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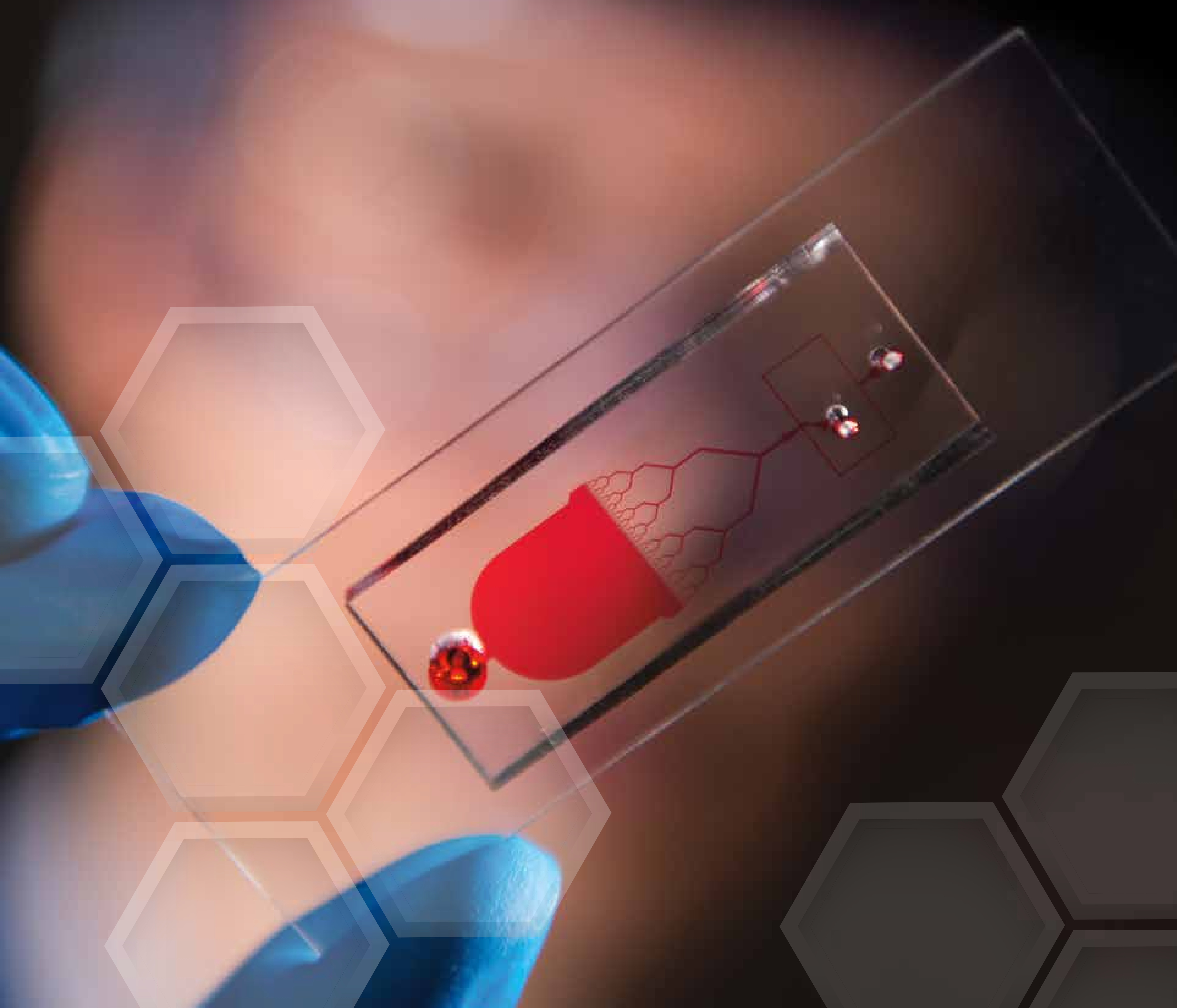
2013-14 DEAN'S REPORT



MICROFLUIDICS ON A ROLL

BY ANNA LYNN SPITZER

NEW I/UCRC CENTER FIRST IN THE NATION DEDICATED TO LAB-ON-A-CHIP RESEARCH

At first glance, it's difficult to discern commonalities between UC Irvine and the Technical Research Centre of Finland.

The university is located in sun-drenched, palm-dotted Southern California; VTT, as the government-funded research institute is known, calls Oulu, Finland, home. There, in the country's subarctic north, winter lasts six months, and the average yearly temperature is 36 degrees Fahrenheit, only slightly above freezing.

While the two institutions differ dramatically in scope, culture and climate, they are in complete synchronicity in pursuit of their common goal: to disrupt the future of point-of-care diagnostics. By meshing VTT's well-developed roll-to-roll manufacturing capabilities with UCI's engineering expertise and innovation in microfluidics, they are on their way to revolutionizing microfluidic lab-on-a-chip devices.

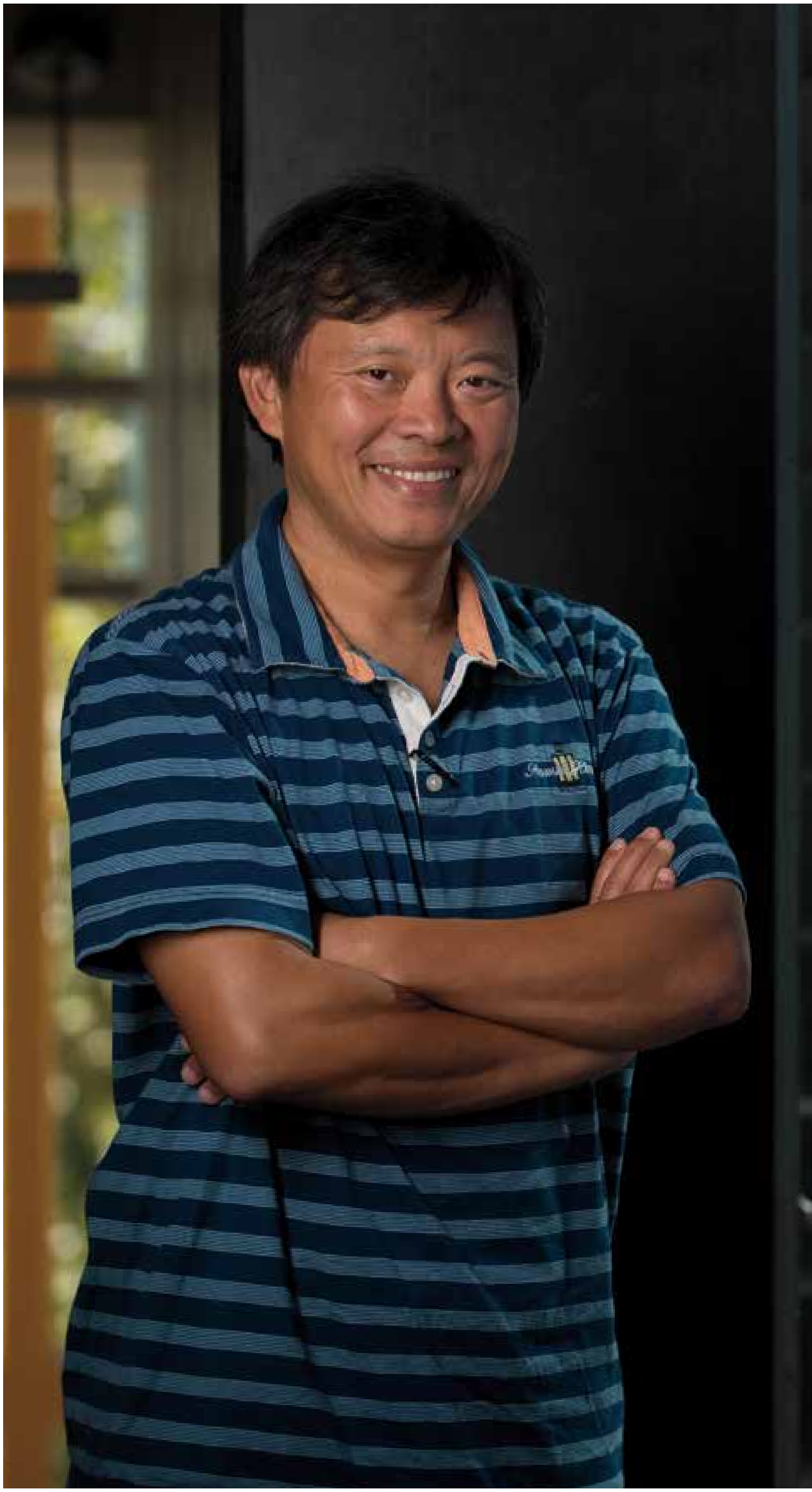
VTT was established in 1942 and develops and houses a variety of roll-to-roll pilot manufacturing equipment at its Centre for Printed and Hybrid Functionalities. The institute successfully produces electronics, solar cells, bio-batteries, LEDs and OLEDs on flexible plastics and paper. UCI's Samueli School of Engineering is home to CADMIM – the Center for Advanced Design & Manufacturing of Integrated Microfluidics – a newly formed Industry/University Cooperative Research Center (I/UCRC) administered by NSF.

CADMIM is a multipronged alliance that encompasses UCI, the University of Cincinnati, and 13 life science, diagnostics and advanced technology businesses. The center, the first I/UCRC led by UCI in the university's history, is in a unique position to effect change: out of 67 of these centers nationwide, it is the sole I/UCRC dedicated to microfluidics research.

Its mission: to develop tools and technologies for manufacturing low-power, integrated microfluidic devices that are cost-effective, fast and user-friendly for applications in environmental, agricultural and health diagnostics. The center foresees a future where completely self-contained microfluidic chips with high sensitivity and short reaction times are manufactured for mere cents, packaged and sold like Band-Aids, and recycled effortlessly.

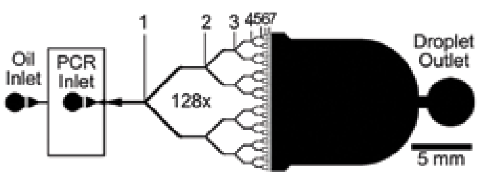
All parties firmly believe roll-to-roll techniques will unlock that future. "Roll-to-roll is not new, but it's not currently suited to production of integrated lab-on-a-chip designs," CADMIM Deputy Director Gisela Lin says. "We're trying to change that."

Until very recently, microfluidics – the science of moving, mixing, separating and processing fluids on very small chips – has involved clean-room fabrication and materials like glass and PDMS, a silicon-based organic polymer. The processes and materials, not to mention the requisite read-out equipment, are costly and inherently prohibitive to mass production. "The devices are still not cheap enough, they're not functional enough and they're not profitable enough," says UCI biomedical engineer Abe Lee, CADMIM's director and principal investigator. "There's not a sustainable market yet."



UCI biomedical engineer Abe Lee (left) and VTT research scientist Ralph Liedert are teaming up to apply roll-to-roll techniques to produce lab-on-a-chip microfluidic devices.

From a very small sample of fluid (blood, urine, saliva, sweat or tears), a microfluidic device can ascertain a great amount of data. It works like this: the sample fluid and an oil are placed in separate input channels. When the oil and sample streams meet, the oil splits the sample into millions of individual droplets. The droplets travel downstream into the holding chamber, where they collect in a honeycomb pattern and the actual analysis takes place.



But the capability of hot embossing tools on roll-to-roll manufacturing equipment is changing that. The tooling can produce the tiny channels through which liquids flow and can integrate the pumps, mixers, chambers, electronics, optics, fluorescence and detection mechanisms required for microfluidic bioassays. The roll-to-roll process also can eliminate the need for read-out equipment, because communication electronics to speed information wirelessly to cell phones or other consumer devices can be incorporated directly onto the chips.

The process moves giant rolls of pre-processed paper or plastic through a continuous web. The material is stamped, printed, pressed, laminated and sealed, producing thousands of tiny chips per foot of material. Roll-to-roll processes could fabricate hundreds of thousands of standard, one-centimeter-square devices per hour.

Ranging from a few square millimeters to a few square centimeters in size, the flexible chips provide an inexpensive way to analyze fluid samples on the fly. "We're looking for devices that can do diagnostics, or any sort of biological assessment that needs to be done quickly, in the field," says Lee, who also serves as chair of the Samueli School's Biomedical Engineering Department.

Microfluidic chips potentially can monitor air, water, the food supply and the human body for toxins, antibodies, pathogens, gene mutations and cell irregularity, all potential precursors of disease. Devices are capable of high-throughput chemical and biological assays, including single-cell and single-organism analysis, DNA assays, drug discovery, protein crystallization, chemical synthesis and single molecule detection. The technology provides the foundation for a new wave of medical diagnostics with wearable sensors that could analyze sweat, tears, blood, saliva, urine and other bodily fluids.

"MICROFLUIDIC DEVICES ARE NOT GOING TO BE THE TWO-DIMENSIONAL, VERY INORGANIC CHIPS THAT WE'RE USED TO NOW," LEE SAYS. "WE DON'T EVEN KNOW HOW TO IMAGINE THE POSSIBILITIES."

It also can play an important role in improving global health. Suddenly, medical providers may have the means to perform diagnostic tests in remote locations without extensive laboratory support.

"We can do a lot of these things today, but we're not doing them fast enough and in enough places," Lee says. "Affordability and immediacy are what we're striving for."

For years, VTT used its roll-to-roll machines primarily for electronics and optics and began experimenting about a decade ago with lab-on-a-chip microfluidic devices. Starting from very simple device formats, VTT and UCI have worked to evolve the complexity and size of diagnostic chips during their year-long collaboration. "We're pushing them; we have ideas and designs that they're beginning to implement for us," Lee says.

"VTT has already demonstrated a lot of electronics and optical components that are pretty fancy. So we decided to take what they can do and what we've developed over the years and put them together."

Ralph Liedert, a VTT research scientist who has been working with CADMIM on the project, says the hot embossing tools enable easy upscaling of manufacturing techniques. "I think very often the reason good designs and good concepts are ending up in a drawer is they are just made out of the wrong materials, and they haven't kept this upscaling in mind," he explains.

"The biggest advantage of roll-to-roll is you can use plastic materials that are immediately suitable for mass manufacturing."

Obviously, equipment is crucial to the effort, but CADMIM itself is equally important if low-cost microfluidic device production is to become reality. The I/UCRC concept emphasizes the coordination of industry and university research efforts to maximize the commercial potential of the developed devices. "Most academics are used to working in their own way and are very different, culture-wise, from industry," Lee says. "This cooperative infrastructure helps bridge a lot of those gaps."

"Industry partners are part of the decision-making, they approve everything that goes on in the center, and they provide the guiding light for the research," adds Lin. "We're very focused on being responsive to industry."

Frank Modica is manager of systems engineering at Canon U.S. Life Sciences, Inc. A CADMIM corporate member, Canon is commercializing a microfluidic diagnostic platform that can detect molecular mutations in DNA. "Canon has a thriving R&D organization, but efforts like this CADMIM partnership widen the opportunities," Modica says. "We hope to gain access and exposure to ideas and research we would otherwise not have the human resources to pursue."

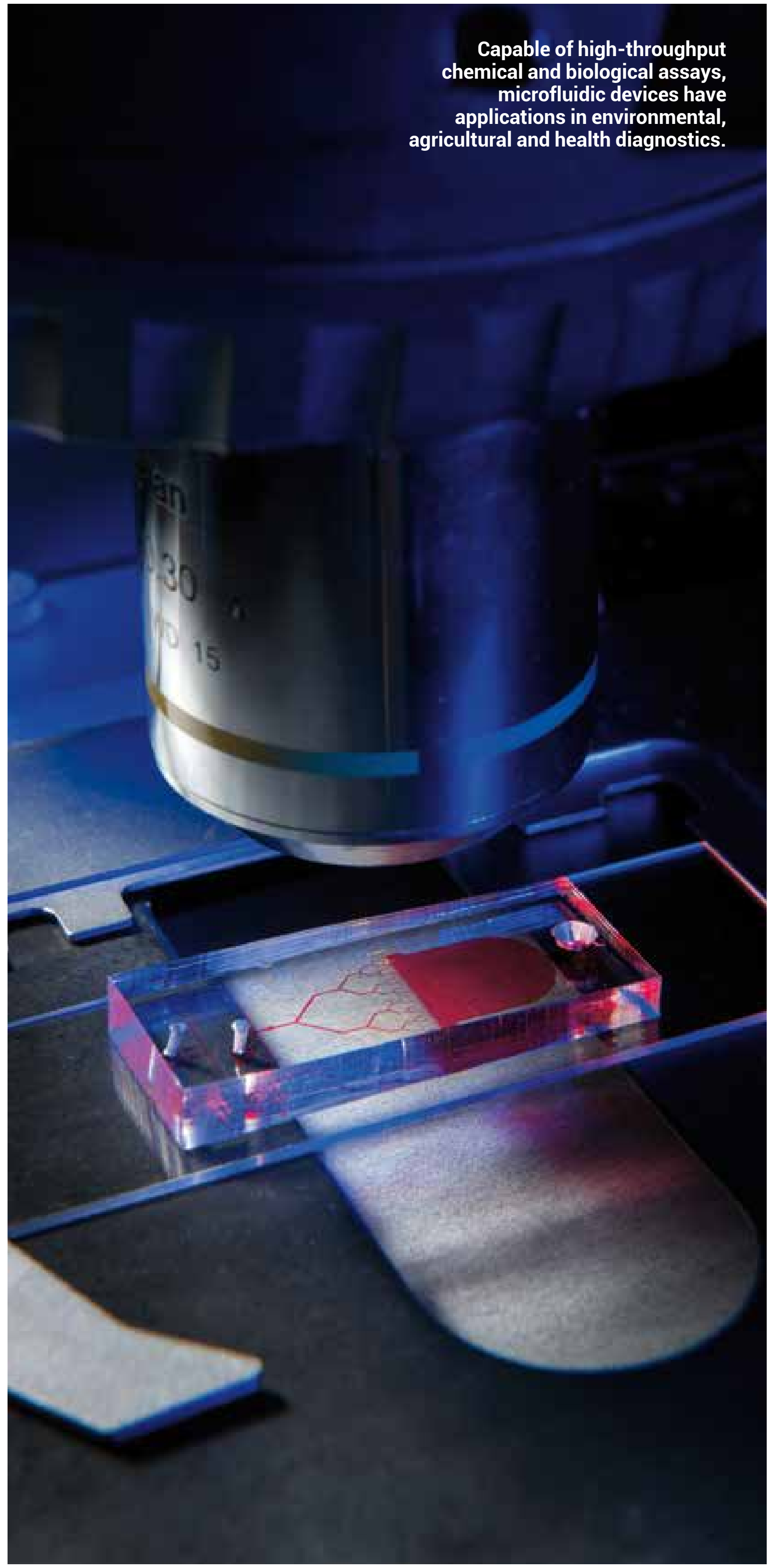
Beckman Coulter manufactures advanced healthcare instruments and systems for diagnosing infectious, cardiovascular and oncological diseases, among others. David Yang, director of science affairs, says the potential for reduced system size and improved sensitivity, along with its unique properties, make microfluidics a good fit for the company; roll-to-roll techniques can make it affordable.

"Participation in CADMIM presents a special and cost-effective opportunity for Beckman Coulter to tap into microfluidic expertise and identify possible solutions to improve patient care," Yang says.

Several projects are already underway at the five-month-old center. There's a DNA library preparation chip, which automates the current time-consuming, six-step procedure used to sequence genomic DNA, while allowing simultaneous processing of multiple samples. Another features a parallel, high-speed device that can generate tiny liquid droplets, enabling researchers to measure precise sample volumes. A third project seeks to demonstrate the integration of multiple microfluidic designs on a single chip.

Additional microfluidic applications are in line for conversion to roll-to-roll techniques, and the prospects are limitless. From wearable sweat sensors to disposable blood tests to ingestible devices that attach themselves to diseased cells, roll-to-roll microfluidics manufacturing promises to transform the world of diagnostics.

"Microfluidic devices are not going to be the two-dimensional, very inorganic chips that we're used to now," Lee says. "We don't even know how to imagine the possibilities."



Capable of high-throughput chemical and biological assays, microfluidic devices have applications in environmental, agricultural and health diagnostics.

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MICROFLUIDICS IN AUGMENTED REALITY

A tiny chip with the same capabilities as a full-size laboratory? That's the science of microfluidics, also known as lab-on-a-chip. Advances in the field are supporting huge strides in point-of-care diagnostics. Employing droplet-based microfluidics, extremely small, often rare liquid samples are broken down into millions of droplets that can be tested individually.

By using your smartphone or tablet, you can download a free augmented reality app to see this microfluidic device in action. Here's how:

Step 1: Download and install the UC Irvine Samueli School of Engineering APP – scan the QR code on the left, or download it from the Android or Apple store.

Step 2: Point your smartphone or tablet over this back cover image.

Step 3: Watch the microfluidic device's amazing process.

Available on the App Store

Available on the Android Market