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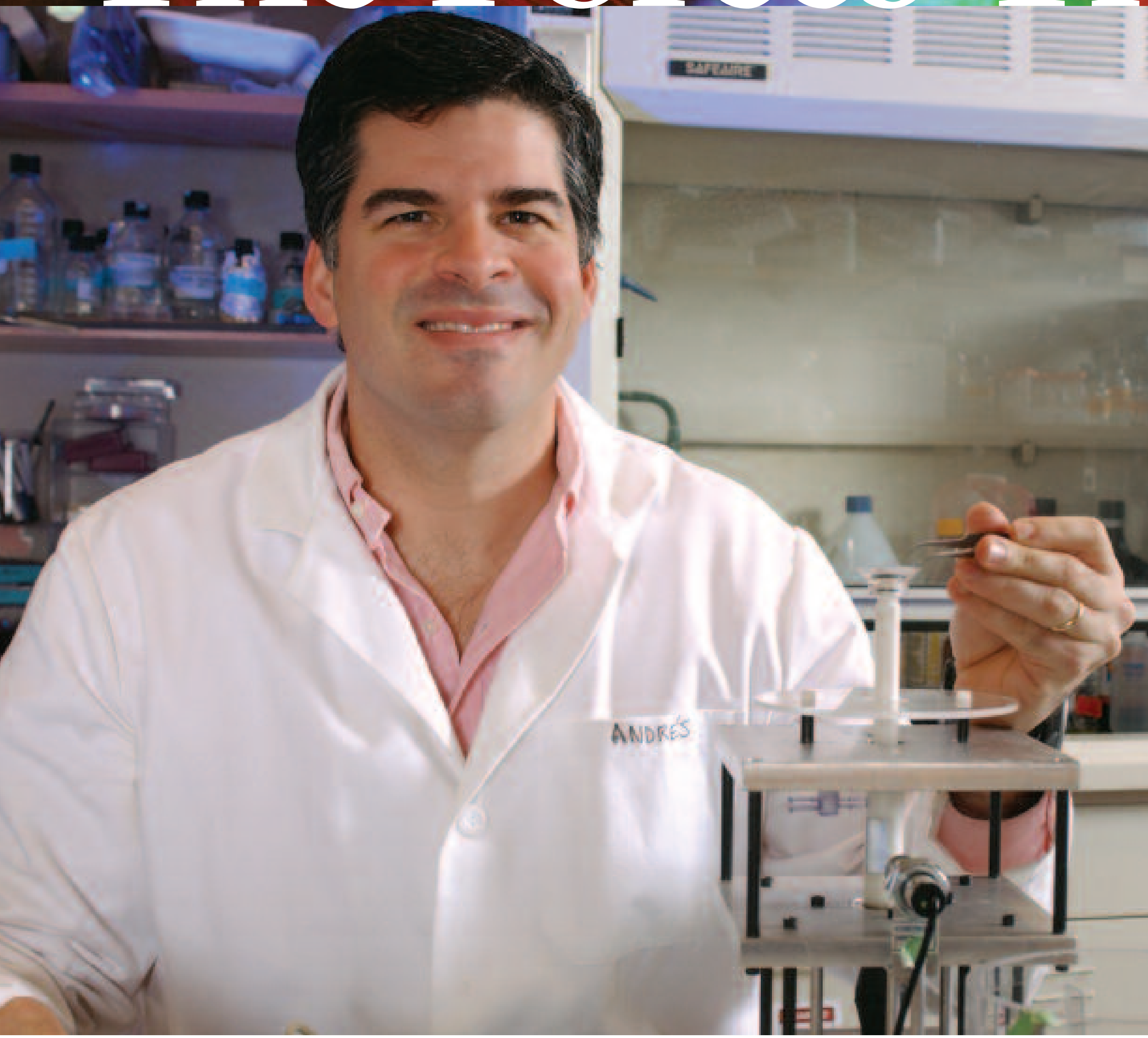

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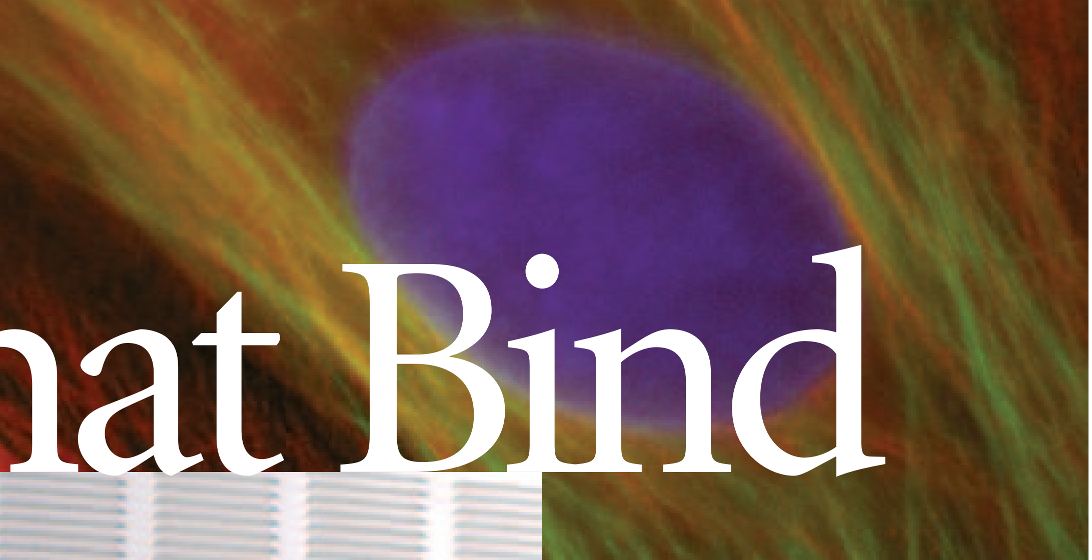


CONLY L. RIEDER

NICOLE CAPPELLO

By Emily Carlson

In one way, Andrés García is different than a lot of other dads. Like many fathers, he plays sports with his two boys, sometimes watches cartoons with them, and leads his older son's Cub Scout den.

But García offers his kids something else, opening their eyes to a world beyond imagination. While visiting their father at work, the boys, 6 and 9, watch objects that are normally invisible to the human eye spring to life under the lens of a microscope. They see a magical machine spit out particles of gold to make new biomaterials that could one day replace broken bones.

García, 35, is an engineer who solves biological problems. He hopes that his work will yield a synthetic bone that could one day help heal fractures and improve the performance of artificial joints. García collaborates in this effort with his wife, Michelle LaPlaca, who is also a biomedical engineer.

An associate professor of mechanical engineering and bioengineering at the Georgia Institute of Technology (Georgia Tech) in Atlanta, García thrives on the challenge of being a successful scientist and a great dad. He and his wife already had kids when they started working at Georgia Tech in 1998. Before long, their careers took off. The young engineers won awards for their work and got research grants to start exciting new projects.

Despite the pressure to push ahead even faster, the couple always made time for their kids, Andrés and Rafael.

"Early on, Michelle and I said that family would be one of our top priorities."

Andrés García is an engineer at Georgia Tech. By studying cell stickiness, García aims to create new biomaterials that can heal bones and other body tissues.

"Here was this biomaterial that improved my life."

Sticking to It

To balance work and family, García makes the most of his time on campus. "You have to be very efficient," he says, explaining that he starts doing research the minute he steps into the lab.

With the goal of designing new types of biomaterials—synthetic products that interact with living systems—García and his graduate students study the mechanics of cellular adhesion, the process by which cells attach to a surface.

Just like tape sticks to paper, a cell sticks to a three-dimensional scaffolding that keeps it in place. This scaffolding, called the extracellular matrix, surrounds the cell and contains nutrients, proteins, and other molecules necessary for living. The matrix holds together the millions of cells that make up our blood vessels, organs, skin, and other tissues.

Paradoxically, the same mechanism that makes cells stick to a surface also helps them change shape and move around the body. Without adhesion, cells in the bloodstream couldn't grab onto vessel walls, crawl to the site of a cut, and repair a wound. Cellular adhesion also plays a major role in the development of embryos into babies.

On the other hand, cellular adhesion can cause problems, too. Gone wrong, this process helps cancer cells spread to other organs and allows arteries to harden, which can lead to heart disease.

Cells can stick to a variety of surfaces because they have specialized proteins that poke through their outer surfaces. These proteins link the extracellular matrix with the signaling circuitry inside the cell. Where the two connect, molecules gather and form tiny "feet" that take a cell where it needs to go. In scientific language, the feet are called focal adhesions.

In the case of cellular adhesion, stickier isn't necessarily better. Too much adhesion makes cell movement difficult, resulting in a sort of molecular flypaper that keeps cells stuck on a surface. And too little sticking power provides no traction whatsoever, preventing a cell from moving forward.

"It's like walking on ice," explains García. "You move your legs, but you don't go anywhere."

Measure of Strength

But cellular adhesion is much more complicated than creating friction between two surfaces. It requires force (see sidebar on page 7).

Cells, like people, need to exert force to move around. This force lets us run, talk, and even breathe. Cells apply their force through focal adhesions, explains García.

The molecules that create this cellular muscle power are fairly well known. What gives them their strength, however, is less understood because adequate tools haven't been developed to measure adhesion strength reliably and reproducibly, says García.

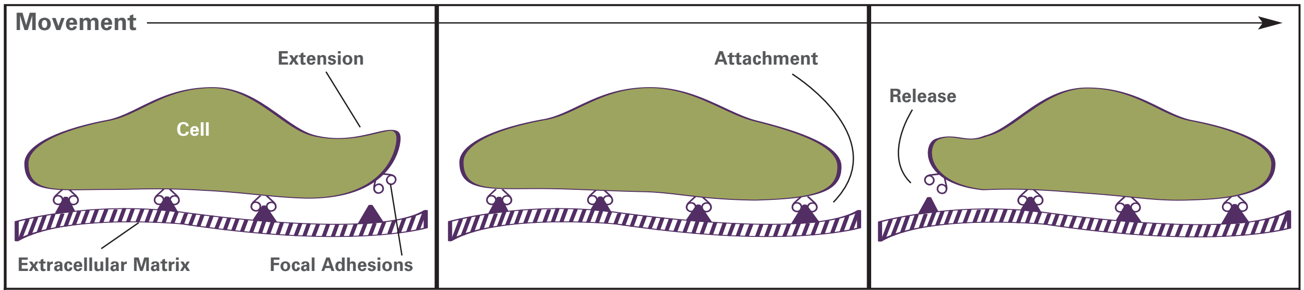
One way to fashion the right tools is to bring together biology and engineering. But, according to García, that's difficult.

"The biggest challenge is to integrate emerging concepts from engineering and cell biology, two very diverse disciplines," he says. "Very few people are trained in both."

Biologists, García explains, are generally more interested in studying the complexities of living systems. Engineers, on the other hand, like to use a different approach. They tend to take the systems apart so they can measure them, he says.

By merging these two problem-solving approaches, García built a tool to determine just how tightly cells stick to a surface and then find out what can change that adhesion force.

Accurate measurements of cellular adhesion strength, says García, will help researchers understand how cells control their stickiness and why they attach to certain surfaces but not others. Scientists could also use this information to design new medicines or even medical devices that aid or hinder a cell's ability to migrate.



Cells walk along body surfaces via tiny "feet," called focal adhesions, that connect with the extracellular matrix.

NICOLE CAPPELLO

A cell-spinning device designed and built by García and his coworkers measures how much force is required to pull cells off a surface.

Putting Ideas in Motion

The idea that synthetic materials can do all this has kept García excited about his research for more than 20 years. When he was 11 years old, the engineer experienced first-hand the awesome ability of implanted devices to substitute for the real thing.

"I developed a condition in my thigh bones that required the use of surgical pins to prevent further degeneration," he says. "After recovering, I was able to run and play basketball again. I was really excited—here was this biomaterial that improved my life."

Although he initially thought he wanted to be an orthopedic surgeon, García's interest gradually shifted more toward basic research. He saw research as the wellspring of exciting new discoveries and technologies.

After college, García earned a Ph.D. in bioengineering from the University of Pennsylvania in Philadelphia. He stayed on as a postdoctoral fellow in the School of Medicine to learn more about cell biology and started to focus his attention on cellular adhesion.

The first step in building a tool for studying adhesion was to create a special surface that would let García control where and how strongly cells stick. Without this material, he says, he wouldn't have been able to accurately measure adhesion strength.

One Size Fits All

If cells have enough room to move around freely, they change shape and shift the position of their focal adhesions. For example, when a spherical cell attaches to a surface, it flattens out and the focal adhesions shift from the center to the edges.

To keep the size and place of the cellular feet constant, García decided on a one-size-fits-all approach. He created a surface in which he could confine each cell to its own space.

Borrowing photolithography methods commonly used to etch patterns onto small electronic circuit boards, García and other scientists generated plates with tiny indentations big enough to hold just one cell each. The researchers treated the surface of the plates with gold and a blend of chemicals that enabled cells to grab on in certain spots. With this lab-made material, García could manipulate the focal adhesion complexes and examine their strength under various conditions.

Now able to precisely control cellular adhesion, García needed a way to measure how much force kept the cells stuck down. Relying on his engineering background, he built a spinning device that he likens to a low-speed blender.

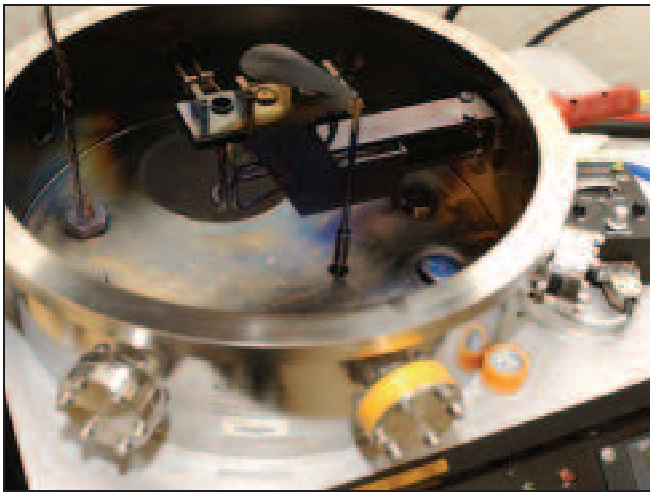
Here's how it works.

García puts the plate containing cells on a disk holder that spins inside a chamber filled with liquid (see photo, left). Like the blades of a blender, the disk holder and plate circle around, bathed in fluid, at a particular speed. As the disk spins, it generates a three-dimensional flow pattern that applies precise detachment forces to adherent cells. It's kind of like the wind blowing in your face when you drive around with the car windows down, García says.

He knows exactly how much force he needs to apply to detach the cells, so by counting the number of cells still sticking to the plate at the end of the experiment, he can calculate adhesion strength.

To the surprise of some of his colleagues, García's experiment did what it was supposed to do, and it worked over and over again.

"A lot of people thought we wouldn't be able to get reproducible results or that the device wouldn't work as we expected," says García. "It's exciting to test something, and sometimes you get surprising results."



NICOLE CAPPELLO

García uses a “gold-making machine,” or electron beam evaporator, to build surfaces for his cell adhesion experiments. Inside the chamber, an electron gun heats a piece of gold until it evaporates, depositing a thin layer of gold onto a glass slide where cells can grow in a special pattern.

Gaining Momentum

García uses his spinning gadget to find out what factors beef up adhesion strength. Through his experiments, he has learned that cellular stickiness depends on the size of the focal adhesion complexes. The more feet a cell has in one spot, the stronger the grip. García has also discovered that adhesion strength depends on the molecular makeup of the cells themselves. Without certain kinds of proteins, a cell loses its ability to develop forces enabling it to strongly stick to a surface.

Taken together, this information leads not only to a better understanding of focal adhesion mechanics, but also to a new framework that García and other researchers can use to study the role of cell stickiness in human health and disease.

Knowledge gained in García’s lab could have broader implications for the field of biomaterials, too. For example, understanding how cells stick to synthetic materials could lead to new medical devices that doctors implant in the body.

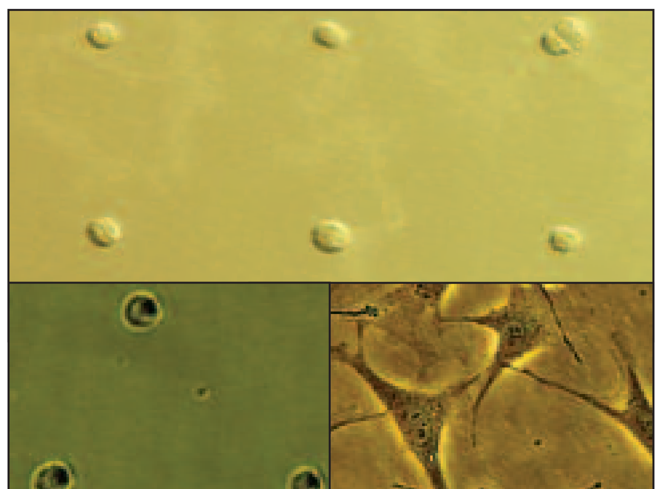
As García explains, the body often “labels” implanted devices as foreign and launches an immune attack, like it would do with a virus. The result can be chronic inflammation, which is a bad thing. A better understanding of cellular adhesion could yield new biomaterials less likely to trigger such reactions.

In fact, García has already developed a material that directs cells to produce substances such as bone mineral. Similar materials might be used to make bone grafts and coatings for artificial hip and knee joints as well as other tissues.

Managing the Load

Out of the lab by 5:00 p.m. most days, García spends the next few hours with his family, coaching his sons’ baseball and basketball teams or helping them with homework. Once the kids are tucked in, García and LaPlaca often work more by reading scientific papers, writing manuscripts about their research, or planning experiments. The long nights aren’t necessarily fun, says García, but he and his wife understand and appreciate the load each one carries.

“It’s a good thing we’re both in similar situations,” he says. “We really help and support each other, both professionally and emotionally.”



ANDRÉS GARCÍA

García’s gold-making machine creates a specialized surface (top) on which cells grow in a pattern (bottom, left). Without a patterned surface to adhere to, cells stretch out any which way when growing on a glass slide (bottom, right).

An example is attending out-of-town scientific meetings. Going to these conferences is an important part of being a researcher. There, scientists talk to each other, discuss their findings, and get new ideas.

García and his wife take turns going to these meetings so one parent will always be home with the kids. When they want to go to the same conference, they juggle their schedules.

"I'll go for the one day, come back, and then Michelle will go for one day," says García. "It's a matter of setting priorities and sharing the load."

If necessary, they'll turn the trip into a family excursion. "We'll take the kids, and they'll sit in the back of a session. They ask really good questions!" jokes the engineer.

The Perfect Balance

In between work and family, García finds time for another passion: sports. For most of his life, he has found himself on the basketball court several times a week. Now he plays an occasional round of hoops with his graduate students or a game against another engineering department. Three days a week, he starts off his day with a 3-mile jog.

"I run at 5:45 a.m.," García says, "and I make the most of it."

García always makes the most of his free time, including plane rides to and from meetings, some of which take him overseas. Like most scientists, García uses this time to catch up on reading scientific journals. But he freely admits he can only read so many in one sitting. For variety, he'll read thrillers, murder mysteries, and other books. Recently, he finished a biography of Benjamin Franklin.

Back at the lab, García does more experiments that help connect engineering and biology, with the hope of blazing new frontiers in medicine. He can't help but share his excitement with young Andrés, Rafael, and their friends who visit the lab.

García hopes these experiences match the marvel he felt that day in the doctor's office when he first saw the healing power of science. ■

Forces Are With You

CONLY L. RIEDER

When you turn the page of a magazine or kick a soccer ball across the field, you exert force that sets something in motion. Similarly, your body uses force to move itself. Force is a measure of the energy exerted over a given distance. It is the push or pull on an object necessary to make it move or change direction. For this to happen, the object (or person) must interact with another object, either close-up or at a distance. Here are a few examples of forces at work.

Applied force is the force one object exerts on another. This happens when you push a book across a desk or use your bicep muscle to lift your arm. When your heart pumps, it creates pressure that forces blood throughout your body.

Gravitational force is the pull that massive celestial bodies, like Earth and its moon, exert on objects. Your skeleton supports your body and stops gravity from tugging your organs and tissues to the ground.

Frictional force happens when one object slides across the surface of something else. For example, brake pads rub against metal rotors to stop tires from turning. Since friction resists movement, your body fights it in certain ways. For example, it reduces friction in joints like your shoulder or knee by coating them with slippery fluids that allow them to move freely.—*E.C.*