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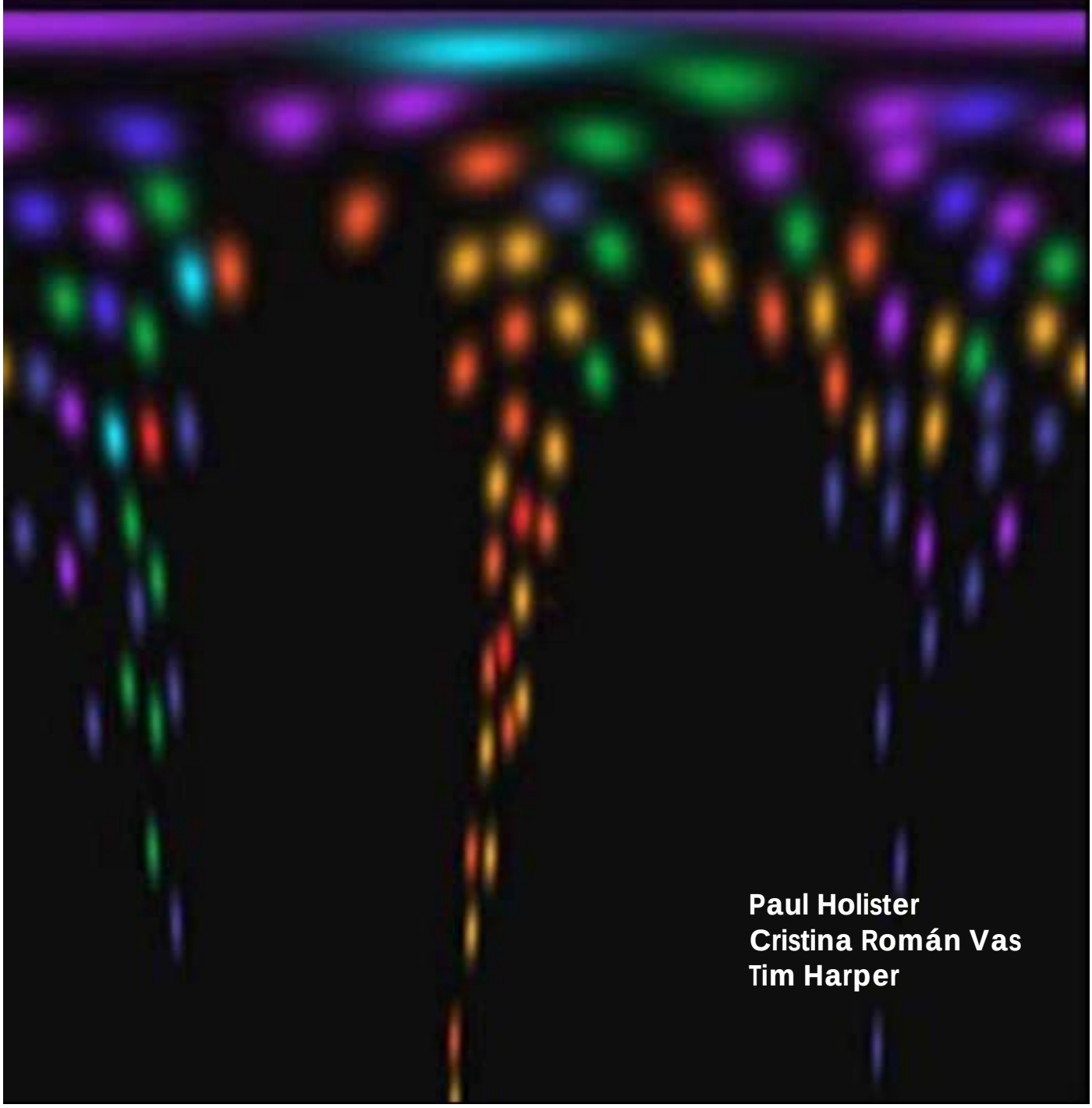

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Origin of content

The free reports in this series are extracted from the technology reports that make up the Nanotechnology Opportunity Report collection and are designed to offer an introduction to the variety of technologies that fall under the nanotechnology umbrella. The full reports also include 'opportunities' sections, covering the various applications of the technology and their effects on markets, and a list describing the companies involved in the technology.

Introduction to NEMS and nanofluidic systems

MEMS-based mechanical devices are shrinking in thickness and width to reduce mass, increase resonant frequency (for example in oscillators), and decrease forces involved in the systems. New methods for creating and detecting motion at the nanoscale are emerging. As with much nanotechnology, developing features smaller than the wavelength of light causes new properties to emerge. Arrays of nanoscale ridges can create a diffraction grating that makes the material refract (bend) light in a different way from the bulk material.

Making nanoscale mechanical objects move, or detecting their movement, presents new challenges. Optical interference or deflection of a laser beam are classic ways of detecting motion. Quantum tunneling currents have also been used. Electric fields can be used to create and control motion (the creation of movement is called actuation and resulting devices designed to move things are called actuators). Tips of scanning tunneling microscopes have also been used to induce motion and may provide the means to create tunable oscillators.

Microfluidics is already a well-established discipline and used in lab-on-a-chip systems. In microfluidic systems fluids are transported in channels with lengths of tens to a few hundreds of micrometers. The equivalent distances in nanofluidic systems will likely be a few to a few hundred nanometers. These dimensions will be down to levels corresponding to typical distances involved in natural phenomena in fluids such as diffusion and electrostatic effects of ionic fluids (any fluid containing salts is ionic, and this includes all biological fluids). Biomolecules are also measured on these scales. These factors present both new challenges and opportunities when comparing with microfluidics. Design of nanofluidic systems needs to be approached quite differently from that of microfluidic systems.

Fabricating valves and pumps at the nanoscale represents a real challenge since at this level biological or other macromolecules will tend to obstruct these mechanical components. Researchers have encountered several difficulties pumping fluids through the tiny passages inside nanoscale devices. Fluids start to behave differently at the nanoscale, with the replacement of turbulent systems by laminar flow.

Researchers at the Ohio State University have reported that a very small amount of electrical current may facilitate flow in nanochannels. The technique was proven effective in tests with actual nanometer-sized channels where electrical potentials as small as one volt were able to drive saline through the channels. Engineers at iMEDD

were able to flush nearly 0.5 nanoliters of saline per minute through a channel only 7 nm wide. The principle is based on the fact that when a fluid is positively or negatively charged, and a like charge is applied to the inner surfaces of a channel, the charges will repel each other and the fluid will flow down the channel.

This technique could have applications in implants for sustained drug release or automatically controlled (on demand) drug delivery to target sites of disease in the body, such as tumors.

An alternative pumping method has been investigated by researchers at Arizona State University. The technique relies on photocapillarity rather than on mechanical parts. Light-responsive molecules can be synthesized and attached to a surface, forming a monolayer. When a light beam is directed at them, they become hygroscopic (attract water) and cause water to advance along the surface.

The fact that channel sizes in nanofluidic systems can approach the scale of biomolecules presents both issues of maintaining flow and opportunities, such as potential sorting of molecules based only upon their characteristic thermal vibration and size. Current work on developing ways of rapidly sequencing DNA or proteins using a nanopore (covered in the report on nanoporous materials) also suggests functions that may be built into nanofluidic systems.

Large polymeric molecules behave quite differently at the nanofluidic level than at the micro level. This is problematic when trying to analyze DNA molecules. The analysis is usually hindered by the molecule's globular shape in solution (bound proteins can be hidden inside the globule formed by the DNA and thus be shielded from detection). Researchers are therefore investigating different techniques for straightening the DNA chains and making them flow though a nanochannel. One inherent difficulty in doing this lies in the additional energy that needs to be added to the system to overcome the entropy barrier (the random coil conformation of the molecule is the most energetically stable; to straighten the molecule this energy barrier has to be overcome).

If the DNA molecules were driven towards an array of channels a few nanometers across simply by fluid flow, the globules would just block the openings. To make the change of entropy smoother, and therefore easier to overcome, researchers have designed different arrays of channels going gradually from micro to nano dimensions.

Scientists at Princeton University use an array where the gaps between rows of micrometer columns are gradually decreased, allowing the DNA molecules to flow between the pillars and comb out little by little so that they are more able to fit into the nanoscale channels at the end of the array.

At Cornell University, researchers use similar energetic barriers as an alternative to gel electrophoresis for separating large polymeric molecules (such as DNA). The scientists use a 30 µm wide channel with repeated, alternating regions of different depths (typically ~ 90 nm and ~ 1400 nm). Every time a globular molecule has to

enter a thin gap, it has to overcome an energetic barrier (due to deformation of the molecule) that depends on the size of the molecule, leading to a sorting effect that correlates reasonably with different molecular lengths.

The most common method used to make the arrays and channels for nanofluidic systems is the same as that currently used with MEMS and is often called micromachining. A pattern is made on a surface using lithography, sections etched out, and then the layer is undercut to separate it from the base and make the remaining sections of the pattern into freestanding structures. Freestanding objects can be created, in silicon and other materials, down to about 20 nanometers, using serial lithographic techniques based on electron beams or ion beams, for example. Parallel lithographic techniques have a larger limit, still around 100 nanometers, at least those implemented commercially. Prototype next-generation systems can create smaller structures, but systems capable of mass-production with features comparable to those achievable with e-beam or ion beam approaches are a long way off. This has serious implications for the commercial viability of applications of NEMS or nanofluidic systems.

However, there is another technology that is already used to make microfluidic systems and that has resolutions equivalent to those of electron beam lithography (20 nm or less). This is the variety of approaches collectively called soft lithography, or nanoprinting, that offers the potential of scaling to mass-production. These approaches are covered in the report on top-down production techniques.

Other techniques can be used to create nanoscale channels. One such technique consists of making a nanowire with a coating, and then dissolving the wire, leaving a tube. The smallest to date using this approach has used silicon nitride and silicon dioxide.

Although silicon tends to be the chosen material for MEMS, interesting work has been done on using softer materials, specifically elastomers, which often suit fluid-based applications better and are also well suited to fabrication using soft lithography techniques. Researchers from Cornell University have developed a method of making flexible polymeric tubes. With diameters of 100 nm, the tubes are ten times narrower than those currently available in microfluidic applications. In fluidic systems, the material's greater flexibility makes much more sense for elements such as interconnected networks and valves. Elastomers can also be made into optical components, such as diffraction gratings and wave guides.

Bottom-up techniques, for example using biomolecules as building blocks in microelectronic circuitry, are likely to see increasing use in the future compared to current top-down techniques such as lithography, etching, and soldering methods. A fusion of top-down approaches and self-assembly may hold the greatest promise for many tasks and quite a lot of research has been done on making nanostructures using such combinations but, as yet, not too much within NEMS and nanofluidics. The light-operated pumping system mentioned earlier is, though, one such example.

However, when it comes to the basic components of NEMS, i.e. the basic components of any device, such as levers, pumps, resonators, pulleys, biomolecules seem to hold considerable potential and are seeing significant research. Nature provides the most beautiful and impressive examples of molecular engineering known. Every part of a living organism is formed by extremely complex systems that work in a smooth and efficient way to perform the multiple tasks needed to maintain life. These systems have long served as a source of inspiration for scientists working on the design of nanomechanical devices. More than this, though, scientists are looking at taking the basic components nature provides and modifying or recombining them to create nanodevices. Despite such work being at a very early stage, some very interesting results have been reported. Primitive tools and machinery have been manufactured by several researchers. Even though these tools are still extremely rudimentary when compared with biological systems, they represent notable scientific achievements and are the first steps towards a deeper understanding of the way nature's toolbox works and of how to exploit it to develop artificial nanodevices.

Molecular motors have been investigated as a source of power for NEMS. In general, molecular motors work on the principle of conversion of chemical energy, provided by the hydrolysis of ATP molecules (adenosine triphosphate) into ADP (adenosine diphosphate), into mechanical energy. Many proteins can change their shape using this energy, which results in some kind of motion, depending on the type of protein.

Many molecular motors in biological systems appear to be driven by Brownian motion, in which thermal fluctuations at the molecular scale are responsible for continuous random changes in the conformation of molecules. Molecular interactions (mainly of an electrostatic nature) can create a force that induces order in the chaotic Brownian movements simply by favoring movements in one direction and inhibiting them in others, thus turning random motion into motion in a specific direction.

An example of this movement is the migration of kinesin molecules along microtubules (25 nm diameter polymers found in all the cells of multicellular organisms). This is responsible for transport of membrane organelles and nucleic acids within the cells. Although the ability of cells to move their internal contents has fascinated biologists for many years, the exact mechanism is still not completely understood, but the kinesin/microtubule combination has already been leveraged in the laboratory, notably for an imaging application.

The following list gives some of the recent research developments in the investigation of biological molecular motors, and other components, and their use in fabricating nanodevices.

Date	*Development*
1998	First DNA motor. DNA is a versatile molecule. Its ability to self-assemble makes it a good building block for molecular machinery. Scientists at New York University assembled DNA strands into cubes and sheets of interlinked rings. The following year they made a nanomotor in which a DNA rod repeatedly twisted between a C and an

S shape, pulling its free ends apart

1999 Using a biological motor (based on the ATP synthase molecule), a group of researchers at Cornell University was able to fabricate the first ATP-powered nanodevice—rotating microspheres on a metal substrate.

2000 The same group attached nickel micropropellers to ATP synthase that were able to rotate continuously for several hours with high efficiency (up to 80%).

Through clever design of complementary DNA strands, researchers at Lucent Technologies' Bell Labs and the University of Oxford in England managed to create a DNA motor that changes from a rigid rod-like form to a soft string form.

2001 A team of biophysicists at the University of California, Berkeley, and the University of Minnesota unveiled one of the most remarkable examples of molecular motors known, the biomolecular device responsible for DNA packing inside a bacteriophage T4 virus. This system is one of the most powerful molecular motors ever observed, able to compact the DNA of the viral genome into a space nearly 6,000 times below its normal volume, reaching a final pressure inside the virus of almost 60 bars (870 psi). To achieve this, the motor has to overcome DNA's resistance to bending, the electrostatic forces of repulsion encountered when pushing charged atoms close together, and the forces of entropy that continually urge the DNA to adopt its usual larger form. The stored energy inside the capsid of the virus is released when a bacterium is infected through cell puncturing, which contributes to rapid DNA injection into the bacterium.

2002 An international group of researchers described for the first time how the bacteriophage T4 virus uses a needle-like, biochemical puncturing device to invade its host, the *E. Coli* bacterium. Understanding the exact mechanism used by viruses to enter cells is significant. This information could be used to develop drugs to prevent viral infections, as well as to create 'designer viruses' that could become the antibiotics of the future.

Angela Belcher and colleagues at the University of Texas engineered long, thin viruses to have a peptide sequence at one of their ends that binds semiconductor nanoparticles (quantum dots). The viruses then aligned themselves, forming a liquid crystal film so strong that it looked like a thin plastic-like film. Such a regular array of quantum dots could form the basis for new kinds of displays. Using other nanoparticles, the approach could be used to create a very dense magnetic memory.

Researchers at the University of North Carolina at Chapel Hill and co-workers made frayed wires from single strands of DNA bundled into clusters about 2 nm wide and between 5 and 200 nm long. The wires can be linked together into networks through complementary strands of

DNA.

At the University of Florida scientists built a molecular motor from DNA that extends and contracts "like an inchworm".

Researchers at the University of Arizona started exploring ways to 'grow' microchips, using microtubules from living cells. Microtubules are long strings of proteins, uniform in size, and with the ability to self-assemble. These tiny tubes can have aspect ratios up to 1,000 (length/diameter), which makes them a good candidate for manufacturing extremely small connectors.

January 2003	French researchers constructed a DNA strand that stretches and shrinks, cycling from an elongated double strand to a more tightly coiled four-strand form. Previous research resulted in DNA machines that rotate and that open and close like scissors.
March 2003	Bell Labs researchers improved their DNA motor and managed to keep it running continuously.