Fermentation and Anaerobic Respiration

How cells extract energy from glucose without oxygen. In yeast, the anaerobic reactions make alcohol, while in your muscles, they make lactic acid.

Introduction

Ever wonder how yeast ferment barley malt into beer? Or how your muscles keep working when
you're exercising so hard that they're very low on oxygen? Both of these processes can happen thanks to alternative glucose breakdown pathways that occur when normal, oxygen-using (aerobic) cellular respiration is not possible—that is, when oxygen isn't around to act as an acceptor at the end of the electron transport chain. These fermentation pathways consist of glycolysis with some extra reactions tacked on at the end. In yeast, the extra reactions make alcohol, while in your muscles, they make lactic acid.

Fermentation is a widespread pathway, but it is not the only way to get energy from fuels anaerobically (in the absence of oxygen). Some living systems instead use an inorganic molecule other than $O_2$, such as sulfate, as a final electron acceptor for an electron transport chain. This process, called anaerobic cellular respiration, is performed by some bacteria and archaea.

In this article, we'll take a closer look at anaerobic cellular respiration and at the different types of fermentation.

**Anaerobic cellular respiration**

Anaerobic cellular respiration is similar to aerobic cellular respiration in that electrons extracted from a fuel molecule are passed through an electron transport chain, driving
ATP synthesis. Some organisms use sulfate (SO$_4^{2-}$) as the final electron acceptor at the end of the transport chain, while others use nitrate (NO$_3^-$) as a terminal electron acceptor, sulfur, or one of a variety of other molecules. What kinds of organisms use anaerobic cellular respiration? Some prokaryotes—bacteria and archaea—that live in low-oxygen environments rely on anaerobic respiration to break down fuels. For example, some archaea called methanogens can use carbon dioxide as a terminal electron acceptor, producing methane as a by-product. Methanogens are found in soil and in the digestive systems of ruminants, a group of animals including cows and sheep. Similarly, sulfate-reducing bacteria and Archaea use sulfate as a terminal electron acceptor, producing hydrogen sulfide (H$_2$S) as a byproduct. The image below is an aerial photograph of coastal waters, and the green patches indicate an overgrowth of sulfate-reducing bacteria.
Fermentation

It’s the process of using microorganisms, such as bacteria or yeast, to convert carbohydrates to alcohol or organic acids under anaerobic conditions.

There are two types of fermentation: alcoholic and lactic acid. Alcoholic fermentation, or ethanol fermentation, is where pyruvate (from glucose metabolism) is broken down into carbon dioxide and ethanol by bacteria and yeast. Alcohol fermentation has been used to produce beer, bread and wine.

Pyruvate molecules from glucose glycolysis may be further fermented into lactic acid. Lactic acid fermentation converts lactose into lactic acid. (1)

There are several benefits to fermenting food. First, fermentation serves to enhance the digestion of food. Your body needs adequate digestive enzymes to properly absorb, digest, and utilize nutrients in food. When vegetables like cabbage
and cucumbers are left to steep and sit until the sugars are broken down to promote the growth of bacteria, this is when the vegetables are fermented.

Fermented foods are also filled with beneficial bacteria that work as reinforcement for the good bacteria in the digestive system. Since 70 percent to 80 percent of the immune system lies in the gut, having proper balance of gut flora is important.

What else is fermentation good for? It preserves food. How? During fermentation, organisms produce acetic acid, alcohol and lactic acid, which are all “bio-preservatives” that retain nutrients and prevent spoilage. Lactic acid acts as a preservative by reducing pH, which inhibits the growth of harmful bacteria. (2) It also influences physical properties of casein to induce a finer suspension, which appears to help promote digestibility.

**Lactic Acid Fermentation**

In lactic acid fermentation, NADH transfers its electrons directly to pyruvate, generating lactate as a byproduct. Lactate, which is just the deprotonated form of lactic acid, gives the process
its name. The bacteria that make yogurt carry out lactic acid fermentation, as do the red blood cells in your body, which don’t have mitochondria and thus can’t perform cellular respiration.

Diagram of lactic acid fermentation. Lactic acid fermentation has two steps: glycolysis and NADH regeneration. During glycolysis, one glucose molecule is converted to two pyruvate molecules, producing two net ATP and two NADH. During NADH regeneration, the two NADH donate electrons and hydrogen atoms to the two pyruvate molecules, producing two lactate molecules and regenerating NAD+. Muscle cells also carry out lactic acid fermentation, though only when they have too little oxygen for
aerobic respiration to continue—for instance, when you’ve been exercising very hard. It was once thought that the accumulation of lactate in muscles was responsible for soreness caused by exercise, but recent research suggests this is probably not the case.

Lactic acid produced in muscle cells is transported through the bloodstream to the liver, where it’s converted back to pyruvate and processed normally in the remaining reactions of cellular respiration.

**Alcohol fermentation**

Another familiar fermentation process is alcohol fermentation, in which NADH\text{NADH}NADH, A, D, H donates its electrons to a derivative of pyruvate, producing ethanol.

Going from pyruvate to ethanol is a two-step process. In the first step, a carboxyl group is removed from pyruvate and released in as carbon dioxide, producing a two-carbon molecule called acetaldehyde. In the second step, NADH\text{NADH}NADH, A, D, H passes its electrons to acetaldehyde, regenerating NAD+\text{NAD}^+NAD+ and forming ethanol.
Diagram of alcohol fermentation. Alcohol fermentation has two steps: glycolysis and NADH regeneration. During glycolysis, one glucose molecule is converted to two pyruvate molecules, producing two net ATP and two NADH.

During NADH regeneration, the two pyruvate molecules are first converted to two acetaldehyde molecules, releasing two carbon dioxide molecules in the process. The two NADH then donate electrons and hydrogen atoms to the two pyruvate molecules, producing two ethanol molecules and regenerating NAD+. 
Alcohol fermentation by yeast produces the ethanol found in alcoholic drinks like beer and wine. However, alcohol is toxic to yeasts in large quantities (just as it is to humans), which puts an upper limit on the percentage alcohol in these drinks. Ethanol tolerance of yeast ranges from about 55\% to 21\%, depending on the yeast strain and environmental conditions.

**Facultative and obligate anaerobes**

Many bacteria and archaea are facultative anaerobes, meaning they can switch between aerobic respiration and anaerobic pathways (fermentation or anaerobic respiration) depending on the availability of oxygen. This approach allows them to get more ATP out of their glucose molecules when oxygen is around—since aerobic cellular respiration makes more ATP than anaerobic pathways—but to keep metabolizing and stay alive when oxygen is scarce.

Other bacteria and archaea are obligate anaerobes, meaning they can live and grow only in the absence of oxygen. Oxygen is toxic to these microorganisms and injures or kills them on exposure. For instance, the *Clostridium* bacteria that are responsible for botulism (a form of food poisoning) are obligate anaerobes.
end superscript. Recently, some multicellular animals have even been discovered in deep-sea sediments that are free of oxygen

**Health Benefits of Fermentation**

**1. Improves Digestion**

Fermentation breaks down nutrients into more easily digestible forms. When lactobacilli in fermented foods proliferate, their vitamin levels increase and digestibility is enhanced. When it comes to soybeans, this protein-rich bean is indigestible without fermentation. Fermentation breaks down the soybeans complex protein into readily digestible amino acids, giving us traditional Asian ingredients, such as miso, tamari (soy sauce) and tempeh. (4)

Milk is also difficult for many individuals to digest. A type of bacteria present in fermented dairy products converts lactose, the milk sugar that many individuals cannot tolerate, into digestible lactic acid. In a study out of France on women who reported minor digestive problems, those women reported improved gastrointestinal digestive
symptoms when fermented milk containing *Bifidobacterium lactis* was consumed. (5)

2. Suppresses H. pylori

**H. pylori** (Helicobacter pylori infection) is an important risk factor for many gastrointestinal diseases. Some fermented foods serve useful for suppressing H. pylori infection.

An observational study published in *World Journal of Gastroenterology* involving 464 participants found lower prevalence of H. pylori seropositivity in those who consumed yogurt more than once a week compared to those who did not. (6) This confirms other research findings that fermented milk improves gastrointestinal symptoms in patients who tested positive for H. pylori. (7)

3. Has Anticancer Effects

Cancer is caused by activation or mutation of abnormal genes, which control cell growth and division. Researchers believe probiotic cultures and fermented foods might decrease the exposure to chemical carcinogens by: (8)

- detoxifying the ingestion of carcinogens
- altering the environment of the intestine and decreasing metabolic activities or populations of
bacteria that may generate carcinogenic compounds
• producing metabolic products that cause programmed cell death or apoptosis
• producing compounds that inhibit the growth of tumor cells
• stimulating the immune system to defend itself against cancer cell proliferation

There are several reports on the ways fermented foods can help treat cancer:

• Large cohort studies in the Netherlands and Sweden have observed the effects of regular consumption of fermented dairy products in reducing the risk of bladder cancer.
• Strains of bacteria called lactobacillus prevent toxicity of heavy metals by excreting harmful heavy metals and heterocyclic aromatic amines, carcinogens found in overcooking meat.
• **Kimchi**, a fermented cabbage cuisine, contains strains that promote the degradation of organophosphorus pesticides, by breaking down a cancer-causing food preservative called sodium nitrate.

4. Enhances Bioavailability of Nutrients

Fermentation helps create new nutrients and has been shown to improve the availability, digestibility
and quantity of some dietary nutrients. As microorganisms go through their life cycles, microbial cultures create B vitamins, including folic acid, riboflavin, niacin, thiamine and biotin. The bioavailability of fat and protein are enhanced by bacterial enzymatic hydrolysis, and the production of lactic acid, butyric acid, free amino acids and short chain fatty acids (SCFA) are increased by lactic acid bacteria.

When SCFAs are absorbed, they may help protect against pathological changes in the colonic mucosa. They play an important role in maintaining an appropriate pH in the colon, which is important in the expression of various of bacterial enzymes and in carcinogen and foreign compound metabolism in the gut.

5. Reduces Symptoms of Lactose Intolerance

Lactobacillus consumes lactose in milk and transforms it into lactic acid that may be easier for individuals to digest. Lactic acid in yogurt reduces symptoms of lactose intolerance in individuals who are lactase-deficient. The beneficial effect appears to be a result of the lactic acid bacteria in fermented milk, increasing lactase in the small intestine.
In clinical practice, replacing milk with fermented dairy products allows for decreased diarrhea, better digestion and improvements in other symptoms of intolerance in participants with lactose intolerance in subjects with short-bowel syndrome and children with diarrhea. Enhanced digestion of sucrose was shown in infants with sucrase deficiency as well. (9)

6. Helps Treat Hepatic Disease

Non-alcoholic fatty liver disease is the buildup of extra fat in the liver cells not caused by alcohol. Liver disease can cause liver swelling, scarring, and even lead to cancer or liver failure.

In a double-blind, randomized, controlled clinical trial, some participants consumed 300 grams a day of fermented probiotic yogurt containing lactobacillus acidophilus and bifidobacterium lactis, while those in the control group consumed 300 grams a day of conventional yogurt for eight weeks. The group who consumed the probiotic yogurt had reductions in alanine aminotransferase, aspartate aminotransferase, total cholesterol and low-density lipoprotein cholesterol compared to the control group. The reduction in these parameters
may be useful in management of liver disease risk factors. (10)

7. Improves Arthritis Symptoms

Most people know someone with arthritis. It is the leading cause of disability, with symptoms including aching, pain, stiffness and swelling of the joints. It is thought that inflammation associated with *rheumatoid arthritis symptoms* may be modulated by the consumption of fermented foods.

A randomized, double-blind, placebo-controlled pilot study of probiotics in active rheumatoid arthritis found that “patients with at least four swollen and four tender joints and stable medications with no steroids for at least one month prior to and during the study, showed a significant improvement in the Health Assessment Questionnaire score after three months of probiotic treatment.” (11)

8. Treats Inflammatory Bowel Disease

Fermented milk supplemented with probiotics can exhibit a direct effect in the gut in managing inflammatory and functional bowel disorders. Clinical trials show that probiotics help reduce abdominal pain, bloating, constipation and
flatulence in patients with inflammatory bowel disease, including Crohn’s disease. (12)

**Best Fermented Foods**

1. **Kefir**

Kefir is a unique cultured dairy product due to combined lactic acid and alcoholic fermentation of lactose in milk. Kefir is produced by microbial activity of kefir grains, which have a relatively stable and specific balance of lactic acid bacteria and yeast.

Due to the **benefits of kefir**, including reduction of lactose intolerance symptoms, stimulation of the immune system, lowering cholesterol, and antimutagenic and anticarcinogenic properties, it has become an important functional dairy food. Consequently, research on kefir has increased in the past years.

2. **Kimchi**

Kimchi is a spicy and popular fermented food enjoyed in Korea. Since it is low in carbohydrates, fat, and has a high content of vitamins, minerals,
dietary fiber and phytochemicals, it is a perfect fermented food for weight control.

3. Kombucha

A sour tonic beverage, like rejuvelac and kvass in Russia, kombucha is a sweetened tea cultured with a gelatinous colony of bacteria and yeast. **Benefits of kombucha** include reducing blood pressure, improving cholesterol levels, increasing the body’s resistance to cancer and detoxifying the body.

4. Miso

Miso is a paste-like, half-solid food with sweet and salty taste, which has been gaining popularity worldwide. It has been a staple food in Japan and is used to cook **miso soup** and side dishes as seasoning. The bioactive compounds formed or released by the enzymes during miso production have been shown to exhibit antioxidant, antidiabetic, anticancer and antihypertensive properties.

5. Natto

A traditional Japanese food made from fermented soy with *Bacillus subtilis* is natto. The enzymes during the fermentation process produce mucilage
that contains nattokinase. **Natto** a natural blood thinner.

### 6. Sauerkraut

**Sauerkraut** is finely chopped cabbage that has been fermented by lactic acid-producing bacteria. Studies have shown that the fermentation of cabbage enhances protective activities, such as protection of blood vessels, vitamin C, dietary folates and manganese.

### 7. Tempeh

Tempeh is a soybean ferment from Indonesia that has become a popular vegetarian food in the United States. In a clinical study, daily consumption of boiled tempeh for two months among patients with active pulmonary tuberculosis on standard therapy showed a positive effect on weight gain and physical function change. (13)

### 8. Yogurt

No cultured food is more well-known or acknowledged for its health benefits than yogurt. Probiotic yogurt is extremely high in calcium, zinc, B vitamins, probiotics and protein.