SYMPOSIUM HH
Integrated Nanosensors
March 29 - 31, 2005

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* Invited paper
SESSION III: Perspectives on Research and Application Needs
Chair: Ivan Schuller
Tuesday Morning, March 29, 2005
Room 3014 (Moscone West)

9:30 AM *HH1.1
Harold Weinstock
Abstract: Not Available

9:30 AM *HH1.2
Frontiers in Integrated Nanosensors: Perspectives from the National Science Foundation. Arthur B. Ellis, Janice M. Hicks and Fillmore J. Bartoli; National Science Foundation, Arlington, VA, Virginia.

The National Science Foundation (NSF) is supporting a variety of basic research and education projects in sensor development and deployment that are related to the symposium theme of integrated nanosensors. Workshops have been held to identify emerging opportunities in sensor science and technology. In collaboration with professional organizations, NSF has also piloted outreach activities designed to foster novel sensor developments accessible to non-technical audiences.

10:00 AM *HH1.3
Integrated Nanosensors: Perspectives from DOE.
Terry Michalase, Center for Integrated Nanotechnologies, Sandia National Laboratories, Albuquerque, New Mexico.

To be determined.

SESSION HH2: Sensing Techniques I
Chair: Yvan Bruynseraede
Tuesday Morning, March 29, 2005
Room 3014 (Moscone West)

10:30 AM *HH2.1
Cluster Beam Deposition of Nanostructured Arrays for Chemical Sensing and High-Throughput Screening Applications. Emanuele Barborini, Enamante Staronczyn, Paolo Piseri, Gero Bongiorno, Antonella Taurino, Pietro Siciliano, Roberta Carbone, Ida Marangi and PierGiuseppe Pelicci; 1 Physics, Universita, Milan, Italy; 2 IMM, CNR, Lecce, Italy; 3 Experimental Oncology, IEO, Milano, Italy.

Deposition of clusters from the gas phase is becoming an enabling technology for the production of nanostructured devices. Among different experimental approaches, supersonic cluster beam deposition (SCBD) has been shown as a viable route for the production of nanostructured thin films. By using SCBD and by exploiting aerodynamic effects typical of supersonic beams it is possible to obtain very high deposition rates with a control on neutral cluster mass distribution, allowing the deposition of thin films with tailored nanostructure. Due to high deposition rates, high lateral resolution, low temperature processing, SCBD can be used for the integration of clusters with micro- and nanofabricated platforms with limited or no post-growth processing. Here I present the production and characterization of chemical microsensors for volatile organic compounds (VOC) based on nanostructured titania deposited on micromanipulated platforms. Aerodynamically filtered SCBD allows to control the nanoparticle size and the parallel deposition of arrays by using stencil masks. Since the material retains the memory of the precursor clusters, it is possible, by thermal annealing, to fabricate arrays with elements characterized by different crystalline phase, grain size and porosity. This allows a combinatorial approach to the large-scale fabrication of multi-element nanostructured devices. The interaction of the arrays with proteins, virus and cells will be also presented in view high-throughput screening applications.

11:00 AM *HH2.2
Porous Si Photonic Crystals as Sensors for Chemical Agents, Viruses, and Bacteria. Michael J. Sailor, Michael P. Schwartz*, Sara D. Alvarez*, Austin Derfus, Benjamin Migliori*; 1 Department of Bioengineering, University of California - San Diego, La Jolla, California; 2 Department of Biology, University of California - San Diego, La Jolla, California.

The synthesis of nanostructured porous silicon films and particles that possess the properties of photonic crystals will be described. With appropriate modification of the electrochemical preparation conditions, multilayered structures can be generated that behave as 1-D photonic crystals. These structures can be encoded and used as refractometric sensors. The particles contain a periodic porous nanostructure that defines the code. The periodic structure displays sharp maxima in the optical reflectivity spectrum at wavelengths that are controlled by the etch parameters. The intensity and wavelength of reflected light is determined in part by the refractive index of the porous nanostructure, which can be modified by binding of molecules within the porous matrix. The use of the optical properties of these materials in sensing of chemical agents, biomolecules, viruses and bacteria will be described.

11:30 AM *HH2.3
Immobilisation of Proteins by Size-Selected Nanoclusters on Surfaces. Richard Edward Palmer, Nanoscale Physics Research Laboratory, University of Birmingham, Birmingham, United Kingdom.

The controlled deposition of size-selected nanoclusters represents a novel route to the fabrication of nanostructured surfaces, generating lateral features of size 1-10 nm. This is precisely the size scale of biological molecules and provides a new method to immobilize individual proteins, with potential applications in structural biology, protein complex formation and high throughput medical diagnostics (microarrays). Scaling relations which describe both the implantation [1] and pinning [2] of the clusters enable the controlled preparation of 3D, nanoscale surface features, stable to temperatures as high as 700K. We report the pinning of size-selected AuN clusters (N = 1 to 100) to the (hydrophobic) graphite surface to create films of arbitrary (sub-monolayer) density. Gold presents an attractive binding site for such clusters and thus potentially for the cysteine amino acids in proteins, suggesting the possibility of residue-specific immobilization of oriented protein molecules. AFM measurements in liquid (buffer) solution show that GroEL chaperonin molecules (15 nm rings), which contain free cysteine residues, bind to the clusters and are immobilized [3]. The cysteine residues pair up to form disulfide bonds, and oncostatin molecules may similarly be immobilized. In both cases protein clusters are also formed. By contrast, green fluorescent protein (GFP) and luciferase molecules do not bind to the nanoclusters. Molecular surface area calculations confirm a model in which the availability of cysteine residues at the outer surface of the folded protein regulates whether the molecules attach to the clusters. The results demonstrate the general rules for, and generality of, protein immobilisation by metal cluster films. Finally, I will discuss very recent experiments with human IgG molecules which appear to present the first evidence that protein immobilization depends on cluster size. 1. S. Pratontep, P. Preece, C. Xirochaki, R.E. Palmer, C.F. Sanz-Navarro, S.D. Kenny and R. Smith, Phys. Rev. Lett. 90 055503 (2003). 2. S.J. Carroll, S. Pratontep, M. Streun, R.E. Palmer, S. Holoday and R. Smith, J. Chem. Phys. 113 7723 (2000); also Nature (News & Views) 408 331 (2000). 3. R.E. Palmer, S. Pratontep and H.-G. Boyen, Nature Materials 2 443 (2003). 4. C. Leung, C. Xirochaki, N. Berovic and R.E. Palmer, Adv. Mater. 15 223 (2004). www.nprl.bham.ac.uk

SESSION HH3: Sensing Techniques II
Chair: Michael Sailor
Tuesday Afternoon, March 29, 2005
Room 3014 (Moscone West)

1:30 PM *HH3.1

Traditional sensing approaches require one sensor for every analyte. As the number of analytes to be measured increases the array becomes more complex and the possibility for interference grows. An alternative sensing approach is based on principles derived from the mammalian olfactory system. Mammalian olfactory has sensor cells, each with a receptor protein that interacts with a range of volatile odorant molecules. The brain learns to recognize the pattern of signals associated with certain odors, rather than the response of individual highly selective cells. Here, we mimic Nature by fabricating single-walled carbon nanotubes into arrays of nanosensors on a single chip. We are using two-layer nanodevice assembly, which allows us to control each component to change the operation of the devices. While the nanotube layer defines the density and complexity of nanodevice arrays on the chip, we can fine-tune the devices by using an additional recognition layer. We use different catalytic metals and polymers as the recognition layers for the nanotube devices in order to achieve chemical diversity. Interactions between the recognition layer and the species result in a measurable change in the electrical characteristics of the nanotube transducer. We fabricate sensor arrays by polymer micro-spotting and electroplating several catalytic metals on the same

We have developed a novel bio-chemical sensor system based on silicon chip technology for electronic detection of biomolecules. The sensing element is an integrated MOSFET transistor, placed at the high stress region of the microcantilever. The reverse side of the microcantilever is functionalized with appropriate sensing layer. As selective binding occurs during bio-chemical exposure, the well-known bending of the cantilever leads naturally to significant, measurable and reproducible change in the output current - thereby providing a novel signal transduction mechanism. Such MOSFET-embedded microcantilevers in the present configuration provide significant advantage over conventional optical detection, including sensitivity, liquid-gas cell operation, and compactness. Our initial results indicate clear high sensitivity of MOS detection, down to less than 2 nm cantilever deflection. The location of the MOS chip is precisely calculated after numerous modeling and simulation. MOSFET platform not only improves the sensitivity, but also has almost negligible noise figure (large signal to noise ratio), ease of integration with CMOS and RF components. By use of stress sensitive MOSFETs as active loads, the size of the transistor is considerably reduced when compared to diffused piezoresistors. We have demonstrated the efficiency of this approach in a wide variety of biomolecular system, including DNA hybridization, protein-protein binding, among others. The presentation will cover device architecture and proof-of-concept sensing examples of biological and gas-chemical analytes.

In this presentation, I will describe an efficient, labor-free, site-specific, and high-throughput production of high-quality and individually addressable conducting polymer nanowire electrode junctions (CPNEJs) in a parallel-oriented array. Poly-aniline, poly-pyrrole and poly(EDOT) nanowires with uniform diameters (90-150 nm) were fabricated into CPNEJ in a precise manner by performing sequential electrochemical polymerizations in their respective monomer solutions. We have demonstrated this CPNEJ array functions as a miniaturized sensor for the parallel and real-time detection of gases and organic vapors. In principle, the number of CPNEJs can be scaled up indefinitely by increasing the number and packing density of the electrodes. Our ultimate goal is to generate a large library of CPNEJs into a densely packed sensor array by individually addressing certain junction electrodes in the presence of particular types of monomers.

Design Considerations of Solid State Devices for Integration with Immobilized Ion Channels. Daniel Fine1, Debarshi Basu1, Randolph Duran2 and Ananth Dodabalapur1

Semiconductor devices will be used will make it easy to incorporate signal processing circuitry and allow for easy scalability and low cost. Materials Science and Engineering, Northwestern University, Evanston, Illinois; 2Institute for Nanotechnology, Northwestern University, Evanston, Illinois; 3Material Science and Engineering, Northwestern University, Evanston, Illinois.

SESSION HH4: Physical Sensors

3:00 PM HH4.1 Spintronics Product Applications. Jim Daughton, NVE Corporation, Eden Prairie, Minnesota.

The past 15 years have seen revolutionary changes in the understanding and applications of phenomena involving electron spins. Beginning in 1989 with the first practical demonstrations of Giant Magnetoresistance (GMR), hardly a year has passed without some significant technical or product milestone. GMR multilayers were applied to magnetic field sensors in 1995 and GMR spin valves were applied to commercial read heads for hard drives shortly thereafter. A modified version of spin valves was also used for high performance, high density electronic isolators. Practical Magnetic Tunnel Junctions (MTJs) were demonstrated in 1995, and soon thereafter Magnetoresistance Random Access Memory (MRAM) development programs using MTJs were begun. MRAM product releases are planned in the near term by at least two companies. Modern MTJs use synthetic antiferromagnets which are “pinned” by an antiferromagnetic material. The first commercial MTJ read head has been introduced. Future products should make use of Spin Momentum Transfer (SMT), a mechanism by which a magnetic moment can be switched by spin injection. SMT has the potential of greatly reducing the power required to switch MRAM cells at very high densities. SMT devices may also have applications for very high frequency circuits. New data on all-epitaxial MTJs show promise for much higher magnetic sensitivity for new magnetic sensors.

3:30 PM HH4.2 Infrared Sensors for Small Scale Focal Plane Arrays. Gail J. Brown, Air Force Research Laboratory, Wright-Patterson AFB, Ohio.

Infrared imaging provides the means to detect and identify objects in the dark or under conditions of poor visibility such as fog or smoke. Infrared cameras are being used on a wide variety of commercial and military applications. The heart of the infrared camera is the focal plane array. The fundamental issues of implementing infrared imaging with small scale focal plane arrays will be reviewed. Special consideration will be given to issues involving small scale optical elements, area of regard, and image resolution. New infrared sensor
materials and devices with potential for integration on nanosensor chips will be presented. Results from recent studies of InAs/GaSb superlattice materials for uncooled, low power, mid-infrared detection will be highlighted.

4:00 PM HH4.3
Composite Nanowire-Based Sensors for Magnetic Resonance Force Microscopy. Mladen Barbić1 and Axel Scherer2; 1Physics and Astronomy, California State University, Long Beach, Long Beach, California; 2Electrical Engineering, Caltech, Pasadena, California.

We will present a nanowire-based methodology for the fabrication of ultra-high sensitivity and resolution probes for atomic resolution magnetic resonance force microscopy (MRFM). The fabrication technique combines electrochemical deposition of multi-functional metals into nanoporous polycarbonate membranes and chemically selective electroless deposition of an optical nanorefractor onto the nanowire. The completed composite nanowire structure contains all the required elements for ultra-high sensitivity and resolution MRFM sensor with: (a) magnetic nanowire segment providing atomic resolution magnetic field imaging gradients as well as large force gradients for high sensitivity, (b) noble metal enhanced nanowire segment providing efficient scattering cross-section from a sub-wavelength source for optical readout of nanowire vibration, and (c) non-magnetic/non-plasmonic nanowire segment providing the cantilever structure for mechanical detection of magnetic resonance.

4:15 PM HH4.4

We report on the investigation of mass sensitivity of cantilever based mass sensors as a function of mass-position. The experimental data are compared with results obtained using finite element analysis. The presented method can be used to enhance the performance of cantilever based mass sensors by using a functionalized particle and by scanning several modes of vibration of the cantilever. Hereby it is possible to achieve a significant increase in the mass resolution (g/Hz) and moreover the method makes it possible to determine the position of the added mass. In most cantilever based mass sensor systems the entire cantilever is coated with gold to which a reagent can bind. Adding a layer of gold degrades the performance of a resonating cantilever by lowering the Q-factor. As an alternative to use the entire cantilever surface for molecular adsorption (distributed mass) we investigate the effect of having an added point-mass and by moving this point-mass in the length direction of the cantilever we find the position yielding the highest mass sensitivity. The work consists of measurements on a micro cantilever with a single gold-particle positioned at different locations along the length axis, and the experimental data is compared to simulations performed using CoventorWare simulation tools. The experimental setup consists of a HeNe laser, which is focused on a micro cantilever with a length of 150 µm a width of 11 µm and a thickness of 1 µm positioned in a vacuum chamber. The position of the reflected beam is registered by a photo-diode, and the signal is measured using a HP4194A gain/phase analyzer. By scanning the cantilever using a nano-manipulator driven by the gain/phase analyzer the amplitude and phase of the resonating cantilever can be detected. A single gold-bead with a radius of 0.9 µm (corresponding to a mass of approximately 90 pg) is positioned on the micro cantilever. After which the first and the second resonance frequency of the cantilever is measured. This is performed several times for different positions of the gold-bead along the cantilever. The change in resonance frequency for the first four modes of the cantilever as a function of particle position along the length axis has been recorded. The theoretical results obtained using CoventorWare are compared with the experimental data and excellent agreement is obtained. The method presented can be used for enhancing the performance of cantilever based mass sensors since the Q-factor degrading gold deposition can be avoided. Using higher modes for detection it is possible to achieve a significant increase in the mass resolution (g/Hz) compared to the fundamental mode and moreover the method in principle grants a spatial resolution to the cantilever based mass sensor.

3:30 PM HH4.5
Dependence of Metallophthalocyanine Thin Film Structure on Substrate Temperature and in situ Annealing. Casey Miller, Ames Sharoni, Ge Liu, C. N. Calestine, Bernd Frühberger and Ivan K. Schuller; Physics, University of California, San Diego, La Jolla, California.

The crystal structure and topology of metallophthalocyanine (MPC) thin films were investigated by X-ray diffraction (XRD) and atomic force microscopy. The deposition temperature was varied in situ and the film properties were measured as functions of temperature and in situ annealing. FePc was deposited on A-plane sapphire (Al2O3) in an organic molecular beam epitaxy (OMBE) system equipped with a low temperature effusion cell. XRD data shows that all films were grown to thicknesses of the order of 50 nm for uncooled, low power, mid-infrared detection. The base pressure of the OMBE was better than 5x10-10 Torr and rose to 5x10-9 during deposition. The substrates were held at constant temperatures ranging from ambient to 300 °C during deposition. For each substrate deposition temperature, post-deposition in situ annealing at the same temperature was performed for 4, 8, and 16 hours. XRD results show the emergence of higher order peaks as deposition temperature increases. AFM results show the transition from a granular morphology at low temperatures and interesting, high density, pinhole-free MPC films. OMBE grown films are compared to others deposited using a simple thermal evaporator with a deposition pressure of 2x10-7 Torr. This work was supported by AFOSR MURI # FA9550-02-1-0288.

8:30 AM HH5.1
Metallophthalocyanine Chemosensors. William C. Trogler1, Karla Miller2, Andrew C. Kuromel3, Ivan K. Schuller4, Michael Hals1, Forest Bohrer5, Jeongwon Park6, Richard D. Yang7, Casey Miller2, Ngoc Tran8 and Bernd Frühberger9; 1Chemistry, University of California, San Diego, La Jolla, California; 2Physics, University of California, San Diego, La Jolla, California.

Chemosensors fabricated from amorphous and crystalline phthalocyanines on interdigitated electrodes have been prepared by both organic molecular beam (OMBE) deposition in ultra high vacuum conditions, as well as by spin coating. Film thicknesses have been varied between 20 and 1000 nm and the influence of annealing, electrode composition (Au, Pt, Pt, and Ni) have been evaluated. Variation of the central metal (Fe, Co, Ni, Cu, and Ti) alters the selectivity of the sensors to analytes. Toxic organic solvents, chemical warfare agent simulants, gaseous pollutants, and explosive vapors were among the analytes explored using an automated dosing system that allows simultaneous testing of up to 10 sensors. The role of the film structure (X-ray, STM, theoretical modeling) and molecular properties in detection selectivity will be discussed. Second generation devices employing interdigitated electrodes with a backside contact (field effect geometry) have been fabricated and offer improved stability and sensitivity.

9:00 AM HH5.2
NanoSensor Hemocyanin. Heinz Decker, Institute for Molecular Biophysics, Johannes Gutenberg University Mainz, Mainz, Germany.

Hemocyanins are freely dissolved multi-subunit respiratory proteins with up to 100 oxygen binding sites (1,2). Binding of oxygen is highly cooperative with Hill-coefficients of up to 11. The slope and position of the curve are strongly influenced by replacing competitive oxygen at the active site with other ligands such as CO (3,4) leading to an allosteric effect such as organic compounds (lactate, urate, phenols etc.), salts and heavy metals (1,5). In most cases hemocyanin remains stable and keeps the quaternary structure, although spectroscopical properties are affected. Thus, hemocyanins offer themselves as useful biosensors to detect those compounds and heavy metals in very low concentrations (1 to 100 000 molecules). The binding of a molecule oxygen between two copper atoms in a side on coordination quenches almost all tryptophan fluorescence within a subunit by a Förster process (7). In the case of the 24-meric tarantula hemocyanin about 340 tryptophans are involved. Two-photon excitation with high light intensity bleaches the Try-ﬂuorescence (8), so single hemocyanin molecules can not be observed by confocal microscopy. But at low light intensity oxygen binding could be monitored in vivo under non invasive conditions (9). In addition several fluorescence labels allow to record the amount of bound oxygen molecules by the hemocyanin (10) and opens the chance to identify single hemocyanin molecules by confocal microscopy. We calculated that depending on the surface, the immobilisation of the hemocyanin and the SVR of the device clusters less than 100 000 hemocyanin molecules could be monitored which allow to detect metals and organic compounds at a similar amount in future. Granted by BMWF Germany and DFG References 1. van Holde KE, Miller KL. (1995) Adv Protein Chem. 47:1-81. 2. van Holde KE, Miller KL, Decker H. (2001) J Biol Chem. 276:15563-6. 3. Decker H, Connelly PR, Robert CH, Gill SJ. (1988) Biochemistry 27:6901-4. 4. Menze MA, Heller M, Decker H, Grieshaber MK. (2000) Biochemistry 39:10806-11. 5. Kuiper HA, Forteini L, Chiancone
Adapting Molecules to Machines. Andrew Ellington, Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, Texas.

The best nanotechnology devices currently available are biopolymers. However, it is clear that many of the technical and engineering breakthroughs in the nanotechnology arena would make possible the design of very small devices with novel functionalities. To fully take advantage of both the potentialities inherent in biomimetic technology and the physical capabilities of designed nanostructure devices, it will be necessary to develop the other partners of the nanotechnology team: the sensors that can adapt via evolution (natural or directed), and the conformations of nucleic acid binding species (aptamers) that will be adapted to machines, rather than the other way around. To this end, we will describe several schemes for the selection of nucleic acids that will have specific binding and sensor functions in the context of engineered devices. In addition to being optimized via selection, the conformations of nucleic acid binding species (aptamers) can be engineered by simply changing Watson-Crick base-pairs. Between in vitro selection and secondary structural ("flatland") engineering, it should in general be possible to adapt nucleic acid biosensors to multiple different optical, electrochemical, and mechanical platforms.


Array based vapor sensing has emerged as a powerful approach toward the detection of chemically diverse analytes. We have developed a unique chemical detection technology [1-4] in which colorimetric changes in an array of dyes constitute a signal much like that generated by the mammalian olfactory system; each dye is a sensor that will be adapted to machines, rather than the other way around. To this end, we will describe several schemes for the selection of nucleic acids that will have specific binding and sensor functions in the context of engineered devices. In addition to being optimized via selection, the conformations of nucleic acid binding species (aptamers) can be engineered by simply changing Watson-Crick base-pairs. Between in vitro selection and secondary structural ("flatland") engineering, it should in general be possible to adapt nucleic acid biosensors to multiple different optical, electrochemical, and mechanical platforms.


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frequencies were monitored in the range of 100 kHz to 5 MHz. Methanol and nerve gas simulants dispropoportionate phosphonate (DIMP) vapors were found to shift the resonance frequency by 6 kHz and -2 kHz with respect to that of clean air. The magnitude of frequency shift in our thin films suggests that we are probing electronic charge relaxation processes. Since the magnitude of the shift is fixed and the mechanical analysis of the nanorods, it can be used to identify different analytes, thereby allowing chemically selective detection of gases on a single film. The technique holds great promise for chemical selective detectors which will not require the complicated recalibration process used with electronic noses.

**HH6.1**

*High Thermal Stability W2B Ohmic Contacts to ZnO Ozone Sensors and pH Sensors.* Laura Vasquez1, Kelly Ip1, Rohit Khanna1, C. J. Kuo1, I. Kravchenko1, B. S. Kang2, F. Ren3, Y. W. Heo1, D. P. Norton1, G. C. Chiu1 and S. J. Pearton1; 1Materials Science and Engineering, University of Florida, Gainesville, Florida; 2Electrical Engineering, Nusional Central University, Chung-Li, Taiwan; 3Chemical Engineering, University of Florida, Gainesville, Florida.

Thin films and single nanowires of ZnO can be used for detection of ozone and combustion gases. We have more recently shown that single ZnO nanorods with Ohmic contacts at either end exhibit large changes in current upon exposing the surface region to polar liquids introduced through an integrated microchannel. The polar nature of the electrolyte introduced led to a change in surface charges on the nanorod, producing a change in surface potential at the semiconductor /liquid interface. The nanorods exhibit a linear change in conductance between -12 of 5.8 Su/PF in the dark and 2200/PF when illuminated with 365 nm light. The nanorods show stable operation with a resolution of ~0.1 pF over the entire pH range. The results indicate that ZnO nanorods may have potential in integrated chemical, gas and fluid monitoring sensors. A key aspect of reliable sensor operation is the development of stable Ohmic contacts. We report the initial characterization of boride-based Ohmic contacts (based on W2B) which show exceptional thermal stability on ZnO. Conventional Ti/AI-based contacts show reactivity with ZnO at temperatures as low as 200°C. Our results show that the W2B contacts deposited by sputtering are slightly rectifying up to annealing temperatures of 300°C and convert to Ohmic thereafter. The reduction of contact reactivity with the semiconductor enables the sensors to operate to higher temperatures.

**HH6.2**

*Encoded Nanostructures for Ultra Sensitive Detection of Proteins and Nucleic Acids.* Chad A. Mirkin and Dimitra Georganopoulou; Chemistry, Northwestern University, Evanston, Illinois.

We have developed an ultra sensitive method for detecting protein and nucleic acid analytes in buffer and serum samples. In solution, an excess of magnetic microprobe probes functionalized with protein species and complementary nucleic acid species were added to bind their specific target. Using a magnetic field, the resulting complexes are pulled out of solution and the targets are sandwiched with nanoparticle probes, also functionalized with protein specific polyclonal antibodies or complementary nucleic acid DNA, unique to the target of interest. Magnetic separation of the complexed probes and targets followed by dehybridization of the barcode DNA from the nanoparticle probes allows one to indirectly determine the presence of the target by identifying the oligonucleotide released from the nanoparticle probe. Because the nanoparticle probe releases a large number of oligonucleotides per target binding event, there is substantial amplification and one can detect targets in the femtomolar to nanomolar concentration range.

SESSION HH6: Bio Sensors
Chair: A. Ellington
Wednesday Afternoon, March 30, 2005
Room 3014 (Moscone West)

**HH6.3**

*Highly Sensitive Polymer-Based Cantilever-Sensors for DNA Detection.* Montserrat Calleja1, Maria Nordström2, Mar Alvarez2, Laura M. Lechuga1, Anja Bölsø3 and Javier Tamayo1; 1Biosensors Group, CNM-CSIC, Tres Cantos, Spain; 2Dep. of Micro and Nanotechnology, MIC-DTU, Lyngby, Denmark.

Recent advances in microfabrication technologies have triggered new applications for micro/nano-tools. Microcantilevers, such as those used in Atomic Force Microscopes, have been recently employed as a new class of biosensors [1,2]. The so-called nanomechanical biosensors have demonstrated that they are capable of detecting single-base mismatches in oligonucleotide hybridization [2] as well as performing protein recognition [3]. With ongoing advances in nanotechnology, the advantages of nanomechanical biosensors are the potential for performing local, high resolution and label-free molecular recognition measurements on a portable device. Also, the reduced sensor area allows drastic decrease of the reagent consumption. Here we present a technology for the fabrication of polymeric cantilevers to be used as biochemical sensors. The fabrication process is based on spin coating of a photosensitive polymer and near-ultraviolet exposure. This microfabrication process is inexpensive, fast and reliable. Also, the polymer fabrication technique provides a convenient way to realize arrays of multiple sensors and to integrate them into a microfabricated biochemical analysis system. The feasibility of the application of a polymer cantilever for biological detection is demonstrated by measuring the immobilization process of thiolated single stranded DNA (ssDNA) on a gold-coated cantilever. The resolution of SU-8 cantilevers is compared to that of commercially available silicon and silicon nitride cantilevers. The high sensitivity of polymeric cantilevers envisages the development of sensitive DNA nanomechanical chips that could be integrated with microfluidics for sample delivery, providing fast and sensitive biosensors for real time measurements. References: [1] R. Ralteir, M. Grattarola, H. J. Buz, P. Sbildal, Sensors and Actuators B 79, 115-120 (2001) [2] J. Fritz, M. K. Baller, H. P. Lang, H. Rothuizen, P. Vetetjir, E. Meyer, H. J. G. L. Dehaen, Ch. Gerber, J. W. Gimzewski, Science 288, 316 (2000) [3] G. Wu, R. H. Datar, K. M. Hansen, T. Thundat, R. J. Cote, A. Majumdar, Nature Biotechnology, 19, 856-860 (2001) [4] M. Alvarg, A. Calle, J. Tamayo, L. M. Lechuga, A. Abad, A. Montoya, Biosensors and Bioelectronics, 18, 649 (2003)

**HH6.4**

*Multiplexed, Real-time Detection of Cancer Marker Proteins using Nanowire Arrays.* Guangfeng Zheng1, Fernando Patolsky1 and Charles M. Lieber1; 1Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachusetts; 2Division of Engineering and Applied Science, Harvard University, Cambridge, Massachusetts.

Detection of cancer marker proteins is critical to early diagnosis and subsequent treatment of cancers. Here we report the label-free, real-time multiplexed electrical detection of cancer marker proteins using antibody-functionalized nanowire field effect transistors (FETs). Both p-type and n-type silicon nanowire FETs were fabricated in a same device array to provide complementary electrical signals to the binding of the proteins, and therefore behave as an encoded nanosensor array.
3:30 PM HH6.5
Simultaneous Detection of Insulin, Glucose and pH Using Nanosensor Array, Souheil Zekri 2, Arun Kumar 1 and Ashok Kumar 1; 1Nanomaterial and Nanomanufacturing Research Center, University of South Florida, Tampa, Florida; 2Department of Mechanical Engineering, University of South Florida, Tampa, Florida.

Diabetes mellitus may be broadly described as a chronic, systemic disease characterized by abnormalities in the metabolism of carbohydrates, proteins, fats and insulin and abnormalities in the structure and function of blood vessels and nerves. A clear understanding of glucose insulin level and pH of the blood is helpful for diabetes to have better control over their problem. Keeping this problem in mind a nanosensor array was fabricated for the simultaneous detection of insulin, glucose, and pH. In this approach 23 nm thick nickel islands were deposited by e-beam evaporation on a silicon substrate that was patterned using a photolithography lift-off process. The square regions of 100 by 100 microns with four individual electrode contacts are fabricated for nanosensor array development. Multi wall carbon nanotubes (MWNT) were then grown over the Ni islands at 900°C using a CVD chamber. Carbon nanotubes grown over the nickel islands were further modified with catalyst, enzymes and functional groups to make them highly specific in detection of pH, glucose and insulin. A 0.1 M phosphate buffer containing glucose oxidase was added to a tetra-ethyl-ortho-silicate (TEOS) based sol gel medium to modify the carbon nanotube grown over the islands to detect specifically and selectively glucose molecules. Five micro-liters of this solution were deposited on one of the four distinct areas. Similarly, insulin detection was carried out using modified nanoelectrodes with antibodies and further another set of electrodes are modified with functional group to make them highly specific for pH detection.

Cyclic voltammetry was explored to obtain the analytical information in the form of an electrical signal that results due to the interaction of the target analyte and the recognition layer placed at the electrode surface. Interference and stability of each nanosensor was also performed using the same electrochemistry set up. The enormous surface to volume ratio allows for a very large number of biomolecules binding to the MWNT. Modified nanoelectrodes are currently being characterized using scanning electron microscopy (SEM), Fourier Transform Infrared spectroscopy (FTIR), UV visible spectroscopy.

3:45 PM HH6.6
Nanosensor for Cholesterol Detection, Arun Kumar 1, Thomas Gregale 2 and Ashok Kumar 2; 1Nanomaterial and Nanomanufacturing Research Center, University of South Florida, Tampa, Florida; 2Department of Mechanical Engineering, University of South Florida, Tampa, Florida.

Cholesterol is a lipid, which is a soft, fat like substance that in reasonable quantities is critical to good health. A blood test to determine your blood cholesterol (also called total cholesterol) level is now a routine part of most physical checkups. In fact, it is now recommended that all people over the age of 20 have their cholesterol checked every five years. In addition to checking your total cholesterol, your doctor will probably check your HDL cholesterol.

The main reasons for measuring the cholesterol level is to reduce risk of pulmonary and circulatory disease, and strokes. With early detection a person can reduce their cholesterol by modifying their diet and increased exercise and minimize the risk of heart attack. Studies for persons with high cholesterol show that a reduction of one percent in total cholesterol could possibly result in a reduction of heart attack risk by up to two percent. In the present approach the method has been developed for the detection of high cholesterol at early stage using modified nanoparticles. The modified nanoparticles are modified with functionalized polymers and ferricyanide which acts as an electron mediator. The functionalized polymer is linked with cholesterol oxidase (ChOx) and cholesterol esterase, by covalent coupling method. The modified nanoparticles behave as nanosensor which allows detection of total cholesterol accurately and more specifically in small sample sizes (micro liter) using surface contact voltammetric detection techniques. Nanosensors developed with modified nanoparticles further characterized with FTIR, SEM and UV-visible spectroscopy.

SESSION HH7: Integration
Chair: Ken Suslick
Thursday Morning, March 31, 2005
Room 3014 (Moscone West)

9:00 AM *HH7.1
Flow Cytometry on a Chip for Biological Sensing, Ye-Hwa Lo, Victor Lien and Nicole Justis; Electrical and Computer Engineering,
University of California-San Diego, La Jolla, California.

We present our results of flow cytometry on a chip based on a new technology platform of fluidic-photonic integrated circuit. The technology can potentially reduce the size of a flow cytometer, a key system for analysis, counting, and sorting of biological samples such as cells, by more than 1000 times. An array waveguide architecture and the technique of optical cross-correlation were developed to achieve high sensitivity optical (fluorescence) detection. Other mechanisms such as magnetic, electric, and acoustic fields can also be incorporated because it offers the device to further enhance the performance and functionality of flow cytometry on a chip for biological sensing.

11:00 AM *HH7.4 Nano- and Micropatterned Surfaces for Biointeractions. Bengt Herbert Kasemo, Applied Physics, Chalmers University of Technology, Gothenburg, Sweden.

Biofunctional surfaces [1] require advanced design and preparation to match the sophisticated (bio)recognition properties of biology. This requires combined topographic, chemical and visco-elastic patterns on surfaces, made by preparation and analytical methods from surface and materials science, biochemistry and molecular biology. Examples in this talk are: Cell mimicking membranes, cell force sensing using microfabricated cantilevers, optically active nano-particles for sensing, and microstructured materials, mimicking shark skin surfaces.

Supported biomembranes [2-4] can be made from unilamellar vesicles in the size range 25-200 nm. On SiO2 the vesicles first adsorb intact, and then they undergo a phase transition, where they rupture and fuse to a supported bilayer. We have studied the coverage dependence, vesicle size dependence and T-dependence of this process [4] using QCM-D [5], AFM and SPR. On TiO2, the vesicles (of the type used in our work) adsorb intact. If intact vesicles are deposited, the surface can be patterned by AFM into regions of alternating bilayer, vesicle, and empty surface [6]. These biomembranes are quite inert towards protein adsorption and cell growth [7]. By adding functional molecules to the membrane sensor [8] and surface-specific cell interactions [9] can be achieved. A cell force sensor based on nanofabricated, plasma-grafted gold cantilevers [7,10] promises as fast and cheap point-of-care devices as well as interesting research tools. The detection technique involves no labelling of the components which can increase the sensitivity significantly. Complete devices with polymer channels and polymer cantilevers with integrated metallic and carbon doped polymer strain gauges have furthermore been realized. For the silicon as well as the polymer based cantilever sensors we are currently pursuing hybrid system integration, where the sensor unit is packaged for specific handheld sensor applications. For mass detection we have realized silicon-based microcantilevers with integrated capacitive read-out and bulk-electrical actuations. Due to problems with high stray capacitances the sensor is monolithically integrated with a CMOS chip for on-chip amplification of the signal. The sensor has been used for detection of mass changes caused by controlled deposition of glycerine droplets and from these experiments a mass resolution of 3 ng/Hz has been deduced.

SESSION H8: Applications
Chair: Yvan Bruynseraede
Thursday, March 31, 2005
Room 3014 (Moscone West)

2:00 PM *HH8.1 Converging Technologies for Bioelectronic Applications. S. Borges, NEXT-ART, IMEC, Leuven, Belgium.

Till now the interaction between electronics and biology has been rather limited. Processing techniques well known in micro-electronics are used to fabricate arrays of DNA strands on glass substrates. Using fluorescent labels for detection, this so-called biochip has been very useful in gene research and its success spurs to other developments in the area of diagnostics. Non-labeled detection techniques were sought, which stimulated research in electronic translation of molecular recognition events both for DNA as well as diagnostic tools for protein recognition. But in almost all cases, a clear separation between biological elements and the micro-electronic system is made. Further developments in nano-technology and bottom-up techniques will change this and a new combination between biological elements and micro-electronics will take place. I will discuss the status of our research of a bio-electronic junction based on micro-electronic chips that allow real-time interaction with electrical and chemical neuronal communication on the scale of individual neurons. Some aspects of long term and sensitive neuron-electro interface will be discussed like a more intimate anchoring and interaction of the neuron with a bio-mimetic surface of the transducer. For the detection of...
neurotransmitters, enzymatic receptors adsorbed on a semiconductor surface constitute a hybrid organic/inorganic sensor. Semiconductors hold a considerable promise as chemical sensor platform. Also a lab-on-a-chip type biosensor will be discussed. For the operation of this transducer the analyte molecules have to be labeled with magnetic beads. A magnetic spin valve sensor can detect the magnetic beads. A possible advantage of this transducer is because beads can be used to direct the molecules over the surface of a chip and to attract and repel molecules from the surface.

2:30 PM *HHA.2
Development of Nanomechanical Biosensors for Environmental Control and Functional Genomics.
Javier Tanayo, Biosensors Group, CNM, CSIC, Tres Cantos, Madrid, Spain.

It has been recently demonstrated that molecular recognition on the surface of a microcantilever previously sensitised with biomolecular receptors alters the cantilever curvature and the vibration at nanometer scale. Both changes are referred to nanomechanical response. Among the virtues of this novel sensors are direct detection without need of labelling with fluorescent or radioactive molecules, very high sensitivity, small sensor area of ~1000 nm², and suitability for further integration using CMOS silicon technology. For first time, we have applied this principle for direct detection of the harmful pesticide DDT. A synthetic hapten of the pesticide conjugated with bovine serum albumin (BSA) was covalently immobilized on the gold-coated side of the cantilever by using thiol self assembled monolayers. Direct detection of DDT is proved by performing competitive assays, in which the cantilever is exposed to a mixed solution of DDT and its monoclonal antibody. On the other hand, we have studied the immobilization and hybridization of oligonucleotide monolayers by monitoring the microcantilever bending. The cantilever was functionalised with thiol-derivatised oligonucleotides, which forms self-assembled monolayers on the gold-coated side of the microcantilever. Surprisingly, DNA hybridisation on the cantilever produces a cantilever bending below the detection limit of sensor devices working with a single microcantilever. The different behaviour of the nanomechanical response for these two biological reactions (pesticide/antibody and DNA/DNA) lead us to carry on a comprehensive study of the origin of the nanomechanical response during DNA hybridisation. The nanomechanical response was compared with well-established techniques such as surface plasmon resonance, fluorescence, and radiolabelling. This study implied that the packing and structure of the immobilized single stranded DNA probes is critical to obtain a significant hybridisation response. In addition, the use of passive cantilevers acting as reference is critical to remove non specific signals, such as small temperature, pH and ionic strength variations. For this purpose, we have developed a new technique for readout of cantilever arrays based on the optical beam deflection method. This combines the optical beam deflection technique and the scanning of a laser beam illuminating individual cantilevers of an array, sequentially. The technique provides sub-angstrom resolution in the cantilever deflection and it allows the readout of tens of cantilevers per second. Finally, new developments performed to measure the dynamic response of microcantilever biosensors will be presented.