You Are What You Eat!

Lipids and carbohydrates are the scientific names for fats and sugars. These natural substances do a lot to keep us healthy. Along with giving us energy, they help cells move around the body and communicate.

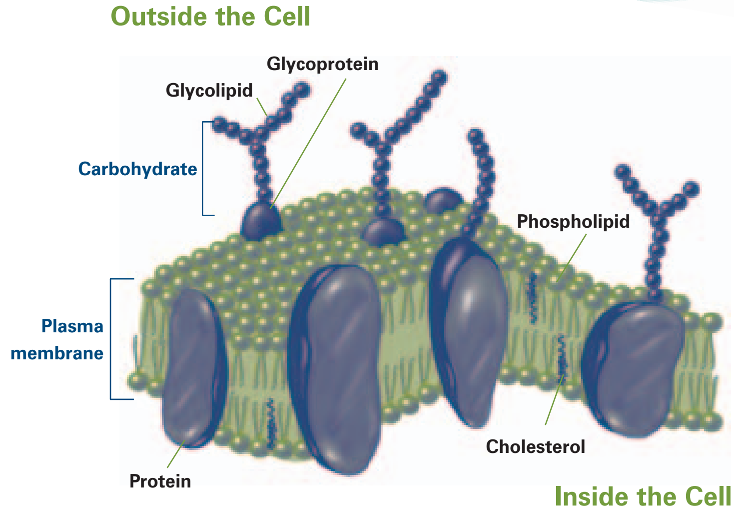
FATS

Eating healthy means that you need to be careful about the amount of fat in your diet. But a certain amount of fat is really necessary: All humans need lipids, called essential fatty acids, from food because our bodies can't make them from scratch. Some body fat is also necessary as insulation to prevent heat loss and to protect vital organs from the strain of routine activities.

Lipids in adipose tissue (fat cells) are a major form of energy storage in animals and people. The "fat-soluble" vitamins (A, D, E and K) are essential nutrients stored in the liver and in fatty tissues. Triglycerides, another type of lipid, are especially suited for stockpiling energy because of their high caloric content. When we need energy, our bodies use enzymes called lipases to break down stored triglycerides into smaller pieces that participate directly in metabolism.

The mitochondria in our cells ultimately create energy from these reactions by generating adenosine triphosphate, or ATP, the main currency of metabolism.

In addition to providing and storing energy, lipids do many other things. They act as messengers, helping proteins come together in a lock-and-key fashion. They also start chemical reactions that help control growth, immune function, reproduction and other aspects of basic metabolism.



The plasma membrane is a perfect example of the rule that oil and water don't mix.

Membranes are a hallmark of how organisms evolved the ability to multitask.

The lipid molecule cholesterol is a key part of the plasma membrane, a coating that wraps around every cell in the human body.

Although it does act as a protective barrier, the plasma membrane is less like a rigid wall and more like a pliable blanket. In addition to lipids, the plasma membrane contains sugars that stick out from its surface and proteins that thread through it.

It is an orderly arrangement of ball-and-stick molecules called glycolipids (lipid chains with sugars attached) and phospholipids (lipids marked with cellular tags called phosphates).

When aligned "tail-to-tail," these fat-containing molecular assemblies resemble a double array of matchsticks lined up perfectly end-to-end.

The membrane forms more or less automatically when the lipid end of each glycolipid or phospholipid matchstick is attracted to oily substances: other lipids. The other matchstick end, containing a sugar or phosphate molecule, drifts naturally toward the watery environment typical of the areas inside or between cells.

Membranes are a hallmark of how organisms evolved the ability to multitask. Membranes allow cells to keep proteins and other molecules in different compartments so that more than one set of reactions can occur at the same time.

In addition to the plasma membranes around cells, organelles inside cells are wrapped by similar, lipid-containing membranes that encase specialized contents.

Meet . . .
Cathy Drennan

CHEMIST AND BIOPHYSICIST, *Cambridge, Massachusetts*

What She's Doing

Our bodies, like nearly all living things on the planet, run chemical reactions in watery fluids at a neutral pH. Naturally occurring metals help these processes occur safely and efficiently.

Cathy Drennan studies how these metals do such important jobs in biology. Since metals are key components of many enzymes, cell proteins and even medicines, this work is really important for our health.

Metals also act as molecular helpers in chemical reactions that rid the atmosphere of pollutants like carbon monoxide. So Drennan's work goes toward protecting the environment, too.

BORN IN
Newton, Massachusetts

FAVORITE TEAM
Boston Red Sox

ALTERNATE CAREER CHOICE
Politician

JOB SITE
MIT

BEST READING
Murder mysteries

"I started my career as a high school science teacher, but I wanted to learn more about research, so I went to graduate school."

Her Findings

Using physics and computer science approaches, Drennan pieces together the three-dimensional shapes of proteins. She did this recently with an iron, nickel and sulfur-containing enzyme that converts carbon dioxide first into carbon monoxide, then into acetyl CoA, a key molecule in energy production.

Drennan was quite surprised to find that metals help this enzyme twist itself in a way that creates a molecular tunnel for the carbon monoxide to travel through. For this experiment, she used an inventive approach that substituted xenon for carbon monoxide. Both are gases of about the same molecular size, but xenon can be used more readily in a freeze-frame molecular snapshot of the enzyme.

Why did nature create such an extremely long tunnel in a protein? Drennan thinks it's an elegant design for an assembly line-like structure that assures the quick and efficient production of the vital molecule acetyl CoA.

Nature's Products

Our world is full of molecules with natural healing power. Chemists examine substances produced for self-defense by microbes, algae, plants and animals to learn how to make powerful antibiotics, painkillers, cancer treatments and other medicines.

Snakes, spiders and sea snails use venom to kill their prey. Poisonous dart frogs, wasps and hemlock trees protect themselves with poison. Penicillin is a bacterial poison made by a mold. The process of evolution has shaped inventive ways for organisms to keep themselves safe from predators.

The enzymes in our bodies are also shaped by millions of years of evolution. Because all living things share the same basic biochemistry, natural products frequently interact with the same molecules in people as they do in other organisms.

So chemists want to understand much more about natural products, and a key step in doing that is figuring out how the molecules are made. That information is important for two reasons. First, it can uncover related, and sometimes even more desirable, molecules. Second, understanding natural processes helps chemists learn how to make and refine chemicals in the lab.

Human use of microorganisms extends back to prehistoric times, when people began making wine and leavened bread. Recently, in an area of chemistry called metabolic engineering, researchers have used the tools of molecular biology to produce chemical substances that, in many cases, never before existed in nature. Sometimes, these are referred to as "unnatural" natural products.

Metabolic engineers use living systems to turn simple sugars and other small molecules into promising new antibiotic medicines, biofuels and other agricultural and veterinary products.

KERRY MATZ

Conus geographus ("geography cone") is one of the few snails that can kill a human. Scientists have retooled cone snail poisons to make the painkiller Prialt.®

Unlike a factory production scheme, metabolic "labs" carry out multiple chemical reactions in a single pot—a cell—without the need for time- and labor-intensive separation and purification steps.

To work their magic, chemists need to understand and be able to reproduce the biochemical circuits these organisms routinely use to break down food and produce energy, as well as those pathways that re-use the building blocks to make bigger molecules. The products of metabolism are called metabolites.

More than a hundred metabolites are currently used as common medicines for people and animals. Examples include the antibiotics erythromycin and tetracycline, a cholesterol-lowering drug called lovastatin (Mevacor®) and a flea-busting pet medicine called avermectin. All of these are polyketides, a class of metabolites that soil bacteria manufacture naturally and abundantly.

Chemicals from nature have also proven effective against not-so-obvious conditions like heart disease,

Tropical rainforests are often rich sources of chemical diversity.

depression and epilepsy. Sometimes, a natural substance will inspire medicines for two or more diseases.

There are also many natural products that look good but simply can't be made in the lab. Many have very complex structures that are too difficult and expensive to manufacture on an industrial scale. One example is the painkiller morphine.

Another is the cancer drug paclitaxel (Taxol®). An entire Pacific yew tree would have to be cut down to extract enough active ingredient from the bark to make a single dose of this medicine. But this slow-growing tree is an environmentally threatened species.

Thankfully, synthetic chemists have figured out a way to make the drug from a readily available ingredient that is abundant in the more plentiful European yew tree.

The process of evolution has shaped inventive organisms to keep themselves safe from preda

Chemists also get creative by inventing techniques unavailable to woodland or jungle creatures. Using lab tools and tricks—changing reaction conditions or adding catalysts—chemists can make huge quantities of molecules whose structures are slight variations of a natural product.

Researchers travel the world to obtain natural samples to analyze and evaluate for the purposes of drug discovery. Collecting natural materials can involve harvesting reptile venom, diving for poisonous marine life and hiking through jungles to identify rare plants.

Scientists have already found lots of promising substances, but they think that many more are still out there.

Having an appreciation for different cultures is really important for this kind of work. Often, talking with locals gives key insights about potential uses for natural products.

Such "bioprospecting" has to be thoughtful and respectful. Many of the areas of rich biodiversity are in tropical forests and coral reefs in some of the poorest parts of the world, and these ecosystems must be protected.

One way to do this is through chemistry that synthesizes natural products and helps minimize the use of natural resources.

Meet… Jay Keasling

CHEMICAL ENGINEER, *Berkeley, California*

Keasling uses bacteria or yeast as factories to make medicines, plant-based fuels and other products that people want and need.

"We could potentially turn any plant—grass, weeds, even paper waste—into energy." *Jay Keasling*

BORN IN: Harvard, Nebraska

FAVORITE FOOD: Beef, but with guilt because of the high energy cost (8 pounds of corn are needed to produce 1 pound of beef)

JOB SITES: Lawrence Berkeley National aboratory and University of California, Berkeley

ORITE TEAM: Nebraska Cornhuskers, football

CATION: On the beach in Hawaii!

Explore more @ http://www.nigms.nih.gov/ChemHealthWeb

Chemistry . . . For a Healthier

Chemists want to understand how biology works so they can manipulate it. Inventing environmentally friendly approaches that make reactions more efficient and produce minimal toxic by-products is an important goal of modern chemistry.

Whether inside the body or in the lab, all chemical reactions do the same thing. They convert starting materials, or reactants, into products. Catalysts make these reactions go faster.

A catalyst works by providing a route for the reaction pathway to make its product using less energy.

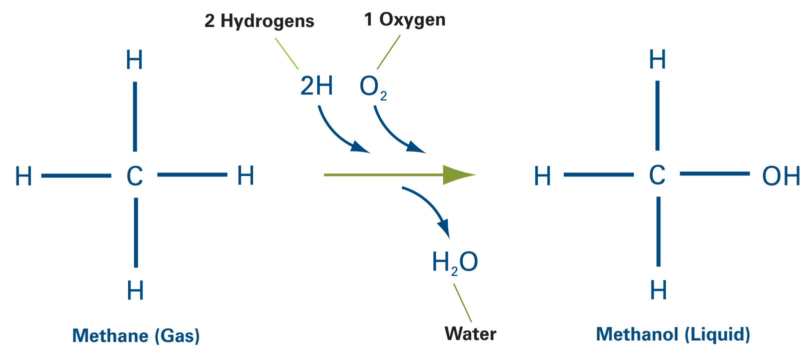
Catalysts are facilitators—they are not used up in the reaction and can be recycled. Researchers are continually looking for catalysts that are more efficient and friendlier to the environment. Such catalysts are an important aspect of "green chemistry."

One recent advance in this area is the development of "click chemistry," which allows chemists to tailor reactions very precisely. Thus, they can generate substances quickly and reliably. Click chemistry also produces fewer byproducts—some of which can be hazardous—and less waste.

BOB TUBBS, WIKIMEDIA COMMONS

In some countries, biodiesel is less expensive than conventional diesel.

Enzyme Reaction



The enzyme methane monooxygenase converts methane into methanol, producing water as a byproduct. Methanol is a liquid that can be transported much more easily than methane, a gas that is hard to keep contained.

Harnessing biology's magic through chemistry underlies the field of biotechnology—the use of biological systems or living organisms to make useful products and processes. Biotechnology has applications in a wide range of areas that benefit the United States and the world.

Examples include genetically engineered medicines and agricultural processes that reduce farmers' dependence on herbicides and insecticides.

Other applications of biotechnology include biodegradable plastics and environmental cleanup tools. For example, fatty acids are used as detergents and as biofuels, which are less damaging to the environment than many coal-based fuels.

Taking advantage of microbes' innovative metabolism and defense mechanisms can help us preserve our environment, as well. This is the case for methane, the main component of natural gas that is used in industrial chemical processes and is second only to carbon dioxide as a greenhouse gas that contributes to global warming.

Methane is chemically inert, meaning it does not break down easily. But for some bacteria that live in extreme environments like hot springs, chewing up methane is a way of life (see diagram, above). Understanding how enzymes in these bacteria convert methane into methanol and water could possibly spur more efficient use of the world's supply of natural gas.

Some chemists study the role of metal-containing molecules in biological systems (see page 9). Many processes in our bodies—like respiration and reproduction—depend on metals like iron, zinc and copper.

Iron, for instance, helps the protein hemoglobin transport oxygen to organs throughout the body. Many metals act to stabilize the shapes of enzymes.

Since metals are elements, the building blocks of all chemical compounds, they are already in their simplest form and our bodies cannot break them down.

World

Thus, our bodies take great care to make sure metals go only where they need to go, and in exactly the proper amount. In many cases that means one or two atoms in an individual cell. That's in contrast to thousands to millions of proteins or other molecules.

Some toxic metals aren't good in any amount. They can poison important enzymes, preventing them from doing their jobs and keeping the body healthy. Lead from the environment, for instance, can mess up the body's synthesis of a vital component of hemoglobin called heme, disabling the blood's oxygen transport system.

Certain forms of mercury can be deadly, causing irreversible damage in the brain. Other dangerous metals, such as arsenic, cause cancer in the skin and lungs. Recently, scientists discovered single-celled algae that thrive in Yellowstone National Park hot springs and that chemically change arsenic to make it less hazardous. Such natural cleansers may find use in reclaiming mine waste or creating safer foods and herbicides.

Scientists are working to eliminate these and other harmful substances from the environment and also to detect and reduce human exposure to such substances.

The medical researchers who study the harmful effects of chemicals on living organisms are called toxicologists.

Some focus on forensics, combining toxicology, chemistry, pharmacology and medicine to help criminal investigations of death, poisoning and drug use.

These researchers record symptoms reported by a victim as well as any evidence collected that could narrow the search for a perpetrator. This evidence could include pill bottles, powders and trace residues of chemicals. Since it is rare for a chemical to remain in its original form after being ingested, toxicologists rely on a solid understanding of metabolism and of chemical reactions to get the job done right.

Researchers are continually looking for catalysts that are more efficient and friendlier to the environment.

Meet... Serrine Lau

TOXICOLOGIST, *Tucson, Arizona*

Lau studies the ways in which tiny variations in human DNA influence whether we get sick when we're exposed to chemicals in the environment.

BORN IN: Hong Kong

JOB SITE: University of Arizona, Tucson

ALTERNATE CAREER: Medical doctor

LAST MOVIE YOU SAW: *The Bourne Ultimatum* and *Ocean's Thirteen*

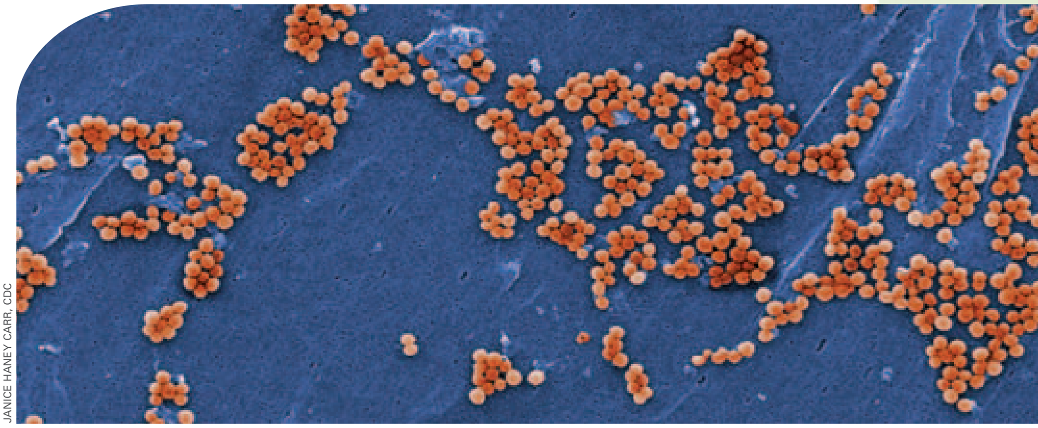
BEST THINGS TO SEE OR DO IN TUCSON: Desert Museum, Gem Show, hiking at Sabino Canyon and Saguaro National Park, bird watching, Kitt eak National Observatory, Mt. Lemmon, Old ucson Studios and the Tombstone Epitaph

"Don't just sit in the dark and wonder what comes next. Instead of panicking, get more information." *Serrine Lau*

Explore more @ http://www.nigms.nih.gov/ChemHealthWeb

Chemistry Meets Medicine

Lots of could-be medicines look good on paper—or on a computer screen—but a drug can only do its intended job of treating a symptom or fighting a disease if it gets to the right place in the body to do its job. That's where chemistry plays such a big role, in tweaking molecules to interact appropriately with the body.



JANICE HANEY CARR, CDC

Staphylococcus aureus bacteria are normal residents of our skin. However, MRSA is a strain of these bacteria that has become resistant to antibiotics like methicillin.

A lot of the most important medical progress in recent history has come from the development of powerful antibiotics and vaccines to treat infectious diseases caused by bacteria, viruses and parasites. But those breakthroughs have come with a cost—microorganisms have learned how to fight back, and with a vengeance.

The misuse of antibiotics is the most common reason why antibiotic resistance is such a significant public health problem. These drugs are sometimes overprescribed by doctors, and many people fail to finish a full prescription.

What's the problem? An antibiotic drug treats infection by knocking out hundreds of strains of "sensitive" bacteria in the body. But left behind are many nonsensitive, or resistant, strains. With no stops in place, the resistant microbes repopulate themselves rapidly.

MRSA, or methicillin-resistant *Staphylococcus aureus*, is a bacterium that causes difficult-to-treat infections in humans, and its prevalence has been on the rise. Making matters worse, MRSA has become resistant to most disinfectants and antiseptics used in hospitals.

Chemists are well aware of the public health danger posed by MRSA and other resistant organisms. They are working hard to outwit microbes that develop resistance. New forms of antibiotic drugs are currently being developed, and researchers are trying to design them to target vulnerable molecular regions of enzymes within bacteria.

As the name suggests, medicinal—also called pharmaceutical—chemistry is an area of research that focuses on designing and making drugs of all sorts. The first step in this process is identifying new molecules.

Years ago, medicinal chemists spent most of their time isolating interesting molecules from living organisms, mainly plants. Today, however, chemists working in this area are equally concerned with finding good ways to make these molecules in the lab. Medicinal chemists also work out the best way to deliver the new drug: as a capsule, tablet, aerosol or injection.

Identifying a molecule with a specific medicinal effect—like lowering cholesterol or killing only tuberculosis bacteria—takes time and patience. But a strategy called combinatorial chemistry can help a lot. In this process, chemists create and then sift through immense collections, or "libraries," of molecules. The newly identified molecules, or "leads," are then tested for their usefulness in treating disease in animals and people.

Just like an online catalog helps you find books in the library or in a bookstore, combinatorial chemistry helps find molecules in a chemical library. It also usually involves computers to help a chemist find molecular matches that meet defined criteria.

Chemical libraries consist of a diverse matrix of thousands or even millions of different molecules made from just a few starting chemical building blocks. Each chemical has associated information about its chemical structure, purity or other characteristics stored in some kind of database.

Synthesizing new molecules or drugs involves much more than following a simple recipe.

Many properties help determine a molecule's potential as a drug. These include its chemical makeup and stability, and its solubility (how well it dissolves in water or body fluids).

Synthesizing new molecules or drugs involves much more than following a simple recipe. That's because chemical reactions turn out two, mirror-image results: a "left" and a "right" version of a molecule.

The molecular building blocks of proteins, sugars and DNA and RNA all have this property, which is called chirality. The term stems from the Greek word for "hands," the most familiar chiral objects.

Chemists call the two mirror images of a molecule enantiomers. Many chemical reactions generate a mixture of equal amounts of the two enantiomers. This matters when it comes to making a small molecule, such as a drug, that must fit precisely into a uniquely shaped cavity of a body protein. Whereas the left-handed version may fit perfectly into the correct space inside the protein, its right-handed counterpart couldn't squeeze in, no matter what.

To manufacture products quickly and cost effectively, pharmaceutical companies used to produce medicines that contained equal portions of the left- and right-handed versions. That is because it is usually much less efficient and more expensive to produce only one enantiomer of a drug. Over time, however, chemistry research has taught us the importance of making single-handed compounds.

This solves two problems. The first is eliminating enantiomers that are dangerous. And in the vast majority of cases, most drugs produced as left- and right-handed mixtures are only half as strong as they could be, because one hand does nothing more than dilute the final mixture.

Hands are familiar chiral objects.

Meet... Andy Combs

MEDICINAL CHEMIST,
Wilmington, Delaware

An executive director at a biotech company, Combs designs and makes new molecules to suppress overactive enzymes that may cause cancer.

"Discovering new medicines is very exciting. It's rewarding to be a chemist working in a field where your research can possibly help so many people. I can't think of a career I would rather do." *Andy Combs*

BORN IN: Argentia, Newfoundland. Then we moved to Maryland, and I grew up in Wisconsin. My dad was in the Navy

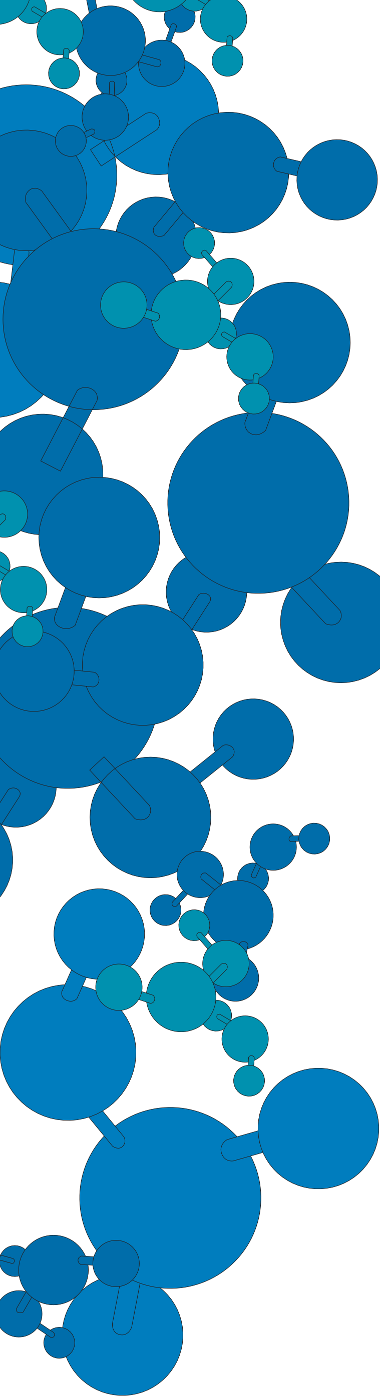
JOB SITE: Incyte Corporation

WHAT YOU WOULD BE IF NOT A CHEMIST: I thought I was going to be an artist and a doctor

HOBBIES: Being outdoors, hiking, boating, fishing, hunting and gardening. Wake boarding on the lakes in Wisconsin and New Hampshire

A RECENT VACATION: Scuba diving with my family at Little Cayman Island and seeing all the cool creatures

Explore more @ http://www.nigms.nih.gov/ChemHealthWeb



What Is Chemistry?

Better Health. Chemists make tools to explore biology, teaching us how disease starts and finding ways to stop it. They study substances from nature to create new antibiotics, pain medicines and cancer drugs.

Help for the Environment. Efficient and clean chemical reactions protect our planet while allowing us to enjoy the foods and other products we need and want. Chemists devise new methods to reduce or eliminate pollutants.

A Creative Pursuit. Making molecules is kind of like sculpting, painting or even composing. Chemists employ the design rules of nature to produce new materials, many of which become part of everyday life.

An Appealing Combination. Many chemists are drawn to the field because it merges science, art and the beauty of nature in interesting ways that help people.

You Could Be a Chemist!

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