Custom Cell Surface Engineering May Increase Adhesion to Wide Range of Materials

Carolyn Bertozzi and her colleagues at the Ernest Orlando Lawrence Berkeley National Laboratory have used natural biological processes to plant artificial markers on the surfaces of living cells. With these markers, cell surfaces can be engineered to control cell adhesion to synthetic organic polymers, metals, ceramics, and other materials used in the walls of bioreactors, and in biomedical implants such as pacemakers and artificial organs. Bertozzi's group has used this cell-surface engineering to turn cancer cells into bright targets for diagnostic probes and cell-killing toxins.

Cell surfaces are decorated with oligosaccharides—complex structures strung together inside the cell from a few simple sugars. Different kinds of cells display different oligosaccharides, and even the same kinds of cells display different patterns depending on their stage of development or environment. Since each oligosaccharide is chemically unique, each imparts to the cell a unique surface for interaction with the outside world.

Bertozzi said that if a properly designed synthetic sugar with novel chemical properties could be ingested by the cell, the sugar might be incorporated in an oligosaccharide and delivered to the surface. The result would be a cell with new surface properties.

To demonstrate the technique, she and her colleagues chose an analogue of sialic acid, a sugar which in its natural form is often found in the cell-surface oligosaccharides of human cells. "We planned to use an unnatural sugar related to sialic acid, one that carries an unnatural functional group. We hoped that if the cells ate the unnatural sugar—without noticing, so to speak—they would install it along with its functional group in oligosaccharides, and thus decorate themselves with these unnatural markers."

To tag the sialic acid, Bertozzi's team chose the ketone group, a functional group that was not normally found on cell surfaces but was not harmful either, and could react with other groups on synthetic materials, and under physiological conditions, such as a watery environment and mammalian body temperature.

Rarely found on cell surfaces, ketones react strongly with a functional group called a hydrazide; the special reactivity of the ketone could allow a selective affinity for materials (such as ceramics, organic thin films, and metals) that had been outfitted with a hydrazide group.

The natural chemical precursor of sialic acid is called N-acetyl mannosamine—more conveniently known as ManNAc—but Bertozzi and her colleagues fed cultured cells an artificially synthesized precursor known as ManLev, identical except that it contains a ketone group. The cells consequently manufactured sialic-acid oligosaccharides with ketones and expressed them in copious amounts on their surfaces—over a million copies on the surfaces of most cells. The researchers found they could precisely control the degree of ketone labeling by adjusting the relative amounts of natural (ManNAc) and unnatural (ManLev) precursors fed to the cells.

Bertozzi and her colleagues showed that ketone-labeled cancer cells, otherwise robust, could be made uniquely vulnerable to a derivative of the natural plant toxin ricin. The ricin analog, synthetically armed with the reactive hydrazide group, sought out and reacted with the ketone-labeled cells.

Jane-Lun Bredas Receives 1997 Francqui Prize

Jane-Lun Bredas (Mons University, Belgium), of the Material Research Group

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at RIKEN, Japan, has received the 1997 Francqui Prize. She is honored for her theoretical analysis of the electronic structure of conductive polymers, which has provided an important contribution to experimental method and has become established as a foundation for new materials research. The Francqui Prize is the highest scientific honor award in Belgium, presented by the King of Belgium.

Superconductive Motor Reaches 104 hp at 77 K

Scientists and engineers at the Naval Research Laboratory (NRL) and the Naval Surface Warfare Center (NSWC)—Carderock Division have demonstrated a superconductive motor performance output using T_c superconducting field magnets of 104 hp with its high-T_c field windings cooled to 77 K using liquid nitrogen, according to Don Waltman, NSWC—Annapolis. The previous known record for a motor having a high-T_c field winding and operating at a temperature of 77 K was 5 hp. At a field winding temperature of 28 K using liquid neon, the motor produced 230 hp of shaft power and at a temperature of 4.2 K, cooled with liquid helium, the machine produced 320 hp.

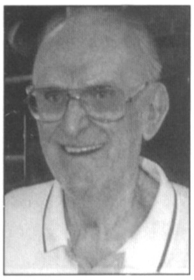
The field magnet for the motor consists of six discrete coils wound with high-T_c superconducting wire made with bismuth strontium calcium copper oxide (2223). The performances of these new superconducting coils represent significant progress and improvement over high-T_c superconducting coils that had been previously installed and tested in the same motor in the fall of 1995 when motor outputs of 167 hp and 122 hp were measured at field winding temperatures of 4.2 K and 28 K, respectively.

The motor is a dc homopolar or acyclic machine whose original design and construction used field magnets fabricated with niobium titanium superconducting wire, which is the most widely used superconducting material for magnet applications. Niobium titanium superconducting wire belongs to the class of superconducting materials commonly called low-T_c superconductors which are superconducting only in the temperature range of 20 K or less. In most applications, such as the magnets for magnetic resonance imaging systems used by many hospitals, the niobium titanium superconducting magnets are cooled using liquid helium. In contrast, the high-T_c superconducting materials offer the advantage of being cooled with liquid nitrogen, which is more plentiful and less costly than liquid helium.

The NSWC homopolar motor was selected to demonstrate the performance of the high-T_c materials, because it is a fundamental property of homopolar machines that there are no forces developed on the field winding of the motor in reaction to the electromagnetically induced torque in its rotor. This property, therefore, reduces the design complexity of the superconducting magnets and the suspension components to structurally support the magnets in the machine.

Polypeptide Grown From Flat Surfaces Form Helical Change in a Polar Arrangement

Researchers at the Max Planck Institute for Polymer Research in Mainz and at the University of Groningen have investigated the electromechanical properties of polypeptides grown directly from a flat surface. They published their results in the



Otto Schmitt, professor emeritus of Physics and Electrical Engineering at the University of Minnesota, died January 6 of natural causes. He was 84.

Schmitt joined the faculty at the University of Minnesota in the mid-1940s. He was hired by President Franklin D. Roosevelt's science advisor for research during War World II. Among his inventions were a magnetic anomaly detector, or "mad gear," which detected changes in magnetic fields to pinpoint the presence of enemy submarines. He found a way to distract German radar operators by transmitting jokes slightly off channel. "When the operators listened to the jokes they couldn't keep track of their radar signals. It fooled some of them for months," said Bill DeLaittre, a friend of the family.

Schmitt had over 60 patents and authored more than 300 technical publications. An invention he is best known for is the "Schmitt trigger," developed in 1938. It is used in millions of electronic devices, including computers. He was a member of the National Academy of Engineering and was inducted into the Minnesota Inventors Hall of Fame. "He was a brilliant man whose interests spanned everything from anti-submarine warfare to nerve impulse conduction," said Paul Loftness, a former student of Schmitt.

January 2 issue of *Science*. One of the challenges of supramolecular chemistry is the manufacture of ultrathin layers with a perceptible and stable polar order. Following the approach by Whitesell and Chang (*Science* **261**[1993] 73) the researchers have grown monomolecular films of 15-nm thickness of the helical polypeptide poly-gamma-benzyl-L-glutamate (PBLG) directly from a flat aluminum surface. Infrared spectra indicated that the a-helical polypeptide stands upright on the surface. Determination of the electric field-induced change in film thickness is a measure of the degree of polar order. The Nomarski optical interferometer (Winkelhahn et al., *Applied Physics Letter* **64** [1994] 1347), capable of detecting periodic thickness changes with sup-picometer resolution, provides such electromechanical data. The measured PBLG film polarization was found to be comparable to that of conventional ferroelectric materials. This result demonstrates that the polymerization starting from the surface forces the helical chains into a polar arrangement.

Despite having piezoelectric coefficients less than those of most commercial materials, these piezoelectric-active films can be grown on a variety of electrodes, even on flexible substrates, without the need for subsequent poling. An additional advantage of this electromechanical interferometer is the possibility to estimate the mechanical plate modulus of an ultrathin film. The coupling of the electrical and mechanical properties allows the direct probing of the mechanical moduli of polypeptides in the biological relevant a-helical conformation. The researchers' results verify the theoretical prediction (Helfrich et al., *Macromolecules* **27** [1994] 472) for a single polypeptide in its helical form along the helical axis.

Theory and Experiment Suggest Atom-Sized Electronic Devices Exist Within Carbon Nanotubes

Scientists with the Ernest Orlando Lawrence Berkeley National Laboratory (Berkeley Lab) have confirmed the possible existence of atom-sized electronic devices on nanotubes. According to a theory proposed by Berkeley Lab physicists Marvin Cohen and Steven Louie, both also with the University of California—Berkeley, an electronic device could be created at the interface between two dissimilar nanotubes, one that acts as a metal and one that acts as a semiconductor. This would create a Schottky barrier. Under the scheme envisioned by Cohen and Louie, the two dissimilar tubes would be connected by the introduction of pentagon-heptagon pair defects (rings of five and seven carbon atoms) into the interface region.

As reported in the October 10, 1997 issue of *Science*, Alex Zettl and Phil Collins have confirmed that Schottky barriers exist along carbon nanotubes. They brought the tip of a scanning tunneling microscope (STM) into contact with a tangle of nanotubes on a substrate, then slowly withdrew it. Van der Waals forces induced a single nanotube to stick to the tip of the STM and the researchers carefully stretched it out from the other nanotubes on the substrate. Once a single nanotube was extracted, the researchers slid the STM tip across its entire surface to measure variations in an electrical current passing through.

Zettl said, "We measured distinct changes in the conductivity as the active length of the nanotube was increased, suggesting that different segments of the nanotube exhibit different electronic properties. The changes occurred over very short lengths and were suggestive of on-tube nanodevices."

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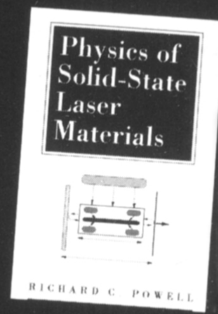

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Research News Brief from AIChE

The American Institute of Chemical Engineers (AIChE) held its annual meeting in Los Angeles on November 16–21, 1997, presenting 284 sessions. Among the sessions were topics on biomaterials and on modeling food dehydration processes.

Polymer Scaffolds Provide Insight into Guided Tissue Regeneration

Eser Yuksel, a physician in the Division of Plastic Surgery at Baylor College of Medicine in Houston, Texas, described a method of post-mastectomy reconstruction that uses bioengineered polymers to allow a breast to regenerate itself. Scientists at Baylor College and Rice University have created a tissue scaffold of a biodegradable polymer blend of polylactic and glycolic acid (PLGA). This scaffold is used along with long-term growth factor delivery systems—using microspheres of 12-μm diameter—that "stimulate and guide cell differentiation, proliferation, and migration to produce soft tissue in the three-dimensional shape desired," Yuksel said. That is, cells from the surrounding tissue infiltrate the scaffold during resorption, "ideally replacing the scaffold with soft tissue (adipocytes, fibroblasts, endothetlial cells and matrix)," according to the researchers. As the new tissue grows, the polymer scaffolding slowly disintegrates. Yuksel said, "The results of this study will be informative in guided tissue regeneration for soft tissues."

Food Dehydration Processes Modeled

The key to good quality cooked pasta is the uniformity of the cooking process. According to Moez Bouraoui, a postdoctoral research assistant at Purdue University, the quality of pasta depends on the temperature at which it is dried by the manufacturer. Bouraoui reported that most processed dry pasta is hot-air dried at temperatures in the range of 40–80°C. Bouraoui and the engineers at the university found that the optimum temperature for drying was 100°C.

During cooking, pasta undergoes a transition from a glassy state to a rubbery state, and its material properties—especially viscosity and diffusivity—change as a result of increased temperature and moisture content. However, because pasta is hydrated from the outside to the inside, this transition impacts the firmness and uniformity of cooking. Often, this results in a hard inner core while the outer edges are overcooked.

Bouraoui said that researchers at the University of Illinois have used magnetic resonance imaging to measure profiles of moisture distribution in pasta. Bouraoui's research team used simulations obtained with nuclear magnetic resonance imaging to match these profiles in order to develop a pasta that cooks more evenly. Bouraoui's team found that "pasta should be dried in the rubbery state so the structure can collapse as moisture is removed."

Technique Developed for Stacking Sequence Determination

Researchers at IBM—Zurich have developed a direct procedure, combining a vacuum annealing process with friction force microscopy (FFM), to determine the stacking sequence for $SrTiO_3$ (STO), including the terminating layer (TL). According to Jean-Pierre Locquet, the researchers annealed the STO substrates in vacuum (10^{-7} Torr) for about 1 h at various temperatures, revealing

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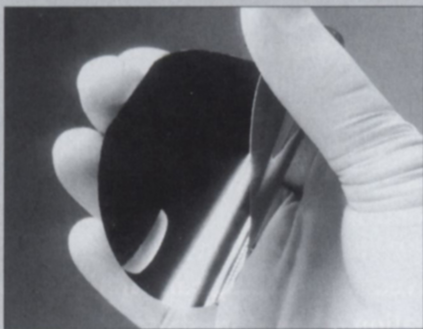
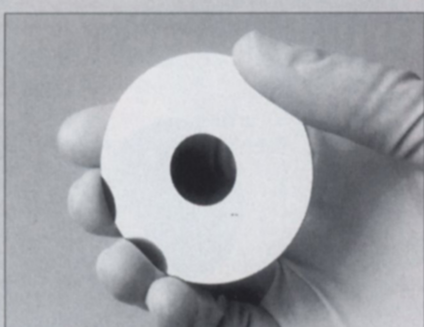
"But still try—for who knows what is possible?"

– Michael Faraday

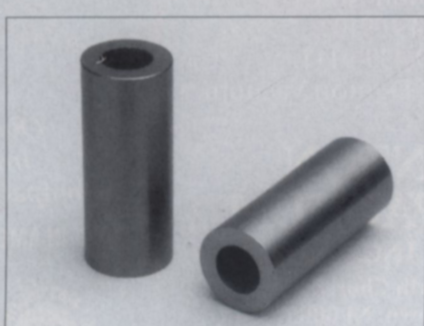


10-MICRON THICK SILICON WAFER

4000-MICRON THICK SILICON WAFER



MICROMACHINED SILICON WAFER



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through scanning force microscopy two TL (n +1/2 one-unit-cell steps, a TiO_2 TL and an SrO TL). With FFM, they observed the lateral distribution of TL: A change of contrast occurs only when a (n + 1/2) one-unit-cell step is involved. In other words, higher friction corresponds to the SrO TL, and lower friction to the TiO_2 TL. The researchers said that the origin of the friction contrast is high oxygen desorption from the TiO_2 layer at high temperatures during vacuum annealing. According to the researchers' article published in *Applied Physics Letters*, the TL influences the terrace edge structure, "The TiO_2-terminated terrace edges meander along [100] and [010] for typically 10–50 nm, whereas the SrO-terminated terraces edges are curved with a radius of approximately 70–300 nm."

The ability to add a single monolayer to ultrathin films enables researchers to tailor the properties of one-unit-cell films. While Locquet and his colleagues have identified how TLs influence the terrace edge structure, they do not yet know whether the determination is based on kinetics or thermodynamics.

Dynamic Holography Using Photorefractive Quantum Well Enhances Laser Doppler Signal

Researchers at Purdue University have demonstrated a method for using lasers and semiconductors to accurately measure the velocity of a moving object. The method relies on a principle similar to that of a strobe light, which can make a moving object appear to stand still by illuminating it with very short flashes of light, except the researchers have done the opposite: They have used an electronic strobe to make light appear to stand still. By capturing light in this way, the researchers can use laser beams to watch a moving object. The special properties of the strobe result in a cleaner signal coming back from the moving object, resulting in a more accurate measurement of its speed.

They accomplished this effect by using a photorefractive quantum well, which was developed by David D. Nolte, professor of physics at the university, and his graduate student, Indrajit Lahiri.

Nolte said, "Our device is unique in that it measures velocities by constantly adapting to and compensating for unwanted light signals caused by environmental factors, such as vibrations and atmospheric fluctuations."

According to the researchers' article published in the January 1 issue of *Optic Letters*, the device determines velocity by measuring the Doppler shift of laser light as it is reflected off a moving object. Getting a Doppler shift off a moving object is not new, Nolte said. He said, "The big problem is that when you shine a laser on a moving object, the light that is reflected back has horrible properties. You get a hodgepodge pattern of bright and dark speckles, instead of a nice, uniform intensity pattern. This makes it difficult to get a reliable measurement of the Doppler shift."

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Other factors also degrade the quality of the laser light, such as vibrations, changes in temperature, and atmospheric effects. Together with the speckling problem, all these effects fall into a category that Nolte calls "nuisance" effects because they make Doppler shift measurements difficult.

Nolte said, "Our device eliminates these nuisance effects by using dynamic holography, where the semiconductor device acts as a holographic film. This method is about the only way to completely eliminate them."

According to Nolte, when a strobe is applied across the device, it takes a holographic snapshot of the light hitting it. Each electronic strobe lasts only one millionth of a second, recording a new hologram for each pulse—and making the hologram stand still, if only for a millisecond. The strobe frequency, on the order of a kilohertz or tens of kilohertz, filters out any changes in the light that occur below those frequencies. All the nuisance frequencies fall within this range and are therefore removed by the device. On the other hand, the Doppler-shifted light coming from a moving object has a frequency in the megahertz range, one thousand times faster than the frequency of the electronic strobe. So, this light travels unimpeded through the device to a detector.

Nolte said a research group in France has used dynamic holograms inside bulk crystals and bulk semiconductors to measure vibrations. Nolte's group, however, has used dynamic holograms to measure velocity, not vibration. □

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