CHAPTER 1

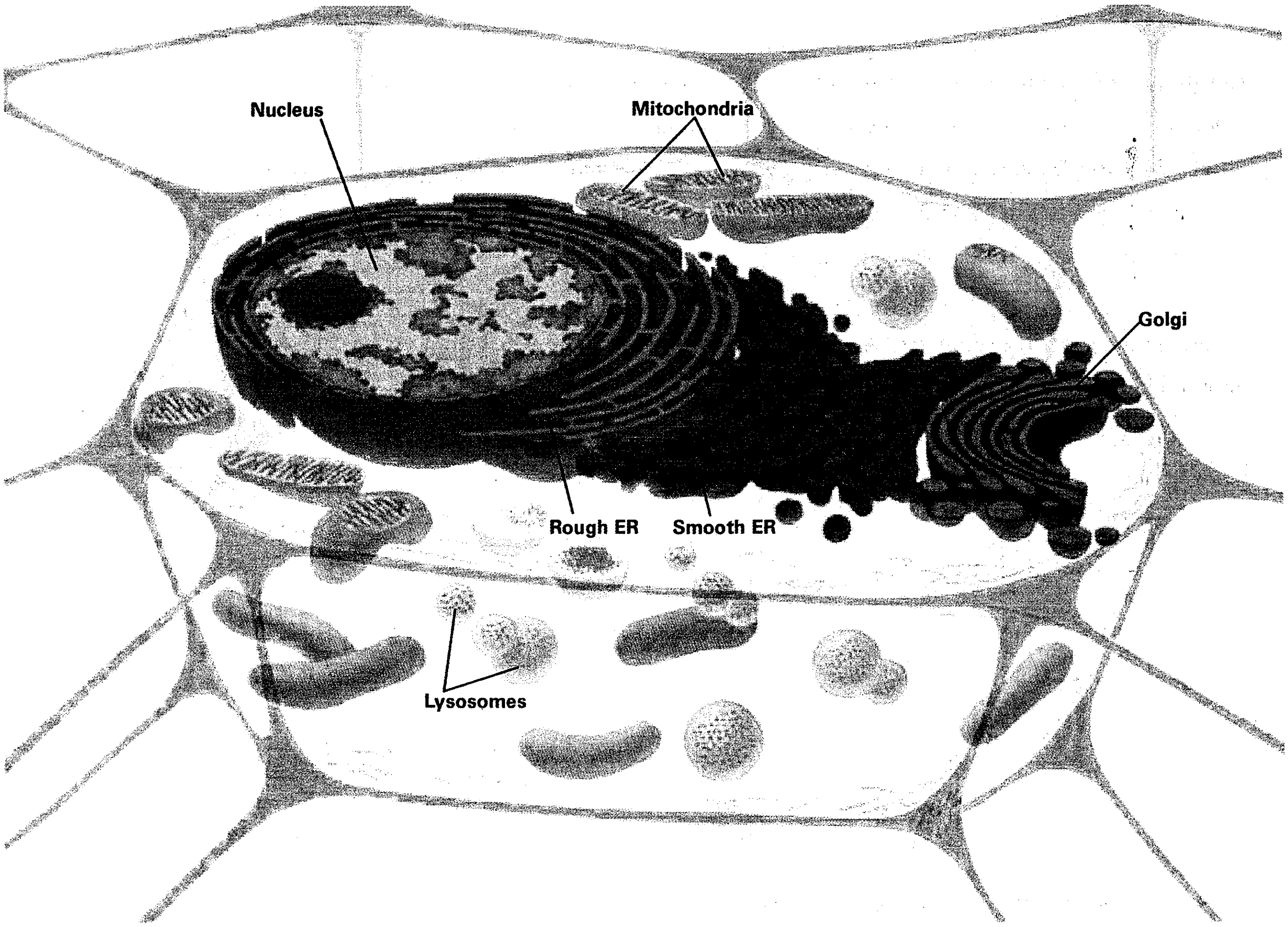
BY ALISA ZAPP MACHALEK

An Owner's Guide to the Cell

Welcome! I hope the transformation wasn't too alarming. You have shrunk down to about 3 millionths of your normal size. You are now about 0.5 **micrometers** tall (a micrometer is 1/1000 of a millimeter). But don't worry, you'll return to your normal size before you finish this chapter.

At this scale, a medium-sized human **cell** looks as long, high, and wide as a football field. But from where we are, you can't see nearly that far. Clogging your view is a rich stew of molecules, fibers, and various cell structures called **organelles**. Like the internal **organs** in your body, organelles in the cell each have a unique biological role to play.

Now that your eyes have adjusted to the darkness, let's explore, first-hand and up close, the amazing world inside a cell.



▲ A typical animal cell, sliced open to reveal cross-sections of organelles.

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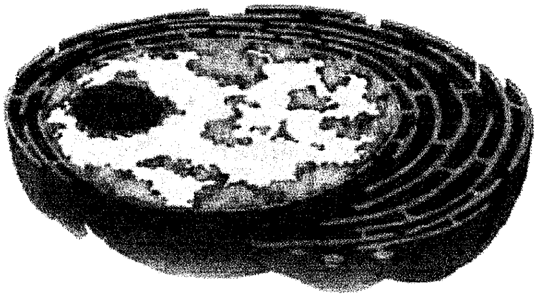
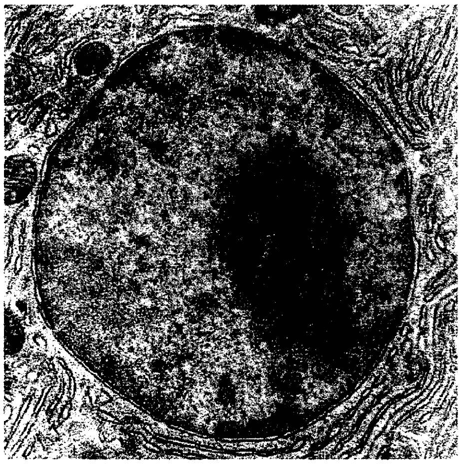




Nucleus: The Cell's Brain

Look down. Notice the slight curve? You're standing on a somewhat spherical structure about 50 feet in diameter. It's the **nucleus**—basically the cell's brain.

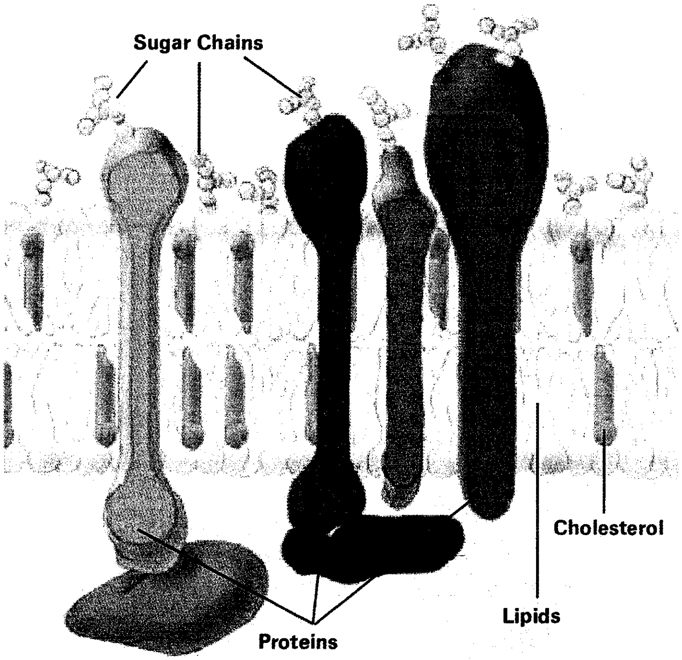
The nucleus is the most prominent organelle and can occupy up to 10 percent of the space inside a cell. It contains the equivalent of the cell's gray matter—its genetic material, or **DNA**. In the form of **genes**, each with a host of helper molecules, DNA determines the cell's identity, masterminds its activities, and is the official cookbook for the body's **proteins**.

Go ahead—jump. It's a bit springy, isn't it? That's because the nucleus is surrounded by two pliable **membranes**, together known as the **nuclear envelope**. Normally, the nuclear envelope is pockmarked with octagonal pits about an inch across (at this scale) and hemmed in by raised sides. These **nuclear pores** allow chemical messages to exit and enter the nucleus. But we've cleared the nuclear pores off this area of the nucleus so you don't sprain an ankle on one.

If you exclude the nucleus, the rest of the cell's innards are known as the **cytoplasm**.

EUKARYOTIC CELLS	**PROKARYOTIC CELLS**
The cells of "complex" organisms, including all plants and animals	"Simple" organisms, including bacteria and blue-green algae
Contain a nucleus and many other organelles, each surrounded by a membrane (the nucleus and mitochondrion have two membranes)	Lack a nucleus and other membrane-encased organelles
Can specialize for certain functions, such as absorbing nutrients from food or transmitting nerve impulses; groups of cells can form large, multicellular organs and organisms	Usually exist as single, virtually identical cells
Most animal cells are 10–30 micrometers across, and most plant cells are 10–100 micrometers across	Most are 1–10 micrometers across

Virtually all forms of life fall into one of two categories: **eukaryotes** or **prokaryotes**.



▲ The membrane that surrounds a cell is made up of proteins and lipids. Depending on the membrane's location and role in the body, lipids can make up anywhere from 20 to 80 percent of the membrane, with the remainder being proteins. **Cholesterol**, which is not found in plant cells, is a type of lipid that helps stiffen the membrane.

Cell Membrane: Specialist in Containing and Communicating

You may not remember it, but you crossed a membrane to get in here. Every cell is contained within a membrane punctuated with special gates, channels, and pumps. These gadgets let in—or force out—selected molecules. Their purpose is to carefully protect the cell's internal environment, a thick brew (called the **cytosol**) of salts, nutrients, and proteins that accounts for about 50 percent of the cell's volume (organelles make up the rest).

The cell's outer membrane is made up of a mix of proteins and **lipids** (fats). Lipids give membranes their flexibility. Proteins transmit chemical messages into the cell, and they also monitor and maintain the cell's chemical climate. On the outside of cell membranes, attached to some of the proteins and lipids, are chains of sugar molecules that help each cell type do its job. If you tried to bounce on the cell's outer surface as you did on the nuclear membrane, all these sugar molecules and protruding proteins would make it rather tricky (and sticky).

Endoplasmic Reticulum: Protein Clothier and Lipid Factory

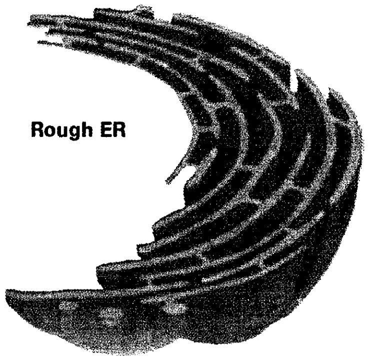
If you peer over the side of the nucleus, you'll notice groups of enormous, interconnected sacs snuggling close by. Each sac is only a few inches across but can extend to lengths of 100 feet or more. This network of sacs, the **endoplasmic reticulum** (ER), often makes up more than 10 percent of a cell's total volume.

Take a closer look, and you'll see that the sacs are covered with bumps about 2 inches wide. Those bumps, called **ribosomes**, are sophisticated molecular machines made up of more than 70 proteins and 4 strands of **RNA**, a chemical relative of DNA. Ribosomes have a critical job: assembling all the cell's proteins. Without ribosomes, life as we know it would cease to exist.

To make a protein, ribosomes weld together chemical building blocks one by one. As naked, infant protein chains begin to curl out of ribosomes, they thread directly into the ER. There, hard-working **enzymes** clothe them with specialized strands of sugars.

Now, climb off the nucleus and out onto the ER. As you venture farther from the nucleus, you'll notice the ribosomes start to thin out. Be careful! Those ribosomes serve as nice hand- and footholds now. But as they become scarce or disappear, you could slide into the smooth ER, unable to climb out.

In addition to having few or no ribosomes, the smooth ER has a different shape and function than the ribosome-studded rough ER. A labyrinth



▲ The endoplasmic reticulum comes in two types: Rough ER is covered with ribosomes and prepares newly made proteins; smooth ER specializes in making lipids and breaking down toxic molecules.

of branched tubules, the smooth ER specializes in synthesizing lipids and also contains enzymes that break down harmful substances. Most cell types have very little smooth ER, but some cells—like those in the liver, which are responsible for neutralizing toxins—contain lots of it.

Next, look out into the cytosol. Do you see some free-floating ribosomes? The proteins made on those ribosomes stay in the cytosol. In contrast, proteins made on the rough ER's ribosomes end up in other organelles or are sent out of the cell to function elsewhere in the body. A few examples of proteins that leave the cell (called secreted proteins) are **antibodies**, insulin, digestive enzymes, and many **hormones**.


SUSUMU ITO

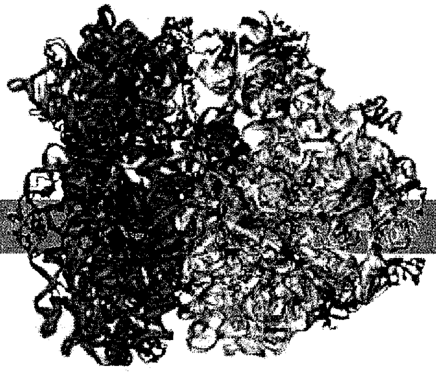
Rough ER

Rx: Ribosome Blockers

All cellular organisms, including **bacteria**, have ribosomes. And all ribosomes are composed of proteins and ribosomal RNA. But the precise shapes of these biological machines differ in several very specific ways between humans and bacteria. That's a good thing for researchers trying to develop bacteria-killing medicines called antibiotics because it means that scientists may be able to devise therapies that knock out bacterial ribosomes (and the bacteria along with them) without affecting the human hosts.

Several antibiotic medicines currently on the market work by inhibiting the ribosomes of bacteria that cause infections. Because many microorganisms have developed resistance to these medicines, we urgently need new antibiotics to replace those that are no longer effective in fighting disease.

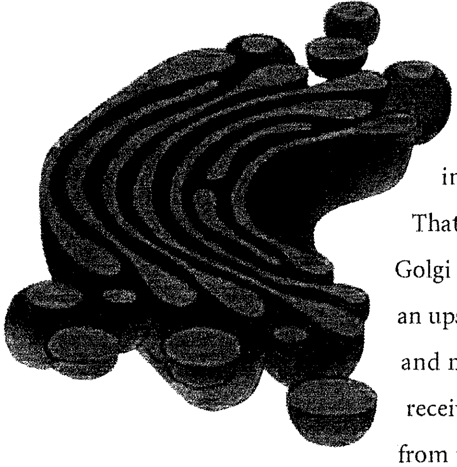
Using sophisticated imaging techniques like X-ray crystallography, researchers have snapped molecular pictures of antibiotics in the act of grabbing onto a bacterial ribosome. Studying these three-dimensional images in detail gives scientists new ideas about how to custom design molecules that grip bacterial ribosomes even more strongly. Such molecules may lead to the development of new and more effective antibiotic drugs. —*Alison Davis*



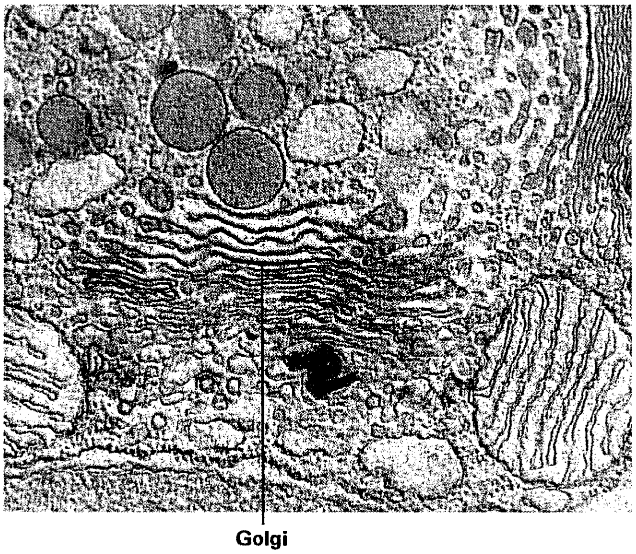
▶ In a dramatic technical feat, scientists obtained the first structural snapshot of an entire ribosome in 1999. This more recent image captures a bacterial ribosome in the act of making a protein (the long, straight spiral in the lightest shade of blue). It also shows that—unlike typical cellular machines, which are clusters of proteins (shown here as purple ribbons)—ribosomes are composed mostly of RNA (the large, light blue and grey loopy ladders). Detailed studies of ribosomal structures could lead to improved antibiotic medicines.

IMAGE COURTESY OF HARRY NOLLER

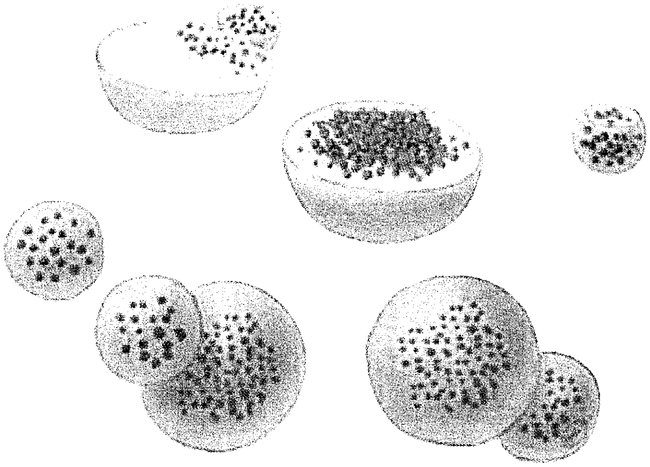
Golgi: Finishing, Packaging, and Mailing Centers



Now, let's slog through the cytosol a bit. Notice that stack of a half dozen flattened balloons, each a few inches across and about 2 feet long? That's the **Golgi** complex, also called the Golgi apparatus or, simply, the Golgi. Like an upscale gift shop that monograms, wraps, and mails its merchandise, the Golgi receives newly made proteins and lipids from the ER, puts the finishing touches on them, addresses them, and sends them to their final destinations. One of the places these molecules can end up is in **lysosomes**.



TINA CARVALHO



Lysosomes: Recycling Centers and Garbage Trucks

See that bubble about 10 feet across? That's a lysosome. Let's go—I think you'll like this. Perhaps even more than other organelles, lysosomes can vary widely in size—from 5 inches to 30 feet across.

Go ahead, put your ear next to it. Hear the sizzling and gurgling? That's the sound of powerful enzymes and acids chewing to bits anything that ends up inside.

But materials aren't just melted into oblivion in the lysosome. Instead, they are precisely chipped into their component parts, almost all of which the cell recycles as nutrients or building blocks. Lysosomes also act as cellular garbage trucks, hauling away unusable waste and dumping it outside the cell. From there, the body has various ways of getting rid of it.

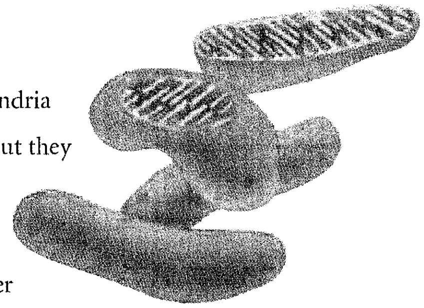
Mitochondria: Cellular Power Plants

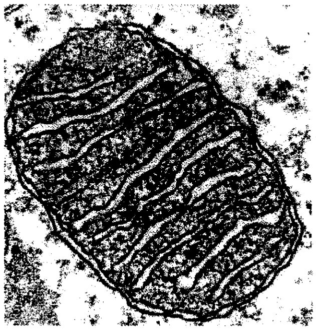
Blink. Breathe. Wiggle your toes. These subtle movements—as well as the many chemical reactions that take place inside organelles—require vast amounts of cellular energy. The main energy source in your body is a small molecule called **ATP**, for adenosine triphosphate.

ATP is made in organelles called **mitochondria**. Let's see if we can find some. They look like blimps about as long as pickup trucks but somewhat narrower. Oh, a few of them are over there. As we get nearer, you may hear a low whirring or humming sound, similar to that made by a power station. It's no coincidence. Just as power plants convert energy from fossil fuels or hydroelectric dams into electricity, mitochondria convert energy from your food into ATP.

Like all other organelles, mitochondria are encased in an outer membrane. But they also have an inner membrane. Remarkably, this inner membrane is four or five times larger than the outer membrane. So, to fit inside the organelle, it doubles over in many places, extending long, fingerlike folds into the center of the organelle. These folds serve an important function: They dramatically increase the surface area available to the cell machinery that makes ATP. In other words, they vastly increase the ATP-production capacity of mitochondria.

The mazelike space inside mitochondria is filled with a strong brew of hundreds of enzymes, DNA (mitochondria are the only organelles to have their own genetic material), special mitochondrial ribosomes, and other molecules necessary to turn on mitochondrial genes.

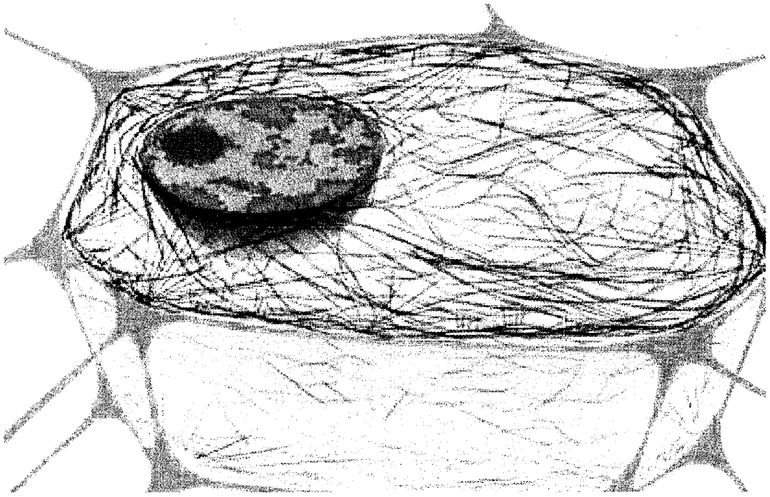




D.S. FRIEND, BRIGHAM AND WOMEN'S HOSPITAL

	ACTUAL SIZE (AVERAGE)	**PERCEIVED SIZE WHEN MAGNIFIED 3 MILLION TIMES**
Cell diameter	30 micrometers*	300 feet
Nucleus diameter	5 micrometers	50 feet
Mitochondrion length	Typically 1–2 micrometers but can be up to 7 micrometers long	18 feet
Lysosome diameter	50–3,000 **nanometers***	5 inches to 30 feet
Ribosome diameter	20–30 nanometers	2–3 inches
Microtubule width	25 nanometers	3 inches
Intermediate filament width	10 nanometers	1.2 inches
Actin filament width	5–9 nanometers	0.5–1 inch

*A micrometer is one millionth (10^{-6}) of a meter. A nanometer is one billionth (10^{-9}) of a meter.



The three fibers of the cytoskeleton—microtubules in blue, intermediate filaments in red, and actin in green—play countless roles in the cell.

Cytoskeleton: The Cell's Skeleton...and More

Now, about all those pipes, ropes, and rods you've been bumping into. Together, they are called the **cytoskeleton**—the cell's skeleton. Like the bony skeletons that give us stability, the cytoskeleton gives our cells shape, strength, and the ability to move, but it does much more than that.

Think about your own cells for a moment. Right now, some of your cells are splitting in half, moving, or changing shape. If you are a man, your sperm use long tails called **flagella** to swim. If you are a woman, hairlike fibers called **cilia** sweep newly released eggs from your ovaries into your uterus. And all that is thanks to the cytoskeleton.

As you can see, the cytoskeleton is incredibly versatile. It is made up of three types of fibers that constantly shrink and grow to meet the needs of the cell: **microtubules, intermediate filaments**, and **actin filaments**. Each type of fiber looks, feels, and functions differently.

The 3-inch-wide flexible pipes you just banged your head on are called microtubules. Made of the strong protein tubulin, microtubules are the heavy lifters of the cytoskeleton. They do the tough

KATHRYN HOWELL

Golgi Spelunking: Exit Here, There, But Not Anywhere

Scientists use a variety of techniques to study organelles like the endoplasmic reticulum and Golgi, gaining ever more detailed understanding of these minute but very complicated structures. For example, Kathryn Howell of the University of Colorado School of Medicine in Denver uses a specialized high-voltage electron microscope, rapid freezing methods, and a computer modeling program to obtain a vivid three-dimensional view of the Golgi and the pathways that proteins use to exit it.

Howell begins by quick-freezing living cells, embedding them in plastic, and slicing the plastic-coated sample into thin sections. As she tilts the microscope stage, she can capture many images of the same region of the sample. A computer assembles these images to form a three-dimensional view, called a tomogram, of the Golgi and other organelles. Based on the tomogram, Howell's research team can produce a movie of a virtual journey through the cell. You can see one such movie at http://publications.nigms.nih.gov/insidethecell/extras.

Howell's research shows that there are several pathways for proteins and other molecules to exit the Golgi. The findings are revealing, as earlier studies using different methods had suggested that there was only one road out of this organelle. No doubt new chapters to this story will be written as biologists and computer scientists create even more sophisticated tools for imaging cells. —*A.D.*