Structural Biochemistry/Metabolism

General

Metabolism regulates life through a set of chemical reactions. Chemical reactions are often coordinated with each other and occur in sequence called metabolic pathways, each step of which is catalyzed by a specific enzyme. These pathways are categorized according to whether the reactions lead to the breakdown or synthesis of substances. Catabolic reactions result in the breakdown of molecules into smaller molecules. Such reactions are often exergonic. By comparison, anabolic reactions promote the synthesis of larger molecules from smaller molecules. This process usually is endergonic and, in living cells, must be coupled to an exergonic reaction. These processes are responsible for the growth and reproduction of organisms, maintaining their structures, and responding to changes in the environment. The involvement of enzymes is essential for metabolism because they couple the organisms, which are thermodynamically unfavorable, to other organisms which are thermodynamically favorable and drive the metabolism towards desirable reactions. Not only do enzymes drive organisms toward desirable reactions, but they also regulate metabolic pathways to respond to changes within the cell’s environment as well as signals from other cells. The metabolism of an organism also establishes which substances which enter the organism are nutritious and beneficial and which are harmful. Additionally, the speed of metabolism, or the metabolic rate, of an organism affects how much food the organism consumes.

Metabolic pathways are regulated in three general ways:

1.Gene Regulation Because Enzymes in every metabolic pathway are encoded by genes, one way that cells control chemical reactions is via gene regulations. For example, if a bacterial cell is not exposed to a particular sugar in its environment, it will turn off the genes that encode the enzymes that are needed to breakdown the sugar. Alternatively, if the sugar becomes available, the genes are switched on.

2.Cellular Regulation Metabolism is also coordinated at the cellular level. Cells integrate signals from their environment and adjust their chemical reactions to adapt to those signals. Cell-signaling pathways often lead to the activation of protein Kinases that covalently attach phosphate group to target proteins. For example, when people are frightened, they secrete a hormone called epinephrine into their blood stream. This hormone binds to the surface of muscle cells and stimulates an intracellular pathway that leads to the phosphorylation of intracellular proteins, including enzymes involved in carbohydrate metabolism. These activated enzymes promote the breakdown, an event that supplies the frightened individual with more energy. Epinephrine is sometimes called “fight or flight” hormone because the added energy prepares an individual to either stay and fight or run away. After a person is no longer frightened, hormone levels drop and other enzymes called phosphates remove the phosphate groups from enzymes, thereby restoring the original level of carbohydrates metabolism.

3.Biochemical regulation The other pathway by metabolic reactions are controlled is at the biochemical level. In this case, the binding of a molecule to an enzyme directly regulates its function. Biochemical regulation is typically categorized according to the site where the regulatory molecule binds.

Example(s) of Metabolic Pathways

**Gluconeogenesis**

This metabolic pathway involves the generation of glucose from non-carbohydrate carbon substrates (i.e. lactate, glycerol, and glucogenic amino acids). This is one of two main mechanisms (the other being glycolysis) that the human body uses to keep blood glucose levels from dropping to a dangerously low level, which is a condition called hypoglycemia. This mechanism isn’t exclusive to humans, being present in plants, animals, fungi and other microorganisms, with some variation in the locations in which glucogenesis takes place. This mechanism kicks in during periods of fasting, starvation, or intense exercise and is endergonic. It is also associated with ketosis and has been a target of therapy for type II diabetes to inhibit glucose formation and stimulate glucose uptake by cells.

The pathway itself consists of eleven enzyme-catalyzed reactions, which can begin in the mitochondria or cytoplasm (depends on the substrate being used). Many of these steps are just reversible reactions found in glycolysis.

• It begins in the mitochondria with the formation of oxaloacetate through carboxylation of pyruvate. This part requires ATP and catalytic help by pyruvate carboxylase, which is stimulated by high levels of acetyl-CoA and inhibited by high levels of ADP.

![Chemical reaction diagram](image1)

• Oxaloacetate is then reduced to malate using NADH, which will prepare it for mitochondrial exit. Afterwards, it is oxidized in the cytoplasm again to oxaloacetate using NAD+, in which the remaining steps of glucogenesis will take place.

• The next step is the decarboxylation and phosphorylation of oxaloacetate to produce phosphoenolpyruvate, which is catalyzed by phosphoenolpyruvate carboxykinase (PEP carboxykinase). This step also hydrolyses one molecule of GTP to GDP.

![Chemical reaction diagram](image2)

• The next steps of the reaction are essentially the same as those involved in reversed glycolysis, with the only difference being that fructose-1, 6-bisphosphatase converts fructose-1,6bisphosphate to fructose-6-phosphate. Note that this conversion is the rate limiting step of the whole process of glucogenesis.
Next, glucose-6-phosphate is formed from fructose 6-phosphate with the help of phosphoglucoisomerase. This product can be used in other metabolic pathways or can be further dephosphorylated to make free glucose. Cell control of intracellular glucose levels is attained by the fact that free glucose can diffuse in and out of the cell, whereas the phosphorylated form is locked in the cell. Glucose formation happens in the lumen of the endoplasmic reticulum. Here, glucose-6-phosphate is hydrolyzed by glucose-6-phosphatase to produce glucose, which is then shuttled into the cytosol by glucose transporters located in the membrane of the endoplasmic reticulum.
Biochemicals

Amino acids, carbohydrates, and lipids are essential for life and, therefore, metabolism focuses on the production of these molecules during the creation of cells and tissues, or when breaking them down and using them as a provider of energy, in the digestion and use of food.

Amino Acids/Proteins

When amino acids arrange themselves within a linear chain, joined together by peptide bonds, proteins are formed. Many proteins are the enzymes that catalyze the chemical reactions that make up metabolism.

The name protein came from the Greek word proteios, meaning "first place." 50% of the dry mass of most cells are proteins. Almost all organisms contain proteins.

Different kind of protein include the following:

1. Enzymatic proteins
   a. Specifically speed up reactions that are endogonic.
   b. Examples:
      1) Digestive enzymes catalyze the hydrolysis of foods.

2. Structural proteins
   a. Supporting the shape of the cell.
   b. Examples:
      1) Collagen is a type of fibrous framework that made up the connective tissues in animals.
      2) Keratin is another type of fibrous proteins are the supplement of the hair, horns, feathers and other skin.

3. Storage proteins
   a. Storage of amino acid.
   b. Examples:
      1) Ovalbumin is a protein used as an amino acid source for the developing embryo in egg white.
      2) Casein is protein with major source of amino acid for baby mammals in milk.

4. Transport proteins
   a. Transportation of substances.
   b. Examples:
      1) Hemoglobin is a protein of vertebrate blood that carries oxygen from the lungs to other parts of the body.
      2) Membrane protein attached the membrane of the cell, transporting substances that unable to cross the membrane itself.

5. Hormonal proteins
   a. Regulation of an organism's activities.
   b. Examples:
      1) Insulin is a hormone secreted by the pancreas that sends signals to the cells to regulate the concentration of sugar in the blood steam for vertebrates.

6. Receptor proteins
   a. Response of cell to stimuli from chemicals, neighboring cells, etc.
   b. Examples:
1) Receptors that attached cell membranes to detect signals from hormonal proteins.
7. Contractile and motor proteins
   a. Movement of organelles.
   b. Examples:
      1) Actin regulates the contraction of muscles
      2) Cilia responsible for the movement of organelles
8. Defensive proteins
   a. Protection against foreign substances.
   b. Examples:
      1) Antibodies.

Amino acids are organic molecules that contain a carboxyl and amino groups attaching an alpha carbon as the center. The alpha carbon also contains another various groups symbolized by R and a hydrogen. The R groups usually called the side chain and it differ from each amino acids.

Amino acids includes the following:

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycine (Gly or G)</td>
<td>Nonpolar, Smallest R group with only a hydrogen atom, evolutionary conserves because most other R group cannot fit into the small space, alpha carbon is achiral</td>
</tr>
<tr>
<td>Alanine (Ala or A)</td>
<td>Nonpolar, R group is a methyl, alpha carbon is chiral</td>
</tr>
<tr>
<td>Valine (Val or V)</td>
<td>Nonpolar, alpha carbon is chiral</td>
</tr>
<tr>
<td>Leucine (Leu or L)</td>
<td>Nonpolar, alpha carbon is chiral</td>
</tr>
<tr>
<td>Isoleucine (Ile or I)</td>
<td>Nonpolar, alpha carbon is chiral</td>
</tr>
<tr>
<td>Methionine (Met or M)</td>
<td>Nonpolar, alpha carbon is chiral, First amino acid of proteins</td>
</tr>
<tr>
<td>Phenylalanine (Phe or F)</td>
<td>Nonpolar, alpha carbon is chiral</td>
</tr>
<tr>
<td>Tryptophan (Trp or W)</td>
<td>Nonpolar, alpha carbon is chiral</td>
</tr>
<tr>
<td>Proline (Pro or P)</td>
<td>Nonpolar, alpha carbon is achiral</td>
</tr>
</tbody>
</table>
10. Serine (Ser or S)
   - Polar
   - alpha carbon is chiral
11. Threonine (Thr or T)
   - Polar
   - alpha carbon is chiral
12. Cysteine (Cys or C)
   - Polar
   - alpha carbon is chiral
13. Tyrosine (Tyr or Y)
   - Polar
   - alpha carbon is chiral
14. Asparagine (Asn or N)
   - Polar
   - alpha carbon is chiral
15. Glutamine (Gln or Q)
   - Polar
   - alpha carbon is chiral
16. Aspartic acid (Asp or D)
   - Electrically charged (Acidic)
   - alpha carbon is chiral
17. Glutamic acid (Glu or E)
   - Electrically charged (Acidic)
   - alpha carbon is chiral
18. Lysine (Lys or K)
   - Electrically charged (Basic)
   - alpha carbon is chiral
19. Arginine (Arg or R)
   - Electrically charged (Basic)
   - alpha carbon is chiral
20. Histidine (His or H)
   - Electrically charged (Basic)
   - alpha carbon is chiral

A proteins consist of one or more polypeptides. Polypeptides consist of different level of structures.

1) Primary structure
   - with unique sequence of amino acids
2) Secondary structure
   - hydrogen bonds interact between polypeptide backbones.
   - polypeptides can fold into structures such as alpha helix, beta pleated sheet, etc..
3) Tertiary structure
   - hydrophobic interaction and disulfide bridges between side chains of polypeptides
4) Quaternary structure
   - overall protein structures consist of two or more polypeptide chains combine into one functional macromolecule.
Carbohydrates

Carbohydrates are the most abundant biological molecules found in organisms and are responsible for the storage and transport of energy, such as starch and glycogen, and structural components, like cellulose in plants or chitin in animals.

Carbohydrates are a class of macromolecules - polymers built from monomers. Carbohydrates include both sugars and polymers of sugars. The simplest carbohydrates are monosaccharides also known as simple sugars. Another group of carbohydrates are disaccharides that joining two monosaccharides together by a covalent bond. Polysaccharides consist of many monosaccharides as building blocks.

1. Monosaccharides
   a. simple sugar with general formula, (CH2O)n
   b. the most common monosaccharide is glucose
   c. the molecule contains a carbonyl group and many hydroxyl groups attached to the carbon atoms
   d. a monosaccharide can either be an aldose (aldehyde sugar) or a ketose (ketone sugar) depending on the location of the carbonyl group
   e. monosaccharides can categorize by the number of carbon on the chain starting with three carbon

2. Disaccharides
   a. two monosaccharides join together by a glycosidic linkage - a covalent bond formed by dehydration reaction
   b. examples:
      1) maltose - two molecules of glucose
      2) sucrose - a molecule of glucose joining a molecule of fructose

3. Polysaccharides
   a. polysaccharides are polymers of multiple monosaccharides joined by glycosidic linkages.
   b. some polysaccharides are storage material and some are for structures.

Storage polysaccharides

1. storage polysaccharides store sugar for later use
2. usually joined by 1-4 linkages of alpha glucose monomers
3. usually form helical shape
4. starch
   a. a storage polysaccharide in plants that joined by glucose monomers
   b. the simplest form of starch is amylose, unbranched
   c. a more complex form of starch is amylpectin, branched
5. glycogen
   a. a storage polysaccharide in animals that joined by glucose monomers
   b. a amylpectin like polymer but more branches
   c. glycogen mainly store in the liver and muscle cells

Structural polysaccharides

1. structural polysaccharides usually give protection to the cell as a form of membrane
2. usually joined by 1-4 linkages of beta glucose monomers
3. usually form beta sheets
4. cellulose
   a. major components of cell walls in plants
   b. cellulose is unbranched
   c. hydroxyl groups on the glucose are able to interact with other hydroxyls of other molecules and form hydrogen bonds
   d. the cellulose molecules are grouped into units called microfibrils.
   e. humans are unable to digest cellulose
**Lipids**

Lipids are the most diverse group of biochemicals. Structurally, the lipids primary function is to be part of biological membranes, such as the cell membrane, or as a source of energy in organisms. Another major class of lipids that is produced in cells are steroids, such as cholesterol.

Lipids are grouped together by their hydrophobic behavior - meaning they mix poorly with water. Lipid consist mostly hydrocarbons.

Different kind of lipid include the following:

1. **Fats**
   a. Fats consist of a glycerol and three fatty acid, constructed from hydrocarbon and the carbon at one end contain carboxyl group.
   b. The fatty acids are join to the glycerol by ester linkage.
   c. Saturated fats are fats that does not contain any double bond on the hydrocarbon chain.
   d. Unsaturated fats are fats that contains double bond on different position of the hydrocarbon chain.
      1) Most double bonds in the hydrocarbon chain are cis- double bond.
      2) Trans fats are trans- double bond.

2. **Phospholipids**
   a. Phospholipids consist of a glycerol, two fatty acid and a phosphate group attaching to an alcohol group.
   b. Phospholipids consist of hydrophilic head and hydrophobic tail.
   c. Phospholipids made up the cell membranes' bilayer.
      1) Hydrophobic tails dislike water and try to get away by getting as close to other hydrophobic tail as possible.
      2) Hydrophilic heads contact with water and protecting the hydrophobic tails in the bilayer.

3. **Steroids**
   a. Steroids consist of four fused rings skeleton.
   b. Different steroids consist of the steroid skeleton and other chemical groups attaching to it.
   c. Example
      1) Cholesterol
         a) Common component of animal cell membranes.

4. **Glycolipid**
   a. Glycolipids consists of a fatty acid unit and a sugar unit.
   b. Derive from sphingosine.
   c. Simplest glycolipid is cerebroside.
   d. More complex glycolipid is ganglioside.
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