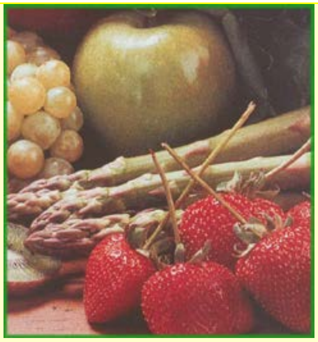
Overview of the Macronutrients Used in Metabolism



The body functions like a machine, and the fuel for the body machine is food. Food provides the carbohydrate, fat, protein, water, electrolytes, vitamins, and other micro-nutrients essential for optimal health and well-being.

The early study of energy nutrients obtained from food is important to master further knowledge and research inquiry into the muscle metabolism content within exercise physiology. For example, many of the molecules of key energy pathways are modifications of energy nutrients. Glycolysis is a great example of this, where the substrates and products of these sequential reactions are all modifications of the simple sugar - glucose. Pyruvate and lactate are two end products of the catabolism of glucose through glycolysis. Conversely, the very different chemical structure of palmitate, a 16 carbon fatty acid, helps explain the need for a separate energy pathway to fatty acids into multiple molecules of acetyl Co-A. Similarly, the different chemical structure of amino acids provide the background for understanding where amine groups come from and why we have ammonia and urea production in different tissues of the body.

Metabolism is a series of reactions where specific enzymes (not all of them!) can be regulated by **activators** and **inhibitors** to change the rate of product formation. Other enzymes for specific reactions remain unregulated but are influenced by subtle changes to substrate and product concentrations that result in a relatively controlled or orderly change in the direction in which substrates are converted to products.

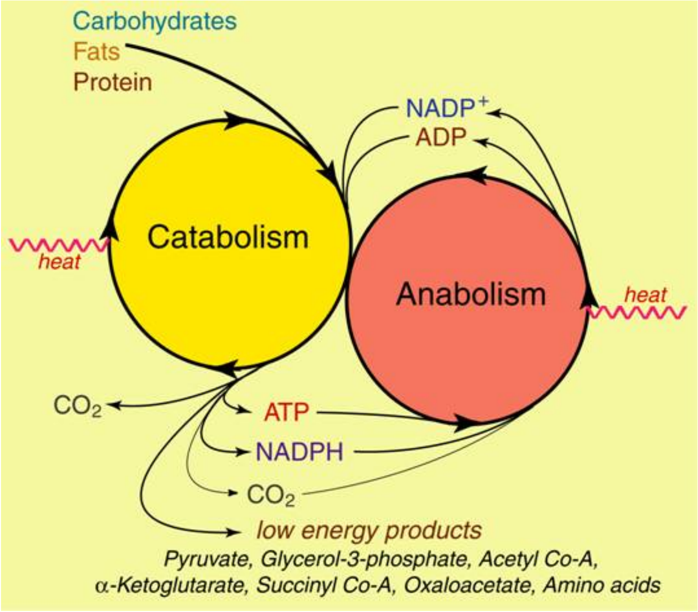


Figure 1. A schematic overview of the connections between catabolism and anabolism.

Metabolism is divided into two opposing functions; catabolism and anabolism (Figure 1). **Catabolism** involves the release of free energy while molecules are broken down into smaller, less energy liberating end product. **Anabolism** involves the harnessing of the free energy from catabolism to build more complex molecules from the combination of complex **nutrients** and the many small end products of catabolism. For both anabolism and catabolism, the reactions and **pathways** can be grouped based on the type of energy substrate used. For skeletal muscle such substrates are **carbohydrates**, **fats**, **proteins** and **amino acids**, and stored **phosphorylated compounds** (e.g. ATP and creatine phosphate).

Overview of the Macronutrients Used in Metabolism

It is very important to understand the role of **macronutrients** in the overall design of energy metabolism, as well as the reactions of **energy metabolism** (Figure 2). A sound grounding in nutrition also assists the study of sports nutrition and **ergogenic aids**. However, one of the most important reasons to understand the “big picture” of metabolism is that it provides an overall perspective of how each component of metabolism relates to each other. For example, when you plan to go on a road trip, the first map you get is a small scale (large area) map that covers the entire distance of travel. This gives you the “big picture” of the route you take, and reveals all of the options for side-roads, scenic stops, and any obstacles to avoid along the way. I propose to you that the study of metabolism is not that much different to your plans for a road trip. Studying the “big picture” first provides perspective to the entire metabolic map. Where, and perhaps how, **carbohydrate catabolism** and **lipid catabolism** share the same reactions. Where, and why, certain amino acids enter the catabolic pathways in different locations. Where oxygen is used and **carbon dioxide** (CO_2) is produced. Why **glycolysis** is always **anaerobic**. How muscle metabolism regenerates cytosolic **NAD^+** and why this is so important for repetitive muscle contractions.

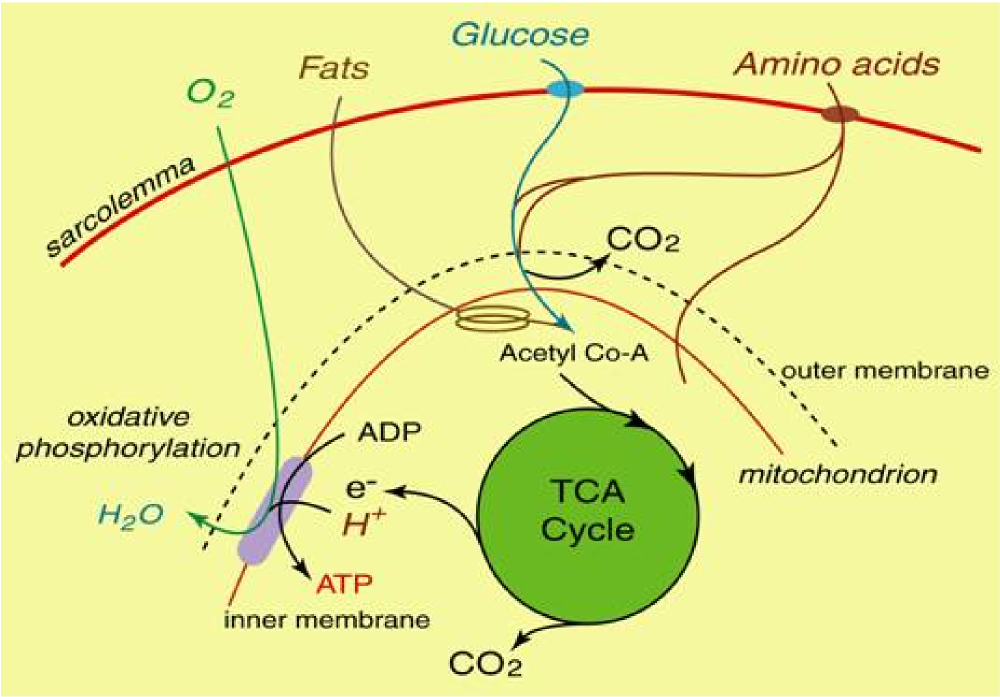


Figure 2. The role of carbohydrates, fats and proteins in cellular energy metabolism.

The macronutrients of cellular metabolism comprise carbohydrates, fats and proteins. The combined illustrative summary of the role of macronutrients in energy metabolism is provided in Figure 2. Basically, the macronutrients are used to release free energy and smaller metabolite by-products from which to fuel cell work and support cellular anabolism. Carbohydrates are used to first fuel glycolysis, and then **mitochondrial respiration** via the **tricarboxylic acid cycle (TCA Cycle or Kreb’s cycle)** and **electron transport chain**. **Fatty acid** molecules are used to fuel a pathway inside mitochondria called **β-oxidation**, which in turn fuels the TCA cycle and electron transport chain. Proteins are degraded, releasing amino acids, which depending on their chain length and chemical structure, can enter into either of glycolysis or the TCA cycle.

Note that the CO_2 released from metabolism comes from the TCA cycle, and also from 3-carbon carbohydrate substrate entry into the TCA cycle. **Oxygen** is used solely within the **mitochondria** at the end of the electron transport chain.
There are some additional important observations from Figure 2. The catabolism of which of the three macronutrients is totally dependent on **oxygen consumption**? Carbohydrate is not as glucose catabolism first and always requires glycolysis, which is always anaerobic. Protein is not as some amino acids enter into catabolism in the glycolytic pathway. Some amino acids can also be used to form intermediates of the TCA cycle, improving mitochondrial function for a given oxygen availability. As all of lipid catabolism occurs in the mitochondria, it is totally dependent on the availability and consumption of oxygen at the cellular level.

Why are these distinctions important? Well, if there is a lack of oxygen, or if the cell's energy demands far exceed the capacity of the mitochondria, then clearly lipid catabolism cannot be relied on for the free energy needed to support muscle contraction. Thus, which pathways and macronutrients must therefore have an increased role on ATP production during intense muscle contractions? The answer; carbohydrate and protein catabolism to fuel glycolysis and mitochondrial respiration.

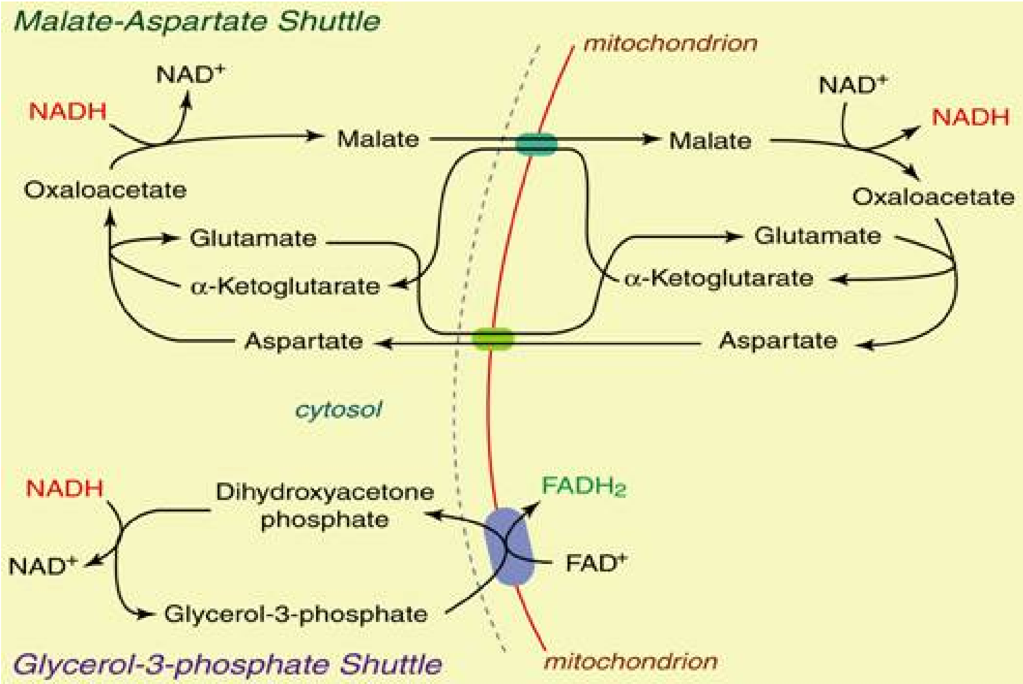


Figure 3. The two methods of NAD^+ regeneration in the cytosol that involve mitochondrial respiration. Note that only one (glycerol-phosphate shuttle) is believed to be operable in skeletal muscle.

Overview of the Macronutrients Used in Metabolism

The interactions between the mitochondria and cytosol are extremely important. During conditions of cellular energy balance, the mitochondria can function to have mitochondrial respiration maintain normal concentrations of key metabolic substrates and products to ensure correct free energy release from ATP. One such important metabolite in NAD^+ as it is necessary for phase II of glycolysis Cytosolic NAD^+, which is an important substrate for glycolysis, is regenerated in two ways. Firstly, by the mitochondria with the help of reactions that essentially shuttle electrons and **protons** between the **cytosol** and mitochondria (Figure 3), and secondly, by the production of **lactate** in the cytosol (Figure 4).

You will learn more about how mitochondria are involved in sustaining a desirable cytosolic NAD^+ concentration, and for how muscle lactate production is a necessary trait of intense muscle contraction that supports the ability to sustain repeated intense muscle contractions. In this context, lactate is a beneficial, not detrimental consequence of intense exercise.

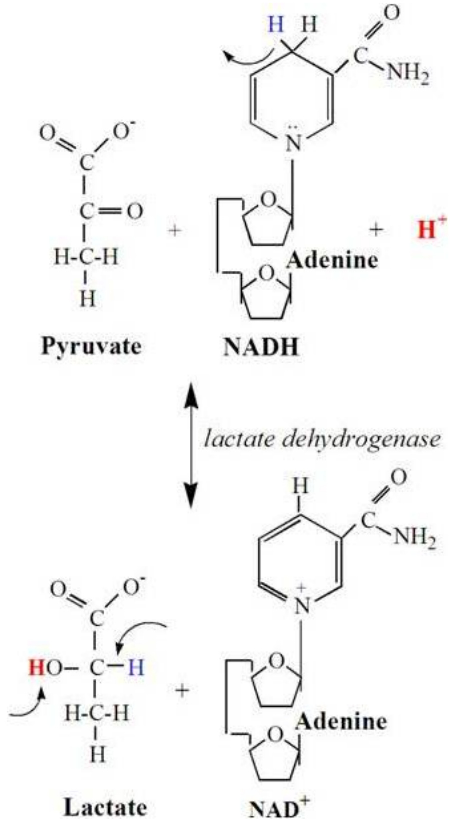


Figure 4. The production of lactate from pyruvate in the cytosol. This reaction is another means to regenerate cytosolic NAD^+ for glycolysis.

Glossary Words

metabolism is the net sum of all reactions of a cell, tissue or organism.

activators are molecules that bind to an enzyme (non-covalently) and increase the catalytic effectiveness of the enzyme.

inhibitors are molecules that bind to an enzyme (non-covalently) and decrease the catalytic effectiveness of the enzyme.

catabolism refers to reactions of the body that break down larger molecules into smaller molecules and waste products, with a net release of free energy.

anabolism refers to reactions of the body that use the free energy and reducing power of catabolism to make larger molecules needed for cell and tissue maintenance, growth and repair.

Overview of the Macronutrients Used in Metabolism

nutrients are molecules obtained from foods and fluid ingested that are essential for supporting life and all bodily functions.

pathways are a series of sequential chemical reactions that link substrates and products to the production of an important end product.

carbohydrates are molecules that are classed as poly-hydroxyl aldehydes or ketones, or substances that yield these molecules after hydrolysis reactions. While most have ratios of carbon to hydrogen to oxygen (C:H:O) of the formula 1:2:1, many do not and also contain phosphorous, nitrogen and sulfur elements.

fats are also known as lipids or oils. Fats and oils are highly hydrogenated long chain carbon molecules (have few oxygen elements) that serve as energy stores as well as important structural components of cell membranes.

proteins are also known as peptides. Proteins are comprised of chains of amino acids, and are coded and regulated by genetic material.

amino acids are the building blocks of proteins. There are 20 amino aids in the human body, with each amino acid consisting of an α-carbon, from which are attached a carboxyl group (-COOH), an amine group ($-NH_2$), a hydrogen (-H) and a unique side chain (-R). Eight of the 20 amino acids cannot be produced by the body and are termed "essential amino acids".

phosphorylated refers to the addition of a phosphate ($-HPO_3$) group to another molecule.

molecule strictly speaking, a molecule is the smallest multiple atomic unit of matter that retains the properties of the element. For example, gaseous oxygen (O_2), nitrogen (N_2) and hydrogen (H_2) are examples of diatomic molecules. However, physiologists often use the word molecule synonymous with compound.

compounds are substances that contain two or more different elements, such as water, lactate, glucose, etc.

macronutrients are the three energy nutrient molecular classes of nutrient; carbohydrates, fats and proteins.

energy metabolism is the part of catabolism that functions to release free energy that is used to form ATP, which in turn is used to fuel cell work.

ergogenic aids are anything that improves performance.

carbohydrate catabolism Catabolism of carbohydrates.

Overview of the Macronutrients Used in Metabolism

lipid catabolism Catabolism of lipids.

carbon dioxide (CO_2) Gas by-product of energy catabolism within the mitochondria, most often released from dehydrogenase reactions.

glycolysis Pathway of catabolism within the cytosol of a cell responsible for the catabolism of glucose (6carbons) to 2 pyruvate compounds (3 carbons).

anaerobic Without oxygen.

NAD^+ Nicotinamide adenine dinucleotide in the oxidized form.

mitochondrial respiration Overall process of mitochondrial metabolism where carbohydrate, lipid and amino acid compounds are catabolized, oxygen is consumed, carbon dioxide is produced, and ATP is regenerated. This process includes pathways of the TCA cycle, β-oxidation, amino acid oxidation, and the electron transport chain.

tricarboxylic acid cycle (TCA Cycle or Kreb's cycle) Pathway within mitochondria that catabolizes acetyl Co-A to products of carbon dioxide, electrons and protons (FADH2 and NADH) and 1 ATP.

electron transport chain Pathway within mitochondria that received electrons and protons gained from prior catabolism pathways and used them to regenerate ATP, consume oxygen and produce water.

fatty acid Type of lipid consisting of a densely hydrogenated carboxylic acid side-chain of between 4 to 36 carbons.

β-oxidation Pathway within the mitochondria involving the catabolism of fatty acids to acetyl CoA and released electrons and protons (NADH and $FADH_2$).

oxygen Element which exits mainly in a gaseous diatomic structure (O_2).

mitochondria Organelle within skeletal muscle responsible for the consumption of oxygen and the regeneration of large amounts of ATP, albeit at a slow rate.

protons Hydrogen atoms that have lost an electron.

cytosol Region of a cell immediately surrounded by the cell membrane.

lactate Three carbon product of the reduction of pyruvate in the cytosol via the lactate dehydrogenase reaction.

oxygen consumption Cellular use of oxygen. This is often measured from expired gas analysis, and represents the difference in the oxygen inhaled vs. exhaled.