

ANALYTICAL CURRENTS

Moving droplets by vibrations

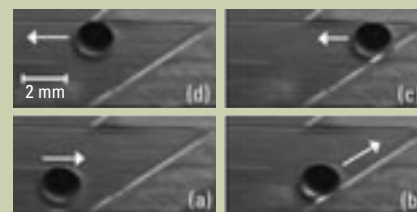
Manoj Chaudhury and colleagues at Lehigh University and Institut Curie Recherche (France) have developed a new method to move individual drops on a hydrophobic surface by vibrations. The method can be used to carry out biological processes, such as cell sorting and DNA hybridization, in microfluidic devices.

Discrete drops can be moved around by other techniques, such as dielectrophoresis and electrowetting, but these methods have problems with speed, lack of reversible drop motion, and heat control. The new method by Chaudhury and colleagues uses asymmetric lateral vibrations to exert an inertial force that thrusts the drop in the direction of the net force. By precisely

controlling the frequency and amplitude of the vibration, 1–10- μ L drops can be propelled around a network, paused, and even reversed.

Chaudhury and colleagues demonstrated drop movement both on a hydrophobic silicon wafer coated with an alkyltrichlorosilane self-assembled monolayer and in a device made out of PDMS and glass. To generate forces on the drop, the substrate on which the droplet sat was mechanically vibrated.

The investigators designed three prototype devices in which vibrations were used to move drops on a chip. Actions such as drop mixing, temperature cycling, and phase separation could be combined to



(a–d) Vibration actuation moves a drop along a channel in a network. The drop changes direction when it contacts the edge of the channel. The arrows show the direction of the net force acting on the drop.

carry out reactions such as PCR. Chaudhury and colleagues say that vibration-actuated drop movement can be automated, and they expect such devices to be inexpensive and simple. (*Langmuir* **2005**, *21*, 4240–4248)

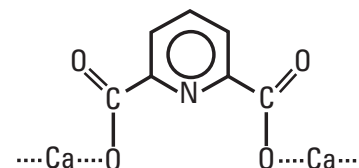
Rapid anthrax detection by SERS

First responders could soon have a new tool for detecting anthrax spores in the event of a biological terrorist attack. Richard Van Duyne and colleagues at Northwestern University have developed a protocol for detecting bacillus spores by surface-enhanced Raman spectroscopy (SERS) with a low-cost, battery-powered, portable Raman spectrometer. The speed and sensitivity of the SERS sensor make it applicable for field detection of harmful environmental agents.

In laboratory experiments, the researchers extracted the biomarker calcium dipicolinate (CaDPA) from *Bacillus subtilis* spores, which are harmless simulants of *Bacillus anthracis* (anthrax). They detected the CaDPA on

silver film over nanosphere (AgFON) substrates by SERS. The entire procedure took 11 min, including a data acquisition period of 1 min, and the limit of detection was $\sim 2.6 \times 10^3$ spores for a laser power of 50 mW. According to the researchers, previous SERS studies of the CaDPA biomarker were 200 \times less sensitive and required 3 \times more laser power. Similarly, those using normal Raman spectroscopy were 200,000 \times less sensitive and required 8 \times more laser power.

To demonstrate the portability and robustness of SERS for field detection, the researchers used a commercially available compact Raman instrument to detect 10^4 *B. subtilis* spores dosed on a one-month-old AgFON substrate. A high-S/N spec-



Calcium dipicolinate.

trum was obtained with a data acquisition period of only 5 s. The SERS spectra of the spore sample compared well with CaDPA spectra obtained with the same device, in terms of peak positions and intensity patterns. Although the results show the specificity of SERS for detecting anthrax, the researchers still need to test the method in the presence of potential interferences. (*J. Am. Chem. Soc.* **2005**, *127*, 4484–4489)

ANALYTICAL CURRENTS

More sensitive SOPs

The sensitivity of semiconducting organic polymers (SOPs) for detecting organic vapors can be greatly enhanced by taking advantage of their inherent lasing ability. Timothy Swager and colleagues at the Massachusetts Institute of Technology developed a new SOP with a high thin-film quantum yield, high optical damage threshold, and low lasing threshold. When the polymer film is pumped with pulsed laser light at intensities near its lasing threshold, stimulated emission occurs. This emission is significantly decreased when trace vapors of the explosives 2,4,6-trinitrotoluene (TNT) and 2,4-dinitrotoluene (DNT) bind to the SOP. By measuring the change in lasing, the researchers were able to detect subparts-per-billion levels of TNT and DNT. They report a 30-fold gain in sensitivity with the new approach compared with spontaneous emission from SOPs. (*Nature* **2005**, *434*, 876–879)

Capacitance-based nanotube sensor

By coating single-walled carbon nanotubes with a thin layer of chemoselective material, Eric Snow and colleagues at the U.S. Naval Research Laboratory have created a low-power sensor that rapidly responds to various chemical vapors. The sensor relies on a change in surface capacitance that occurs when an analyte adsorbs to the nanotubes.

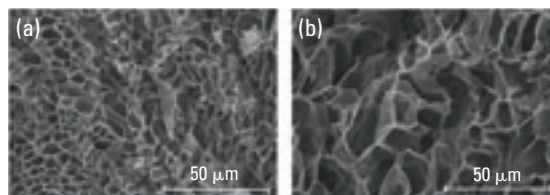
In comparison with previously reported chemicapacitors, which are coated with relatively thick layers of a dielectric material and can take several minutes to respond and recover, the new sensor uses very thin layers of material, down to a single-molecule monolayer. Such thin monolayers reduce the time required to load and remove the analyte and thus allow for real-time sensing.

According to the researchers, the sensor is general enough to detect a wide range of chemical vapors, including volatile organics and low-vapor-pressure explosives. To demonstrate its sensitivity, they used the device to detect dimethylmethylphosphonate (DMMP), a simulant for the chemical nerve agent sarin. Using a hydrogen-bonding chemoselective polymer, they achieved a minimum detection limit (MDL) of 0.5 ppb for DMMP. When they replaced the polymer with a molecular monolayer, the response time improved; however, the MDL increased to 50 ppb. (*Science* **2005**, *307*, 1942–1945)

Hybrid hydrogel with proteins

Sylvia Daunert and colleagues at the University of Kentucky and the University of California, Irvine, have developed a novel stimuli-responsive hydrogel with genetically engineered proteins. The hybrid hydrogel has potential applications in microfluidic devices and drug delivery systems.

The investigators incorporated a modified version of calmodulin (CaM) in the hydrogel. CaM is a protein that binds Ca^{2+} , antipsychotic drugs, and certain peptides. The protein has three conformations—a native conformation, one with Ca^{2+} , and another with antipsychotic drugs. The conformations provide three specific swelling stages to the hybrid hydrogel in response to different stimuli. Conventional hydrogels only have two stages.



The CaM hybrid hydrogel (a) shrinks in the presence of Ca^{2+} and (b) swells in the presence of a Ca^{2+} chelating agent. (Adapted with permission. Copyright 2005 Nature Publishing Group.)

The reversible stimuli-responsive properties of the hybrid hydrogel were demonstrated in the presence and absence of Ca^{2+} . The hydrogel shrank when exposed to Ca^{2+} and swelled in the presence of a Ca^{2+} chelating agent. The material was stable and responsive over a period of six months.

The investigators demonstrated that the hydrogel could be incorporated into microfluidic systems as a gate. In a swollen state, the material prevented the release of a blue dextran solution from a reservoir. When exposed to a stimulus, the hydrogel shrank and allowed the solution to flow from the reservoir.

The material also responded to an antipsychotic drug, chlorpromazine. Daunert and colleagues showed that the hydrogel could control the transport of molecules through its pores on the basis of the size of the molecules. The researchers suggest that it therefore could be used as a micro-actuator in drug delivery systems. (*Nat. Mater.* **2005**, *4*, 298–302)

Conical gold nanotube-based biosensor

Charles Martin and colleagues at the University of Florida and GSI Darmstadt (Germany) have developed a new protein biosensor that features a conical gold nanotube embedded in a polymeric membrane. An ionic current is passed through the nanotube. When an analyte binds to its molecular recognition agent (MRA), which is immobilized at the small opening of the conical nanotube, it permanently binds and completely blocks the current.

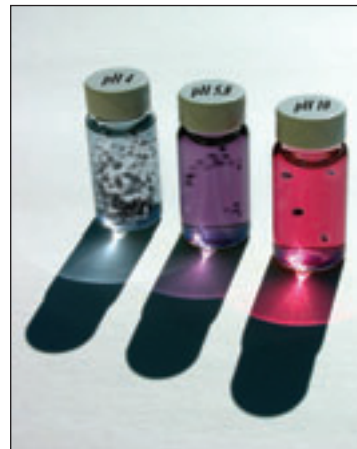
Martin and co-workers obtained current–voltage (I – V) curves for three different MRA–analyte systems: biotin–streptavidin, protein G–immunoglobulin, and ricin antibody–ricin. A baseline I – V curve was constructed for the system before analyte exposure. The researchers then obtained I – V curves after adding a protein that does not bind the MRA and after adding the appropriate binding partner. The ion current was only blocked when the binding partner was added to the biosensor system.

The current was permanently and completely blocked in the biosensor system because the MRAs and analytes strongly bound to each other and the analytes were about the same size as the nanopore opening. Weaker binding analytes could be used to produce reusable biosensors in the future. (*J. Am. Chem. Soc.* **2005**, *127*, 5000–5001)

Colorful shape shifting

Richard Zare and colleagues at Stanford University have developed a colorimetric sensor that detects protein conformational changes. The inexpensive, gold-nanoparticle sensor can be adapted to study the folding of many proteins in different environments.

The researchers coated gold nanoparticles with cytochrome *c*. As they lowered the pH, they observed a shift in the absorption peak to a higher wavelength. The nanoparticles also aggregated over time at lower pH values. In another set of experiments, Zare and his team coated a gold film with cytochrome *c* and obtained surface plasmon resonance measurements. The refractive index of the protein-coated gold layer varied with pH, an indication that the protein conformation changed. The data from both sets of experiments were similar, which suggests that gold nanoparticles can be used to detect conformational changes. (*Chem. Biol.* **2005**, *12*, 323–328)



Cytochrome *c*-coated gold-nanoparticle solutions change from red to blue and aggregate with decreasing pH.

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Nanoscale biosensor detection limits

Because S/N tends to increase as the size of the measurement device decreases, considerable effort is being made to reduce the dimensions of analytical instruments. But Paul Sheehan and Lloyd Whitman at the U.S. Naval Research Laboratory caution that without directed transport of biomolecules in micro- and nanoscale biosensors, any gain in S/N will be offset by a limitation to picomolar sensitivities.

The investigators examined wire and disk-shaped biosensors of various sizes and

detection sensitivities. They calculated that in a hemispherical sensor of submicrometer dimensions containing a 1-fM solution of DNA-like molecules, it would take days for a sufficient number of molecules to accumulate on the detector and be measured. And even if the length of time wasn't a concern, the measurement would be inaccurate because of issues such as nonspecific adsorption and sample degradation.

The limitation does not come from the detector but from the transport of analytes

by mass action. It could be overcome by using, for example, flux to direct analytes toward the detector. But flux only enhances detection sensitivity by a small amount in nanodevices. Sheehan and Whitman suggest that if the increase in S/N is less than the decrease in device dimensions, then miniaturization of the device may not be the appropriate approach because of the limits imposed on analyte flow by conventional microfluidics. (*Nano. Lett.* **2005**, *5*, 803–807)