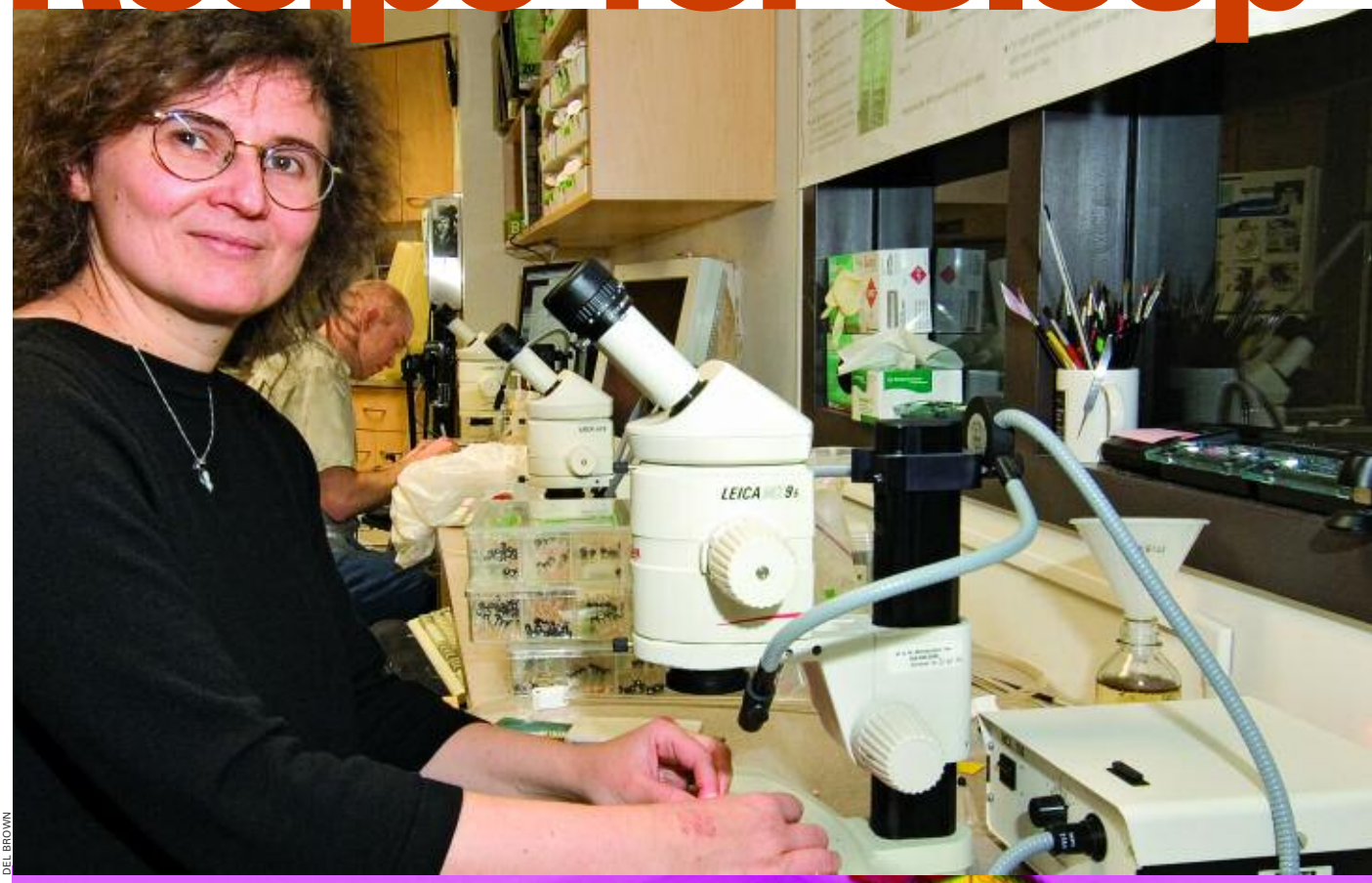
Recipe for Sleep



DEL BROWN

BY EMILY CARLSON

Do you like playing with your food?

Not molding it into sculptures, but experimenting with it—putting syrup instead of jelly on a peanut butter sandwich or microwaving marshmallows to see if they'll explode.

This creativity can have tasty results or teach you new kitchen tricks to show your friends. With the right utensils and training, you could even call yourself a chef…or a scientist.

Like chefs, scientists enjoy using their knowledge and tools of the trade to mix up lab recipes that can lead to new outcomes or ideas.

Or, you could be both. Take Chiara Cirelli, a neuroscientist at the University of Wisconsin-Madison. While her friends devour the fresh soups, pasta, and pizza that she creates at home, other researchers eat up the findings about sleep that she churns out in the lab.

Settling Down

Born in a region of northern Italy famous for its first courses, Cirelli came to the United States 12 years ago for a research position in California. At that point, she already had M.D. and Ph.D. degrees. In 2001, she faced a tough decision: Should she stay in the United States, or return to Italy?

Cirelli, now 41, was being recruited by the University of Wisconsin to join a group of scientists who study the reasons we need shuteye. Without losing much sleep over the decision, she settled into a new life in the Midwest.

Today, she lives in a log cabin surrounded by woods and occasionally visited by white-tailed deer. "I grew up in cities, but I really like it here," says Cirelli.

The researcher, now a U.S. citizen, doesn't regret her choice to stay.

"The general attitude toward research is very different in Italy," Cirelli says, explaining that students in Italy typically get less experience teaching and sharing results with the public.

As Cirelli searches for answers about sleep—a quest she started as a graduate student in Pisa—she hopes that her work ultimately will lead to new sleep aids that might help people snooze more soundly.

"We have no good drugs that have the same restorative power as sleep," says Cirelli, suggesting that an ideal drug might be able to compress a night's sleep into a power nap.

Why do we all need sleep?

Sleeping Habits

All animals sleep—at least all those that scientists have studied. They don't necessarily do it the same way, though. Cows sleep standing up, armadillos snooze during daylight, and some birds nap with one eye open. Researchers have shown that dolphins sleep with one side of their brain still awake, probably because they need to be conscious to breathe.

Cirelli herself keeps a regular sleep schedule.

"I always get at least 7 hours," she says. She usually dozes off a few hours after dusk and rises before the sun—without an alarm clock.

"I wake up spontaneously," she adds. She doesn't nap, because she never feels sleep deprived, but she always encourages others to enjoy an afternoon siesta if they feel tired.

Cirelli sticks to this schedule no matter what may come up.

"I like to entertain and have people over for dinner, but at 9:30 p.m., I say 'goodbye.'" Her guests know that they're welcome to stay after their hostess hits the sack.

But still: Why do we sleep? From the savanna to the city, snoozing comes at a cost. A gazelle that's not keeping watch could get picked off by a hungry lion. For other species, like humans, sleep consumes valuable time that could be spent working, studying, or even partying.

Some researchers think that sleep gives the body a chance to repair itself, or that it provides the brain time to organize its thoughts. But Cirelli thinks something different.

"Sleep is still very much a mystery."

Her idea is that sleep helps us learn more the next day.

"When you're awake, you are always learning new things," she explains. As a result, the connections between the brain's neurons, called synapses, get stronger. The synapses also get bigger and need more fuel.

"We can't afford this in terms of space and energy," says Cirelli.

Research suggests that the slow brain activity produced during sleep shrinks your brain synapses, making you a more efficient learner in the morning.

Cirelli has been testing this hypothesis in rats. If proven true, she will be one step closer to explaining why we sleep.

Slowing Down

Down a quiet hallway in an even quieter room that gets completely dark and stays a constant, cool temperature, 20 rats spend their days and nights. Tiny electrodes touching the rodents' brains record electrical activity, while other monitors record movement. Comparing the two helps Cirelli distinguish between a sleeping rat and one that's just lazing around.

The data translates into waves on a computer screen. For both brain and muscle activity, slow waves are usually tall and wide, whereas fast waves are short and narrow. As you get groggier, your brain starts producing slower waves. During the rapid-eye movement (REM) phase of sleep, when most dreams occur, the waves can be just as fast as they are during wakefulness.

Cirelli and her team run a variety of sleep experiments with the rodents.

To test the synaptic-strength hypothesis, they study the snoozing patterns of normal and "gifted" rats. While the average rats spend their time lounging around, the smarter ones get a mental workout in a more stimulating environment, where they're challenged by tasks like grabbing food pellets from a small opening.

The scientists analyze brain activity patterns of all the rats during sleep and wakefulness, and they look for physical differences in their actual brains during both states. Identifying dissimilarities between the two rat groups could point to a connection between learning and sleep.

Fly by Night

For Cirelli, cooking and science share other common ingredients. Here's a hint: They're full of protein, but not particularly tasty.

Fruit flies! Yep, the same annoying pests that circle ripe peaches in the kitchen are a staple of the Cirelli lab. There, the flies go by their scientific (Latin) name, *Drosophila melanogaster*. Cirelli uses these insects to search for genes that may play a role in sleep.

At first, not everyone thought this genetic approach was a bright idea.

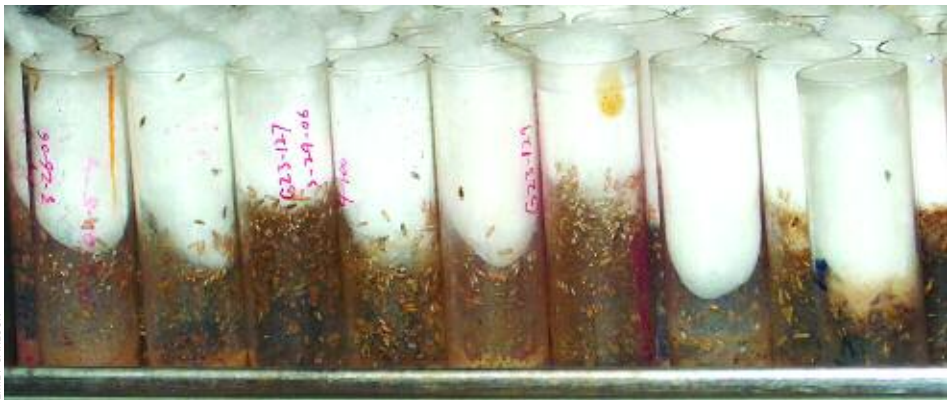
"In the research community, sleep was always considered something that happened only in mammals," says Cirelli. "The idea of studying sleep in flies was considered strange, to put it mildly!"

Lots of recent studies done by Cirelli and others confirm that fruit flies sleep. It might be hard to imagine a fruit fly (about the size of a rice grain) tucked into bed, but they get more sleep than we do—an average of 12 hours every night.

When flies sleep, they're completely still. Only loud noises or other disturbances wake them. If you give them medicines that induce sleep, they snooze longer. If you give them caffeine, they stay alert longer.

After sleep deprivation, the flies are more sluggish the next day and may need a nap to make up for it. Does any of this sound familiar?

Not only do flies sleep, they offer researchers a perfect tool for studying heredity, or genetics. With a fly life-span of just a few months, researchers can examine many generations of these organisms. Doing the same with humans would take hundreds of years!



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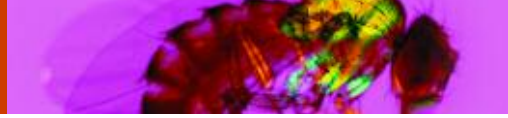
In the lab, fruit flies bunk in glass vials stuffed with food.



Female flies lay eggs every day, making for a ready supply of flies. Plus, scientists know almost all the genes for about a dozen different species of *Drosophila*. That's important because by comparing the genes of related fly species, researchers can track changes in certain genes for a given behavior, like sleeping.

Cirelli searches for flies that can sleep less without becoming impaired. This trait, she explains, would probably come from a genetic mutation, a small change in a gene's DNA spelling that offspring can inherit. By locating the gene mutation, she and others could then explore its role in mammals, like mice, rats, and possibly humans.

Alternatively, the researchers could purposefully change a fly's genetic information and then look for any effect on sleep habits.

Before Cirelli and others proposed the idea of studying the molecular underpinnings of sleep, most sleep researchers focused primarily on brain activity. According to Cirelli, monitoring brain activity identified brain regions involved in sleep, but did little to explain what happens at the molecular level.

Cirelli wanted to figure out what genes and proteins contribute to normal sleep. So far, the researcher has identified several genes that appear to have a powerful effect on sleep and ultimately could lead to new clues about the causes of sleep disorders.

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This contraption turns on its side like a carnival ride to keep the flies inside each vial awake.

Sleepless in Madison

Unlike her research rats, Cirelli's flies sleep in a much noisier room. For the first part of a typical experiment, the insects bunk in a quiet closet, where each fly sleeps in its own glass vial stuffed with food. An infrared beam cuts through the "beds" to monitor movement. If a fly doesn't cross the light beam for 5 minutes, the monitor records that fly "asleep."

Next, Cirelli makes the flies really tired. She places the fly vials in a 4-foot-long robotic arm built by the campus machine shop. There, the flies try to sleep during what probably feels like a carnival ride. Every couple of minutes, the arm tilts and drops the frame containing the vials on its side.

This action not only changes the insects' orientation, it sends a rude awakening—the clank of metal against metal. Another sleep-depriving contraption includes a gadget that scrapes credit cards against the glass vials.

Before she had these gizmos, Cirelli herself kept the flies awake.

"It [used to be] me tapping on the glass or knocking the frames against my knee," she recalls, not very fondly.

Now tired, the flies return to the peaceful closet for a nap. At this point in the experiment, Cirelli looks for flies that spend less time catching up on lost sleep. These flies may have a genetic mutation that keeps them alert after sleep deprivation.

Normally, this type of genetic analysis can take years, and often researchers never find the mutation that causes the behavior they're studying.

"You need a lot of patience," Cirelli admits. "You also need a lot of luck."

Against these odds, her group hit the jackpot last year—they found the gene mutation that allows the "mini-sleeper" flies to get by on just a few hours of sleep each night without showing signs of sleep deprivation.

Working with another scientist who also studies *Drosophila*, Cirelli discovered that the minisleeper flies displayed another telltale inherited trait: They shook after being exposed to the anesthetic chemical ether.

"The idea of studying sleep in flies was considered strange, to put it mildly!"

"Only three or four genes in the entire set of *Drosophila* genes are known to cause shaking," Cirelli explains. Her team immediately knew where to find their needle in the gene haystack.

The information provided a shortcut to identifying the minisleeper gene, since genetic mutations that are physically close to each other on the same chromosome are often inherited together.

As it turns out, the mystery gene was one called "shaker," which encodes a protein that helps nerve cells transmit electrical signals. Because humans have a similar gene and protein, the finding offered a new target for drug development. But there's a problem: Minisleeper flies don't live nearly as long as the sleepier ones, so more work needs to be done to sort this out.

Despite her research successes, Cirelli says that it may be a long time before scientists completely understand the function of sleep.

"Sleep is still very much a mystery," she says. "But I'm optimistic we'll [have some answers] in my generation or the next."

Espresso, Anyone?

While Cirelli likes to talk about her sleep research with family, friends, and coworkers during her regular dinner parties, the food she cooks is still the main attraction.

"She is the *best* at both molecular biology and cooking," says Ugo Faraguna, a visiting graduate student from Italy who was looking forward to joining Cirelli at her cabin for a lab dinner.

Faraguna's favorite dish is Cirelli's tortelloni alla zucca—homemade pasta stuffed with squash, most likely grown in Cirelli's own vegetable garden. Faraguna says that Cirelli's love for cooking is in part cultural.

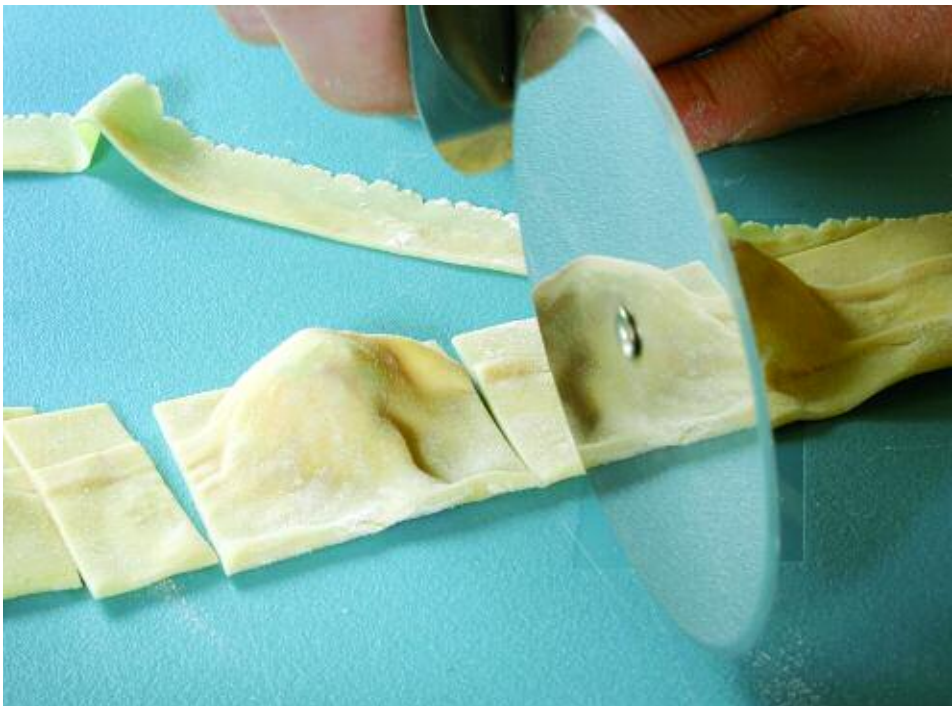
"In Italy, we spend hours and hours cooking. It's a ritual," he says. "Here, people think food is energy you put in your body, like the gas you put in a car."

When she's not working on lab or dinner recipes, Cirelli enjoys the outdoors. From April to October, she tends to her garden, hikes the trails near her house, or chops firewood for the winter months.

Once the Wisconsin winter brings frigid air and biting winds, Cirelli stays indoors. She reads or catches up on classic American movies—but not on television.

"I don't have a TV," she says matter-of-factly. Instead, she installed her own movie theater, complete with

Homemade pasta is a staple of Cirelli's Italian cooking.



a large screen, projector, and surround sound. Even though her friends tell her she should spend more time relaxing, Cirelli always says they have nothing to worry about.

"I absolutely love what I do!" she says.

Her colleagues can't complain: They enjoy Cirelli's company in the lab as much as they do at her dinner table.

"Chiara makes science fun," says Ruth Benca, a research psychiatrist who collaborates with Cirelli. According to Benca, Cirelli isn't interested in competing with other researchers, but instead prefers to work side-by-side with them.

"That's what science is all about," says Benca.

To her students, Cirelli is a fairy tale brought to life. Faraguna, who attends the same prestigious Italian university that Cirelli did, jokes that he came to the United States to find out if she was the "goddess" everyone said she was.

"She's a myth at our school [in Italy]," explains Faraguna, listing all her research accomplishments. "I love what I'm doing even more because of Chiara."

Given all that his teacher manages to accomplish, Faraguna lightheartedly wonders if Cirelli already has found the recipe for making more wakeful hours in a day. ■

Taste Tests

Take a bite of mushy peas or a sip of sour milk. Yuck, right? Well, maybe, but stop and consider that you just observed science in action!

When vegetables boil in water, the heat softens the rigid structure of the plants' cells. Milk, on the other hand, serves as its own chemical and biological laboratory. The few natural bacteria in milk that aren't killed during pasteurization can reproduce and generate enough acid to sour milk.

Scientists who study the properties and interactions of different ingredients are called food chemists. Their labs look like kitchens, with refrigerators, ovens, blenders, and other culinary tools. By concocting new recipes—their experiments—these scientists examine how different products or cooking techniques can change the flavor, smell, shelf life, or even color of what we eat.

Besides knowing a lot about chemistry, these specialized researchers also know a lot about food, which is composed primarily of different combinations of water, proteins, fats, carbohydrates, and minerals. Water makes up 93 percent of an eggplant, for example, but only 3 percent of a peanut. Processing, however, can alter these compositions, changing a food's characteristics and its potential market appeal.

Since sampling the results is a key part of the food scientist's job, in this profession an above-average sense of smell and taste can be as important as scientific training. Sometimes, members of the public are invited to volunteer for taste tests. At the University of Wisconsin-Madison, food scientists who are trying to improve certain aspects of cheese and ice cream regularly call on a herd of experienced tasters to try their latest experiment.—*E.C.*