Chapter 8

8.1: Cellular Respiration

1.	(Complete) glucose breakdown: $\mathbf{C_6H_{12}O_6 + 6\ O_2 = 6\ CO_2 + 6\ H_2O}$ **+ energy**
2.	Glucose is *oxidized* & O_2 is *reduced*.
3.	Glucose → high-energy molecule, CO_2 and H_2O → low-energy molecules ∴ CR is ***exergonic*** b/c it releases energy.
4.	Electrons removed from substrates & received by O_2, which combines with H^+ to become H_2O
5.	Glucose breakdown is **gradual** (if broken down rapidly, most energy lost as non-usable heat).
6.	Glucose breakdown yields synthesis of 36 or 38 ATP; preserves ≈ **39%** of energy available in glucose. Relatively efficient compared to e.g. **25%** efficiency of a car burning gasoline.

NAD^+ and FAD

1.	NAD^+ & FAD: *redox coenzyme;* accepts & gives up electrons. ✓ $\mathbf{NAD^+ + 2e^- + H^+ \rightleftharpoons NADH}$ ✓ $\mathbf{FAD + 2e^- + 2H^+ \rightleftharpoons FADH_2}$
2.	Each metabolic reaction in CR is catalyzed by specific enzyme.
3.	FAD coenzyme of oxidation-reduction can replace NAD^+
4.	Electrons received by NAD^+ and FAD are high-energy e^-; **carried to ETC.**
5.	Only small amount of NAD^+ needed in cells b/c each NAD^+ molecule is used repeatedly.

4 Phases of Cellular Respiration

1.	**Glycolysis:** breakdown of 1 glucose molecule (C_6) in cytoplasm into 2 pyruvate molecules (2 C_3) ✓ Enough energy released for immediate yield of 2 ATP ✓ Anaerobic
2.	**Preparatory (prep) reaction**, pyruvate enters mitochondrion, oxidized to 2-carbon acetyl group & CO_2 removed, electrons go to NAD^+. Occurs twice per glucose molecule.

3. Citric acid cycle: ✓ Matrix; produces NADH and $FADH_2$ ✓ Series of reactions that gives off CO_2 & produces 1 ATP ✓ Twice b/c 2 acetyl-CoA molecules enter the cycle per glucose molecule ✓ Produces **2** immediate ATP molecules per glucose molecule
4. Electron transport chain: ✓ Series of carriers in *inner mitochondrial membrane* that accept electrons from glucose – electrons passed from carrier to carrier until received by O_2. ✓ Passes electrons from higher to lower energy states, allowing energy to be released & stored for ATP production.

8.2: Glycolysis

1. Divided into energy-investment steps where ATP is used to "jump start" glycolysis, & energy-harvesting steps, where more ATP is made than used.
2. Energy-Investment Steps: ✓ 2ATP are used to activate glucose which is split into 2 C_3 (G3P) molecules, each carries a phosphate group.
3. Energy-Harvesting Steps: ✓ 2G3P are oxidized by removal of **$2e^-$ & $2H^+$** → accepted by NAD^+ → 2 NADH ✓ When NADH molecules pass 2 electrons to ETC → become NAD^+ ✓ **Substrate-level phosphorylation:** oxidation of G3P & subsequent substrates results in 4 high-energy phosphate groups which are used to synthesize **4 ATP molecules**. ✓ Enzyme **(kinase)** passes a high-energy phosphate to ADP & ATP results. ✓ 2 of 4 ATP molecules produced are required to replace 2 ATP molecules used in initial phosphorylation of glucose ∴ *net* gain of 2 ATP from glycolysis. ✓ Pyruvate enters mitochondrion (**if** O_2 is available) & or undergoes *fermentation.*

Input	Output
glucose (C_6)	2 pyruvate ($2C_3$)
2 NAD^+	2 NADH
2 ATP	2 ADP
4 ADP + 4 P	4 ATP (2 ATP net)

8.3: Fermentation

1. **Anaerobic**; in cytoplasm.
2. Pyruvate from glycolysis **reduced** by NADH to either lactate (lactic acid fermentation) or alcohol & CO_2 (alcoholic fermentation).
   - ✓ Pyruvate + NADH → **lactate + NAD^+**
   - ✓ Pyruvate + NADH → **alcohol + NAD^+ + CO_2**
3. NADH passes its electrons to pyruvate instead of to ETC; NAD^+ is then free to return & pick up more electrons during earlier reactions of glycolysis.

4. **Advantages and Disadvantages of Fermentation**
   - ❖ Provides quick burst of ATP energy for muscular activity despite low yield of 2 ATP mol.
   - ❖ **Yeasts**: unicellular fungi that carry on alcoholic fermentation ∴ produce ethyl alcohol & CO_2.
   - ❖ **Animals**: humans, certain bacteria & fungi carry on lactic acid fermentation.
     - ✓ Lactic-acid bacteria produce lactic acid; production of cheese & yoghurt.
   - ❖ During **vigorous exercise**, O_2 is not enough to carry pyruvate into mitochondria ∴ muscle tissue ferments pyruvate into lactate to free some NADH so glycolysis can continue to produce 2 ATP by **substrate level phosphorylation**.
     - ✓ Fermentation products are **toxic** to cells. When blood cannot remove all lactate from muscles, lactate changes pH & causes muscle fatigue.
     - ✓ Recovery occurs after lactate is sent to liver where it is converted into pyruvate; some pyruvate is then respired (in mitochondria) or converted back into glucose.

5. **Efficiency of Fermentation**
   - ❖ 2 ATP produced per glucose molecule during fermentation is equivalent to **14.6 kcal**.
   - ❖ Complete glucose breakdown to CO_2 & H_2O → **686 kcal** per molecule.
   - ❖ Fermentation efficiency → **14.6/686 ≈ 2.1%**; less efficient than breakdown of glucose (39%).

Input	Output
glucose	2 lactate or 2 alcohol & 2 CO_2
2 ADP + 2 P	2 ATP net gain

8.4: Inside the Mitochondria

1. **Mitochondrion** has a double membrane with intermembrane space (b/w outer & inner mem).
2. **Cristae:** inner folds of membrane that jut into the *matrix*, innermost compartment of mitochondrion that is filled with gel-like fluid.
3. Prep reaction & citric acid cycle enzymes → in matrix; **ETC** → in cristae.

4. Preparatory Reaction

- Connects glycolysis to Krebs cycle. Pyruvate is converted (**oxidized**) to acetyl group (C_2) & attached to *coenzyme A (CoA)* → compound **acetyl-CoA**.
- Electrons go to NAD^+; occurs twice for each glucose molecule.
  - ✓ **$2\ C_3H_4O_3 + 2\ CoA \rightarrow 2\ C_2H_3O\text{-}CoA + 2\ CO_2$**
  - ✓ **2 pyruvate + 2 CoA → 2 acetyl-CoA + 2 carbon dioxide**

5. Krebs/ Citric Acid Cycle

- **Matrix**; twice for each glucose molecule.
  - ✓ Products (per glucose molecule): **4 CO_2, 2 ATP, 6 NADH & 2 $FADH_2$**
- Acetyl-CoA from prep reaction carry **acetyl group** (C_2) to Krebs cycle to join w/ **oxaloacetate** (C_4) to form **citrate** (C_6).
- At 2 different times, 2 electrons & 1 H^+ accepted by **NAD^+ → NADH**.
- At 1 time, 2 electrons & 1 H^+ accepted by **FAD → $FADH_2$**
  - ✓ **NADH & $FADH_2$** carry these electrons to the ETC.
- **Acetyl group** oxidized to 2 CO_2 molecules.
- Some **energy** is released & used to synthesize ATP by ***substrate level phosphorylation***.
- **6 C atoms** in glucose molecule become C atoms of 6 CO_2 molecules (2 from prep reaction + 4 from Krebs cycle).

2 acetyl groups (C_2)	4 CO_2
6 NAD^+	6 NADH
2 FAD	2 $FADH_2$
2 ADP + 2 P	2 ATP

6. Electron Transport Chain

- In cristae of mitochondria & plasma membrane of aerobic prokaryotes.
- Series of carrier proteins that pass electrons from one to another.

Members of the Chain

- ✓ Some protein carriers are **cytochrome** molecules: complex carbon rings with heme (iron) group in the center. Iron becomes reduced when it accepts electrons, vice versa.

Cycling of Carriers

- ✓ NADH gives up its electrons → NAD^+; next carrier then gains electrons ∴ reduced.
- ✓ **Oxidative phosphorylation:** at each sequential redox reaction, energy is released to form ATP molecules.
- ✓ H^+ remains in the matrix.
- ✓ By the time electrons are received by O_2, **3 ATP** have been made.
- ✓ $FADH_2$ delivers electrons to ETC → FAD, **2 ATP** formed.
- ✓ **O_2:** final electron acceptor; receives low-energy e^- from last carrier **(cytochrome oxidase)**, combines with H^+ → H_2O in matrix.

$$\frac{1}{2} O_2 + 2e^- + 2H^+ \rightarrow H_2O$$

- ✓ Recycling of coenzymes & ADP increases cellular efficiency.

Cristae of a Mitochondrion and Chemiosmosis

- ✓ ETC consists of 3 protein complexes & 2 protein mobile carriers that transport electrons.
- ✓ <u>3 protein complexes:</u>
  - NADH-Q reductase complex
  - cytochrome reductase complex
  - cytochrome oxidase complex
- ✓ <u>2 protein mobile carriers:</u> coenzyme Q & cytochrome c

- ✓ Energy released from flow of electrons down ETC is used to pump H^+ ions (low concentration, active transport) in matrix to intermembrane space (high concentration, 10x as much H^+ as in matrix).
- ✓ H^+ flow from intermembrane space (high H^+ conc., facilitated transport) → to matrix (low H^+ concentration through ATP synthase complex.
- ✓ As H^+ flow, enzyme ATP synthase synthesizes ATP from ADP + P in matrix by **chemiosmosis.**
- ✓ Accumulation of H^+ ions in intermembrane space creates strong electrochemical gradient.
- ✓ **Chemiosmosis:** ATP production tied to electrochemical (H^+) gradient across a membrane.
- ✓ Once formed, ATP molecules diffuse out of mitochondrial matrix through channel proteins.
- ✓ ATP → ADP + P (return to mitochondrion for recycling).
- ✓ ATP synthase must continuously produce ATP for organism to survive.
- ✓ Active tissues require greater amount of ATP; have more mitochondria.

7. Energy Yield from Glucose Metabolism

❖ **Substrate-Level Phosphorylation**

- ✓ Per glucose molecule: net gain of 2 ATP from glycolysis in cytoplasm.
- ✓ Krebs cycle in matrix of mitochondria produces 2 ATP per glucose.
- ✓ ∴ total of 4 ATP (from 2 NADH) formed by substrate-level phosphorylation outside of ETC.

❖ **ETC and Chemiosmosis – where most ATP is produced**

- ✓ Per glucose, 10 NADH and 2 $FADH_2$ molecules provide electrons & H^+ ions to ETC.
- ✓ For each NADH formed within mitochondrion, 3 ATP produced.
- ✓ For each $FADH_2$ formed by Krebs cycle, 2 ATP produced.
- ✓ For each NADH formed outside mitochondria by glycolysis, 2 ATP produced as electrons are shuttled across mitochondrial membrane by organic molecule & delivered to FAD.

Efficiency of Cellular Respiration

- Energy difference b/w total reactants (glucose + O_2) & products (CO_2 + H_2O): **686 kcal**
- ATP: **7.3 kcal**; 36 to 38 ATP produced during glucose breakdown for total of at least **263 kcal**.
- **Efficiency**: 263/686, or 39% of available energy in glucose is transferred to ATP; rest is lost as heat.

- **Catabolism:** break down molecules; degradative reactions; exergonic. Drives anabolism.
- **Anabolism:** build molecules; synthetic reactions; endergonic.