Lecture Outline: Fuel Catabolism

I. **Energy, Matter, and Ecosystems**

A. Energy Flow vs. Material Recycling in Ecosystems

1. Energy flows through an ecosystem: enters as sunlight, gets transformed, and eventually leaves as heat.
2. Materials (matter) get recycled within an ecosystem: transformed into other compounds and passed between members.

B. Producers vs. Consumers

1. **Producers**: Organisms that can produce their own food.
    a. Vast majority are photosynthetic (plants, algae, cyanobacteria).
    b. Perform a complex set of reactions that feeds them and provides raw materials for macromolecules.
    c. Have the ability to make organic compounds from inorganic sources of carbon, including carbon dioxide.
    d. This process is called **carbon fixation**.
2. **Consumers**: Organisms that cannot produce their own food.
    a. Must eat producers or other consumers.
    b. Rely on producers for organic compounds as they cannot use inorganic carbon sources (like CO_2) to make organic compounds.

C. Organic Macromolecules

1. All organisms are made of organic macromolecules (polysaccharides, lipids, polypeptides, polynucleotides) plus

other smaller molecules.

2. Organic compounds contain carbon skeletons.
3. Carbon dioxide is considered inorganic, despite containing carbon, and is useless to consumers as a carbon source.

II. **Reciprocal Relationship Between Photosynthesis and Complete Fuel Oxidation**

A. **Photosynthesis**: Uses carbon dioxide and water as inputs to produce organic molecules and oxygen.

B. **Complete Oxidation of Fuel**: Uses organic molecules and oxygen as inputs to produce carbon dioxide and water.

C. These two processes have a **reciprocal relationship**, each effectively undoing the other.

D. The carbon dioxide exhaled by consumers is the leftover from the complete dismantling of organic food that was eaten.

III. **Redox Reactions (Reduction-Oxidation)**

A. Definition: Redox is shorthand for reduction-oxidation, involving the transfer of electrons.

B. Key Terms:

1. **Reduction**: The gain of electrons (reduces the overall charge).
2. **Oxidation**: The loss of electrons.

C. Coupled Process: Reduction and oxidation always occur together; electrons are conserved.

D. Agents:

1. **Reducing Agent**: The substance that becomes oxidized (loses electrons) and causes another substance to be reduced.
2. **Oxidizing Agent**: The substance that becomes reduced

(gains electrons) and causes another substance to be oxidized.

E. Combustion as a Redox Reaction:

1. A reaction with oxygen, where a fuel (e.g., methane) is combusted.
2. The fuel is always oxidized.
3. Oxygen does the job of receiving electrons, thus being reduced.
4. In hydrocarbons, shared electrons are relatively far from nuclei (higher energy).
5. During combustion, bonds rearrange, and electrons move closer to highly electronegative oxygen (lower energy level), releasing energy.

IV. **Energy Carriers: Co-enzymes (NAD+ and FAD)**

A. Definition: Co-enzymes are molecules that pick up something from one process and drop it off at another; often called "taxis" for electrons.

B. **NAD (Nicotinamide Adenine Dinucleotide)**:

1. Structure: A dinucleotide composed of two nucleotides hooked together.
2. Forms:
   a. **NAD+**: The oxidized form (empty taxi, lower energy).
   b. **NADH and H+**: The reduced form (passenger-filled taxi, higher energy), carrying two electrons and one proton.
3. Function: Picks up electrons/hydrogens from fuel (oxidizing the fuel), becomes reduced (NADH and H+), and delivers this energy elsewhere for later ATP production.
4. A single NADH and H+ molecule has more energy than an ATP molecule.

C. **FAD (Flavin Adenine Dinucleotide)**:

1. Similar to NAD but with flavin as its other nitrogenous base.
2. Forms:
    a. **FAD**: The oxidized form.
    b. **FADH2**: The reduced form, carrying two full hydrogen atoms (two electrons and two protons).
3. Function: Also picks up electrons/hydrogens from fuel and carries energy to be dropped off later.

V. **Complete Oxidation of Glucose (Central Catabolic Pathway)**

A. Overall Process:

1. Stepwise breakdown of glucose (C6H12O6) to gradually release energy.
2. Prevents explosive release of energy (like direct combustion), allowing cells to capture energy as ATP.
3. The overall change in free energy (delta G) is the same whether in one step or many steps.
4. Glucose is the primary or "master fuel" for cells.

B. Dehydrogenation: The process of removing hydrogen atoms (and thus electrons) from the fuel by dehydrogenase enzymes, which constitutes oxidation and releases energy.

C. Major Components of Complete Oxidation of Glucose:

1. **Glycolysis** (First major component)
    a. Location: Cytosol (main interior liquid compartment of the cell).
    b. Process: A 10-step biochemical pathway that splits one 6-carbon glucose molecule into two 3-carbon pyruvate molecules.
    c. Phases:

(1) **Energy Investment Phase**: Requires an input of 2 ATP molecules per glucose to energize the sugar.

(2) **Energy Payoff Phase**: Produces 4 ATP and 2 NADH and H+ per glucose.

f. Net Yield (per glucose):

(1) 2 ATP (produced via **substrate-level phosphorylation**).

(2) 2 NADH and H+ (carrying energy from the glucose).

(3) 2 Pyruvate molecules (partially spent fuel, still contains significant usable energy).

2. **Cellular Respiration** (Second major component, occurs in the mitochondrion for eukaryotes)

a. Uses pyruvate as its fuel, not glucose.

b. Pyruvate must be transported into the mitochondrial matrix.

c. Three Major Parts:

(1) **Oxidative Decarboxylation of Pyruvate** (First part of Cellular Respiration)

1. Location: Mitochondrial matrix.
2. Process: Each 3-carbon pyruvate is decarboxylated (one carbon removed as CO_2) and oxidized.
3. The remaining 2-carbon unit (acetate) is attached to Coenzyme A, forming **Acetyl CoA**.
4. Yields (per glucose, as there are two pyruvates):
    1. 2 CO_2 (fully spent fuel).
    2. 2 NADH and H+.

3. 2 Acetyl CoA (remaining usable fuel).

5. No ATP is produced in this step.

(2) **Citric Acid Cycle (Krebs Cycle / TCA Cycle)** (Second part of Cellular Respiration)

1. Location: Mitochondrial matrix.
2. Process: A cyclic biochemical pathway where Acetyl CoA enters, combines with a 4-carbon compound (oxaloacetate) to form a 6-carbon citrate, which is then systematically dismantled.
3. Completes the oxidation of the original glucose fuel; all remaining carbons are released as carbon dioxide.
4. Outputs (per glucose, as two Acetyl CoA enter the cycle):
    1. 4 CO_2 (representing the remaining carbons from glucose, completely spent fuel).
    2. 6 NADH and H+.
    3. 2 $FADH_2$.
    4. 2 ATP (produced via **substrate-level phosphorylation**).

(3) **Oxidative Phosphorylation** (Third part of Cellular Respiration, where the largest amount of ATP is produced)

1. Location: Inner mitochondrial membrane.
2. This process has two components:
    1. **Electron Transport Chain (ETC)**
        1. Composed of protein complexes (Complexes I, II, III, IV) embedded in the inner mitochondrial membrane.

2. NADH and H+ and FADH2 deliver their high-energy electrons (from the original fuel) to the chain.
3. Electrons are passed sequentially from one complex to the next (a series of redox reactions).
4. As electrons move down the chain, they drop to lower energy levels, releasing energy.
5. This released energy powers proton pumps (Complexes I, III, and IV).
6. Protons (H+) are pumped from the mitochondrial matrix into the intermembrane space, creating an electrochemical **proton gradient** (a form of stored energy).
7. **Oxygen** serves as the **final electron acceptor** at the end of the chain, combining with electrons and protons to form **water**.
8. No ATP is produced directly during electron transport.

2. **Chemiosmosis**
    1. The proton gradient established by the ETC drives the synthesis of ATP.
    2. Protons flow back down their concentration gradient (from the intermembrane space back into the matrix) through a molecular machine called **ATP Synthase**.

3. ATP Synthase acts as an ion channel and an enzyme. The flow of protons causes the rotor part of ATP Synthase to spin.
4. This mechanical energy drives the catalytic knob of the enzyme, which phosphorylates ADP (adds an inorganic phosphate) to synthesize **ATP**.
5. More than 90% of the ATP from complete glucose oxidation is generated in this final step.

VI. **Fermentation**

A. Context: An alternative pathway that operates when oxygen is absent or insufficient for cellular respiration.

B. Primary Purpose: To **re-oxidize NADH back to NAD+**.

1. This is crucial because glycolysis requires NAD+ to continue functioning.
2. If NAD+ is not regenerated, glycolysis would halt, stopping all ATP production.

C. ATP Production: Fermentation itself does not produce any ATP. The only ATP generated is the 2 net ATP from glycolysis.

D. Less Efficient: Offers a much smaller ATP yield per glucose compared to cellular respiration.

E. Types of Fermentation (examples relevant to humans):

1. **Lactic Acid Fermentation**:
   a. Performed by human muscle cells during strenuous exercise when oxygen supply is limited.
   b. Pyruvate from glycolysis is converted directly to lactate (lactic acid).
   c. This reaction re-oxidizes NADH to NAD+, allowing

glycolysis to continue.

d. Buildup of lactic acid contributes to muscle fatigue.

2. **Alcohol (Ethanol) Fermentation**:

a. Performed by yeast and some bacteria.

b. Pyruvate is first decarboxylated to acetaldehyde, which is then reduced to ethanol.

c. This process re-oxidizes NADH to NAD+ and produces CO_2 (e.g., carbonation in beer, rising in bread).

VII. **Catabolism of Other Fuels**

A. Central Pathway: The complete oxidation of glucose serves as the central metabolic pathway for energy extraction.

B. Other Nutrient Classes: Proteins, carbohydrates (other than glucose), and fats can be catabolized for energy by feeding into this central pathway.

1. **Proteins**:

a. Digested into individual amino acids.

b. Amino acids must be **deaminated** (amino group, NH_3, removed) because nitrogen is problematic for energy metabolism.

c. The resulting carbon skeletons can enter the pathway as pyruvate, Acetyl CoA, or various intermediates of the Citric Acid Cycle.

d. Ammonia (NH_3) byproduct is toxic and converted to urea by the liver for excretion.

2. **Carbohydrates (other monosaccharides)**:

a. Polysaccharides like starch are digested into monosaccharides (e.g., glucose, fructose).

b. Other monosaccharides are easily converted into glucose

or other intermediates that can enter glycolysis directly.

3. **Fats (Lipids)**:
    a. Digested into their components: glycerol and fatty acids.
    b. **Glycerol**: Can be converted into glyceraldehyde 3-phosphate (G3P), an intermediate of glycolysis.
    c. **Fatty Acids**: Long hydrocarbon chains that can be broken down two carbons at a time into Acetyl CoA units, which then enter the Citric Acid Cycle.

VIII. **Control of Fuel Catabolism**

A. Regulation: The rate of ATP production (and thus glycolysis and cellular respiration) is adjusted based on the cell's energy demands.

B. Feedback Mechanisms: Key enzymes act as control points in the pathway.

1. **Phosphofructokinase**: A major control enzyme in glycolysis.
2. Inhibition:
    a. High levels of **ATP** (signal sufficient energy) inhibit the enzyme, turning down glycolysis.
    b. High levels of **citrate** (an intermediate of the Citric Acid Cycle) also inhibit, indicating adequate fuel processing.
3. Activation:
    a. High levels of **AMP** (adenosine monophosphate, a signal of very low energy) activate the enzyme, dramatically increasing ATP production.