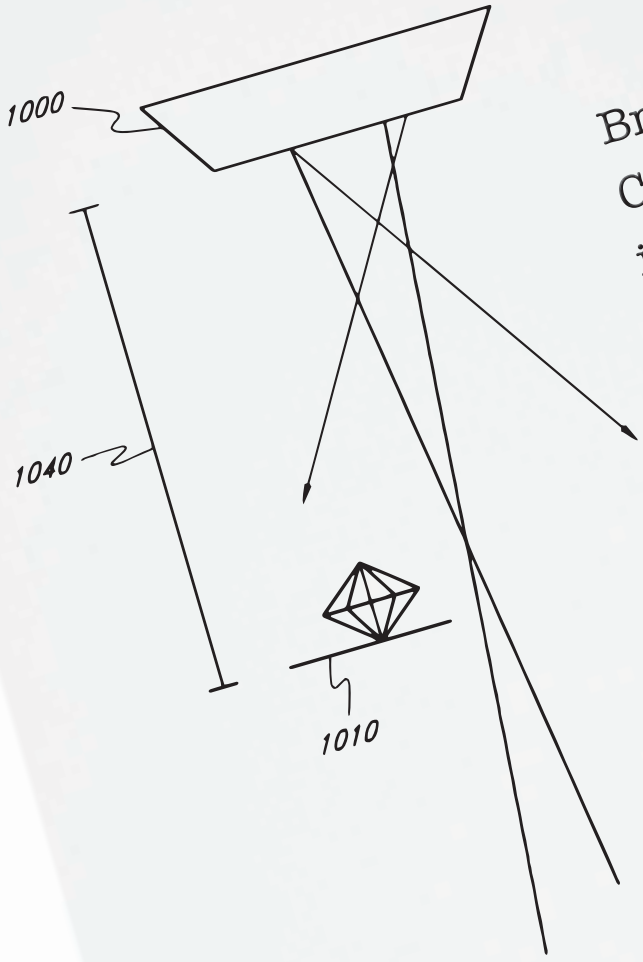
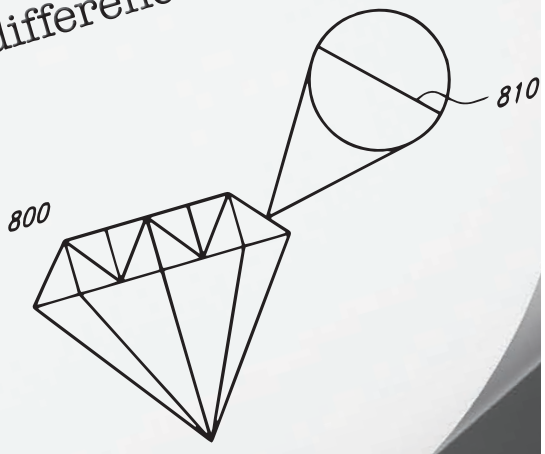
FROM LAB BENCH TO MARKETPLACE

By Kimm Fesenmaier



Brimming with innovation, Caltech is more than an institution of thinkers. Its culture and policies also encourage researchers to get their discoveries and inventions out into the world, where they can make a difference.



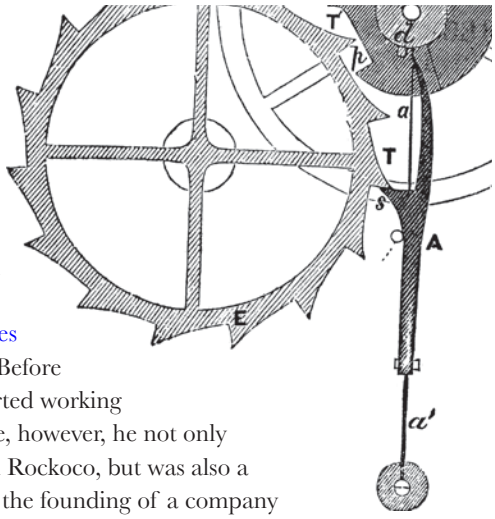
In 2005, George Maltezos was 11 months away from getting his PhD, working as a graduate student in the lab of nanofabrication expert Axel Scherer—and just a month away from marrying his fiancée, Suzy. The couple wanted to give special gifts to all of the members of their wedding party, but didn't have a lot of money with which to buy them.

What's a poor-but-generous young scientist to do? A little dumpster diving, a little repurposing of some outdated laser equipment (it's a long story), and voilà: Maltezos found himself with a lab-grown rod of titanium-doped sapphire crystal—basically an enormous ruby—to work with, and a Caltech advisor who certainly knew a thing or two about etching semiconductors.

Necessity being the mother of invention, Scherer and Maltezos soon came up with a new way to facet, or cut, crystals using the tools of modern microelectronics. They then etched nanoscale diffraction gratings very precisely onto the bottom of the stones, making grooves in the stone to diffract light and produce fire and sparkle. The outcome? Not only did Maltezos's loved ones get jewelry adorned with breathtaking laser rubies, but he and Scherer also realized they could extend the idea to diamonds. Within a month, the Scherer group had filed a patent on the process, which they now call Nanocut plasma etching, and started a company called Rockoco, which uses the method in the jewelry industry.

"We've changed the paradigm of diamond optics," Maltezos says. "In a hundred years, nobody will think of buying a diamond that hasn't been Nanocut because it just makes diamonds look better."

Today, Maltezos is developing a low-cost, easy-to-use diagnostic device that could transform the way diseases such as HIV are detected and monitored around the globe. He's working on the project with Scherer and Nobel Prize–winning biologist David Baltimore, with funding from the Bill and Melinda Gates Foundation. Before Maltezos started working on this device, however, he not only helped found Rockoco, but was also a key player in the founding of a company called Helixis—which produced a polymerase chain reaction (PCR) device much smaller and much less expensive than the standard machines then available.



AN OBLIGATION TO THE PUBLIC

Although Maltezos's story might be a bit unusual—not every grad student gets to help launch one company, let alone two—it's not entirely surprising either. Caltech researchers are an innovative and productive lot, and while many focus on basic science, a significant number make discoveries or collaborate on projects that go on to be applied to the development of new products, processes, or therapies. As a result, work at Caltech has led to such transformative and practical advances as ultraefficient thin solar cells, high-performance materials for medical products and personal electronics, and environmentally friendly chemical processes. In other words, Caltech research frequently has

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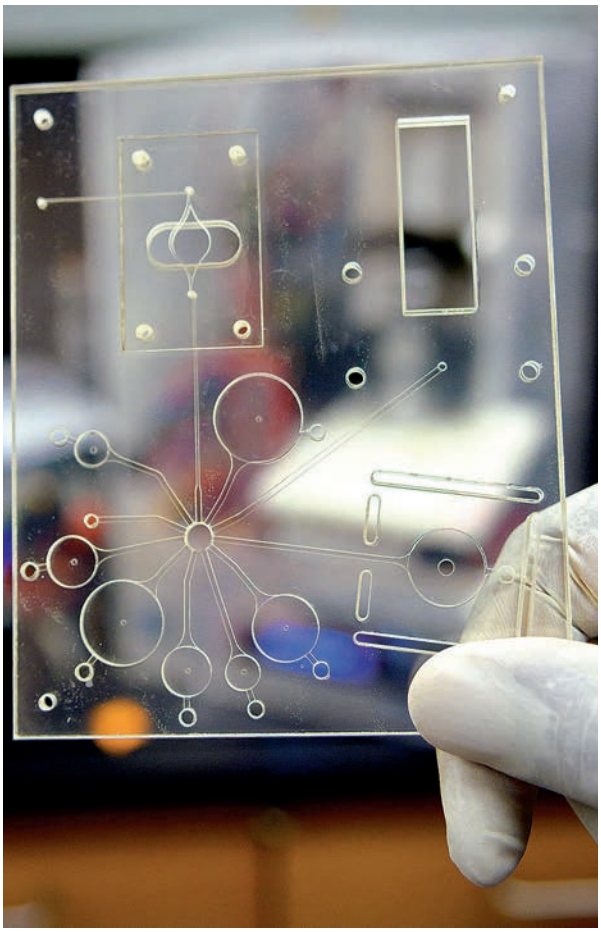
7
COMPANIES STARTED
&
104
PATENTS ISSUED

an impact that extends beyond—or actually knocks down—the walls of the Ivory Tower.

And that's no coincidence, says Fred Farina (MS '92), executive director of Caltech's Office of Technology Transfer (OTT) and Caltech's chief innovation officer. "Taxpayer money is a large portion of Caltech's funding, so we have an obligation to the public," he says. "The public is interested in science to some extent, but they also want to know that there is a return on their investment—that there are things that come out of the research that benefit society."



Above: A piece of the new, inexpensive, backpack-sized PCR device that George Maltezos, Axel Scherer, and David Baltimore are building for the Gates Foundation.

Next page: Chemist Theodor Agapie works with some air-sensitive chemicals in a glove box in his lab.

Since its founding in 1995, OTT has worked to foster a culture on campus that encourages and empowers faculty members to protect their intellectual property and to bring their ideas to the marketplace, where they can make a difference to the world at large.

That work has paid off. Caltech regularly reports a higher number of invention disclosures—initial filings of ideas that have the potential to eventually be patented—per research dollar than any of its peer institutions. During the fiscal year that ended last September, the faculty filed 246 such disclosures; about half of those disclosures will eventually go on to be filed as full patent applications. Over the last five years, Caltech has, on average, been granted more than 115 patents and started five new companies per year.

"I think one of the keys to this level of success is that the faculty trusts our office, and they come to us when they need us," says Farina. "We are here to serve the faculty. We strive to provide them with excellent service, as well as knowledge, experience, and connections that they don't have to go outside to get."

DEVELOPING ENTREPRENEURS

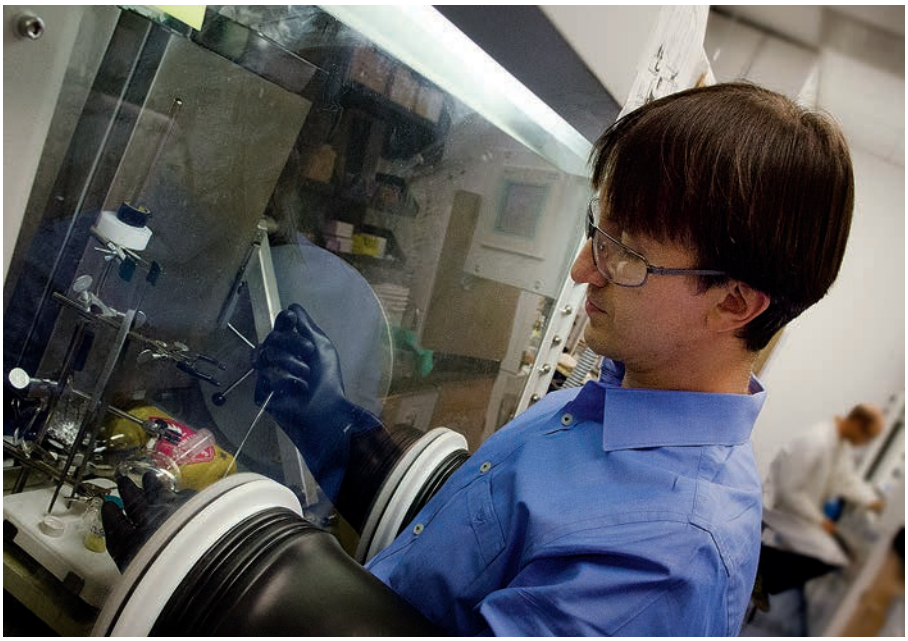
For chemical engineer and biochemist Frances Arnold, one of the most valuable services OTT provides is assistance with licensing deals, which give an individual or a company the right to use a piece of intellectual property, such as a patent. Arnold's patents have been licensed to companies interested in developing her work, and she has started companies of her own based on inventions developed by her group. She, like many other Caltech faculty members, thanks Larry Gilbert, senior director of technology transfer at Caltech, for her success in licensing her patents. "His attitude is, 'Let's make it happen,'" Arnold says.

Indeed, Gilbert was instrumental in getting the Institute and its faculty members to recognize that, in order to be competitive, companies often need exclusive licenses to patented ideas and technologies. Caltech granted its first exclusive license in 1988. "It was a novel philosophy at the time," Arnold says.

As is Caltech's enthusiastic promotion of entrepreneurship. Although the Institute holds the title to patents issued to its employees for inventions made in the course of work or using Caltech facilities, it is also Caltech policy to facilitate the transfer of useful technologies to those who can make them available to the public. Therefore, while some schools charge faculty members up front for use of the intellectual property they developed, Caltech often grants researchers an option agreement, which puts a hold on the intellectual property they intend to license while they develop a business strategy and seek investors. To further help the young start-up, Caltech will defer reimbursement of patent expenses for a period of time, allowing the company to focus its resources on developing, marketing, and selling products. In exchange, the Institute will take a modest equity stake in the fledgling business.

Arnold says this approach makes sense both from her own point of view as a scientist and from the Institute's perspective, given its desire to see Caltech work make its way out into the world. "It's essentially the Institute saying that it will take the risk along with you," she says. After all, what sense does it make to demand cash from a start-up that has yet to make a dime?

Scherer's success as an entrepreneur, like Arnold's, began with one-on-one conversations with OTT employees. Though Scherer has now started three companies, he says he never imagined



as a young professor that he would start even one. "But Caltech has the best tech-transfer office I know of, and they convinced me that my ideas had value," Scherer says. "They are flexible, efficient, and have a knack for matching the needs of the staff, the professors, and the students."

And that knack is important, Scherer notes, because Caltech's diverse faculty members have an equally diverse set of needs. "Some people don't know where to find funding, other people don't know how to write patents. Some people have no concept of the value of their ideas, others just need connections to find a management team. Caltech's OTT has people who can help you navigate all of those challenges."

START AT THE VERY BEGINNING

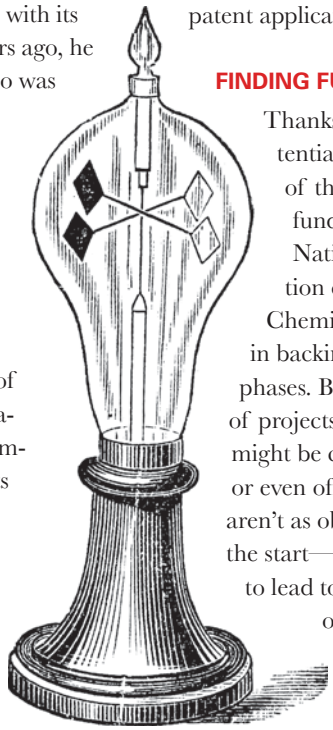
What chemist Theodor Agapie (PhD '07) needed was help navigating the process of filing a patent application. Agapie's lab had recently synthesized a new catalyst that drives the chemical reactions of polymerization—reactions in which chemical monomers (the original reactants) are combined to produce molecular chains, known as plastics, with desired properties such as elasticity and strength. The catalyst Agapie's group designed allows for the incorporation of chemicals with functional groups that had previously been difficult to incorporate in these reactions, opening up new possibilities in terms of the properties the resulting polymers can possess. For example, the new catalyst holds promise for developing polymers with improved adhesive and antimicrobial properties.

When Agapie joined the Caltech faculty in 2009, he had already participated in the patenting process once with his graduate advisor, Caltech chemist John Bercaw. Together they had developed and then patented a catalyst, also for polymerization. So when Agapie's group started having success with its new catalyst a couple of years ago, he knew that the first thing to do was to contact OTT.

"We, as a society, make a lot of plastics for applications as diverse as construction materials, electronics, medical equipment, and packaging," Agapie says. "Catalysts that control the structure and performance of plastics open up new applications, and there's a lot of commercial interest in these sorts of materials."

For instance, Agapie can see using his group's newly developed catalyst to make antimicrobial plastics for use in biomedical applications. After some optimization of the design, he can also imagine using the catalyst to produce building materials, such as PVC piping, under lower-temperature conditions and with more control over the polymer's structure at the molecular level than current fabrication methods allow.

But to commercialize any of those ideas, he would have to begin the patent process. So in 2011, he filed an invention disclosure, a simple form that documents the basics of the discovery. OTT used that disclosure to file a provisional patent application on his behalf with the United States Patent and Trademark Office; this provided a year of protection for his ideas, during which he could continue his research and decide whether the catalyst was truly promising enough to make it worth filing a full patent application. After about 10 months, OTT contacted him to talk about the status of his work and the next steps in the patent process. After he decided that it made sense to continue pursuing the patent, OTT referred him to an outside attorney who had the expertise to work with him to write up the full patent application.



FINDING FUNDING

Thanks to its commercial potential, Agapie's research is of the type that traditional funding sources, such as the National Science Foundation or companies like Dow Chemical, might be interested in backing, even in its earliest phases. But Caltech is chock full of projects whose basic premises might be considered high-risk or even off-the-wall, and which aren't as obviously commercial at the start—but have the potential to lead to some form of technology transfer down the road. For these,

Caltech has started a program called the Caltech Innovation Initiative (CI2), with the help of a generous gift from trustee Jim Rothenberg. Steve Mayo (PhD '87)—now William K. Bowes Jr. Foundation Chair of the Division of Biology and then vice provost for research—and his successor in that role, bioinspired engineer and vice provost for research Mory Gharib (PhD '83), worked with OTT to set up the initiative in 2009. Their goal? To encourage innovative thinking. In the less than four years since its inception, CI2 has provided grants ranging from $50,000 to $125,000 per year to more than a dozen projects—enough money to get such early research ideas off the ground.

Electrical engineer Ali Hajimiri was among the first recipients of CI2 funding. A promising idea had sprung up in his lab—an approach that he thought could lead his team to develop handheld magnetic biosensors for the detection of diseases in parts of the world where there is little or no access to medical facilities. "When we submitted a proposal, the idea was in a very early stage," Hajimiri says. "The CI2 funding enabled us to take the project to the next level." His group pressed forward, and today they hold several patents based on the work they did, and are considering forming a company based on their technology.

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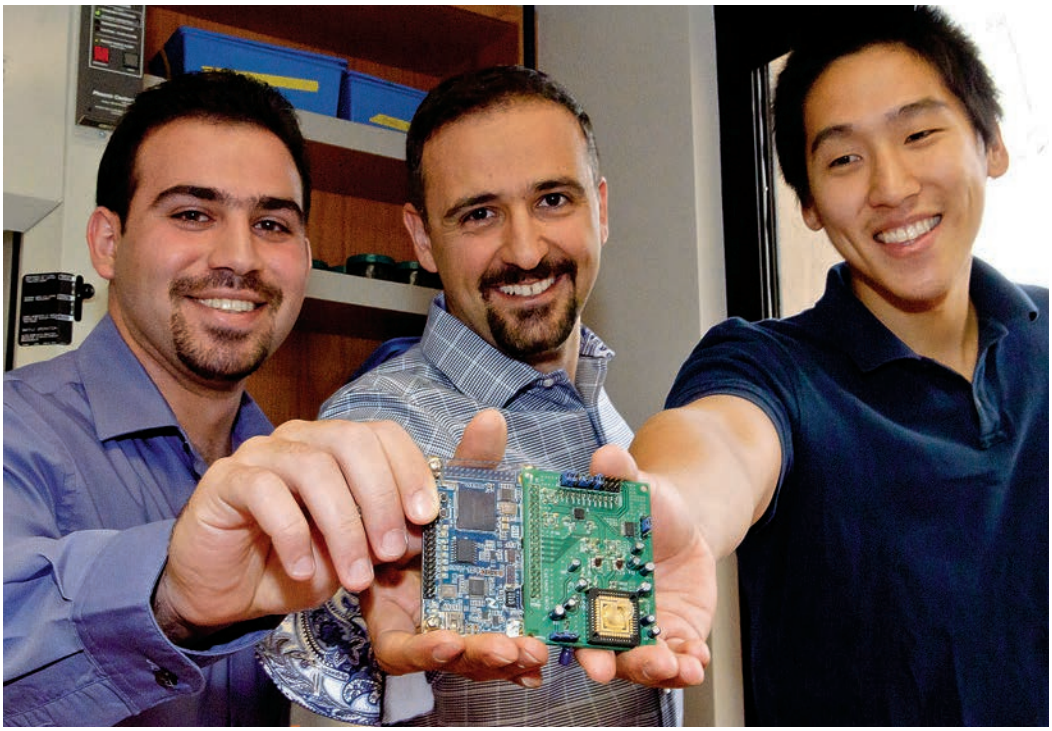
Gharib considers Hajimiri's story a perfect example of why the CI2 program was created—to encourage excellent, high-risk research and to boost the technology transfer process at Caltech. Gharib has another reason for his interest in the process, he says—he wants to prevent other Caltech researchers from repeating the mistakes he made earlier in his career.

"Before I came to Caltech, I had many inventions that I basically lost because I never protected them," he explains. "I just published, and industry used my ideas. That's a problem because, at the end of the day, those are the fruits of your labor." Now, after having started several companies of his own, he realizes the information and guidance OTT can provide would have been invaluable back when he was starting out. "We let faculty talk to ventures, but we give them all the data points—what they should look for, what their expectations should be," he says. "If you know from day one what to expect and you have an experienced group backing you, it helps."

Gharib also hopes to dispel the myth that researchers involved in tech transfer spend so much time on their commercial ventures that their research programs suffer. He points to both himself and to chemistry Nobel laureate Bob Grubbs as proof to the contrary. Both, after all, hold dozens of patents and have each started successful companies, and yet both continue to publish prolifically. "You can be an entrepreneur and a dedicated academic researcher if you're in an environment that helps you to cultivate both without interfering with each other," Gharib says. "That's what Caltech provides."



Undergraduate student Aroutin Khachaturian (left), electrical engineer Ali Hajimiri, and grad student Alex Pai (right) show off the integrated circuit at the heart of their handheld diagnostic device.

FOLLOWING AN IDEA TO THE MARKETPLACE

In fact, Caltech also provides rules that prevent the blurring of the line between academic research and entrepreneurial endeavors. For instance, faculty members cannot take on management roles in the companies they start. "You cannot hire, fire, or sign checks," Gharib says. Postdocs who want to work for such companies have to leave the Institute, and students must take a leave of absence.

That's exactly what George Maltezos did when he went to work as chief engineer for Helixis, the company he helped found, along with Scherer and Baltimore, in 2007. As a grad student, he had worked with Scherer and Baltimore to develop a PCR device—a system that can copy and analyze any short sequence of DNA or RNA—that is small enough to sit on a lab bench, less than a quarter the cost of standard PCR devices, and able to provide a more uniform temperature for amplifying genetic materials. Scientists use PCR devices to search samples for evidence of cancer, genetic mutations, and pathogens such as HIV, malaria, tuberculosis, and sexually transmitted diseases, thereby diagnosing these conditions quickly. While typical PCR devices cost more than $50,000, Helixis's first product sold for $13,000 and is now used around the world.

When Maltezos and Scherer first started working on the PCR device, they were responding to the H5N1 bird flu pandemic that had erupted in Asia in late 2003; becoming entrepreneurs was not their initial goal. And yet that's exactly what they became; in 2010, Helixis was acquired by the San Diego–based biotech company Illumina for approximately $105 million. "I never anticipated that," Scherer says.

These days, Maltezos is back on campus. He's working with the Scherer and Baltimore labs and clinical researchers at Dartmouth-Hitchcock Medical Center to take the idea of an inexpensive, small, accessible PCR device to the next level—making the entire sample-to-answer system compact enough to fit in a backpack, and delivering a technology that can operate at a cost of no more than $5 per test.

"We're working toward the goal of making this technology available to places that desperately need it in the developing world," says Maltezos. "Even with Helixis, that *always* was our goal." E&S

Caltech holds

1,700

active U.S. patents

Frances Arnold is the Dick and Barbara Dickinson Professor of Chemical Engineering, Bioengineering and Biochemistry. Her work is funded by the U.S. Army, the Department of Energy, the National Science Foundation, DARPA, and the CI2 program. She cofounded Gevo and was on the founding advisory boards of Maxygen, Fluidigm, and Mascoma.

Theodor Agapie is an assistant professor of chemistry. His work is funded by the Dow Chemical Company, the National Science Foundation, BP, and Caltech faculty start-up funds.

Morteza (Mory) Gharib is the Hans W. Liepmann Professor of Aeronautics and professor of bioinspired engineering. He is also Caltech's vice provost for research and is affiliated with the Kavli Nanoscience Institute. His work is funded by the Office of Naval Research, NASA, Boeing, and Zambon Pharma. He cofounded Arges Imaging.

Ali Hajimiri is the Thomas G. Myers Professor of Electrical Engineering and leads the Caltech High-speed Integrated Circuits group. His work is funded by several government agencies and industry partners, including DARPA and the Air Force Research Laboratory. He cofounded Axiom Microdevices.

Axel Scherer is the Bernard Neches Professor of Electrical Engineering, Applied Physics and Physics. He leads the Caltech Nanofabrication Group and is affiliated with Caltech's Kavli Nanoscience Institute. His work is funded by the Gates Foundation, the Air Force Office of Scientific Research, DARPA, Boeing, Sanofi, the Advanced Energy Consortium, and the CI2 program. Scherer has cofounded three companies: Luxtera, Helixis, and Rockoco.