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Detecting DNA with Carbon Nanotube Arrays

- **Nanotube arrays are a thousand times more sensitive than current electrochemical biosensors**
- **Multiple targets can be detected at the same time**
- **Preparation of samples is much easier, and no labels are required**

Gene chips, biochips, DNA chips—they're all names for microarrays about the size of a postage stamp that help detect and identify specific sequences of DNA present in a sample solution. These amazing little chips capture and separate the DNA sequences onto hundreds of thousands of tiny cells or "spots" on the chip for subsequent analysis. The analysis, however, is often a complex process requiring bulky optical microscopes and/or readers, computer workstations, highly trained personnel, and of course time.

"That's less than ideal for NASA space missions," says Harry Partridge, deputy director of the Center for Nanotechnology at NASA Ames Research Center. "It would be better if astronauts could carry small chips that contain everything they need to diagnose their health—a small chip that could detect targeted DNA sequences from a drop of blood or small bit of body tissue and quickly provide an interpretive read-out right there on the chip."

Researchers funded by CICT's Information Technology Strategic Research (ITSR) Project have found a way to make this possible. According to Partridge, who is also manager of ITSR's bio-nanotechnology subproject, "Lead scientist Jun Li and his associates—including Hou Tee Ng, Alan Cassell, Wendy Fan, Hua Chen, Qi Ye, Jessica Koehne, Jie Han, and Meyya Meyyappan, director of the Center for Nanotechnology—have created a nanoscale electrochemical platform that can revolutionize the sensitivity and cost of the next-generation gene chips."

Targeting next-generation gene chips

Jun Li says, "The electrochemical approach has miniaturized biosensors beyond the limits of optical technologies and made it easy to interface with microelectronics, but until now it has not been able to effectively analyze small samples, such as a drop of blood.

"We have overcome this obstacle with an ultrasensitive nanoelectrode array that is based on carbon nanotubes," says Li. "We plan to use this technology to develop small, fast, low-cost, ultrasensitive and highly specific biosensors for next-generation gene chips."

A new electrochemical sensor platform

Current electrochemical biosensor platforms consist of metal or carbon electrodes functionalized with specific DNA probes—

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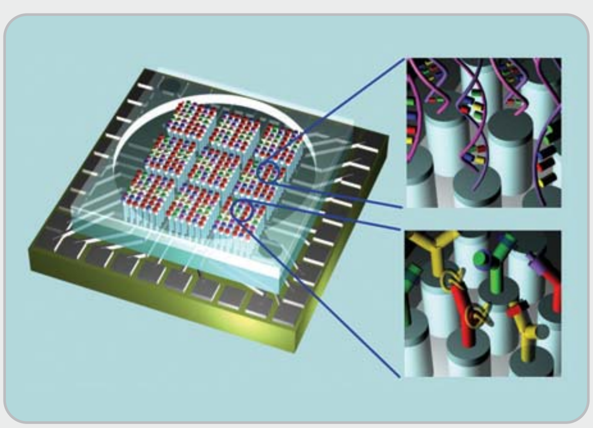

At left is an artist's conception of an ultrasensitive multiplex electronics biosensor based on a carbon nanotube nanoelectrode array. The insets on the right represent applications in DNA (top) and antigen detection (bottom).

Technology Spotlight

Technology

New electrochemical platform for biosensors and chemical sensors based on multiwalled carbon nanotube (MWNT) nanoelectrode arrays

Function

Detect and measure multiple DNA and/or chemical targets

Relevant Missions

- Exploration missions
- Space science missions
- Earth science missions

Applications

- Protecting crew in spacecraft and planetary habitats
- Early cancer detection and other medical diagnoses
- Homeland security

Features

- A thousand times more sensitive than current technology—detects target DNA sequences from less than one thousand strands
- Lower detection limits—less than 1,000 molecules
- Electrode radius sizes approaching biomolecules

Benefits

- Supports analytical applications that require reliable statistics and multiplex detection
- Supports use of lithography to precisely fabricate probe density
- Replaces optical sensor technology —no need for fluorophore labels

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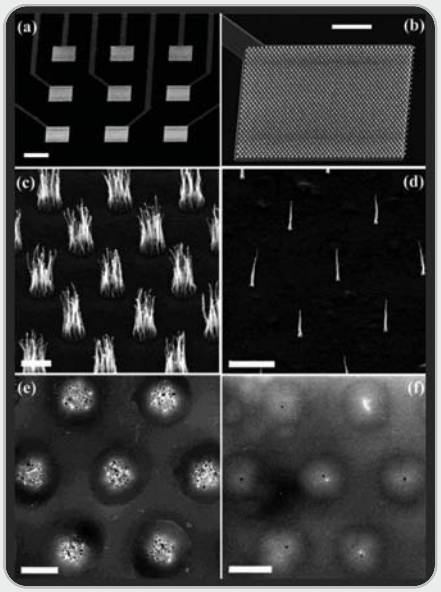

At left are scanning electron microscope (SEM) images of:
(a) a 3x3 array of electrode pads,
(b) an array of MWNTbundles on one of the electrode pads,
(c, d) an array of MWNTs at UV lithography and e-beam patterned Ni spots, respectively,
(e, f) the surface of polished MWNT array electrodes grown on 2-micrometer and 200-nanometer spots, respectively.

Panels (a-d) are 45 degree perspective views, and panels (e-f) are top views. The scale bars are 200, 50, 2, 5, 2, and 2 micrometers, respectively.

single-strand sequences, or one half of a potential pair. When a complementary DNA strand (the other half) is introduced to the sensor via a sample solution, the two strands combine, or hybridize, on the surface of the electrode. The potential of the electrode is then changed by the sensor, creating a chemical reaction that generates an electrical signal to indicate that the molecule is present (see illustration of matched pair on first page, top right).

By fabricating nanotube electrode arrays to replace the metal or carbon electrodes in this process, Li and his team have demonstrated a new technique that multiplies by a thousand the number of electrodes in the same small space. This increases the sensitivity of the sensor, and the probability of detection.

“Prior to our research, the electrochemical approach was limited by how small the radius of the metal or carbon electrodes could be,” says Li. “The smaller the radius, the higher the signal-to-noise ratio, and the faster the measurement,” says Li. “Unfortunately, when metal or carbon electrodes get too small, they become very difficult to fabricate. Multiwalled carbon nanotubes, however, have extremely high mechanical strength and high aspect ratios, making them much easier to fabricate as vertical nanoelectrode arrays. The individual nanotubes are also much smaller—a thousand times smaller—than conventional microelectrodes.”

With this new technology, an entire nanoelectrode array can fit into the area taken by just a single metal electrode in today’s arrays—about 20-30 micrometers (one micrometer equals 1,000 nanometers).The diameter of each multiwalled nanotube can be between 30 and 100 nanometers, and the spacing between them precisely controlled.

Growing the nanoelectrodes

Using the plasma-enhanced chemical vapor deposition (PECVD) technique, Li and his team grew a vertical array of nanotubes from nickel catalyst film. The spots of nickel were defined and spaced precisely using UV and e-beam lithography. The number of tubes grown at each spot can be varied by changing the thickness of the nickel film.

The nanotubes and their substrate are then encapsulated in silicon dioxide, using a tetraethoxysilane CVD process. This creates a mechanically stable and well-insulated matrix. The array is then chemically and mechanically polished to plane the top and expose just the tips of the vertical tubes, which become the electrodes. These electrodes are ultra-small in radius, extremely strong, precisely spaced, and well insulated from crosstalk.

“Carbon nanotubes offer a wide electrochemical window, flexible surface chemistry, and biocompatibility,” says Li. “By placing a thousand nanotube probes in the space of one of today’s metal electrodes, we can detect DNA sequences from less than a thousand strands. This is sensitive enough to directly measure mRNAs in a drop of blood or a piece of tiny tissue sample. It matches the upper limit of sensitivity of conventional laser-based fluorescence techniques, but doesn’t require time-consuming sample preparation and expensive and bulky analytical equipment.”

A wide range of applications

This new technology will benefit a wide range of fields, from clinical molecular diagnostics to pathology and drug discovery.

“Our technology can be developed into handheld devices for early diagnosis of diseases such as cancer in space and on Earth,” says Li. “The technology can be used to create immunosensors, too. By functionalizing the appropriate biomolecules with enzymes or antibodies and immobilizing them on the nanoelectrode arrays, you can build sensors to detect and quantify the presence of viruses or bacteria, and target specific pathogens, such as anthrax. The enzyme-based biosensors can be used for healthcare at home, and the pathogen sensors can be used for homeland security.”

–Larry Laufenberg

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