cover STORY

Science on a small scale

With help from NanoFabrication Kingston, researchers are making technology smaller, faster, and better.

BY MARK WITTEN

Richard Oleschuk was watering the plants in his garden when he noticed an unusual effect upon dousing the large Elephant Ear (*Colocasia*) plants. "As soon as the water hit the surface of the leaves, it rolled off. You could never make the leaves wet," says Dr. Oleschuk, a professor in the Department of Chemistry.

A drop of water sits on a superhydrophobic surface. This photo by Timothy Hutama, a master's student in the Oleschuk lab in the Department of Chemistry, received honourable mention in the Queen's 2016 Art of Research photo contest.

TIMOTHY HUTAMA

Intrigued by the plant's water-repelling properties, Dr. Oleschuk brought leaves to his lab for further investigation. He asked graduate student Lili Mats (now PhD'16) to analyze the micro- and nanostructural features of the *Colocasia* leaf with a scanning electron microscope to learn more about how it repels water. "She looked at me like I had three heads," he says.

They soon learned that the leaf had a superhydrophobic surface, with a high water-contact angle of 150° (much greater than water-repelling Teflon® at 115°) and a low roll-off angle, which measures the ability of a surface to shed a droplet. These surface features provide very low frictional resistance, so water droplets can move easily across the surface with minimal applied force. "The *Colocasia* leaf really dislikes water. Certain plant species have evolved superhydrophobic, self-cleaning leaves that shed water, dust, and debris following a rain to maintain a high photosynthetic efficiency," explains Dr. Oleschuk.

On-the-spot diagostics

Inspired by this chance observation of a natural superhydrophobic surface, he began a series of experiments that led to the development of laser-patterned microfluidic chips with different wetting properties that could be used to perform on-the-spot diagnostic tests for plant viruses and bacteria, water quality, or infections and other diseases in humans.

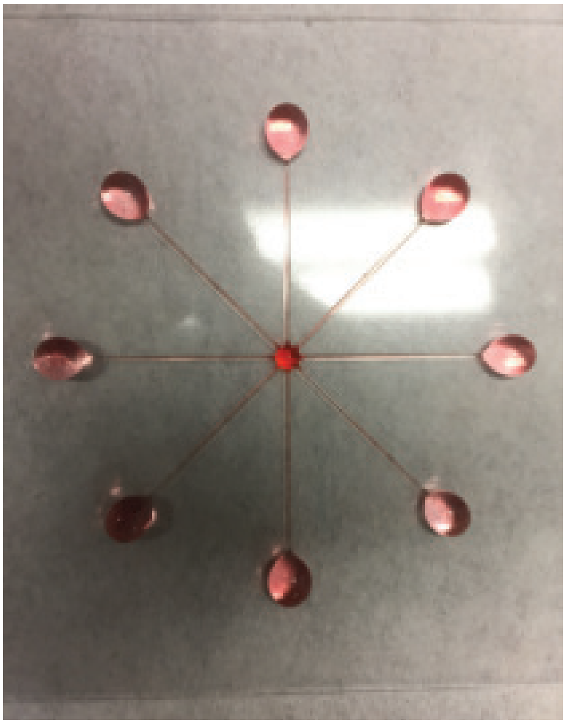
Microfluidics is the science of manipulating fluids at the micron scale (one-millionth of a metre). It involves making tiny little channels of flowing liquids on a chip, and being able to do chemistry or biology on tiny volumes using very sensitive detectors all fabricated on a chip.

In the initial experiment, Dr. Oleschuk tried using a bar magnet to move and direct water droplets less than one nanolitre in volume (a nanolitre is one-billionth of a litre) on the water-repellant leaf surface attached to a glass microscope slide. He then identified a commercially available superhydrophobic coating based on fluorinated silica nanoparticles, applied the coating to a glass slide, and found that the magnet moved the droplets at a much higher velocity on the coated surface than on the leaves.

Dr. Oleschuk and his team of grad students then built a microfluidic chip with alternating hydrophilic (water-attracting) and superhydrophobic (water-repelling) areas. Using the Oxford Lasers laser micromachining system at NanoFabrication Kingston, they burned off the water-repellant coating on certain areas of the glass slide to create a pattern of circular, water-attracting channels of different sizes on the glass substrate. Nano-sized water droplets were deposited on the channels and fluorescence-based chemical analyses were performed on the chip. "The glass surface loves water and is very wetting. Certain areas can't get wet and others can, so the droplets travel on the water-loving channels. You can then conduct different tests on each channel on the chip," he says.

Their new method of manipulating and analyzing minute sample concentrations on a chip (recently published in the American Chemical Society journal *Applied Materials and Interfaces)* is a promising advance in the emerging field of droplet-based microfluidics. It's a fast, easy, and inexpensive way to do chemical analyses or biological tests on a drop of blood, saliva, serum, or urine. It has many advantages over current methods of chemical and biological testing, which can be expensive and cumbersome, requiring complicated instruments, large amounts of sample, and long processing times. Using fewer reagents for chemical analyses also reduces the environmental impact. "The star-shaped, portable device we designed and fabricated allows you to conduct a very large number of tests in a short period of time. You can do five or six different tests on a single device and it takes 30 seconds to get a result," Dr. Oleschuk says.

He is now collaborating with Ephyra



KYLE BACHUS

This star-shaped device pumps liquids from the central hub toward the outer edges using Laplace pressure. It can be used to conduct multiple tests simultaneously on a single drop of fluid. The star device was laser micromachined at NFK.

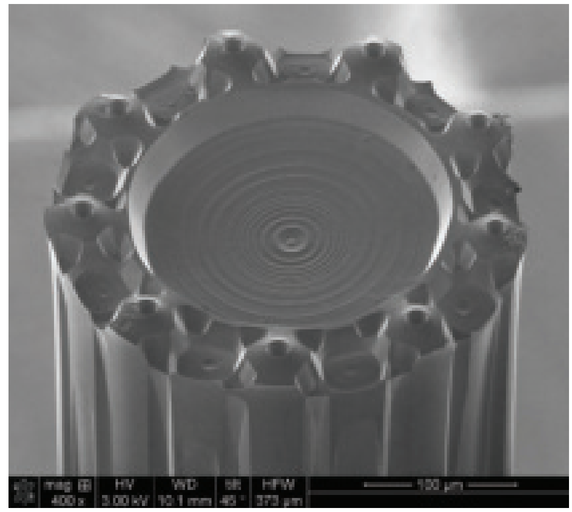
Biosciences, a company that sells antibody tests to detect plant pathogens in fruits and vegetables – to develop easy tests to characterize plant disease in potato as well as beer bacteria contamination. The "potato chip," for example, would use a superhydrophobic/hydrophilic approach and incorporate antibodies specific to the plant pathogens that growers want to test to help improve crop yields. "It's personalized medicine for the potato plant. The 'potato chip' could do rapid, on-the-spot tests for specific viruses and the result could guide the grower in treating the crop in a certain way," Dr. Oleschuk says.

Creating a map for surgeons

He is also working with cancer researcher David Berman, director of the Queen's Cancer Research Institute, to develop tools that use superhydrophobic/hydrophilic materials and incorporate antibodies for imaging of tumours. One imaging application might be to aid in biochemical mapping of the regions within and around a tumour to narrow the margins for surgical removal. A more accurate, detailed map of the tumour could allow the surgeon to be more precise in removing cancerous tissue, while leaving more healthy tissue intact. "Without the laser micromachining capabilities of the NFK facility, none of this work would have happened," says Dr. Oleschuk.

In another line of nanotechnology research, Dr. Oleschuk has developed and patented a microfluidic shower head with nine microfabricated nozzles that can efficiently generate and spray nanometre-sized droplets into spectrometers capable of analyzing chemical compounds and human disease biomarkers. This next-generation, nanoelectrospray emitter, developed in collaboration with Université Laval researchers, is much more sensitive and less likely to clog than current devices and could lead to improved detection of diseases such as cancer. "We are making shower heads smaller than a human hair-width using ultra-fine glass tubes. These devices are cost-effective and you can do tests with more sensitivity and much faster than with the current technology," he says.

In 2016, Dr. Oleschuk and the Laval researchers formed a partnership with Trajan Scientific and Medical in Australia, which licensed the patent, to develop and commercialize the next generation of devices and components to enhance the sensitivity of electrospray mass spectrometry. Funding from CMC Microsystems and an NSERC grant in the early stages of development were helpful in attracting an industrial research partner to commercialize the technology. "Doing research for general interest and contributing to background scientific knowledge are important. But if you can create a device that has an impact and get the device to the stage that it is commercializable, that's very satisfying," he says.



KYLE BACHUS

This microfluidic shower head, patented by Dr. Oleschuk, could lead to improved detection of disease.

The creation of laser-patterned microfluidic chips is just one example of the kind of cutting-edge research carried out at NanoFabrication Kingston (NFK), an $8-million lab established at Innovation Park in 2015 as a partnership between Queen's and CMC Microsystems. NFK is an open-access lab that offers access to leading-edge equipment, methodology, and expertise for designing and prototyping microsystems and nanotechnologies. It's funded through the Canada Foundation for Innovation and the Ontario Ministry of Research and Innovation, as well as Queen's and CMC.

"We are making shower heads smaller than a human hair-width."

A machine shop for research innovation

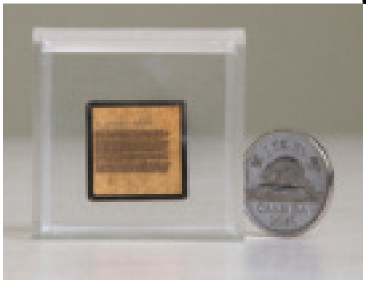
"This is like a modern machine shop for making things on a tiny scale. We help solve problems, whether it's with tools and equipment or the expertise of people here, through CMC, or other partners on campus and across Canada," says Rob Knobel, a Queen's physics professor and lead researcher at NFK.

The facility enables individuals and companies to explore new frontiers in the design, creation, and testing of innovations on the scale of the nanometre, one-billionth of a metre or one-thousandth of a micron. (Microtechnology is on the scale of a micrometre or micron, one-millionth of a metre.) "The difference in this lab is on the scale of what we can make. In nanotechnology, you're talking about being able to place one or a few atoms or molecules where you want them. You can even manipulate atoms one by one for a

BERNARD CLARK

During a 2016 tour of the NFK facility, Graham Gibson presented Ontario Premier Kathleen Wynne with a tiny plate etched with the logos of Queen's University and CMC Microsystems to thank the Ontario government for its contribution to the lab. The plate was created through laser ablation, in which the material absorbs the laser energy and vaporizes. The short pulse length of the laser allows for high-precision machining with well-defined edges. The process can be used on plastics, metals, and even paper.

Another example can be seen at right. Principal Woolf's column, "From micro-history to nanotechnology," has been replicated on a 2 cm-square piece of gold-plated metal.



BERNARD CLARK

few materials, controlling and measuring them," says Dr. Knobel.

Why can't we make them small?

Richard Feynman, the famous American physicist, is credited with proposing the concept of nanotechnology at a 1959 lecture in which he said:

> *I don't know how to do this on a small scale in a practical way, but I do know that computing machines are very large; they fill rooms. Why can't we make them very small, make them of very little wires, little elements – and by little, I mean **little**. For instance, the wires should be 10 or 100 atoms in diameter ... There is nothing I can see in the physical laws that say the computer elements cannot be made enormously smaller than they are now."*

But it took some time for people to work on it, first in microelectronics and later in chemistry, physics, and other fields. Today, nanotechnology is emerging as the go-to field for new innovations with the potential to improve dramatically the speed, performance, and cost of almost any device you can imagine.

Dr. Knobel's own research focuses on nano-electronics and nano-mechanics, making tiny moveable objects with the extreme sensitivity needed to measure quantum effects. Using the techniques of lithography, etching, and deposition, he fabricates nanometre-scale structures that can move. In one project, he and his students are building tiny vibrating sensors made from graphene, a form of carbon a single atom thick. Only a few molecules absorbed on the membrane will change its vibration, potentially enabling vapour sensors. "We're developing graphene chemical sensors with the goal of detecting vapours in parts per billion or trillion concentrations. These could be used for detecting explosives or biological agents," says Dr. Knobel.

The NFK facility houses state-of-the art tools for fabricating and prototyping new nano-scale inventions. There is specialized equipment for picosecond laser micromachining, electron beam evaporation, plasma etching, and scanning electron microscopy. Earlier this year, the lab added three pieces of new equipment for deposition, patterning, and etching of materials with greater ease, speed, and precision. "With our deposition tool, you can deposit less than a nanometre of material on a surface," explains Graham Gibson, NFK lab operations manager and CMC employee, who trains users in nanofabrication techniques for their specific applications. "We enable a lot of research. We help users with our tools and expertise, and then they will often do the fabrication themselves here. We help them create the device, and then they go away and use it."

Design. Make. Test.

NFK offers special learning advantages for students too. "The design-make-test cycle is greatly accelerated with this equipment. My students can design a prototype in the morning, fabricate it in the afternoon, and test it that evening. They learn a lot from the hands-on experience of making the product themselves rather than having to send it off to be made somewhere else," says Dr. Oleschuk.

Hannah Dies used NFK's maskless lithographic system to create a chip with a novel metallic nanosubstrate that can detect a wide range of substances. "I was one of the first users of NFK in 2015. The lithographic system gives you lots of flexibility in how you design the chip. I worked very closely with Dr. Gibson to learn how to do this and now it's quite routine to go in and make my chips," says Ms. Dies, who is pursuing a combined PhD in chemical engineering and MD from the School of Medicine.

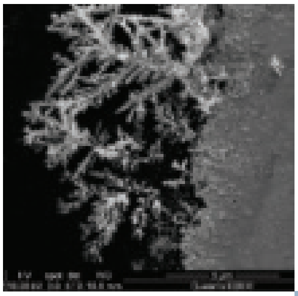
A key to her device's exceptional sensitivity is its tree-shaped nanostructure surface, a series of extended and interconnected dendritic nanoparticles that amplify signals from attached electrodes on the chip. "We built the device from the bottom up. We didn't originally expect this to have the shape that it did, a dendritic, branched nanostructure. It looks like a little nanoforest of trees. The theory is that creating branches allows for greater amplification and also extends the area available for sensing," says Ms. Dies.

A chemistry lab on a chip

She built into the chip the capacity to use a powerful technique called SERS (surface-enhanced Raman scattering), which can provide highly sensitive detection of chemical and biological substances at low concentrations. "Conventional SERS substrates require expensive pieces of equipment and take time to produce. Our SERS-on-a-chip substrates can be fabricated in only a few minutes and are simple to use."

Ms. Dies was the primary author of a recent paper (published in the Royal Society of Chemistry's *Nanoscale* journal) that showed how well this point-of-use fabrication method works. Her PhD supervisors, Aris Docoslis and Carlos Escobedo (Chemical Engineering), were co-authors, as was PhD student Joshua Raveendran. As proof of concept, the study demonstrated that their SERS-on-a-chip device could detect melamine in infant formula at 1 part per million (ppm), well below the World Health Organization's safe allowable concentration of 2.5 ppm. The researchers spiked apple juice with thiram, a pesticide toxic to the liver. The chip detected thiram at 1 ppm, seven times below the prescribed maximum residue limit. Cocaine was detected in distilled water (saliva is 99.5 per cent water) at concentrations below federal workplace testing limits.

Ms. Dies followed this up with an experiment showing the SERS-on-a-chip sensor could do very specific tests to detect *multiple* illicit drugs from saliva samples: "We have promising results about the identification of specific illicit drugs and the ability to differentiate one from the other. We tested cocaine, THC, heroin, and OxyContin and found we can successfully run tests on all four."



She sees commercial opportunities for this nano-sensing technology in fields such as food safety, drug screening, and hazardous materials testing. The researchers are filing for a patent and a team of students from the Queen's Innovation Centre Summer Initiative – a boot camp for budding student entrepreneurs – is working on business strategies to develop and market the technology. "They are a super-competent, energetic group of students looking at all aspects of developing and commercializing this technology. It's cool to be able to stay in science but have a team support the business side of things. You need that to have an impact with your research. A lot of great scientific ideas would stay in the lab without it," she says.

When Ms. Dies arrived at Queen's in 2014 and spoke with Dr. Docoslis, a nanomaterials expert, about possible research projects, he took her down the hall to chat with Dr. Escobedo, a biosensor technology expert. They needed a graduate student to assist with their project on microfluidic devices as portable biochemical sensors and they saw her background in physics as an asset. Although the fields of chemical- and bio-sensing were new to her, she was up for the challenge. "It's fun to get addicted to a project that has a lot of different aspects to it," says Ms. Dies, who earned a prestigious Vanier Doctoral Scholarship in 2015 for her early work on the project.

Now that she has created a portable sensing device to detect food contaminants and illicit drugs, the future doctor wants to further develop the technology for medical applications. After completing her second year of medical school, Ms. Dies plans to tackle this as a research project next summer: "Medical diagnostics are more challenging. My goal would be to look at a biomarker of cancer and see if we can modify our sensor by adding in some bioselectivity, so it can detect a complex disease biomarker at low concentrations. That's my dream project. And because nanotechnology is an emerging field, there is a lot of room for discovery." ■

Learn more about NFK: nanofabkingston.ca.

Left, detail of the "nanoforest of trees" on Hannah Dies' lab-on-a-chip. The line at the bottom labelled 5μm is 5 microns long, or the size of a dust particle.

Below, Hannah Dies at work at NFK.

MATT MILLS