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Micro Electro Mechanical Systems

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ABSTRACT

The last two decades have seen significant advances in the development of micro electro mechanical systems (MEMS) for use as sensors. MEMS based sensors have applications in fields of science ranging from physical and chemical sensing to biological disease diagnosis. The major advantages of MEMS sensors over conventional sensors include their potential for higher sensitivity, lower cost, smaller sample size, and label-free detection. Another important distinction is that MEMS sensors can easily be multiplexed to simultaneously detect multiple analytes. MEMS technology holds promise as the next generation of high sensitivity sensors.

Keywords: MEMS, cantilevers, microcantilevers, nanocantilevers.

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INTRODUCTION

Most conventional micro and nano electro mechanical systems (MEMS and NEMS, respectively) are designed for detecting and sensing. The sensing principle varies according to the device, the nature of the analyte molecules, and the precision required. Capacitance, piezo resistance and resonance frequency are among the sensing principles depending upon the mechanical properties of the device. Micro machined cantilevers were first used as force probes in Atomic Force Microscopy (AFM). Their extreme sensitivity to several environmental factors, such as noise, temperature, humidity and pressure was immediately evident¹

Recent advances in microfabrication techniques have boosted the discovery of novel applications for micro and nano tools. Micro and nanocantilevers have been used as a new class of biosensors: they recognize proteins with exquisite sensitivity and can detect small amounts of materials, especially pathogen bacteria. This is a very useful property for medical diagnosis and food control. Directed micro and nanoelectromechanical devices, are also useful as highly sensitive and immunospecific multifunctional biological detectors. By measuring the change in resonance frequency, microcantilevers were shown to be sensitive to mass changes, with a better yield than piezoelectric gravimetric conventional sensors. The laboratories with MFA instruments displayed a substantial interest in cantilevers as a new platform for a variety of chemical and physical biosensors².

Cantilevers

Cantilevers (springboard) are nano mechanical biosensors, microfabricated with the standard silicon technology. Their sizes are in the micrometer or nanometer ranges (Figures 1 and 2). Due to their intrinsic flexibility, together with the availability of techniques designed to monitor bending, cantilevers have become versatile tools for SF This technology is already established and well documented as a multifunctional and highly sensitive technique, and a real time method useful for a variety of applications, such as plastic explosive detection using gas biosensors, whole microorganism detection as part of liquid biosensors, or DNA and proteins studies³.

Types of cantilevers

Nano cantilever

A strip of silicon carbide, a few hundred nanometres in width, whose vibrational frequency varies in proportion to the mass of objects resting on it. It can detect masses as small as one attogram. Over the last few years, nanocantilevers have even been developed to achieve attogram level sensitivity. Smallest micro electro mechanical system (MEMS) that can be easily machined

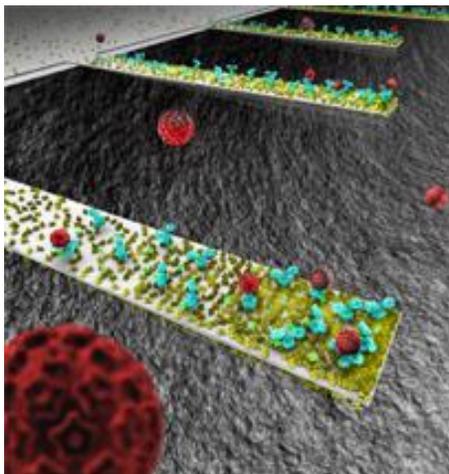


Figure 1. Nano cantilever

and mass-produced via the same techniques used to make computer chips. The ability to detect extremely small displacements make nanocantilever beams an ideal device for detecting extremely small forces, stresses and masses. Nanocantilevers coated with antibodies, for example, will bend from the mass added when substrate binds to its antibody, providing a detector capable of sensing the presence of single molecules of clinical importance⁴.

Micro cantilever

Microcantilevers are the most simplified MEMS based devices available for analyte sensing applications. Microcantilevers have been used successfully for physical, chemical and biological sensing work. In the field of medicine, microcantilever technology is specifically well-suited to disease screening, point mutation analysis, blood glucose monitoring, and chemical and biological warfare agent detection^{1,2}.

Although micro and nanocantilevers sensors are robust, their high throughput applications have been limited due to the technical hurdles involved in functionalizing these elements. A method for easy and reliable microstructure functionalization has been needed to drive cantilever technology into the realm of practical sensing applications. To meet this need, NanoInk has developed instrumentation and associated technology for directed placement of materials at the nano- to microscale. Here, we demonstrate the deposition of proteins on microcantilevers⁵.

1) Types of microcantilever:

Duo-/ Octosensis Microcantilever-Arrays are chips with mono crystalline silicon cantilever. These cantilever sensors can be used in static as well as in dynamic mode. Therefore the sensors are available with a cantilever thickness of 1 μm and 5 μm . Each thickness is available in 3 different kinds of length⁶.

a. Standard Cantilever

- Low tolerance: 300 nm thickness tolerance
- Precise resonance frequency: well defined bracing
- Easy handling: chips with vertical side walls, packed in sticking free PMMA Carrier on request.

Contamination free package: PMMA Carrier on request

b. Precision Cantilever

- Precision-Cantilever: 50 nm thickness tolerance
- Protocol available: Each cantilever measured with +/- 20 nm accuracy

Suitable for calibration of AFM's

Duo-/ Octosensis micro cantilever

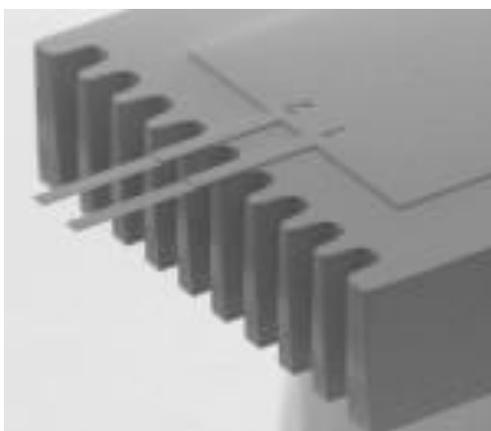


Figure 2. Duosensis Chip

- Duosensis: 2 cantilever per chip
- Octosensis: 8 cantilever per chip
- Cantilever length: 500 μm , 750 μm and 1000 μm
- Static mode: 1 μm cantilever thickness
- Dynamic mode: 5 μm cantilever thickness

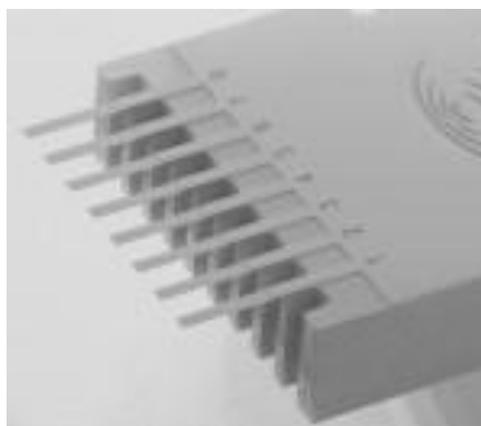


Figure 3. Octosensis Chip

FABRICATION OF CANTILEVERS

Materials Used in Commercial Cantilevers

The commercial cantilevers are typically made of silicon, silicon nitride, or silicon oxide and are available in a wide variety of different shapes, dimensions, and force sensitivities. Recent developments combine the latest integrated circuit (IC) and complementary metal oxide semiconductor (CMOS) technologies to produce intelligent extremely small cantilevers in the form of an array⁷.

Cantilevers Use in Non-Contact Modes

Recent years have witnessed a second evolutionary step in the use of cantilevers whereby they are no longer brought into contact with a surface. They are now used in sensor systems providing a completely new type of miniaturized transducer based on fundamental principles of physics like the bimetallic effect, surface stress, or the harmonic oscillator⁸.

APPLICATION OF CANTILEVER

Biosensing applications demand fast, easy-to-use, cheap and highly sensitive methods for detecting analytes along with the capability for high-throughput screening. All these points can be fulfilled by micromachined cantilever sensors, which are therefore ideal candidates for biosensing applications. The various applications of microcantilever based sensors are summarized in Figure 4⁸.

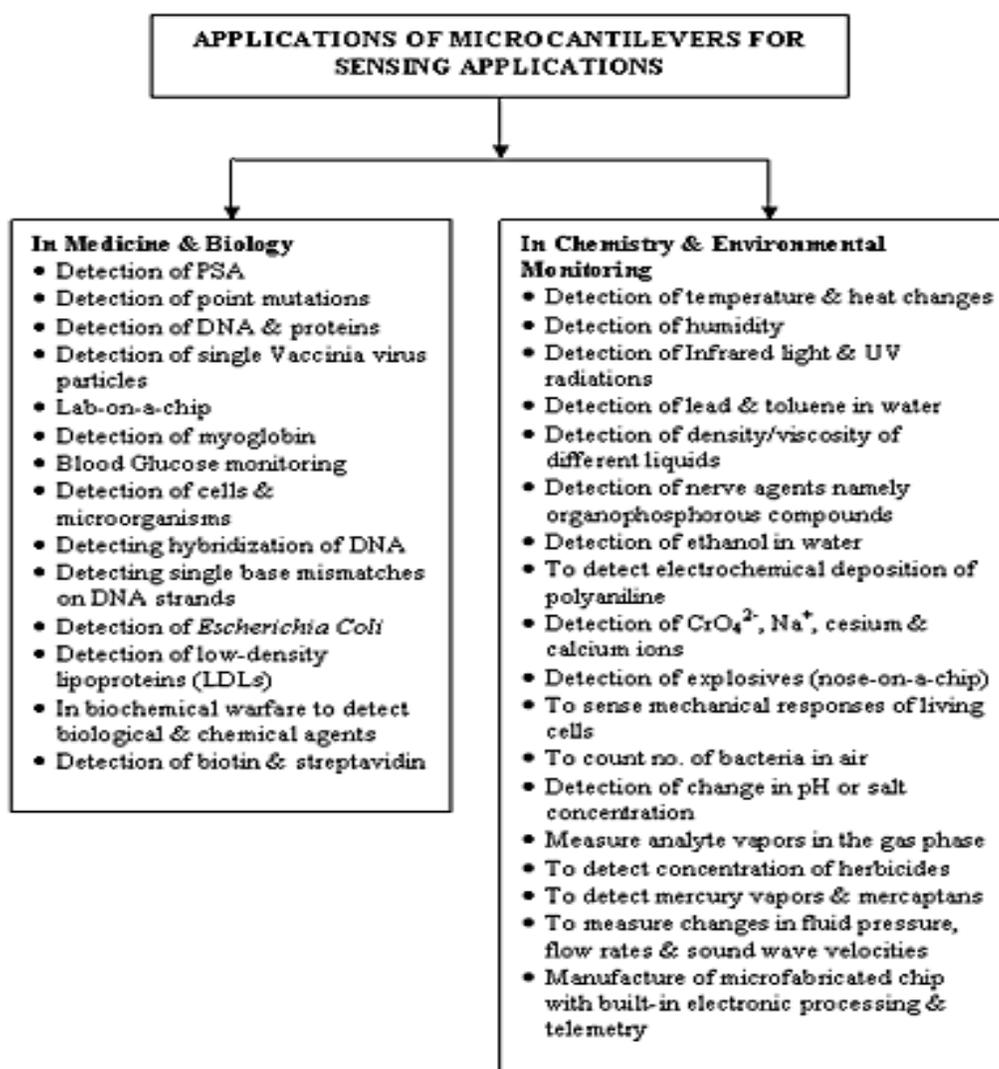


Figure 4. Applications of microcantilever-based sensors.

Microcantilever based sensors are the simplest MEMS devices that offer a very promising future for the development of novel physical, chemical and biological sensors. They are the most recent and most advanced analyte detection systems with the detection limit far lower than the most advanced techniques currently employed. The adsorbed mass of the analytes causes the nanomechanical bending of the microcantilever. The change in mass on the microcantilever surface due to the binding of the analyte molecules is directly proportional to the deflection of the microcantilever. Thus, qualitative as well as quantitative detection of analytes can be performed⁹.

Advantages of Microcantilever-Based Sensors

Microcantilever based sensors have enormous potential for the detection of various analytes in gaseous, vacuum and liquid medium. They have aroused considerable interest because of their high specificity, high sensitivity, simplicity, low cost, low analyte requirement (in μl), non-hazardous procedure with fewer steps, quick response and low power requirement. Substances at trace levels are currently detected by various techniques like high performance liquid chromatography (HPLC), thin layer chromatography (TLC), gas chromatography (GC), gas liquid chromatography (GLC) etc. However, these techniques are complex, time consuming, costly and require bulky instrumentation. Also sample preparation is a prolonged complex procedure and requires skilled personnel. But the microcantilever-based sensors can detect trace amounts of substances in parts-per-billion (ppb) and parts-per-trillion (ppt). They translate biomolecular recognition into nanomechanical bending of the microcantilever. Intermolecular forces arising from the adsorption of analyte molecules onto the microcantilever induce surface stress, directly resulting in nanomechanical bending of the microcantilever¹⁰.

TYPES OF SENSORS BASED ON MICRO AND NANOCANTILEVERS

Sensing Applications of Microcantilevers in Physics and Chemistry:

The cantilever-based sensors have extensive applications in physics and chemistry. They can be used to measure sound wave velocities, fluid pressures and flow rates, and can be tuned to selectively pick up acoustic vibrations. Biotoxins could be detected with sensitivity at the ppt level by coating one side of the cantilever with monoclonal antibodies specific for the particular biotoxin. The effects of small atmospheric-pressure changes can be felt in the resonance of the vibrating cantilever. Effects of exposure to ultraviolet radiations can be sensed by choosing the proper polymeric coating. It has been observed that silicon nitride cantilevers coated with gold on one side are quite sensitive to pH changes. Based on this, cantilever based sensors can be

made to detect the pH change. They have also been used to detect mercury vapor, humidity, natural gas, gas mixtures, toluene and lead in water¹¹.

Humidity Sensors

The humidity in the environment can be measured if one side of microcantilever is coated with gelatin. Gelatin binds to the water vapors present in the atmosphere, thereby causing the bending of the cantilever. Researchers at Oak Ridge National Laboratory (ORNL), USA showed that cantilevers coated with hygroscopic materials such as phosphoric acid can be used as a sensor for detecting water vapour with picogram mass resolution. When water vapors are adsorbed on the coated surface of the cantilever, there is change in the resonance frequency of microcantilevers and cantilever deflection. Sensitivity of microcantilevers can be increased by coating its surface with materials having a high affinity for the analyte¹².

Herbicide Sensors

Microcantilevers have been used to detect the concentration of herbicides in the liquid environment by Roberto Raiteri and co-workers. The herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) was coated on the upper surface of the cantilever. The monoclonal antibody against 2,4-D was then provided to the cantilever. The specific interaction between the monoclonal antibody and the herbicide caused the bending of the cantilever. A lot of research is going on to develop antibody coated cantilever immunobiosensors for the detection of organochlorine and organophosphorous pesticides and herbicides present at ng/l concentration in aqueous media. Alvarez and Co-workers demonstrated the use of microcantilevers for the detection of pesticide dichloro diphenyl trichloroethane (DDT)]¹³.

Metal Ion Sensors

Microcantilever sensors have been employed to detect a concentration of 10^{-9} M CrO_4^{2-} in a flow cell. In this device, a self-assembled layer of triethyl-12-mercaptododecyl ammonium bromide on the gold-coated microcantilever surface was used. Microcantilevers could be used for the chemical detection of a number of gaseous analytes. A multielement sensor array device employing microcantilevers can be made to detect various ions simultaneously¹⁴.

Temperature Sensors / Heat Sensors

Changes in temperature and heat bend a cantilever composed of materials with different thermal expansion coefficients by the bimetallic effect. Microcantilever based sensors can measure changes in temperature as small as 10^{-5} K and can be used for photo thermal measurement. They can be used as microcalorimeters to study the heat evolution in catalytic chemical reactions and enthalpy changes at phase transitions. Bimetallic microcantilevers can perform photothermal

spectroscopy with a sensitivity of 150 fJ and a sub-millisecond time resolution. They can detect heat changes with attojoule sensitivity¹⁵.

Viscosity Sensors

Changes in the medium viscoelasticity shift the cantilever resonance frequency. A highly viscous medium surrounding the cantilever as well as an added mass will damp the cantilever oscillation lowering its fundamental resonance frequency. Cantilevers can therefore be vibrated by piezoelectric actuators to resonate and used as viscosity meters¹⁶.

Calorimetry Sensors

In these sensors, only the temperature changes are to be measured. Most of the chemical reactions are associated with a change in heat. So, calorimetry has got tremendous potential to identify a wide range of compounds. Enzymes like glucose oxidase can be immobilized and coated on the surface of the microcantilever, which will react specifically with glucose in the solution producing a recognizable calorimetric signal. Due to the tiny thermal mass and sensitivity of the cantilever, calorimetry sensors employing cantilevers will be next generation of sensors for detecting temperature changes^{17, 18}.

Sensor Detecting Magnetic Beads

Microcantilevers can be used as force transducers to detect the presence of receptor-coated magnetic beads. It is possible to detect the presence of single μm size magnetic bead sticking onto the functionalized cantilever surface by applying an external magnetic field and measuring the deflection of the microcantilever. An extremely sensitive sensor can be made by labelling the analyte with magnetic beads¹⁹.

Cantilever Based Telemetry Sensors

Cantilever based telemetry sensors will deploy fieldable devices to relay pertinent data to central collection stations. They will enable the use of mobile units worn or carried by personnel and will replace wired sensors in some applications. Researchers at ORNL are building a microfabricated chip with built-in electronic processing and telemetry. They are also working on a method to detect different species²⁰.

Microsensors to Monitor Missile Storage and Maintenance Needs

Miniaturized microcantilever based sensors with remote wireless monitoring capability have been employed to gain insight into stockpile condition. This technology will evaluate ammunition lifetime based on environmental parameters like humidity, temperature, pressure, shock and corrosion as well as number of other indicators of propellant degradation including NOx. Single chip detectors with electronics and telemetry could be developed with several

hundred cantilevers as an array to simultaneously monitor, identify and quantify many important parameters. Corrosion sensors have limited life in moderate to severe environments. Systems have to be build to collect environmental data for better knowledge of environmental conditions. There is a need to develop materials like zeolites for use as sensitizing coatings for specific detection. Zeolites are thermally stable aluminosilicate framework structures used commercially as molecular sieves, catalysts, ion-exchangers and chemical absorbers. They show excellent selectivity and selective thermal desorption properties²¹.

Remote Infrared Radiation Detection Sensors

A remote infrared (IR) radiation detection sensor has been developed by Oden and co-workers. The sensor is made up of a piezoresistive cantilever coated with a heat absorbing layer. Piezoresistive microcantilevers represent an important development in uncooled IR detection technology. The cantilever undergoes bending due to the differential stress between the coating and the substrate. The cantilever bending causes a change in the piezoresistance, which is proportional to the amount of the heat absorbed. Temperature variations can be detected by coating the cantilever with a different material, which causes the bimetallic effect resulting in the bending of the cantilever. Thus, calorimetric detection of chemical reactions can be done. Gold-black would serve as the IR absorbing material. High thermal expansion bimaterial coatings such as Al, Pb and Zn could be used to increase the thermally induced bending of the microcantilever. Two dimensional cantilever arrays can be used for IR imaging as they are simple, highly sensitive and fast responding²².

Explosives Detection Devices

It is believed that dogs have got amazing smelling power, the reason they are widely employed in the detection of explosives. Dogs can detect explosives by sniffing easily vaporized organic chemicals present at concentration as low as parts-per-billion. Many groups are conducting active research with the intention of making a 'nose-on-a-chip' device having the smelling power exactly similar to the dog's nose. In this 'nose-on-a-chip' device, a microcantilever array could be used in which each cantilever will be coated differently to pick up a specific organic compound. It can be incorporated in our everyday use item like shoes, walking cane, purse etc. to detect the explosives without letting the culprits know about the search operation. The device would be a great achievement from the security point of view and would prevent large accidents. A microcantilever coated with platinum or a transition metal can react with trinitrotoluene (TNT) if it is heated to 570°C and held at that temperature for 0.1 second. The reaction of TNT with the cantilever coating will cause a mini-explosion. Thundat and his group. are developing a

matchbox-size device to detect explosives in airport luggage and landmines based on this technique^{23,24}.

Sensing Applications of Microcantilevers in the Field of Disease Diagnosis:

Cancer Detecting Microchips

Microcantilever based sensitive assay for the diagnosis of cancer. The surface of the microcantilever was coated with antibodies specific to prostate specific antigen (PSA), a prostate cancer marker found in the blood of patients having prostate cancer. When the PSA-coated microcantilever interacted with the blood sample of the patient having prostate cancer, antigen-antibody complex was formed and the cantilever bent due to the adsorbed mass of the antigen molecules. The nanometer bending of cantilever was detected optically by a low power laser beam with sub-nanometer precision using a photo detector. This microcantilever based assay was more sensitive than conventional biochemical techniques for detection of PSA as it can detect antigen levels lower than the clinically relevant threshold value. The technique is as good as and potentially better than ELISA. Moreover, the cost per assay is lesser as there is no need to attach fluorescent tags or radiolabel the molecules. The detection of PSA based on the resonant frequency shift of piezoelectric nanomechanical microcantilever had been demonstrated also by Lee and co-workers²⁵.

Myoglobin Detection Sensors

Raiteri and his group employed microcantilevers with anti-myoglobin monoclonal antibody coated on the upper surface by sulfosuccinimidyl 6-[3-(2-pyridyldithio)-propionamido] hexanoate (sulfo-LC-SPDP) cross-linker. When the human serum was provided, myoglobin bound to the anti-myoglobin, thereby causing a deflection of the microcantilever. 85 ng/ml of myoglobin was easily detected, which is the physiological concentration in the healthy human serum²⁶.

Glucose Biosensors

Pei and co-workers reported a technique for micromechanical detection of biologically relevant glucose concentrations by immobilization of glucose oxidase onto the microcantilever surface. The enzyme-functionalized microcantilever undergoes bending due to a change in surface stress induced by the reaction of glucose oxidase immobilized on the cantilever surface with glucose in solution. Experiments were carried under flow conditions and it was demonstrated that the common interferences for glucose detection had no effect on the measurement of blood glucose²⁷.

Biosensors for Coronary Heart Disease

A clinical biochemical sensor application was presented, where the adsorption of low-density lipoproteins (LDL) and their oxidized form (oxLDL) on heparin were differentiated by measuring the surface stress employing biosensing microcantilevers. The ability to differentiate these two species is of interest because their uptake from plasma principally favoured the oxidised form, which is believed to be responsible for the accumulation of cholesterol in the aorta in time and is associated with the first stage of coronary heart disease. The method was also used to detect conformational changes in two plasma proteins, Immunoglobulin G (IgG) and Albumin (BSA), induced by their adsorption on a solid surface in a buffer environment. This phenomenon is of crucial importance in biomedical applications involving solid surfaces, but has been difficult to measure with conventional adsorption techniques²⁸.

Cantilever Based Sensors to Detect Single-Nucleotide Polymorphisms

Single nucleotide polymorphisms (SNPs) within the known gene sequences and the genome are the main concern of the genomics research. Point mutations cause several diseases such as Thalassaemia, Tay Sachs, Alzheimer's disease etc. Therefore, efforts to detect the single nucleotide polymorphism will aid in the early diagnosis of these diseases and will help in the treatment of patients having such disorders. An effective and reliable way of detecting such single base pair mismatches is by using microcantilevers which are extremely sensitive to specific biomolecular recognition interactions between the probe DNA sequence and the target DNA sequence. They can detect concentration in the pico- to femtogram range. Thiolated DNA probes specific for the particular target DNA sequence are immobilized on the gold-coated microcantilever. Hybridization with the fully complimentary target DNA sequence will cause the net positive deflection of the cantilever. Net positive deflection is a result of reduction in the configurational entropy of dsDNA versus ssDNA, which causes the reduction of compressive forces on the gold side of the cantilever. Hybridization of the probe DNA with target DNA having one or two base-pair mismatches results in a net negative deflection of the cantilever due to increased repulsive forces exerted on the gold-coated surface of the microcantilever. The deflection is greater for target DNA having two base pair mismatches than for target DNA having one base pair mismatch. The degree of repulsion increases as the number of base pair mismatches increase^{29, 30}. McKendry demonstrated multiple label-free biodetection and quantitative DNA-binding assays on a nanomechanical cantilever array.

These DNA based microcantilever deflection assays would be a boon to the field of pharmacogenomics, which will develop drugs specifically made to target the SNPs. These assays

have a quick response time of less than 30 minutes and are much cheaper than the other techniques currently used to detect the SNPs. It is a simple procedure and the output i.e. the cantilever deflection is a simple +/- signal. Current hybridization detection techniques like Southern blotting require highly stringent reaction conditions while the microcantilever-based technique requires only a physiological buffer and room temperature (25°C). Details about the transformation of biomolecular recognition into nanomechanics are given in. Southern hybridization is very tedious, costly, hazardous and time consuming procedure. On the other hand, microcantilevers hold a great promise for the medical diagnosis because not only the presence but the location of the mismatches can be found³¹.

Biochips

Recent advances in biochips have shown that sensors based on the bending of microfabricated cantilevers have potential advantages over previously used detection methods. Biochips with mechanical detection systems use microcantilever bimaterial (e.g. Au–Si) beams as sensing elements. The Au side is usually coated with a certain receptor. Upon the binding of the analyte (e.g. biological molecules, such as proteins or biological agents) with the receptor, the receptor surface is either tensioned or relieved. This causes the microcantilever to deflect and the deflection was found to be proportional to the analyte concentration. Examples of bindings in biomolecular (receptor/analyte) applications are: antibody–antigen bindings or DNA hybridization of a pair of DNA strands (receptor/analyte) having complementary sequences. Biochips having microcantilevers as sensing elements do not require external power, labelling, external electronics or fluorescent molecules or signal transduction for their operation. These types of biochips can be used in screening certain diseases such as cancer and detecting specific chemical and biological warfare agents such as botulinum toxin, anthrax, and aflatoxin. A chemical sensor based on a micromechanical cantilever array has been demonstrated by Battison and co-workers^{32, 33, 34}

APPLICATION OF NANOCANTILEVERS

Detection of DNA Sequences

Nanocantilevers, 90 nm thick and made of silicon nitride, have been used by the group of researchers led by Harold Craighead, Cornell University to detect a single piece of DNA 1578 base pairs in length. The group claimed that they can accurately determine a molecule with mass of about 0.23 attograms (1 attogram = 10^{-18} gram) employing these nanocantilevers. The researchers placed nanoscale gold dots at the very ends of the cantilevers, which acted as capture

agents for sulfide-modified double-stranded DNA. But in principle, gold nanodots could be used to capture any biomolecule having a free sulfide group. Scanning laser beams were used to measure the vibrational frequency of the cantilevers. The researchers believe that nanodevices based on nanocantilevers would eliminate the need for PCR amplification for the detection of defined DNA sequences, thereby simplifying methods used to screen for specific gene sequences and mutations.

Similarly, N. Nelson-Fitzpatrick *et al.* at the University of Alberta, Canada have made ultra thin resonant nanocantilevers, of the order of 10 nm, in aluminum-molybdenum composites. The group claims that the development of NEMS-based devices in metallic materials would enable new areas of applications for the direct sensing of various chemical compounds thus obviating the need of intermediate surface derivatization^{35,36}.

Detection of Carcinoma

Nanoscale cantilevers - microscopic, flexible beams resembling a row of diving boards are built using semiconductor lithographic techniques. These can be coated with molecules capable of binding specific substrates-DNA complementary to a specific gene sequence, for example. Such micron-sized devices, comprising many nanometer-sized cantilevers, can detect single molecules of DNA or protein.

As a cancer cell secretes its molecular products, the antibodies coated on the cantilever fingers selectively bind to these secreted proteins. These antibodies have been designed to pick up one or more different, specific molecular expressions from a cancer cell. The physical properties of the cantilevers change as a result of the binding event. Researchers can read this change in real time and provide not only information about the presence and the absence but also the concentration of different molecular expressions. Nanoscale cantilevers, constructed as part of a larger diagnostic device, can provide rapid and sensitive detection of cancer-related molecules.

Detection of viruses, bacteria and pathogens

Nanocantilevers are used in designing a new class of ultra-small sensors for detecting viruses, bacteria and other pathogens.

The nanocantilevers, which resemble tiny diving boards made of silicon, could be used in future detectors because they vibrate at different frequencies when contaminants stick to them, revealing the presence of dangerous substances. Because of the nanocantilever's minute size, it is more sensitive than larger devices, promising the development of advanced sensors that detect minute quantities of a contaminant to provide an early warning that a dangerous pathogen is present.

The researchers were surprised to learn that the cantilevers, coated with antibodies to detect certain viruses, attract different densities — or quantity of antibodies per area — depending on the size of the cantilever. The devices are immersed into a liquid containing the antibodies to allow the proteins to stick to the cantilever surface. But instead of simply attracting more antibodies because they are longer, the longer cantilevers also contained a greater density of antibodies. The research also shows that the density is greater toward the free end of the cantilevers.

The engineers found that the cantilevers vibrate faster after the antibody attachment if the devices have about the same nanometer-range thickness as the protein layer. Moreover, the longer the protein-coated nanocantilever, the faster the vibration, which could only be explained if the density of antibodies were to increase with increasing lengths.

The work, funded by the National Institutes of Health, is aimed at developing advanced sensors capable of detecting minute quantities of viruses, bacteria and other contaminants in air and fluids by coating the cantilevers with proteins, including antibodies that attract the contaminants. Such sensors will have applications in areas including environmental-health monitoring in hospitals and homeland security. So-called "lab-on-a-chip" technologies could make it possible to replace bulky lab equipment with miniature sensors, saving time, energy and materials. Thousands of the cantilevers can be fabricated on a 1-square-centimeter chip.

The cantilevers studied in the recent work range in length from a few microns to tens of microns, or millionths of a meter, and are about 20 nanometers thick, which is also roughly the thickness of the antibody coating. A nanometer is a billionth of a meter, or approximately the length of 10 hydrogen atoms strung together. A cantilever naturally "resonates," or vibrates at a specific frequency, depending on its mass and mechanical properties. The mass changes when contaminants land on the devices, causing them to vibrate at a different "resonant frequency" which can be quickly detected. Because certain proteins attract only specific contaminants, the change in vibration frequency means a particular contaminant is present^{26,37, 38}.

CONCLUSION

Now the researchers reckon that the next step is to have on-chip electrical-based resonant frequency detectors, rather than using optical-based detectors. "There is also the challenge of [developing] a robust technique for attaching antibody molecules to the surface of the cantilever beams. And they are currently working towards techniques that will allow them to perform detection using the cantilevers in a viscous medium such as blood.

REFERENCES

1. Yue M, Stachowiak JC, Datar R, Cote R, Majumadar A. Label-Free Protein Recognition Two-Dimensional Array Using Nanomechanical Sensors. *Nano Letters*. 2008; 8: 520.
2. Grayson ACR, Shawgo RS, Johnson AM, Flynn NT, Li Y, Cima MJ, Langer R. A BioMEMS Review: MEMS technology for physiologically integrated devices. *Proc. IEEE*, 2004; 92(1): 6-21.
3. Arntz Y, Seelig JD, Lang HP, Zhang J, Hunziker P, Ramseyer JP, Meyer E, Hegner M, Gerber C. Label-free protein assay based on a nanomechanical cantilever array. *Nanotechnology*. 2003; 14: 86-90.
4. www.news.uns.purdue.edu/images/+2006/bashir-nanocant.
5. Sensor-microstructure-functionalization. www.nanoink.net.
6. www.micromotive.de/ggl/technology_e.php.
7. Stoney GG. The tension of metallic films deposited by electrolysis. *Proc. Roy. Soc. London A Mater*. 1909; 82: 172-75.
8. Polla DL, Erdman E, Robbins WP, Markus DT, Diaz JD, Rinz R, Nam Y, Brickner H. Microdevices in Medicine. *Ann. Rev. Biomed. Eng*. 2000; 2: 551-76.
9. Thundat T, Oden PI, Warmack RJ. Microcantilevers sensors. *Micro. Thermophys. Eng*. 1997; 1:185-99.
10. Wu G, Ji H, Hansen K, Thundat T, Datar R, Cote R, Hagan MF, Chakraborty AK, Majumdar A. Origin of nanomechanical cantilever motion generated from biomolecular interactions. *Proc. Natl. Acad. Sci. USA*. 2001; 98: 1560-64.
11. <http://monet.physik.unibas.ch/nose/>
12. <http://www.ornl.gov/info/ornlreview/rev29-12/text/instru>.
13. Alvarez M, Calle A, Tamayo J, Lechuga LM, Abad A, Montoya A. Development of nanomechanical biosensors for detection of the pesticide DDT. *Biosens. Bioelectron*. 2003; 18(5-6): 649-53.
14. Ji HF, Thundat T, Dabestani R, Brown GM, Britt PF, Bonnesen PV. Ultrasensitive detection of CrO₄²⁻ using a microcantilever sensor. *Anal. Chem*. 2001; 73: 1572-76.
15. Barnes JR, Stephenson RJ, Welland ME, Gerber C, Gimzewski JK. Photothermal spectroscopy with femtojoule sensitivity using a micromechanical device. *Nature*, 1994; 372:79-81.

16. Oden PI, Chen GY, Steele RA Warmack RJ, Thundat T. Viscous drag measurements utilizing microfabricated cantilevers. *Appl. Phys. Lett.* 1996; 68: 3814-16.
17. Berger R, Gerber C, Gimzewski JK, Meyer E, Guntherodt HJ. Thermal analysis using a micromechanical calorimeter. *Appl. Phys. Lett.* 1996; 69: 40-42.
18. Arakawa ET, Lavrik NV, Rajiv S, Datskos PG. Detection and differentiation of biological species using microcalorimetric spectroscopy. *Ultramicroscopy.* 2003; 97(1-4): 459-65.
19. Cherian S, Thundat T. Determination of adsorption-induced variation in the spring constant of a microcantilever. *Appl. Phys. Lett.* 2002; 80(12): 2219-21.
20. Britton CL, Warmack RJ, Smith SF, Wintenberg AL, Thundat T, Brown GM, Bryan WL, Depriest, JC, Ericson MN, Emery MS, Moore MR, Turner GW, Clonts LG, Jones RL, Threath TD, Hu Z, RochelleMarch JM. Battery-powered, Wireless MEMS sensors for high-sensitivity chemical and biological sensing. Presented at the 1999 Symposium on Advanced Research in VLSI, Atlanta, GA. 1999; 359-68.
21. Scandella L, Binder G, Mezzacasa T, Gobrecht J, Koegler JH, Jansen JC, Berger R, Lang HP, Gerber C, Gimzewski JK. Zeolites materials for nanodevices. *Micropor, Mesopor. Mater.* 1998; 21: 403-09.
22. Oden PI, Thundat T, Wachter EA, Warmack RJ, Datskos PG, Hunter SR. Remote infrared radiation detection using piezoresistive microcantilevers. *Appl. Phys. Lett.* 1996; 69: 2986-88.
23. Yinon J. Detection of explosives by electronic noses. *Anal. Chem.* 2003; 75: 99A-105A.
24. Baller MK, Lang HP, Fritz J, Gerber C, Gimzewski JK, Drechsler U, Rothuizen H, Despont M, Vettiger P, Battison FM, Ramseyer JP, Fornaro P, Meyer E, Guntherodt HJ. A cantilever array-based artificial nose. *Ultramicroscopy.* 2000; 82: 1-9.
25. Lee JH, Hwang KS, Park H, Yoon KH, Yoon DS & Kim TS. Immunoassay of prostate-specific antigen (PSA) using resonant frequency shift of piezoelectric nanomechanical microcantilever. *Biosens. Bioelectron.* 2005; 20: 2157-62.
26. Arntz Y, Seelig JD, Lang HP, Zhang J, Hunziker P, Ramseyer JP, Meyer E, Hegner M, Gerber C. Label-free protein assay based on a nanomechanical cantilever array. *Nanotechnology.* 2003; 14: 86-90.
27. Chen GY, Thundat T, Wachter EA, Warmack RJ. Adsorption-induced surface stress and its effects on resonance frequency of microcantilevers. *J Appl Phys* 1995; 77: 3618-22.

28. Battison FM, Ramseyer JP, Lang HP, Baller MK, Gerber C, Gimzewski JK, Meyer E, Guntherodt HJ. A chemical sensor based on a microfabricated cantilever array with simultaneous resonance-frequency and bending readout. *Sens. Actuators B*.2001; 77: 122-31.
29. Hansen KM, Ji HF, Wu G, Datar R, Cote R, Majumdar A, Thundat T. Cantilever-based optical deflection assay for discrimination of DNA single-nucleotide mismatches. *Anal Chem* 2001; 73: 1567-71.
30. McKendry R, Zhang J, Arntz Y, Strunz T, Hegner M, Lang HP, Baller MK, Certa V, Meyer E, Guntherodt HJ, Gerber C. Multiple label-free biodetection and quantitative DNA-binding assays on a nanomechanical cantilever array. *Proc Natl Acad Sci USA*. 2002; 99(15): 9783-88.
31. Fritz J, Baller MK, Lang HP, Rothuizen H, Meyer E, Vettiger P, Gunterodt HJ, Gerber C, Gimzewski JK. Translating biomolecular recognition into nanomechanics. *Science* 2000; 288: 316-18.
32. Fodor SPA, Rava RP, Huang XC, Pease AC, Holmes CP, Adams CL. Multiplexed biochemical assays with biological chips. *Nature*.1993; 364: 555-56.
33. Rowe CA, Tender LM, Feldstein MJ, Golden JP, Scruggs SB, MacCraith BD, Cras JJ, Ligler FS. Array biosensor for simultaneous identification of bacterial, viral, and protein analytes. *Anal Chem*1999;71(17): 3846-52.
34. Battison FM , Ramseyer JP, Lang HP, Baller MK, Gerber C , Gimzewski JK , Meyer E, Guntherodt HJ. A chemical sensor based on a microfabricated cantilever array with simultaneous resonance-frequency and bending readout. *Sens. Actuators B*.2001; 77:122-31.
35. Llic B, Yang Y, Aubin K, Reichenbach R, Krylov S, Craighead HG. Enumeration of DNA molecules bound to a nanomechanical oscillator. *Nanoletters*. 2005; 5(5): pp. 925-929.
36. <http://www.nsti.org/Nanotech2006/showabstract.html?absno=488>
37. Wu GH, Datar RH, Hansen KM, Thundat T, Cote RJ, Majumdar A. Bioassay of prostate-specific antigen (PSA) using microcantilever. *Nat. Biotechnol*. 2001; 19: 856-60.
38. Raiteri R, Nelles G, Butt HJ, Knoll W, Skladal P. Sensing of biological substances based on the bending of microfabricated cantilevers. *Sens. Actuators B*. 1999; 61:213-17.