Quantifying the nano-world: new tools for nanoscientists

Richard Feynman, a renowned physicist gave a presentation in 1959 titled "There's Plenty of Room at the Bottom" to describe his vision of what we now call 'nanotechnology'. Nanotechnology concerns the manipulation of objects at the nanoscale (one nanometre = one millionth of a millimetre), which is the scale of individual atoms and molecules. Dr. Murali Ghatkesar, assistant professor in the Department of Precision and Microsystems Engineering, lives by a slightly modified motto: "There's Plenty of Need for Quantification at the Bottom". Ghatkesar develops tools to experimentally access the nanoworld, to measure parameters and manipulate objects at the nanometre scale. "To do nanoscience, we need micro and nanotools."

Micro-nanotools

Ghatkesar explains how he takes questions from the biology and chemistry domains to his engineering drawing board. The questions that drive his work include How do we do a biopsy, not of a piece of tissue but from a single cell?" and "How do the interactions between tiny particles result in the macroscopic behaviour of colloidal liquids?" Starting point in developing the tools that help answer such questions is the current state of the art in micro and nano-engineering. By adding smart features to existing microsystems, they become 'micro-nanotools'.

Femtopipette

One such tool is the femtopipette: a pipette that is able to dispense or aspirate the smallest droplets of liquid, with a volume in the femtolitre range. This is truly a challenge considering the fact that a femtolitre is only 10^{-15} or 0.000000000000001 litre. Ghatkesar uses an atomic-force microscope (AFM) and modified cantilever to do the trick. An AFM is a widely used apparatus that scans surfaces with a very sharp needle mounted on a flexible cantilever. By measuring the deflection of the cantilever while the needle is tracing a surface, surface features can be imaged down to the sub-micrometer scale. "We develop micro and nanofabrication techniques to hollow out the cantilever and needle, and create an aperture of typically a few hundred nanometre in diameter at the tip." By connecting the hollow cantilever to a pressure control system, it can be made to either suck-up or disperse tiny volumes of liquids.

Label, extract, carry, freeze, study

The resulting instrument can thus pick up a tiny droplet and put it down somewhere else. What's the use of that? Ghatkesar describes an example application: "If we want to understand how the complex system of life functions, we need to zoom in on its basic building block – the cell – and study

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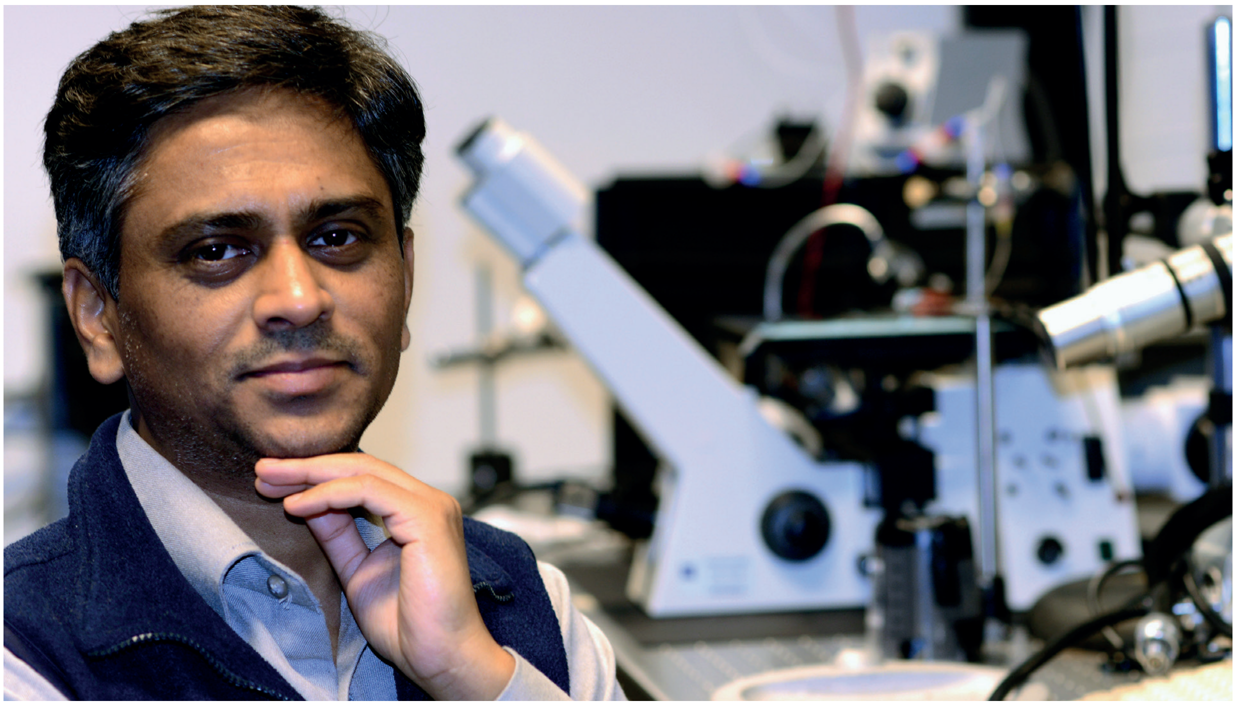

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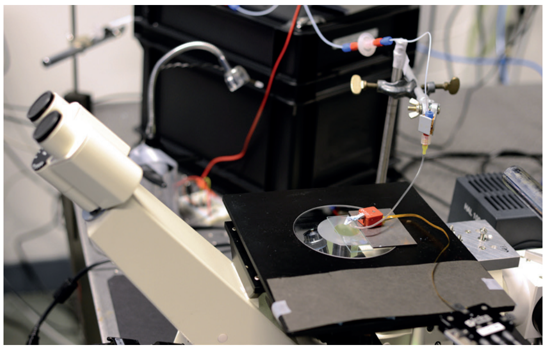


The femtopipette (not visible) is mounted on the arm of a sugar cube sized mini-robot (red cube). The robot takes the pipette to the desired location for dispensing. Fluids from the external world are connected to the chip using flexible tubes. The entire setup is mounted on an inverted optical microscope to monitor the pipetting of the fluid.

the many different components inside it. Currently this is done by freezing the complete cell and cutting it into many thin slices, which are investigated using an electron microscope. Hopefully, in one of the slices, the component of interest is found. This is quite an inefficient way to study a specific component of the cell. Our approach is to use our femtopipette to inject fluorescent labels inside the cell, to make the the components of interest light up. Then we direct our femtopipette towards the fluorescence where it extracts the labelled component. The extracted component is dispensed on to the microscopy substrate that is quickly frozen and studied under the cryo-electron microscope. This method of sample preparation technique is very efficient and saves a lot of time and cost.” The methodology can be used to study variety of sub-cellular components. “Our new tool will be perfectly suited to prepare bio-samples that are available in extremely tiny amounts (inside one single cell) and thus help shed light on the structure of the molecules that are responsible for a particular biological function.”

More parameters

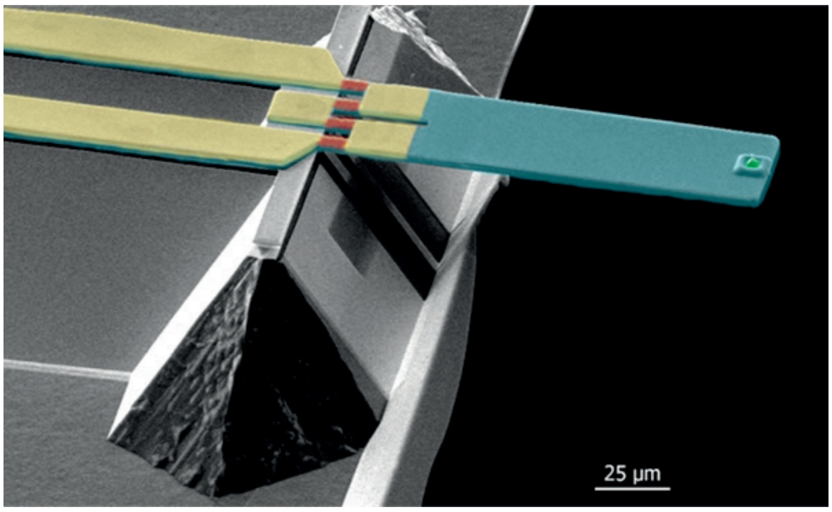
Yet, the ‘quantification at the bottom’ that Ghatkesar is poised to achieve is not limited to handling femtolitres to reveal molecular structures. “The same system can be used to quantify other parameters of the nanoworld as well, such as interaction strength, mass and stiffness.” As an example, Ghatkesar imagines using his flexible cantilever system to pick up nanoparticles. When the aperture in the needle is smaller than the nanoparticle, the particle can’t enter the hollow cavity inside the needle. Instead, it becomes attached to the sharp end of it, fixed in place due to the suction force. The dynamics of the cantilever now says something about the mass of the particle being picked up. Moreover, by carefully moving the needle and the particle attached to it towards another particle, bringing them into close vicinity, the cantilever deflection provides information about the interaction between two particles. This is an important parameter in the field of colloidal chemistry, where the interactions among nanoparticles determine the behaviour of particle-packed fluids, such as milk, paint or foam.

Building nanofeatures

The capability of moving nanoparticles from one place to another, with nanometre precision, might even be used to build nanofeatures onto microchips. Ghatkesar envisions strategically placing nanoparticles of a few nanometres in size, one particle at a time, thus creating nanoscale structures and electrical connections. “We can position the particles very precisely and then apply a heating step to get the particles to fuse together and create nanoscale connections.”

Multidisciplinary

How does Ghatkesar describe the field he works in? Although his personal expertise is in physics and microsystems, he operates in a highly multidisciplinary environment where precision engineering, biology and chemistry come together. “While each of us has own specialization, we have learned each other’s languages to enable close collaboration.” The NanoEngineering Research Initiative (NERI) of his department is a development Ghatkesar calls “fantastic”. “It is an opportunity to bring all the expertise in our department together, and puts us in a unique position in the field of nanoscience. There is so much synergy.” He emphasizes the potential of NERI in establishing collaboration with industry. His own work on the femtopipette as well as his vision on new ways to exploit AFM cantilevers are already attracting the attention of the AFM industry. “I see my innovations getting produced and used in large quantities within 5 to 10 years,” Ghatkesar projects.



Electron microscopy picture of the femtopipette developed by Ghatkesar and co-workers at TU Delft, as seen from below. The image shows the flexible microscale cantilever (blue) with a sharp needle at the end (green). The needle can be positioned over an area of interest with nanometre precision. Because both the cantilever and needle are hollow and connected to a pressure system, femtolitre quantities of liquid can either be taken-in (aspiration) or dispensed from an aperture at the needle.