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RESEARCHERS FIND EFFICIENT WAY OF TESTING FOR PROSTATE CANCER

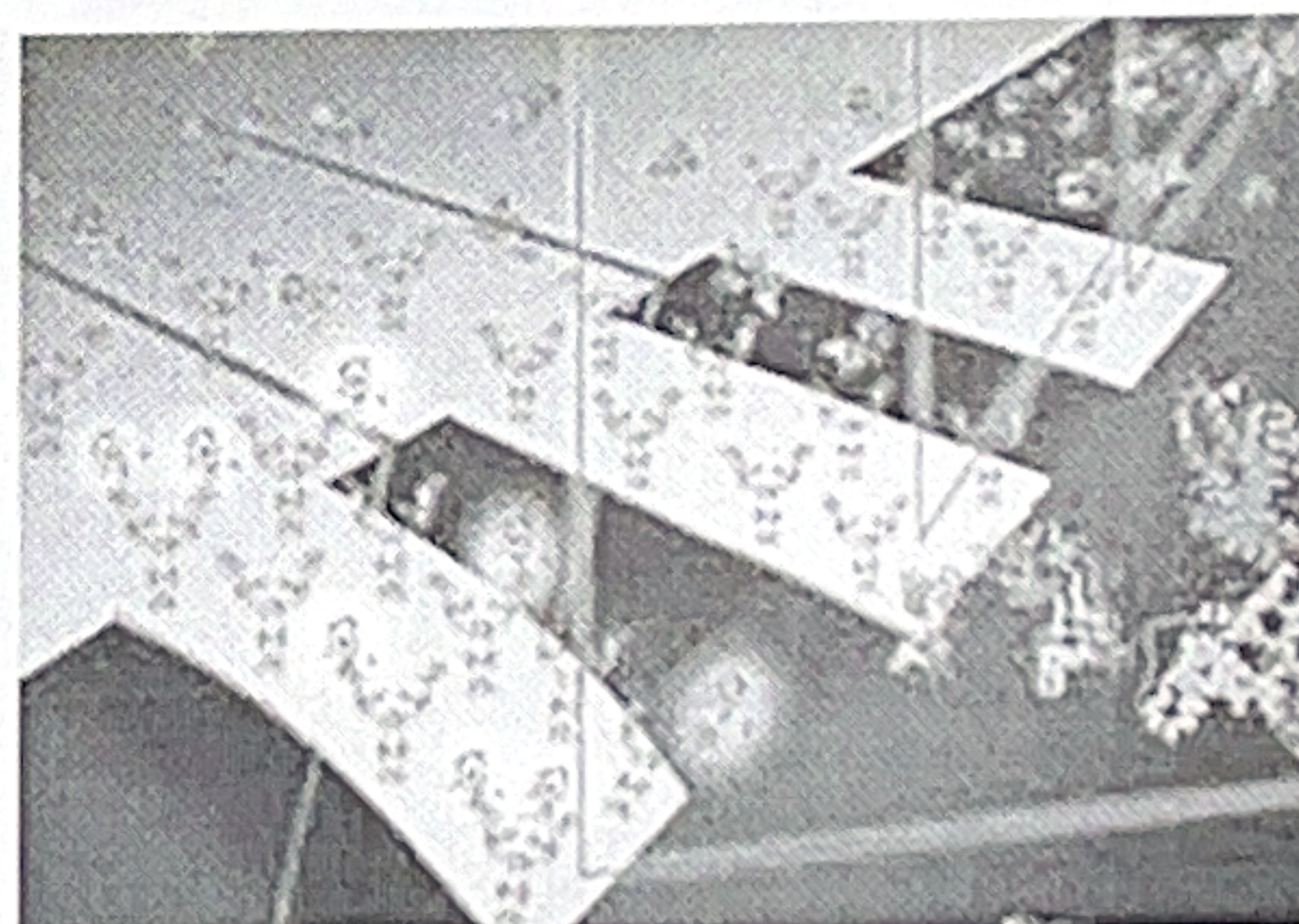
Sep 04, 2001 -

 By Rosemary Clandos
 Small Times Correspondent

Sept. 4, 2001 -- A team of researchers has developed a sensor that uses microscopic "diving boards" -- a technological development that could cut the cost of detecting prostate cancer.

Arun Majumdar, a professor of mechanical engineering at the University of California, Berkeley, published his findings Saturday in the journal *Nature Biotechnology*. The technique brings together tiny cantilevers -- developed in the past few years to detect DNA and other chemicals -- and protein chips, which are being commercially produced for analysis of DNA and RNA.

The researchers fastened a cancer antibody to the underside of a cantilever -- a sort of microscopic diving board -- on a silicon chip. When prostate specific antigen (PSA) was placed onto the device, it attached to the antibody and caused the cantilever to bend. A laser was used to measure the microscopic deflection. Researchers found a correlation between the degree of bend and the amount of PSA present.



The left cantilever bends as the protein PSA binds to the antibody. The other cantilevers are exposed to different proteins found in human blood serum.

This new technique is expected to lower costs because it eliminates the need for dyes and expensive instruments, said project co-researcher Thomas Thundat, a senior scientist at the life science division of the U.S. Department of Energy's Oak Ridge National Laboratory in Tennessee.

The current detection method -- ELISA, or enzyme linked immunosorbent assay -- requires several costly chemicals including a fluorescent color marker to be used with the blood sample.

The research findings indicated that the cantilever technology can detect PSA at .2 nanograms per milliliter, the same level as ELISA, but researchers expect the cantilever approach to become more sensitive as it is developed.

Majumdar's protein detection chip is similar to the DNA chips already being used in research labs and the biotechnology industry to simultaneously conduct hundreds of DNA analyses. Diseases such as diabetes, cystic fibrosis, AIDS and cancer that are characterized by a protein or DNA markers in the blood or urine could be analyzed with Majumdar's application for existing technology.

He said that more cantilevers will have to be used in parallel for each molecule detected, so a comparison can be made between the deflection of bound and unbound cantilevers.

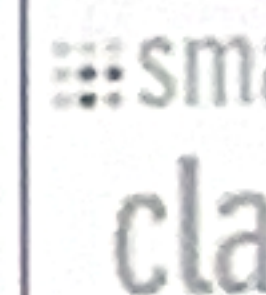
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The team is working on creating an array of cantilevers, but the number will depend on the specific application.

While prostate cancer has one specific marker, PSA, other cancers have many markers and they must be measured by several tests to determine the quantity of cancer-related proteins in the blood serum or specific tissue. Eventually, the technology is expected to be developed using about 100 cantilevers.

"This chip would allow us to do that in one test, not multiple tests and that would reduce costs," said Majumdar.

The research received funding from the National Cancer Institute's Innovative Molecular Technology Program and the U.S. Department of Energy.

A leading health official said she is intrigued by the potential of the emerging technology. "We have a very big investment in attempting to create tools to better define [early] signs of cancer," said Carol Dahl, director of the National Cancer Institute's office of technology and industrial relations. "The type of tools Majumdar is creating is one of the tools for that express purpose."

Other researchers who worked on the project include Guanghua "George" Wu, U.C. Berkeley graduate student; Richard J. Cote, a professor of pathology and urology at the University of Southern California's Keck School of Medicine; Ram H. Datar, USC visiting assistant professor of pathology; and Karolyn Hansen, postdoctoral fellow at Oak Ridge National Laboratory.

Jim Gimzewski, a professor of chemistry at UCLA, was one of the first researchers to develop cantilever technology as a sensor.

"It's a general purpose technology to detect various biological molecules," Gimzewski said. "It uses silicon microfabrication techniques. These techniques permit one to produce massive arrays – you can scale up the number of devices and the number of cantilevers on the device. So there's an established technology; one doesn't have to develop a new technology, it's proven in the field of microelectronics."

Majumdar said his biggest hurdle is to refine a chip with 20 or more cantilevers working together. He expects to be able to demonstrate the basic technology by the end of the year. "We still need to do a lot of work to demonstrate the technique in a clinical setting," Majumdar said.

At Protiveris Inc., a Rockville, Md.-based company, researchers have their radar tuned to Majumdar's new technology.

"We see strong commercial potential in the drug discovery and drug development market and in diagnostics," said Rob Menzi, vice president of operations for Protiveris, a biotech startup in Rockville, Md. "The big benefit is for biopharmaceutical companies who spend millions of dollars on research – they're after information."

Drug companies have a stock of proteins that are known to cause diseases. The proteins are tested against a panel of drug compounds. By using the cantilever technology, researchers will be able to see how strongly the proteins attach to the drug compounds.

Because Majumdar's technology does not include fluorescent dyes or tags, it will be more appealing for drug discovery. Drug molecules are commonly very small and fluorescent tags can interfere with the process of binding to a protein or enzyme, the researchers said.

Having previously funded and licensed some of Majumdar's earlier work with cantilevers and diffractive gratings, Protiveris is trying to incorporate that technology into a platform for drug discovery tools. They expect to launch a product within about 18 months.

Fariba Ghodsian, managing director and head of health care based research at Roth Capital Partners in Los Angeles, said that the technology aligns with the current HMO and cost-containment environment.

"There should be more emphasis on early diagnosis to reduce the cost of treatment," she

said. "If the technology is beyond proof of concept and there is some type of validation in laboratories or in animal models then its more appealing to investors.

"Researchers may have to push their products forward more before they approach venture capitals. They'd have to rely more on [government] funding to advance their project."

(Small Times Staff Writer Jeff Karoub contributed to this report).

