

The Chemistry of Health



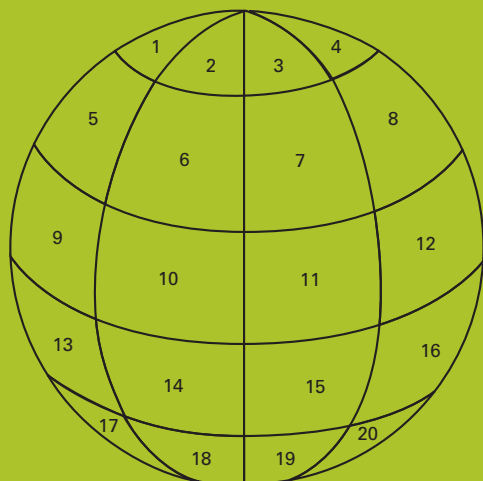
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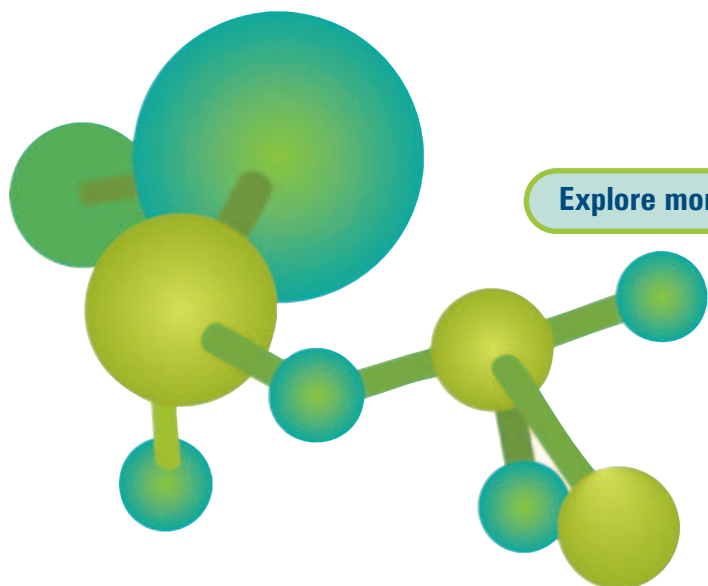
Disease . . . Pollution . . . Hunger . . . Global warming . . .

Did you realize that chemistry plays a key role in helping us solve some of the most serious problems facing our world today?

Chemists want to *know*. They want to find the building blocks of the chemical universe—the molecules that form materials, living cells and whole organisms.

Chemists want to *create*. They want to make useful substances, including some that don't even exist in the natural world.

Many chemists are medical explorers looking for new ways to maintain and improve our health. Others are helping to preserve our planet by developing safe, cheap and efficient ways to make the materials we use every day.



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Actions & Reactions

Chemists want to know about matter and its properties—the density, acidity, size and shape of molecules. Biologists want to understand living things and how they interact with their environment.

And chemistry and biology are more connected than you might think.

Using knowledge about atoms, forces and molecules, chemists learn about unfamiliar substances, but they also learn about organisms and body processes.

One of the most amazing triumphs of the human body is the fact that all we really need to do to keep it running is to eat and sleep. The rest seems to take care of itself.

But a lot of chemical reactions are going on 24/7 to make this happen.

Metabolic factories recycle the components of digestion back into basic building blocks from which our tissues and organs are built.

Using proteins, the genetic material DNA and RNA, sugars and fats, chemical reactions let a sprained ankle heal properly, make our hair and fingernails grow a little bit every day and give us energy to text our friends or ace a geometry test.

The main players in metabolism are enzymes, molecules that speed up the chemical reactions in our bodies. Because they make reactions go faster than they would on their own, enzymes are biological catalysts.

Consider this: Without the help of enzymes, the conversion of nutrients and minerals into usable biological molecules such as proteins, DNA and RNA might take weeks, even years! Enzymes are essential to life, since our bodies



Millions of chemical reactions in our bodies help us stay active.

The main players in metabolism are enzymes, molecules that speed up the chemical reactions in our bodies.

cannot afford to wait that long to receive the important products of chemical reactions.

In speeding up reactions, enzymes act like the accelerator pedal of a car. But they also play the role of matchmaker, bringing together starting materials (substrates or reactants) and converting them into finished materials (products).

Most enzymes reside inside cells. If cells get damaged, they break apart and spill their contents into neighboring body fluids, like blood. That is why higher-than-normal levels of enzymes in blood—revealed in a simple blood test—can signify trouble in tissues or organs where those cells normally live.

When enzymes are not working properly, they can cause disease. For example, cancer can develop

when the enzymes that copy DNA make mistakes. These errors can produce a misspelled gene that makes a defective protein or no protein at all. If that protein is the one that keeps a set of cells from multiplying out of control, you can imagine how its absence could bring about serious problems.

Inside the body, enzymes are never lonely. They link together, forming vibrant networks and pathways. And so our metabolism is really just a collection of enzyme-catalyzed reactions that build and break down organic molecules in food, producing or consuming energy in the process. But to be effective, the reactions need to work together in a coordinated way.

The chemical reactions of metabolism occur over and over again.

Much like a cascade of dominoes, the product of one chemical reaction becomes the substrate for another. By understanding the language of the body's metabolic communication systems, scientists can find ways to patch the circuits when they become broken from injury and disease.

One secret to an enzyme's success is its three-dimensional shape. An enzyme is shaped so that it can hug its substrate tightly. This molecular embrace triggers chemical changes, shuffling attractive forces and producing new molecules. Only enzymes that have an exact fit with their substrates do a decent job of speeding up chemical reactions.

Many proteins need help from one or more other proteins to perform their jobs well. Proteins

that interact often change their shape as a result of the encounter. The differently shaped protein is better able to capture its substrate and make a chemical reaction happen. Sort of like rearranging seats in a room to accommodate more guests, the reshaping of proteins can make extra space for substrates and products to fit.

In addition to proteins, other helper molecules called cofactors are necessary ingredients for many enzyme reactions. Folic acid, a B vitamin, is one of them.

Researchers have known for decades that folic acid can protect against certain birth defects—such as spina bifida—that develop during the first few weeks after conception. For this reason, the U.S. Food and Drug Administration recommends



Folic acid helps enzymes and substrates get together.

that every woman of childbearing age supplement her diet with 400 micrograms of this vitamin.

Folic acid does its good deeds by improving the fit between various enzymes and their substrates. One of these enzymes speeds up the conversion of a potentially harmful molecule called homocysteine to methionine, a nontoxic amino acid that the body needs. Thus, folic acid lowers blood levels of homocysteine, which in excess is a risk factor for heart attacks and strokes.



Meet... Virginia Cornish

CHEMICAL BIOLOGIST, *New York City*

Cornish uses genetic engineering methods to mix and match natural substances in new ways.

“Chemistry is my favorite science because it’s rooted in creativity—inventing new molecules with unanticipated functions.”

Virginia Cornish

BORN IN:
Savannah, Georgia

FAVORITE KIND OF MUSIC:
College music stations that play everything

BEST THING TO DO ON A SNOW DAY:
Go sledding with my young kids

JOB SITE: Columbia University

ORITE SUBJECTS IN HIGH SCHOOL:
Chemistry and poetry

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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.

F A T S

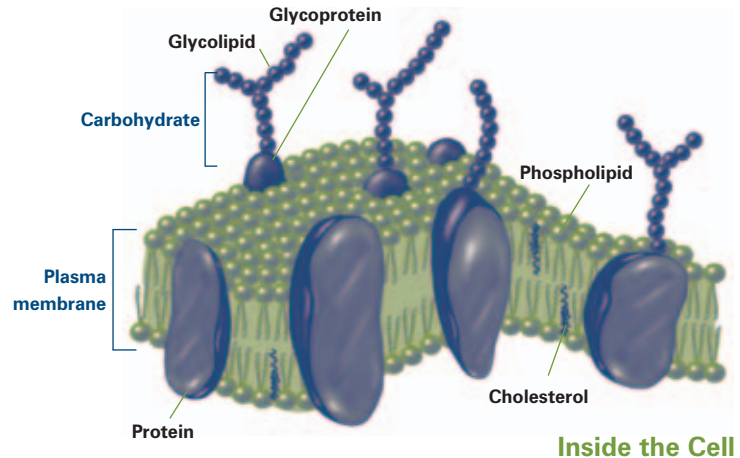
Eating healthy means that you need to be careful about the amount of fat in your diet. But a certain amount of fat is really necessary: All humans need lipids, called essential fatty acids, from food because our bodies can't make them from scratch. Some body fat is also necessary as insulation to prevent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

Outside the Cell



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.

SUGARS

In chemistry, a polymer is a substance that contains repeating units: Polyester and many plastics are examples of synthetic polymers. Proteins, nucleic acids and carbohydrates are natural “biopolymers” that consist of chains of amino acids, DNA, RNA or sugar molecules.

How do our bodies make biopolymers? You guessed it: enzymes. Scientists can also make some biopolymers in the lab. DNA, RNA and proteins are fairly simple to construct—so simple that scientists today routinely synthesize thousands of different versions at once on wafer-like chips similar in size to those used in computers.

But complex carbohydrates—chains of sugars—are a different story.

Why is making sugar chains so hard? The answer lies in their fundamental structure.

Proteins are strings of amino acids that can only fit together one way, head-to-tail. In contrast, long, branched chains of sugars called oligosaccharides can fit together in dozens of different ways. Chemists



Amino acids link head-to-tail to make proteins.



Simple sugars link in many orientations to make oligosaccharides.

have a tough time forcing them to connect one way instead of another.

One reason chemists want to make sugars from scratch is to design vaccines that target the surfaces of bacteria and viruses.

Sugars attached to proteins, called glycoproteins, are an important part of cell membranes. Jutting out from the surface of nearly all cells, these sugary signposts are a cell’s identification. They are sort of like cellular address labels.

Also called glycans, these branched molecules serve as specialized receptors that act as docking stations for proteins on other cells. Each organ and tissue has its own special glycans, which grant access only to those molecules that know the proper molecular “code.”

Every type of virus we encounter can only grip a certain set of glycans with precisely the right connections at their tips. In this manner, the types of glycans that a virus latches onto can determine how it will make you sick. For example, some viruses prefer glycans in the lungs, while others like the intestines or the throat.



Meet ... Ram Sasisekharan

BIOENGINEER, *Cambridge, Massachusetts*

Sasisekharan researches carbohydrates indispensable natural molecules used by all life forms.

“I volunteer to teach in Asia every summer. I enjoy sharing my experiences with the next generation of world health sleuths!” *Ram Sasisekharan*

BORN IN: Chennai, India

FAVORITE FOOD: Pasta

PLAN A: When I was young, I always imagined I’d be a medical doctor

JOB SITE: MIT, Singapore, Bangkok... anywhere the need arises

FAVORITE WEEKEND PASTIMES: Jogging, spending time with family, enjoying and creating art, and being outdoors

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Cool Tools

Chemists are masters of materials, and they often work in the world of the very small. Using tools made from the building blocks of life, chemists can spy on the movements of single molecules and make miniature devices that pick up trace levels of contaminants in food and the environment.

The space between two carbon atoms within a molecule is about one-tenth of a nanometer. The DNA double helix has a diameter of about two nanometers. The smallest bacteria, on the other hand, are much bigger: a few hundred nanometers in length.

A nanometer is one-billionth the length of a meter—or about the circumference of a marble in comparison to that of the Earth!

And nanotechnology is the study of the control of matter on an atomic and molecular scale. Some say it is chemistry by a different name.

Fittingly, some entire modern chemistry “labs” are extremely small—cramming all the necessary tools and molecules onto a rectangular wafer smaller than a business card. Such mini-machines contain an expansive network of miniature

tubes and columns, each only as big as a fraction of a drop of water.

Chemists want to use tiny devices to deliver drugs to specific sites in the body, allowing for highly targeted treatments with minimal side effects. Other devices could measure cholesterol, sugar and electrolytes in blood, saliva, urine or tears.

Small tools also allow scientists to watch biology happen in real time. Bright, rainbow-colored dyes and a green fluorescent protein (GFP) that comes from jellyfish let scientists track how molecules move around in living organisms. Often, these experiments are done in simple organisms like bacteria and yeast, which consist of only a single cell but have inner workings with a striking degree of similarity to human biology.

In studies with human cells, researchers have tagged cancer cells with GFP to watch how they spread to other parts of the body. They mark insulin-producing cells in the pancreas to see how they’re made and gain insights into new diabetes treatments.

Using another technology, called quantum dots, scientists use

microscopic semiconductor crystals to label proteins and genes. Quantum dots enable the study of molecules in a cell as a group, rather than in isolation.

Dots of slightly different sizes glow in different fluorescent colors—larger dots shine red, while slightly smaller dots shine blue, with a whole spectrum in between. Researchers can create up to 40,000 labels by mixing quantum dots of various colors and intensities, much like an artist mixes paint.

Another group of modern chemistry tools includes sensors, devices that measure a physical quantity and convert it into a signal that can be read by an observer or instrument.

We use sensors all the time in our daily lives. A simple example is a thermometer, which transforms a measured temperature into the expansion and contraction of a liquid that can be read on a calibrated glass tube. Another is a touch-sensitive elevator button.

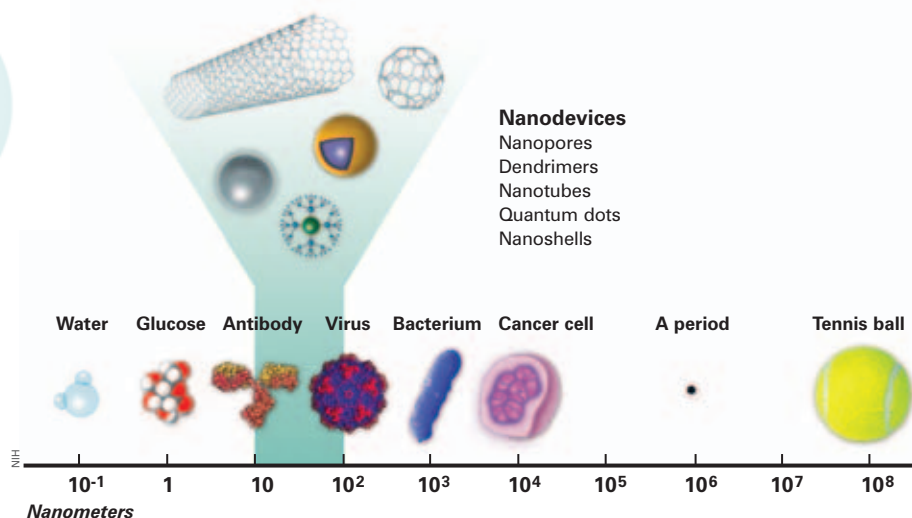
Scientists and doctors use sensors all the time, too. Biosensors can scan a wide range of biological materials, from microbes, enzymes and antibodies to pollutants. The output, or signal, varies widely as well, ranging from color to light to electricity.

One of the most common examples of a health-related biosensor is a blood glucose monitor. This miniature device uses the enzyme glucose oxidase to break down blood glucose and produce a readable signal, which indicates how much sugar is present in a person’s blood. It is a vital tool for people with diabetes who must check their blood sugar several times a day.



Quantum dots are nanocrystals that radiate brilliant colors when exposed to ultraviolet light.

How Small Is Small?



Nanotechnology is the study of the control of matter on an atomic and molecular scale.

Some biosensors rely on modified microorganisms that detect toxic substances at very low levels. They can give us early warning of environmental contaminants, poisonous gases and even bioterror agents, such as ricin or anthrax.

Chemistry also plays a central role in making biomaterials such as artificial joints, implants, heart valves and skin patches filled with hormones or other medicines.

Efforts to engineer artificial organs—like a liver, pancreas or bladder—also hinge on chemistry. Researchers have made test versions of many artificial organs. And some, like artificial skin for the treatment of severe burns and traumatic injuries, are already in wide use.



Meet... Jack Taunton

CHEMIST AND CELL BIOLOGIST,
San Francisco, California

Taunton custom-makes molecules in his lab to figure out how cells do so many amazing things.

“I never took a formal cell biology class, but I’ve been surrounded by talented cell biologists who taught me most of what I know.” *Jack Taunton*

BORN IN: Houston, Texas

BEST WAY TO SPEND A WEEKEND: Playing and listening to music, reading chemistry and cell biology papers, designing small molecules on the backs of discarded envelopes

JOB SITE: University of California, San Francisco

FAVORITE MUSICIANS/COMPOSERS: Sonic Youth, Béla Bartók, Ornette Coleman, Jimi Hendrix, Charles Mingus, J.S. Bach, Tom Waits, The Beatles, John Coltrane, Lee Morgan

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

Meet . . . Gus Rosania

PHARMACEUTICAL SCIENTIST, *Ann Arbor, Michigan*



BORN IN
Barranquilla, Colombia

DREAM CAR
A large, purple van that seats eight and runs on air and sunlight

FAVORITE SEASON
The one we're in! I live in the present

JOB SITE
University of Michigan, Ann Arbor

FAVORITE PASTIME
Laughing until my belly aches

What He's Doing

Sometimes, a drug doesn't work like it's meant to because it isn't absorbed properly or it doesn't reach the correct spot in the body. These adverse drug reactions are one of the leading causes of hospitalization and death in the United States.

Gus Rosania thinks that the precise location of a drug within a cell is a key clue to its effectiveness and safety. And so he is using powerful microscopic techniques to track where drugs go inside cells and what they do when they get there.

To do this efficiently and on a large scale, Rosania is using "machine vision." This technique joins imaging to computer methods that can screen large collections of molecules for their locations inside cells.

"My dream is to develop technologies for making better and safer medicines. I want to help people live longer, healthier and happier."

His Findings

Rosania treated human cells growing in lab dishes with a huge collection of molecules that glow in different colors in response to certain wavelengths of light. Computerized microscopes scanned the treated cells, analyzing more than 15,000 individual molecular pictures.

The experiment was a test to see if such a "high-throughput" approach—beginning with thousands of different potential molecules—could be used in the process researchers use to look for would-be medicines. Rosania concluded that his machine-vision technique was successful in automatically analyzing where the dye molecules traveled inside cells.

One advantage this technique has over manual labor—a person sitting at a microscope—is scale. The process can be done quickly and efficiently, saving time and money and enabling many more molecules to be tested in the search for new and safer medicines.

Meet more chemists @ <http://www.nigms.nih.gov/ChemHealthWeb>

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.



"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.

BORN IN
Newton, Massachusetts

FAVORITE TEAM
Boston Red Sox

ALTERNATE CAREER CHOICE
Politician

JOB SITE
MIT

BEST READING
Murder mysteries

The graphic features a large blue circle with a yellow border containing the text above. Below the circle is a stylized molecular structure composed of yellow and teal spheres connected by grey rods.

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 predators

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 ones they think that market 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 Laboratory and University of California, Berkeley

SPORTS: Nebraska Cornhuskers, football

RELAXATION: 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.

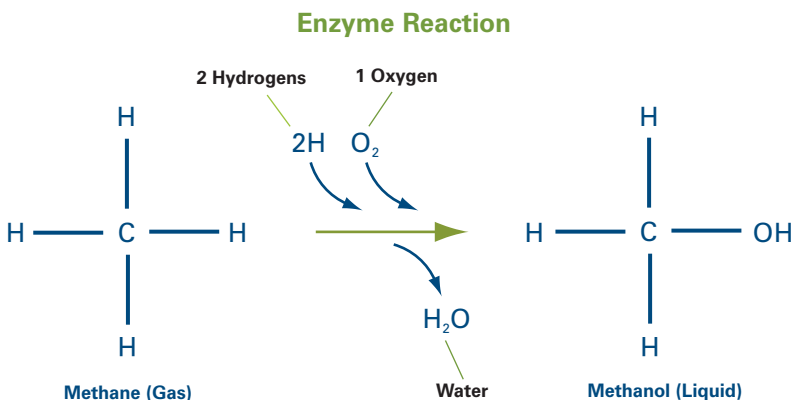
A catalyst works by providing a route for the reaction pathway to make its product using less energy.

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



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



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.

of which can be hazardous—and less waste.

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,

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

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.



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.

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

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 Peak National Observatory, Mt. Lemmon, Old Tucson Studios and the Tombstone Epitaph

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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.

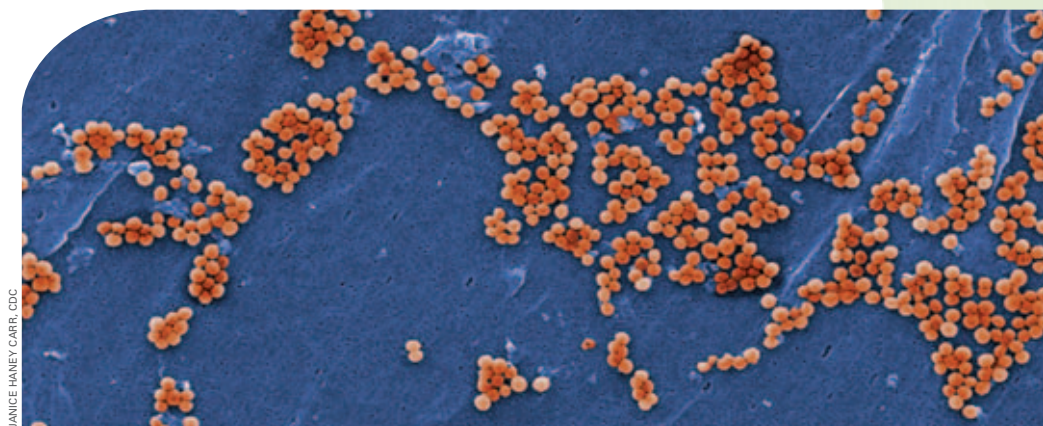
A lot of the most important medical progress in recent history has come from the development of powerful antibiotics and vaccines to treat infectious diseases caused by bacteria, viruses and parasites. But those breakthroughs have come with a cost—microorganisms have learned how to fight back, and with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



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.

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.



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



Hands are familiar chiral objects.

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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