis

### GLYCOLYSIS REACTIONS

<table>
<thead>
<tr>
<th>Reaction</th>
<th>$\Delta G^\circ$(kJ)</th>
<th>$\Delta G$(kJ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>glucose + ATP $\rightarrow$ G-6-P + ADP</td>
<td>-16.7</td>
<td>-33.9</td>
</tr>
<tr>
<td>G-6-P $\rightarrow$ F-6-P</td>
<td>1.67</td>
<td>-2.92</td>
</tr>
<tr>
<td>F-6-P + ATP $\rightarrow$ F-1,6-BP + ADP</td>
<td>-14.2</td>
<td>-18.8</td>
</tr>
<tr>
<td>F-1,6-BP $\rightarrow$ DHAP + G-3-P</td>
<td>23.9</td>
<td>-0.23</td>
</tr>
<tr>
<td>DHAP $\rightarrow$ G-3-P</td>
<td>7.56</td>
<td>2.41</td>
</tr>
<tr>
<td>G-3-P + P_i + NAD$^+$ $\rightarrow$ 1,3-BPG + NADH</td>
<td>6.20</td>
<td>-1.29</td>
</tr>
<tr>
<td>11,3-BPG + ADP $\rightarrow$ 3-PG + ATP</td>
<td>-18.8</td>
<td>0.1</td>
</tr>
<tr>
<td>3-PG $\rightarrow$ 2-PG</td>
<td>4.4</td>
<td>0.83</td>
</tr>
<tr>
<td>2-PG $\rightarrow$ PEP + H$_2$O</td>
<td>1.8</td>
<td>1.1</td>
</tr>
<tr>
<td>PEP + ADP $\rightarrow$ pyruvate$^-$ + ATP</td>
<td>-31.4</td>
<td>-23.0</td>
</tr>
<tr>
<td>ATP $\rightarrow$ ADP + P_i</td>
<td>-30.5</td>
<td></td>
</tr>
</tbody>
</table>

### Glycolysis Control

<table>
<thead>
<tr>
<th>ENZYME</th>
<th>ACTIVATED BY</th>
<th>INHIBITED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexokinase</td>
<td>AMP</td>
<td>Glucose-6-P (minor)</td>
</tr>
<tr>
<td>PFK-1</td>
<td>AMP, Fructose-6-P, Fructose-2,6-BP (liver), Insulin</td>
<td>ATP, Fructose-1,6-BP, Citrate, Glucagon</td>
</tr>
<tr>
<td>Pyruvate Kinase</td>
<td>AMP, Fructose-1,6-BP</td>
<td>ATP, Acetyl CoA, Phosphorylation, Alanine</td>
</tr>
</tbody>
</table>

PFK-1 - Tetramer with different isozymes (combinations of M and L)

Fructose and Galactose entry points into glycolysis
**Gluconeogenesis**

Occurs in the liver and kidneys to provide glucose in the absence of dietary glucose
Can convert pyruvate, lactate, glycerol and α-keto acids to glucose

Pyruvate Carboxylase – converts pyruvate into oxaloacetate
found in mitochondria and requires biotin

Malate Shuttle
Malate Dehydrogenase converts oxaloacetate to malate and then back to oxaloacetate

![Pyruvate oxidation diagram](image)

PEP Carboxykinase – converts oxaloacetate to phosphoenolpyruvate
found in both the cytosol and mitochondrion

Fructose-1,6-Bisphatase – converts fructose-1,6-bisphosphate to fructose-6-phosphate

Glucose-6-Phosphatase – converts glucose-6-phosphate to glucose
allows glucose to enter the blood stream

**Gluconeogenesis Control**

<table>
<thead>
<tr>
<th>ACTIVATION</th>
<th>INHIBITION</th>
<th>ENZYME</th>
<th>ACTIVATED BY</th>
<th>INHIBITED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>High carb diet Insulin</td>
<td>Pyruvate carboxylase</td>
<td>Acetyl-CoA</td>
<td></td>
</tr>
<tr>
<td>Glycerol</td>
<td></td>
<td>PEP carboxykinase</td>
<td>hormonal synthesis</td>
<td></td>
</tr>
<tr>
<td>Amino Acids</td>
<td></td>
<td>Fruc-1,6-BPase</td>
<td>ATP</td>
<td>AMP</td>
</tr>
<tr>
<td>High Fat Diet</td>
<td></td>
<td>Gluc-6-Pase</td>
<td>Gluc-6-P</td>
<td>Glucose</td>
</tr>
<tr>
<td>Prolonged Fasting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Cori cycle**

**Pentose Phosphate Pathway**

Time didn’t allow coverage of either of these topics but you should spend some time on them.
**Glycogen** – glucose storage
Glucose polymer with α-1,4 and some α-1,6 linkages

Control
Insulin activates glycogen synthesis
Glucagon and Epinephrine promote degradation

**Control of Glycogen Phosphorylase**

- **Phosphorylase b** (dephosphorylated)
  - **T State** (Inactive)

  - Activated by AMP

- Inhibited by ATP

- Glucose-6-P

- Glucose Caffeine

- Phosphorylase Kinase

- Phosphoprotein Phosphatase

- Phosphorylase a (phosphorylated)
  - **T State** (Inactive)

  - Inhibited by Glucose Caffeine

- **Phosphorylase b** (dephosphorylated)
  - **R State** (Active)

  - Phosphorylase a (phosphorylated)
  - **R State** (Active)
Citric Acid Cycle

<table>
<thead>
<tr>
<th>ENZYME</th>
<th>ACTIVATED BY</th>
<th>INHIBITED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrate Synthase</td>
<td>ADP, Acetyl-CoA</td>
<td>Citrate, Succinyl-CoA, ATP and NADH (lesser extent)</td>
</tr>
<tr>
<td>Isocitrate Dehydrogenase</td>
<td>ADP, Ca²⁺</td>
<td>ATP and NADH (minor)</td>
</tr>
<tr>
<td>α-Ketoglutarate Dehydrogenase</td>
<td>ADP, Ca²⁺</td>
<td>Succinyl-CoA, NaDH, ATP (minor)</td>
</tr>
<tr>
<td>Pyruvate Carboxylase</td>
<td>Acetyl-CoA</td>
<td></td>
</tr>
</tbody>
</table>
Citric Acid Cycle
Malate Dehydrogenase – Highly endergonic reaction; helped by low [oxaloacetate] in mitochondria

CAC is also used in the catabolism of many amino acids

Anabolic CAC Aspects
Citrate → Lipids (fatty acids and cholesterol)
Oxaloacetate → Glucose
Oxaloacetate → Amino Acids
α-Ketoglutarate → Amino Acids
Also involved in production of heme, purines and pyrimidines

CAC Anapleurotic Reactions (Rxns replenishing CAC intermediates)
Pyrurate → Oxaloacetate (by Pyruvate Carboxylase)
Transamination of Asp, Glu (produce oxaloacetate and α-ketoglutarate respectively)

High ATP/ADP and NADH/NAD\(^+\) Ratios – Biosynthesis activated and Catabolism inhibited
Low ATP/ADP and NADH/NAD\(^+\) Ratios – Catabolism activated and Biosynthesis inhibited

Glyoxalate Cycle
Occurs in glyoxosomes in plants until they begin photosynthesis
Allows for the conversion of fats to carbohydrates (explains why seeds contain so much fat)
Electron Transport Chain

Intermembrane Space
high [H⁺]

Complex I

Complex II

Complex III

Complex IV

Cyt C

NADH → NAD⁺

FADH₂ → FAD

2H⁺ → 1/2O₂ + 2H⁺ → H₂O

ATP Synthase

ADP → ATP

Matrix
low [H⁺]

Succinate

FADH₂ → FeS

FMN → FeS

NADH → NAD⁺

NADH Dehydrogenase

CoQ → FeS → Cyt c → Cyt c → Cyt a → Cu → Cyt a₃ → O₂

Cytochrome c oxidase

Q cycle

Inhibitors

<table>
<thead>
<tr>
<th>Complex I</th>
<th>Complex III</th>
<th>Complex IV</th>
<th>Uncoupler</th>
</tr>
</thead>
<tbody>
<tr>
<td>rotenone</td>
<td>Antimycin A</td>
<td>CN-, CO, N₃</td>
<td>2,4-dinitrophenol</td>
</tr>
</tbody>
</table>
ATP Synthase

**F₁**
alternating 3α and 3β subunits
(β subunits are catalytic)

**F₀**
alternating a and c subunits
-proton channel

---

Open (O): releases ATP
Loose (L): binds ADP
Tight (T): converts ADP to ATP

Oxidative Stress and Anti-Oxidants

**Glycerol phosphate shuttle**
NADH exchanged for FADH₂
Active in brain and skeletal muscle

**Malate-aspartate shuttle**
NADH “transferred” across membrane
Active in kidney, liver, and heart

---

Glycerol-Phosphate Shuttle

<table>
<thead>
<tr>
<th>Cytosol</th>
<th>Outer membrane</th>
<th>Inner membrane</th>
</tr>
</thead>
<tbody>
<tr>
<td>NADH → NAD⁺</td>
<td>DHAP → G-3-P</td>
<td>FADH₂ → FAD</td>
</tr>
</tbody>
</table>

---

Glucose

2ATP 2ADP

2Pyruvate (3C)

2CO₂

6NAD⁺ 6NADH

2NAD⁺ 2NADH

2Acetyl-CoA (2C)

2CO₂

2ADP 2ATP

(1 for each pyruvate)
**Lipid Metabolism**

**Dietary Intake to Storage**

Triacylglycerides converted to fatty acids and monoacylglycerides for absorption out of the small intestine. Reassembled into triacylglycerides and transported via chylomicrons to adipose tissue for storage.

- Triacylglycerides converted to fatty acids and monoacylglycerides for absorption out of the small intestine.
- Reassembled into triacylglycerides and transported via chylomicrons to adipose tissue for storage.

**From Adipose Tissue to Energy Production**

Triacylglycerides converted to fatty acids and glycerol by hormone-sensitive lipases
- Activated by glucagon and epinephrine in response to fasting, exercise, or stress
- Lipases activated in a cAMP-dependent pathway via phosphorylation
- Glycerol transported to liver for glycolysis or gluconeogenesis
- Fatty acids transported through the bloodstream to tissues in need (heart and muscles primary)

**Adipose Tissue**

```
Triacylglycerides → lipases → Glycerol and Fatty Acids → liver → Glycolysis or Gluconeogenesis → Acetyl CoA → CAC Cycle → Other Tissues (mitochondria)
```

**β-oxidation**

- Unsaturated fatty acids produce 1 less FADH₂ for each double bond
- Cis-alkenes are converted to trans-alkenes by enoyl-CoA Isomerase
Catabolism of Stearic Acid (18C)

\[ \text{Acetyl-CoA} \rightarrow 9 \text{Acetyl-CoA} \]

\[ 8 \text{FAD} \rightarrow 8 \text{NAD}^+ \]
\[ 8 \text{FADH}_2 \rightarrow 8 \text{NADH} \]

\[ 8 \text{Rounds of } \beta\text{-oxidation} \]

\[ 9 \text{Acetyl-CoA} \rightarrow 9 \text{GDP} \]
\[ 9 \text{GDP} \rightarrow 27 \text{NAD}^+ \]
\[ 9 \text{FAD} \rightarrow 27 \text{NADH} \]
\[ 9 \text{FADH}_2 \rightarrow 27 \text{NADH} \]

\[ 18 \text{CO}_2 \]

\[ \text{ATP} \rightarrow \text{AMP} + \text{PP}_i \rightarrow 2\text{P}_i \]
(Equivalent to 2 ATP consumed)

\[ \text{Total: 120 ATP} \]

<table>
<thead>
<tr>
<th>NADH</th>
<th>FADH$_2$</th>
<th>ATP</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>8</td>
<td>-2</td>
</tr>
<tr>
<td>27</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>35 (= 87.5 ATP)</td>
<td>17 (= 25.5 ATP)</td>
</tr>
</tbody>
</table>

**Ketogenesis**

Occurs as the result of a build up of acetyl-CoA (due to a lack of oxaloacetate)

Heart and muscle can metabolize ketone bodies

Brain can metabolize ketone bodies only after a period of starvation

Ketoacidosis in diabetes patients – excessive metabolism of fatty acids due to lack of glucose uptake
Fatty Acid Synthesis
Response to high carb/low fat diet

\[
\text{glucose} \rightarrow \text{acetyl-CoA} \rightarrow \text{fatty acids}
\]

Occurs in cytosol so acetyl-CoA must be transported out of the mitochondria

---

**Regulation of Fatty Acid Synthesis**

<table>
<thead>
<tr>
<th>Activated by</th>
<th>Inhibited by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Low [NADPH] (caused by high [palmitoyl CoA])</td>
</tr>
<tr>
<td></td>
<td>Low [acetyl CoA]</td>
</tr>
<tr>
<td></td>
<td>Low [Citrate]</td>
</tr>
<tr>
<td></td>
<td>Inhibited by palmitoyl CoA</td>
</tr>
<tr>
<td></td>
<td>Inhibited by glucagon and epinephrine</td>
</tr>
</tbody>
</table>
Cholesterol

Cholesterol Synthesis
Primary Regulation Point
Enzyme synthesis inhibited by cholesterol
Enzyme degradation enhanced by cholesterol
Inhibition by phosphorylation (glucagon)
Target of cholesterol lowering medications

\[
\text{HMG-CoA} \xrightarrow{\text{HMG-CoA Reductase}} \text{Mevalonate} \xrightarrow{2\text{NADPH}} \text{Isopentenylpyrophosphate (IPPP)} \xrightarrow{22 \text{ Enzymatic Steps}} \text{Cholesterol}
\]

Cholesterol Degradation
Activated by high cholesterol
Occurs in liver

\[
\text{Cholesterol} \xrightarrow{7-\alpha\text{-hydroxylase (degradation)}} \text{7-\alpha\text{-hydroxycholesterol}} \xrightarrow{\text{Cholic Acid}} \text{(a bile salt)}
\]

Lipoproteins
Chylomicrons – 98% lipid (85% TAG)
From dietary absorption (intestine \(\rightarrow\) lymph \(\rightarrow\) blood stream)

VLDL – 50% TAG, 20% cholesterol and esters
Function to transport of plasma TAGs
Synthesized in liver \(\rightarrow\) IDL \(\rightarrow\) LDL
Main protein is ApoB100 (LDL receptor recognition)

LDL – 45% cholesterol (70% of plasma cholesterol)
Formed by loss of TAGs from IDL
Function to deliver cholesterol to extrahepatic tissues

HDL – 55% protein, 20% cholesterol
Smallest of the lipoproteins
Function to recirculate cholesterol back to the liver
Primary protein is ApoAII (binds HDL receptor of liver for uptake of cholesterol by liver)

Prostaglandin Synthesis

\[
\text{Arachidonic Acid} \xrightarrow{\text{COX Major Regulatory Step}} \text{PGG2} \xrightarrow{\text{PGE2, PGF2\alpha, TXA2}} \text{PGH2}
\]

COX-2 Inhibition
- Excess generated in response to inflammation
- Targeted by many anti-inflammatory drugs
Lipids and Membranes

Fatty acids
Triacylglycerols
Waxes
Phospholipids
Sphingolipids
Isoprenoids and steroids

Fatty acids
Saturated vs. Unsaturated
- Trans-fats associated with increased LDL, decreased HDL, and increased triglycerides

Nomenclature
Omega-3 and Omega-6 Fatty Acids

Triacylglycerols
Glycerol backbone bonded to 3 fatty acids via ester linkages
Uses: Energy Storage
- Insulation
- Soap

Phospholipids
Glycerol, 2 fatty acids and phosphate group
Uses: Membranes (Lipid Bilayers)
- Emulsification Agents

Phosphoglycerides: Glycerol, 2 fatty acids, phosphate group and alcohol bonded to phosphate group

Sphingolipids
Contain sphingosine, phosphate, a fatty acid, and an alcohol
Found in nervous tissue membranes

Isoprenoids
Terpenes (Lots of Examples)
- Squalene, β-carotene, vit A, vit E, vit K

Steroids
Cholesterol is the biological precursor for all steroids
- β-estradiol, testosterone, aldosterone, cortisol
- Vit D, bile
Lipid Membranes
Fluid Mosaic Model (Diagram)
Proteins are suspended in the membrane and have some mobility to move around
Unsaturated fatty acids increase mobility while cholesterol increases rigidity
Impermeable to ions and polar molecules but non-polar molecules can typically diffuse across the membrane
Asymmetry: inner and outer layers of the membrane often have differing compositions

Membrane Proteins
Integral Membrane Proteins
Peripheral Membrane Protein
Transmembrane Proteins
Lipid Protein Anchors

Membrane Transport
Simple Diffusion (ex. CO₂, O₂, lipids, some drugs)

Facilitated Diffusion – diffusion of ions/polar solutes via a carrier protein (channel protein) (ex. glucose)

Active Transport - works against the concentration gradient and requires energy (ATP hydrolysis)
1) Primary (ex. Na/K pump—3Na⁺ pumped out and 2K⁺ pumped into cell fueled by ATP hydrolysis)
2) Secondary – use one solutes gradient to accomplish the transport of another (Na⁺/glucose cotransport)
3) Ion-Mediated

Membrane Receptors
College Biochemistry Chapter 10 – Photosynthesis

Light reactions take place in the thylakoid membrane
Dark reactions take place in the stroma

Chlorophylls absorb red light (600-700nm) and blue light (400-500nm)
Antennae chlorophyll molecules pass light energy to reaction centers

Photophosphorylation
Photosystems are part of an electron transport chain that creates a proton gradient
Proton gradient powers ATP synthase

Z Scheme of Photosynthesis
Calvin Cycle (Dark Reactions)

**NET REACTION**

\[
\begin{align*}
9 \text{ ATP} & \quad 9 \text{ ADP} \\
3 \text{ CO}_2 + \text{ H}_2\text{O} & \quad \text{Glyceraldehyde-3-phosphate} \\
& \quad (3\text{C}) \\
6 \text{ NADPH} & \quad 6 \text{ NADP}^+ 
\end{align*}
\]

**Regulation of Photosynthesis**

<table>
<thead>
<tr>
<th>Light Activates</th>
<th>Light Inhibits</th>
<th>Indirect mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>RuBisCo</td>
<td>PFK</td>
<td>pH: most PS enzymes function best @ pH 8</td>
</tr>
<tr>
<td>fruc-1,6-BPase</td>
<td>Gluc-6-PDH</td>
<td>Mg\text{2+}: light increases, enzymes activated</td>
</tr>
<tr>
<td>phosphoribulkinase</td>
<td></td>
<td>Thioredoxin activation--Governs activity of other enzymes</td>
</tr>
</tbody>
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**Regulation of Rubisco**

RuBisCo genes activated by light
Activated by increased pH and [Mg\text{2+}]
Activated by Carbonylation (CO\text{2} rxn with Lys)--Ensures RuBisCo activity only when High [CO\text{2}]
Inhibited by Oxygen

Fruc-1,6-BPase activated by high pH and [Mg\text{2+}]
**RuBisCo Oxygenase Activity and Photorespiration**

![Diagram of RuBisCo Oxygenase Activity and Photorespiration]

**C₄ Plants**
Concentrates CO₂ in bundle sheath cells and minimizes water loss
More energy intensive than C₃ plants:
5 ATP/CO₂ fixed in C₄ vs. 3 ATP/CO₂ fixed in C₃
PEP carboxylase has high HCO₃⁻ affinity and no O₂ affinity

**CAM Plants**
Stomata open at night, closed during the day (minimizes water loss)
CO₂ taken up and stored as malate at night
CO₂ released during the day to participate in the Calvin Cycle

**Sucrose Synthesis**

**Starch Synthesis**

**Cellulose Synthesis**