Bioenergetics and metabolic pathways

BIOB111
CHEMISTRY & BIOCHEMISTRY

Session 17
Session Plan

- Introduction to Bioenergetics
- Metabolism
- Metabolic Pathways
- Metabolism & Cell Structure
- Mitochondria
- Compounds in Metabolic Pathways
- High-energy Phosphates
- Coenzymes NAD & FAD
- Coenzyme A
- Overview of Bioenergetic Pathways
Bioenergetics

• **Bioenergetics':**
  – The study of energy transformation / energy flow through living systems
  – Energy is involved in making & breaking chemical bonds in biological molecules

• Bioenergetics can also be defined as the study of energy relationships & energy transformations in living organisms

• The energy, required to **run the human body**, is obtained from ingested foods
  – Foods are broken down in several different catabolic pathways
Metabolism

Metabolism:
• The **total sum of all biochemical reactions** that maintain the living state of the cells within an organism

**CATABOLISM**: Breaking down
• Metabolic reactions in which large bio-molecules are broken down into smaller one
  – Energy is released
  – E.g. Breakdown of a protein into the individual amino acids

**ANABOLISM**: Building up
• Metabolic reactions in which small bio-molecules are joined together to form larger ones
  – Energy is required
  – E.g. Synthesis of proteins from individual amino acids
Catabolism

Larger molecules

Anabolism

Smaller molecules

Energy

Stoker 2104, Figure 23-1 p842
Metabolic Pathway

• A metabolic pathway a series of consecutive biochemical reactions,
  – Used to convert a starting material into an end product.

• The major metabolic pathways are similar for all life forms
  – Scientists study metabolic reactions in simple life forms to understand the same reactions in humans

• **Linear pathways** – series of reactions generates a final product

• **Cyclic pathways** – series of reactions regenerates the first reactant.

Examples:
- Linear metabolic pathway = breakdown of alcohol
- Cyclic metabolic pathway = Citric acid cycle
Metabolic Pathway Summary View

**STAGE 1**
The process of digestion changes large, complex molecules into relatively small, simpler ones.

**STAGE 2**
Small molecules from digestion are degraded to still smaller units, primarily the two-carbon acetyl group that becomes part of acetyl CoA.

**STAGE 3**
Acetyl CoA is oxidized to produce CO₂ and reduced coenzymes (NADH, FADH₂) in the citric acid cycle.

**STAGE 4**
NADH and FADH₂ facilitate ATP production through the electron transport chain and oxidative phosphorylation.
Metabolism & Cell Structure

• Cell structure knowledge is essential to understanding of metabolism

**Prokaryotic Cell**
• Single compartment organism
  – Bacteria only
  • No nucleus
  • Single circular DNA molecule present near center of the cell (nucleoid)

**Eukaryotic Cell**
• Multi-compartment cell
  – DNA is present in the membrane enclosed nucleus
  – Cell is compartmentalized into cellular organelles
  – ~1,000 times larger than bacterial cells
Eukaryotic Cell Diagram

Plasma membrane

Cytosol

Nucleus

Ribosomes (small dots)

Lysosome

Mitochondria

Stoker 2014, Figure 23-2 p843
Mitochondria

- Mitochondria are the power-stations of the cell that generate cellular energy
  - ATP

- Mitochondria have a double membrane
  - Inner & Outer membrane separated by the Intermembrane space

Mitochondrial Matrix
- The most interior region within the Inner membrane

Outer Mitochondrial Membrane
- 50% lipid & 50% protein
  - Permeable to most molecules & ions

Inner Mitochondrial Membrane
- 20% lipids & 80% protein
  - Highly impermeable to most substances

- The inner mitochondrial membrane is highly folded to increase surface area, forming Cristae
  - Enzymes, ATP synthase complex, are attached to cristae
A schematic representation of a mitochondrion, showing key features of its internal structure.
Compounds in Metabolic Pathways

- Several **Nucleotide-Containing Compounds** play an important role in metabolic pathways

- **Adenosine Phosphates**
  - Adenosine mono phosphate (AMP)
  - Nucleotide containing Adenine
  - Adenosine diphosphate (ADP)
  - Adenosine triphosphate (ATP)
  - Cyclic adenosine monophosphate (cAMP)

\[
\text{AMP} + \text{P}_i \rightarrow \rightarrow \rightarrow \text{ADP} + \text{P}_i \rightarrow \rightarrow \rightarrow \text{ATP}
\]
Compounds in Metabolic Pathways and where they are Required

• Many B vitamins function as coenzymes in carbohydrate metabolism
  – Without B vitamins the body would be unable to utilize carbohydrates as an energy source

• 6 B vitamins in carbohydrate metabolism:
  – Thiamin – as TPP (vitamin B1)
  – Riboflavin – as FAD, FADH₂ & FMN (vitamin B2)
  – Niacin – as NAD⁺ & NADH (vitamin B3)
  – Pantothenic acid – as CoA (vitamin B5)
  – Pyridoxine – as PLP (pyridoxal 5-phosphate)
    • vitamin B6
  – Biotin (vitamin H)
Adenosine Phosphates

Several Adenosine Phosphates exist:
- **AMP** – Adenosine Monophosphate – a DNA/RNA nucleotide
- **ADP** – Adenosine Diphosphate – key molecule in metabolic pathways
- **ATP** – Adenosine Triphosphate – key molecule in metabolic pathways

There are 2 different types of bonds between phosphates:

- **Phospho-ester bond** = the phosphate-ribose bond
- **Phospho-anhydride bond** = phosphate-phosphate bond
  - A very reactive bond, requires less energy to break
Adenosine Phosphates

Adenosine monophosphate (AMP)

Adenosine diphosphate (ADP)

Adenosine triphosphate (ATP)

Phosphoanhydride bonds

Phosphoester bond

Adenine

Ribose

Stoker 2014, Figure 23-4 p846
ATP Hydrolysis

- ATP & ADP molecules readily undergo hydrolysis reaction
  - Hydrolysis of ATP releases Phosphate groups ($P_i$) + energy

$\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + P_i + H^+ + \text{energy}$

$\text{ADP} + \text{H}_2\text{O} \rightarrow \text{AMP} + P_i + H^+ + \text{energy}$

$\text{ATP} + 2\text{H}_2\text{O} \rightarrow \text{AMP} + 2P_i + 2H^+ + \text{energy}$
ATP Hydrolysis

ATP $\rightarrow$ ADP + energy (7.3 kcal/mol) + $P_i$

ADP $\rightarrow$ AMP + energy (7.3 kcal/mol) + $P_i$
ATP Function
• In cellular reactions ATP functions as:
  – Source of a phosphate group
  – Source of energy
• e.g. Conversion of glucose to glucose-6-phosphate
  – Requires phosphate from ATP

![Chemical structures showing the conversion of glucose to glucose 6-phosphate](Image)

The symbol \(\text{PO}_3^{2-}\) is a shorthand notation for a \(\text{PO}_3^{2-}\) unit.
Other Nucleotide Triphosphates

*Other bases can also form nucleotide triphosphates:*

- **UTP**: Uridine Triphosphate
  - Involved in carbohydrate metabolism

- **GTP**: Guanosine Triphosphate
  - Involved in carbohydrate & protein metabolism

- **CTP**: Cytidine Triphosphate
  - Involved in lipid metabolism
What is the difference between ATP and ADP?

What happens when the phosphoanhydride bond within ATP is broken?

Why is it necessary for cells to create a lot of ATP?
Attempt Socrative questions: 1 to 3

Google Socrative and go to the student login

Room name:

City name followed by 1 or 2 (e.g. PERTH1)

1 for 1st session of the week and 2 for 2nd session of the week
**Flavin Adenine Dinucleotide (FAD)**

FAD is a coenzyme required in many metabolic redox reactions

- FAD contains the B vitamin **Riboflavin** (vitamin B2)
  - **Flavin**: heterocyclic amine
  - **Ribitol**: alcohol derived from ribose
FAD Structure

- Flavin
- Ribitol
- Adenosine diphosphate (ADP)

Stoker 2014, Figure 23-6a p849
FAD Function

To be able to participate in redox reactions, FAD exists in 2 forms:

- **FAD** – oxidized form (lacks hydrogen)
  - Acts as an oxidising agent in redox reactions
    - Itself reduced to **FADH\textsubscript{2}**

- **FADH\textsubscript{2}** – reduced form (contains hydrogen)
  - Acts as an reducing agent in redox reactions
    - Itself oxidised to **FAD**

In metabolic pathways FAD:
- Continuously changes between its oxidized & reduced forms
- Functions as an electron carrier
  - Carries electrons to the electron transport chain

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

2 H atoms
FAD Function

\[
\begin{align*}
\text{Oxidised form} & : \text{R} - \text{C} - \text{C} - \text{R} + \text{FAD} & \rightarrow & \text{R} - \text{CH} = \text{CH} - \text{R} + \text{FADH}_2 \\
\text{Reduced form} & : \text{FADH}_2
\end{align*}
\]

\( R = \text{Ribitol} - \text{ADP} \)

Stoker 2014, p850
**Nicotinamide Adenine Dinucleotide (NAD)**

- NAD is another coenzyme required in many metabolic redox reactions
  - Contains B vitamin **Niacin** in the form of **Nicotinamide** (vitamin B3)
NAD Structure

Nicotinamide

Ribose

Adenine

Stoker 2014, Figure 23-6b p849
NAD Function

- To be able to participate in redox reactions, NAD exists in 2 forms:
  - **NAD\(^+\)** – oxidized form (lacks hydrogen)
    - Acts as an oxidising agent
      - Itself reduced to **NADH**
  - **NADH** – reduced form (contains hydrogen)
    - Acts as an reducing agent
      - Itself reduced to **NAD\(^+\)**

- In metabolic pathways NAD:
  - Continuously changes between its oxidized & reduced forms
  - Functions as an electron carrier
    - Carries electrons to the electron transport chain

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

2 H atoms
NAD Function

\[
\text{NAD}^+ \quad \text{(oxidized form)} \quad \quad \text{R} = \quad \text{Ribose} \quad \text{ADP} \quad \text{NADH} \quad \text{(reduced form)}
\]

\[
\text{R-C-R} + \text{NAD}^+ \quad \rightarrow \quad \text{R-C-R} + \text{NADH} + \text{H}^+
\]

\[\text{2° alcohol} \]

Ketone
What types of chemical reactions do the NAD\(^+\) and FAD coenzymes help facilitate? Why?

Out of FAD and FADH\(_2\), which is the electron rich and which is the electron poor version of the coenzyme? Why?

Is the FADH\(_2\) coenzyme in the reduced or oxidised form? How did you determine this?
Attempt Socrative questions: 4 to 6

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Coenzyme A (CoA)

Coenzyme A contains:

- 2-aminoethanethiol
  - The functional group of CoA is –SH (Thiol)

- B vitamin **Pantothenic acid** (vitamin B5)

- **Phosphorylated ADP** with a $P_i$ on 3’ of the ribose
CoA Structure

2-Aminoethanethiol  |  Pantothenic acid  |  Phosphorylated ADP

H—S—CoA
CoA Function

• “A” refers to the metabolic function of CoA
  – To transfer of ACETYL groups (2 carbon fragment)

• Acetyl CoA is a fusion of the acetyl group and CoA
  – Acetyl CoA a central metabolite produced in carbohydrate, lipid and protein metabolism
Overview of Bioenergetic Pathways

- The energy, required to run the human body, is obtained from ingested foods
  - Foods broken down in several different catabolic pathways

- There are 4 general stages in the biochemical energy production:
  - **Stage 1**: Digestion
  - **Stage 2**: Acetyl group formation
  - **Stage 3**: Citric acid cycle
  - **Stage 4**: Electron transport chain & Oxidative phosphorylation
Digestion

- The digestion of carbohydrates, lipids & proteins:
  - Begins in the mouth >>> continues in the stomach >>> completed in the small intestine

- Many digestive enzymes are used in this process
  - Results in production of small molecules that can cross intestinal membrane into the blood
    - The digestion products are absorbed across the intestinal wall into the bloodstream & transported to all body cells

- End-products of digestion
  - Glucose & other monosaccharides from carbohydrates
  - Amino acids from proteins
  - Fatty acids & glycerol from fats & oils
Acetyl Group Formation

- The Acetyl group formation stage involves many reactions, some of which occur in the cytosol & others in the mitochondria.

- The small molecules from digestion like glucose and fatty acids are oxidized to produce the acetyl group.
  - Acetyl groups:

- Acetyl group attaches to CoA >>> forms Acetyl CoA
  - Acetyl CoA is a fusion of the acetyl group and CoA
    - Acetyl CoA is a central metabolite produced in carbohydrate, lipid, and protein metabolism
    - CoA is derived from the vitamin pantothenic acid
  - Acetyl CoA enters the citric acid cycle

\[
\text{CoA} \quad \leftrightarrow \quad \text{Acetyl CoA}
\]

\[
\text{H} \quad \text{S} \quad \text{CoA} \quad \leftrightarrow \quad \text{CH}_3 \quad \text{C} \quad \text{S} \quad \text{CoA}
\]
Citric Acid Cycle (CAC)

- Citric acid cycle (CAC) takes place in the mitochondria

- Acetyl groups are oxidized during the CAC
  - Produces CO$_2$, energy, NADH, FADH$_2$
    - Most energy derived from the CAC is trapped in reduced coenzymes NADH & FADH$_2$
      - Both coenzymes used in the electron transport chain
    - Some energy produced in CAC is lost in the form of heat
  - The CO$_2$ we exhale comes primarily from CAC

- Acetyl CoA

Digestion/metabolism of carbohydrate, protein, lipid

Stoker 2014, Figure 23-11 p861
ETC & OP

- Both ETC and OP take place in mitochondria

Electron transport chain:
- NADH & FADH$_2$ provide H$^+$ & electrons needed for ATP production
  - H$^+$ are transported to the inter-membrane space in mitochondria
  - Electrons are transferred to molecular O$_2$, which is reduced to H$_2$O

Oxidative phosphorylation:
- H$^+$ re-enter the mitochondrial matrix through the ATP-synthase enzyme
  - Produces ATP from ADP
    - ADP + P$_i$ → ATP
What happens when ETC and OP is interrupted?

- Without oxygen both ETC and OP will cease
  - Oxygen needed to accept electrons from the ETC

- Cyanide is deadly because it binds to one of the proteins in the ETC
  - Stops the electrons being passed down the chain to oxygen

- In both cases when ETC/OP stops
  - ATP production stops >>>> cell death
Common Metabolic Pathway

- The CMP is the total sum of the biochemical reactions of the:
  - Citric Acid Cycle
  - Electron Transport Chain
  - Oxidative Phosphorylation

- The CMP reactions constitute the **Common Metabolic Pathway (CMP)**
  - Produce energy in the form of ATP

- The reactions in citric acid cycle and ETC/OP are the same for all types of foods
  - Carbohydrates, fats & proteins

- The CMP takes place in the mitochondria
Attempt Socrative questions: 7 to 11

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Stoker 2014, p859
Readings & Resources

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