

SYMPOSIUM HH
Integrated Nanosensors

March 29 - 31, 2005

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* Invited paper

SESSION HH1: 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 Filbert 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 make sensor developments accessible to nontechnical audiences.

10:00 AM *HH1.3

Integrated Nanosensors: Perspectives from DOE. Terry Michalske, 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. Paolo Milani¹, Emanuele Barborini¹, Paolo Piseri¹, Gero Bongiorno¹, Antonella Taurino², Pietro Siciliano², Roberta Carbone³, Ida Marangi³ and PierGiuseppe Pellicci³; ¹Physics, Università, Milano, Italy; ²IMM, CNR, Lecce, Italy; ³Experimental 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 clusters beam deposition (SCBD) has been shown as a viable route for the production of nanostructured thin films. By using SCBD and by exploiting aerodynamical 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 cluster-assembled films on 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 microfabricated 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. Sailor¹, Michael P. Schwartz¹, Sara D. Alvarez¹, Austin Derfus², Benjamin Migliori³, Lin Chao³ and Sangeeta N. Bhatia²; ¹Department of Chemistry and Biochemistry, University of California - San Diego, La Jolla, California; ²Department of Bioengineering, University of California - San Diego, La Jolla, California; ³Department 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 remote 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 sulphur 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 immobilised [3]. Both peroxidase molecules [4], in which the cysteine residues pair up to form disulphide bonds, and oncostatin molecules can similarly be immobilised. 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 ground 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. Xirouchaki, 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. Hobday and R. Smith, J. Chem. Phys. 113 7723 (2000); also Nature (News & Views) 408 531 (2000). 3. R.E. Palmer, S. Pratontep and H.-G. Boyen, Nature Materials 2 443 (2003). 4. C. Leung, C. Xirouchaki, N. Berovic and R.E. Palmer, Adv. Mater. 16 223 (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

Sensor Arrays Based on Single-Walled Carbon Nanotube Structures. Alexander Star, Vikram Joshi, David Thomas, Sergei Skarupo, Jean-Christophe P. Gabriel and Christian Valcke; Nanomix Inc, Emeryville, California.

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

chip. The data from these nanosensor arrays is collected, processed and analyzed to identify patterns for variety of analytes, including aliphatic and aromatic hydrocarbons, carbon monoxide, hydrogen sulfide, nitrogen dioxide, ammonia, amines and alcohols. The same two-layer nanosensor strategy can be also applied to optoelectronic devices [1], to relative humidity sensing [2], and to electronic detection of specific protein binding [3]. The intrinsic advantages of this technology include small size, low power consumption, and low cost due to the use of conventional semiconductor chip manufacturing techniques. [1] A. Star, Y. Lu, K. Bradley, G. Gruner, *Nano Lett.* 2004, 4, 1587. [2] A. Star, T.-R. Han, V. Joshi, J. R. Stetter, *Electroanalysis* 2004, 16, 108. [3] A. Star, J.-C. P. Gabriel, K. Bradley, G. Gruner, *Nano Lett.* 2003, 3, 459.

1:45 PM HH3.2

MOSFET Embedded Microcantilevers for Novel Electronic Detection of On Chip Molecular Interactions. Soo-Hyun Tark¹, Gajendra Shekhawat² and Vinayak Dravid³; ¹Material Science and Engineering, Northwestern University, Evanston, Illinois; ²Institute for Nanotechnology, Northwestern University, Evanston, Illinois; ³Material Science and Engineering, Northwestern University, Evanston, Illinois.

We have developed a novel bio-chem 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 micro cantilever. The reverse side of the microcantilever is functionalized with appropriate sensing layer. As selective binding occurs during bio-chem exposure, the well-known bending of the cantilever leads naturally to significant, measurable and reproducible change in the drain 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, ease of integration, among others. Our initial result indicates 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 efficacy 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.

2:00 PM HH3.3

Individually Addressable Conducting Polymer Nanowire Electrode Junctions in a Sensor Array. Hsian-Rong Tseng, Molecular & Medical Pharmacology, UCLA, Los Angeles, California.

In this presentation, I will describe an efficient, labor-free, site-specific, and scalable approach for the production of high-quality and individually addressable conducting polymer nanowire electrode junctions (CPNEJs) in a parallel-oriented array. Polyaniline, polypyrrole and poly(EDOT) nanowires with uniform diameters (60-150 nm) were introduced into the CPNEJs 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.

2:15 PM HH3.4

Design Considerations of Solid State Devices for Integration with Immobilized Ion Channels. Daniel Fine¹, Debarshi Basu¹, Liang Wang¹, Wolfgang Knoll³, Ingo Koepfer³, Joanna Long⁴, Peter Anderson⁵, Randolph Duran² and Ananth Dodabalapur¹; ¹Microelectronics Research Center, The University of Texas at Austin, Austin, Texas; ²George and Josephine Butler Polymer Research Laboratories, Department of Chemistry, University of Florida, Gainesville, Florida; ³Max Planck Institute for Polymer Research, Mainz, Germany; ⁴McKnight Brain Institute, University of Florida, Gainesville, Florida; ⁵Whitney Marine Laboratory, University of Florida, St. Augustine, Florida.

There is increasing interest in developing devices which can detect trace amounts of highly toxic chemicals and biological agents. An avenue which has shown a great deal of promise is the integration of immobilized ion channels, such as Maxi-K and the M2 subunit of nicotinic acetylcholine receptor, with solid state devices such as

bipolar junction transistors (BJTs) and junction field effect transistors (JFETs). These sensing devices consist of ion channels encapsulated in a lipid bilayer which is tethered to the surface of the solid state device. The resulting devices can then be used to transduce the small stochastic currents generated by ion translocation through the ion channels to an electronic signal which can be amplified and processed. The ion channels are isolated from living cells, such as *Xenopus* oocytes in the case of Maxi-K, and are voltage gated allowing for additional on-chip potentiometric control including voltage-clamped operation. By genetic modification of selected sites at the extramembranal surface of the channels with various types of receptors, it will be possible to detect very small concentrations of toxic agents such as ricin. A wide range of device types and fabrication methodologies are being pursued to investigate the strengths and weaknesses of the resulting sensors and to allow for a high degree of scalability. Bipolar junction transistors with DC gains of nearly 10,000 have been fabricated with conventional micron scale photolithography techniques using a sequence of epitaxially grown layers. Junction field effect transistors are being fabricated with device widths on the order of tens of nanometers as well. These devices are being produced using electron beam lithography and will allow for high sensitivity, low noise, and easy integration of large packing densities. Organic devices which utilize a gate, source, and drain electrode separation of tens of nanometers will also be explored. In these devices, also patterned by electron beam lithography, a small gate electrode will be used for sensing which will cut down on parasitic capacitance. All or part of this electrode will be made from a metal which forms its own oxide, such as aluminum. The source and drain will then be defined very close to this gate electrode using an electron beam lithography system capable of 20 to 30 nm alignment. These carefully designed and fabricated solid state devices used in conjunction with the corresponding library of biologically isolated channel proteins can make for a highly sensitive sensing apparatus. When incorporated with chemical and biological receptors, there will be a modulation of the ion streams due to gating of the ion channel by interaction of a target analyte molecule. The fact that silicon and organic semiconductor devices will be used will make it easy to incorporate signal processing circuitry and allow for easy scalability and low cost.

SESSION HH4: Physical Sensors
Chair: Bernd Fruhberger
Tuesday Afternoon, March 29, 2005
Room 3014 (Moscone West)

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 products 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 material can be switched by spin polarized currents flowing through the material. SMT and thermal assistance have promise for reducing currents 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 Barbic¹ 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 electrodeless deposition of an optical nanoreflector 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

Mass Sensitivity of Cantilever Based Mass Sensors as a Function of Mass-Position. S. Dohn, R. Sandberg, W. Svendsen and A. Boisen; MIC - Department of Micro and Nanotechnology, Technical University of Denmark, Kgs. Lyngby, Denmark.

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 actuating the cantilever using a piezo-element 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 60 pg) is positioned on the micro cantilever using a nano-manipulation setup after which the 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 compared to conventional 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.

4:30 PM HH4.5

Dependence of Metallophthalocyanine Thin Film Structure on Substrate Temperature and in situ Annealing. Casey Miller, Amos Sharoni, Ge Liu, C. N. Colesniuc, Bernd Frubberger 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 (AFM) as functions of deposition 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 13-14 nm, corresponding to ~10 monolayers. 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 1, 2, 4, and 8 hours. XRD results show the emergence of higher order peaks as deposition temperature increases. AFM results show the transition from a granular morphology to flat, extended molecular layers (with pinholes) with increased temperature. XRD and AFM analyses independently reveal a film roughness corresponding to 1-2 monolayers. Annealing results in different degrees of morphological reorientation. Our results show improvement toward the deposition of 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# F49620-02-1-0288.

SESSION HH5: Chemical Sensors

Chair: Andy Kummel

Wednesday Morning, March 30, 2005

Room 3014 (Moscone West)

8:30 AM *HH5.1

Metallophthalocyanine Chemosensors. William C. Trogler¹, Karla Miller¹, Andrew C. Kummel¹, Ivan K. Schuller², Michael Hale¹, Forest Bohrer¹, Jeongwon Park¹, Richard D. Yang¹, Casey Miller², Ngoc Tran¹ and Bernd Frubberger²; 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, Pd, 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 160 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) or by binding an allosteric effector such as organic compounds (lactate, urate, phenols etc.), salts and heavy metals (1,4,5). 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 Foerster 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 Trp-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 SNR of the device clusters less than 100 000 hemocyanin molecules could be monitored, which may allow to detect metals and organic compound at a similar amount in future. Granted by BMBF Germany and DFG References 1. van Holde KE, Miller KI. (1995) Adv Protein Chem. 47:1-81. 2. van Holde KE, Miller KI, Decker H. (2001) J Biol Chem. 276:15563-6. 3. Decker H, Connelly PR, Robert CH, Gill SJ. (1988) Biochemistry 27:6901-8 4. Menze MA, Hellmann N, Decker H, Grieshaber MK. (2000) Biochemistry 39:10806-11. 5. Kuiper HA, Forlani L, Chiancone

E, Antonini E, Brunori M, Wyman J. (1979) *Biochemistry* 18:5849-54.
6. Erker W, Hubler R, Decker H. (2004) *Eur Biophys J.* 33:386-95 7.
Lippitz M, Erker W, Decker H, van Holde KE, Basche T. (2002) *Proc Natl Acad Sci USA.* 99:2772-7. 8. Decker H., Lippitz M, Erker W., Basche T (2005), in preparation 9. Erker W, Schoen A, Basche T, Decker H. (2004) *Biochem Biophys Res Commun.* 324:893-900

9:30 AM ***HH5.3**

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 occurring in the nano realm may make possible the design of very small devices with novel functionalities. To fully take advantage of both the potentialities inherent in bionanotechnology and the physical capabilities of designed nanoscale devices, it will be necessary to adapt one to the other. Given the abilities of biopolymers to adapt via evolution (natural or directed), it would seem most likely that molecules 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 uniquely 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.

10:30 AM **HH5.4**

Colorimetric Sensor Arrays: Applications and Miniaturization. Ken Suslick, Michael Janzen, Jennifer B. Wilson and Chen Zhang; Chemistry, University of Illinois, Urbana, Illinois.

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 olfaction system; each dye is a cross-responsive sensor. This technology uses a disposable array of chemoresponsive dyes as the primary sensor elements, making it particularly suitable for detecting many of the most odiferous compounds. Striking visual identification of a wide range of VOCs are easily made at parts per billion (ppb) levels, for example to amines, carboxylic acids, and thiols (i.e., sensitivities comparable to GC-MS detection). In order to improve response times and increase sensitivity, we have begun miniaturization of the sensor array by use of the recently available PiezoArrayer from Perkin-Elmer. This non-contact array printer, originally designed for DNA and protein array production, can be utilized for microscopic printing of non-aqueous solutions. We have succeeded in preparing 36 dye spot arrays, for example, in a total area of <2 sq. mm. Effects of this miniaturization will be discussed. [1] Rakow, N. A.; Suslick, K. S. "A Colorimetric Sensor Array for Odor Visualization" *Nature*, 2000, 406, 710-714. [2] Suslick, K. S.; Rakow, N. A. "Colorimetric Artificial Nose Having an Array of Dyes & Method for Artificial Olfaction" U.S. Patent 6,368,558; April 9, 2002.; Suslick, K. S.; Rakow, N. A.; Sen, A. "Colorimetric Artificial Nose Having an Array of Dyes and Method for Artificial Olfaction: Shape Selective Sensors" U.S. Patent 6,495,102; Dec. 17, 2002. [3] Suslick, K.S.; Rakow, N.A.; Kosal, M.E.; McNamara III, W.B.; Sen, A. "Chemsensing: A Colorimetric Array Detector" *Proc. ISOEN 02* (ed. A. D'Amico and C. DiNatale; IEEEE: Baltimore, 2003), pp. 46-52. [4] Suslick, K. S. "An Optoelectronic Nose: Colorimetric Sensor Arrays" *MRS Bulletin*, 2004, 29, 720-725. Suslick, K. S.; Rakow, N. A.; Sen, A. "Colorimetric Sensor Arrays For Molecular Recognition" *Tetrahedron* 2004, in press;

10:45 AM **HH5.5**

Detection of Toxic Chemicals Using Polyaniline Nanofiber Composite Sensor Arrays. Shabnam Virji^{1,2}, Christina Baker¹, Dan Li¹, Richard B. Kaner¹ and Bruce H. Weiller²; ¹Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California; ²Space Materials Laboratory, The Aerospace Corporation, Los Angeles, California.

Polyaniline nanofibers are promising materials for detecting toxic gases since a conductivity change of over 8 orders of magnitude can occur in the presence of strong acids and bases. Polyaniline also responds to organics, polar molecules and redox agents by swelling, chain alignment and redox reactions, respectively. All of these responses are enhanced with the use of nanostructured materials. We now show that polyaniline can be modified with additives to enhance the detection of specific analyte gases. A new sensor for hydrogen sulfide can be made from polyaniline nanofibers decorated with metal salts. Different composite films can be measured simultaneously using

an integrated nanosensor array to find the optimal material that gives the largest and fastest response. In this case, undecorated polyaniline nanofibers give almost no response to hydrogen sulfide, whereas the decorated nanofibers give a conductivity change of over 4 orders of magnitude. Nanostructured polyaniline, in different forms, can be integrated into a sensor array for various applications including homeland security.

11:00 AM **HH5.6**

Integrated Tin Oxide Gas Sensor. Brian P. Mosher and Taofang Zeng; North Carolina State University, Raleigh, North Carolina.

Semiconductor chemical gas sensors have wide applications and are presently a commercial product. The sensors measure the change of electrical resistance upon exposure to certain gases. The scale of change of the resistance distinguishes the gases and their concentration. Selectivity is the key to reliable and multi-functional gas sensors. Recently, new approaches have been proposed to improve the selectivity of tin oxide based gas sensors through modifying the compositions of the sensing materials, modulating the operational temperature, and changing the geometrical structure of the sensors. We use nano-porous tin oxide doped with copper oxide and cerium oxide to enhance the selectivity for detecting NO, CO and CH₄. The oxide and the sensor are prepared using a sol-gel process and screen printing technique. The sensors are integrated with temperature control and are operable at high temperatures.

11:15 AM **HH5.7**

Metallophthalocyanine (MPc) Thin-Film Field-Effect Transistors (FET) for Chemical Selective Sensing. Richard Yang³, Karla Miller¹, Jeongwon Park³, Corneliu Colesniuc², Forest Bohrer¹, Michael Hale¹, Bernd Fruhberger², William Trogler¹, Ivan K. Schuller² and Andrew C. Kummel¹; ¹Chemistry and Biochemistry, University of California, San Diego, La Jolla, California; ²Physics Department, University of California, San Diego, La Jolla, California; ³Material Science and Engineering, University of California, San Diego, La Jolla, California.

MPc-FET based chemical sensors are reported to have parts per billion sensitivity for a number of gases. We report upon the development of chemically sensitive FET devices (ChemFET) based on MPc thin films with tunable selectivity. A conducting channel forms at the insulator-MPc interface when the Fermi level of a source electrode is brought close to the HOMO level of MPc by adjusting the gate bias voltage. Gas adsorption induces small changes in the work function of MPc, but results in large changes in the channel conductivity. By measuring the drain current as a function of gate voltage, the relative sensitivity to different gases will be tuned to improve the chemical selectivity. Gate bias can also be used to compensate the drift in the threshold voltage resulting from film aging. The devices were fabricated using standard silicon lithography technology. Gold interdigitated electrodes were patterned on 450 Å thermal SiO₂ on p-type silicon substrates. Channel lengths of 5 and 10 microns were fabricated. Gate electrodes were deposited on the backside of the substrates. MPc thin films such as CuPc, NiPc and CoPc were deposited using Organic Molecular Beam Epitaxy (OMBE) at 6x10⁻⁹ Torr. X-ray diffraction and AFM were applied to study the film crystallinity and morphology. Current-voltage properties were characterized in detail. Carrier mobility and threshold voltages will be correlated with film properties. Various channel length and thickness of the film were also studied to identify contributions from bulk and interfacial charge transport. Device performances will be tested with organic vapors and chemical warfare stimulants.

11:30 AM **HH5.8**

Chemical Selective Phthalocyanine Thin Film Sensors. Richard Dengliang Yang¹, Jeongwon Park¹, Karla A. Miller², Forest Bohrer², Michael J. Hale², Bernd Fruhberger², William C. Trogler² and Andrew C. Kummel²; ¹Materials Science and Engineering Program, University of California, San Diego, La Jolla, California; ²Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California.

Phthalocyanine is one of the most investigated organic semiconductors for gas sensing applications. Detection limits to parts per billion (ppb) for NO₂ vapor were reported in the literature. However, chemical selectivity is still a challenging issue for all gas sensors. In this paper, we report upon the application of impedance spectroscopy to study phthalocyanine thin films on interdigitated microelectrodes to improve the chemical selectivity. Adsorption of gas analytes induces changes in the charge transport and electronic relaxation properties of phthalocyanine thin films. With an applied alternating electric field, various relaxation processes can be differentiated as a function of frequency. The dissipation factor (DF) is defined as the ratio of the real to the imaginary parts of the complex impedance. Ultra sharp (100 Hz) resonance DF peaks are detected when the phase lag of the current behind electric field is 0° or 180°. In our devices, resonance

frequencies were monitored in the range of 100 kHz to 5 MHz. Methanol and nerve gas simulant diisopropylmethyl 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 above a critical analyte concentration, 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.

11:45 AM HH5.9

High Thermal Stability W2B Ohmic Contacts to ZnO Ozone and pH Sensors. Lars Voss¹, Kelly Ip¹, Rohit Khanna¹, C. J. Kao², I. Kravchenko³, B. S. Kang³, F. Ren³, Y. W. Heo¹, D. P. Norton¹, G. C. Chi² and S. J. Pearton¹; ¹Materials Science and Engineering, University of Florida, Gainesville, Florida; ²Electrical Engineering, National 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 of 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 pH 2-12 of 8.5nS/pH in the dark and 20nS/pH when illuminated with UV(365nm) light. The nanorods show stable operation with a resolution of ~0.1 pH over the entire pH range. The results indicate that ZnO nanorods may have application 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/Al -based contacts show reaction with ZnO at temperatures as low as 200C. Our results show that the W2B contacts deposited by sputtering are slightly rectifying up to annealing temperatures of 300C and convert to Ohmic thereafter. The reduction of contact reaction with the semiconductor enables the sensors to operate to higher temperatures.

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

1:30 PM *HH6.1

Multifunctional Cantilever Arrays for Chemical and Biological Sensing. Martin Hegner¹, Natalija Backmann¹, Karin Gfeller¹, Natalia Nugaeva¹, Hans-Peter Lang^{3,1}, Alexander Bietsch^{3,1}, Andreas Plueckthun² and Christoph Gerber^{3,1}; ¹Institute of Physics, University of Basel, NCCR Nanoscale Science, Basel, Switzerland; ²Dept. of Biochemistry, University of Zurich, Zurich, Switzerland; ³Cantilever Sensors, IBM Research Laboratory Zurich, Ruschlikon, Switzerland.

Biosensing tools are currently undergo a further stage of development increasing efforts have therefore been put into the development of cantilever-based sensors for the detection of physical phenomena and chemical and biological reaction. Micro-fabricated silicon cantilevers arrays offer a novel parallel label-free approach where ligand-receptor binding interactions occurring on the sensor generate nanomechanical signals like bending or a change in mass that is optically detected in-situ. The elegance of these sensing methods is that the detection of an analyte requires no labeling, as well as that the various application fields only differ in the functional layers on the cantilever interface. The detection scheme remains common for all the different applications. In principle, any detection method, which is based on molecular recognition, is able to be implemented. Detection of multiple unlabelled DNA/RNA simultaneously down to picomolar concentrations within minutes is demonstrated. This DNA sensitivity is suitable for detection of specific unlabeled gene fragments within a complete genome (gene fishing). Currently we are able to fish individual gene fragments within a whole genome (rat or human) and have the ability to see whether a gene is turned on or off upon a specific external signal (Interferon) supplied in cell cultures. Such an approach allows non-labeled, non-amplified genetic analysis within a complete genome and will provide a new tool for biomarker screening. We report on new styles of bio-/chemical cantilever activation for sensing applications. To enhance the sensitivity for protein detection we use scFv fragments and antibody mimics (i.e. ankyrins) which can be tailor made and optimized for enhanced binding strength

towards the target of interest. Active growth of micro-organism is detected on micron sized cantilevers. Potential applications include: Fast antibiotic susceptibility testing and fast fungal spore detection in food industry and bio-destruction of materials.

2:00 PM *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 microparticle probes functionalized with protein specific monoclonal antibodies or nucleic acid specific sequences 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 sequences and encoded with barcode 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 sequence 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 zeptomolar to nanomolar concentration range. The implication of this new assay and the identification of markers for HIV, prions and Alzheimer's disease will be discussed.

2:30 PM HH6.3

Highly Sensitive Polymer-Based Cantilever-Sensors for DNA Detection. Montserrat Calleja¹, Maria Nordstrom², Mar Alvarez¹, Laura M. Lechuga¹, Anja Boisen² and Javier Tamayo¹; ¹Biosensors Group, CNM-CSIC, Tres Cantos, Spain; ²Dept. 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[3,4] with extreme sensitivity. Among 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. The cantilever fabrication process presented 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 miniaturized biochemical analysis system. The feasibility of the application of a polymeric cantilever for biological detection is demonstrated by measuring the immobilization process of thiolated single stranded DNA (ssDNA) on a gold-coated cantilever. The response of SU-8 cantilevers is compared to that of commercial silicon and silicon nitride cantilevers. The high sensitivity of polymeric cantilevers envisions 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. Raiteri, M. Grattarola, H.-J. Butt, P. Skladal, Sensors and Actuators B, 79, 115-126 (2001) [2] J. Fritz, M. K. Baller, H. P. Lang, H. Rothuizen, P. Vettiger, E. Meyer, H. J. Guntherodt, 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. Alvarez, A. Calle, J. Tamayo, L. M. Lechuga, A. Abad, A. Montoya, Biosensors and Bioelectronics, 18, 649 (2003)

2:45 PM HH6.4

Multiplexed, Real-time Detection of Cancer Marker Proteins using Nanowire Arrays. Gengfeng Zheng¹, Fernando Patolsky¹ and Charles M. Lieber^{1,2}; 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 silicon 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

internal control to each other. Different cancer marker proteins, such as prostate specific antigen (PSA), PSA- α 1-antichymotrypsin (PSA-ACT) complex, carcinoembryonic antigen (CEA) and Mucin 1 (MUC 1), have been detected simultaneously and quantitatively on a same nanowire FET array, with the sensitivity up to femtomolar concentration. In addition, the measurement of binding and catalytic activity of a reverse transcriptase cancer marker, telomerase, demonstrates the ability of combining both protein markers and nucleic assays within a single nanowire device chip. Moreover, the use of assembly methods to prepare large integrated arrays of nanowire devices can detect up to 100s of different proteins simultaneously and selectively, thereby offers a powerful tool for proteomics based disease diagnosis, drug discovery and medical treatment.

3:30 PM HH6.5

Simultaneous Detection of Insulin, Glucose and pH Using Nanosensor Array. Souheil Zekri², Arun Kumar¹ and Ashok Kumar²; 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 25 nm thick nickel islands were deposited by e-beam evaporation on a silicon substrate that was patterned using a photolithography liftoff process. The square regions of 100 by 100 microns with four individual electrode contacts are fabricated for nanosensor array development. Multi wall carbon nanotubes (MWCNT) were then grown over the Ni islands at 900 oC using a Chemical Vapor Deposition (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 voltametry 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 MWCNT. Modified nanoelectrodes are currently being characterized using scanning electron microscopy (SEM), Fourier Transform Infrared spectroscopy (FTIR), UV visible spectroscopy.

3:45 PM HH6.6

Nanobiosensor for Cholesterol Detection. Arun Kumar¹, Thomas Gressle² and Ashok Kumar^{2,1}; 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 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 a nanosensor which allows detection of total cholesterol accurately and more specifically in small sample sizes (micro liter) using surface contact voltametric detection techniques. Nanosensors developed with modified nanoparticles further characterized with FTIR, SEM and UV-visible spectroscopy.

4:00 PM HH6.7

Applications of Biologically Functionalized Carbon Nanotubes. Alan Dalton^{1,2}, Rockford Draper², Inga Musselman², Gregg Dieckmann², Alfonso Ortiz-Acevedo², Vasiliki Zorbas², Ray Baughman², Joe Razal², Hui Xie² and Steve Collins²; ¹Department of Physics and the UniS Materials Institute, University of Surrey, Guildford, United Kingdom; ²Chemistry Department and the NanoTech Institute, University of Texas at Dallas, Richardson, Texas.

Carbon nanotubes (CNTs) have remarkable physical and chemical properties. As a result, a range of applications is envisioned in both the physical and life sciences. However, as-produced CNTs form as insoluble hydrophobic aggregates and are not biocompatible. Detergents used to solubilize CNTs in water disrupt cellular membranes and are incompatible with many biological applications while covalent modification with soluble moieties interferes with CNT properties. We have developed a family of de novo polypeptides that non-covalently functionalise CNTs providing a biocompatible surface that exploits the structural diversity of the peptides. These peptides allow solubilization, isolation and subsequent hierarchical reassembly of peptide wrapped nanotubes into functional macrostructures. We also utilize a new class of modified peptides called reversible cyclic peptides (RCPs), based on cyclic peptides of alternating L- and D-AAs, for the diameter-selective solubilization of SWNTs. In addition, RCPs covalently closed around SWNTs do not dissociate from the nanotubes unless the disulfide bond is reduced. This stable RCP/SWNT association provides a platform to which ligands are attached, directing the SWNTs to bind to specific targets for potential biosensing application. We also discuss the use of macroscopic assemblies of biologically functionalised carbon nanotubes as responsive sensors. Zorbas, V. et al. (2004). JACS 126(23): 7222-7227 Dieckmann, G. R. et al. (2003). JACS 125(7): 1770-1777

4:15 PM HH6.8

Detection of Protein-Protein Interactions in Nanochannels based on High Frequency Impedance Measurements.

Markus Loehndorf, Antonio Malave, Michael Tewes, Ivan Stoyanov and Thomas Gronewold; CAESAR (Center of Advanced European Studies and Research), Bonn, Germany.

We have developed high frequency impedance sensors with nanofluidic channels by utilizing micro- and nanofabrication techniques. These sensor devices have been used to detect and analyze protein-protein or aptamer-protein interactions in real-time.[1] Measurements of the binding of thrombin to anti-thrombin antibodies as well as to RNA, and DNA aptamers have been studied and compared to results obtained by SAW (surface acoustic wave) devices.[2] Furthermore, the binding process of the receptor molecules within the nanochannel are discussed in view of diffusion limitations for molecules of different molecular weight and size. Using a sacrificial layer technique forms the nanochannels between the two sensor electrodes. The height of the nanochannel is on the order of 90-150 nm, whereas the lateral dimension is 2 μ m x 6 μ m. The detection is based on changes of the sensor impedance within the nanometer gap due to the binding of molecules with low relative dielectric constant ϵ_r on the electrode surface and the associated displacement of water or other buffer molecules with a high relative dielectric constant ϵ_r . Thus, the effective relative dielectric constant ϵ_r of the medium between the electrodes changes the electrical impedance of the sensor. Biological buffers typically have ion concentrations in the range from 100mM to 200mM, which leads to the formation of an electric double layer (EDL) with a characteristic length the so-called Debye-Hueckel length d_{DH} of about 1 nm. Because the electrical field vanishes for distances larger than that critical length d_{DH} , it is evident that for common receptor sizes such as antibodies (~10nm) or aptamers (~1nm) the sensitivity would be very low for ligands bound on top of the receptors. We have solved this problem by measuring at high frequencies of 1-1.5 GHz, where the ions can no longer follow the fast changes of the electrical field and therefore the electrical field fully penetrates the gap between both electrodes. Our work is focussed on the development of a fully electronic multiple parameter chip by combining the high frequency impedance sensor and its high sensitivity to dielectric changes with the mass or viscosity sensitivity of the SAW device. [1] M. Loehndorf et al. Proc. of μ -TAS 2004, Vol.2, 431 (2004) [2] M. Schlensog et al. Sensors and Actuators Vol. B101/3, 308 (2004)

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. Yu-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-photonics 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 into the device to further enhance the performance and functionality of flow cytometry on a chip for biological sensing.

9:30 AM *HH7.2

Cantilever Based Sensing Devices with Integrated Read-Out and Electronics. Anja Boisen, MIC - Department of Micro and Nano Technology, Technical University of Denmark, Lyngby, Denmark.

A micrometer-sized cantilever can be used as a very sensitive, simple and cheap biochemical sensor in ambient and aqueous environments. Basically, a biochemical reaction at the cantilever surface can be monitored as a bending of the cantilever, due to a change in the surface stress. Furthermore, highly sensitive mass detection can be achieved by using resonating nanocantilevers. We have developed cantilever-based sensors with integrated read-out, which hold promises as fast and cheap point-of-care devices as well as interesting research tools. The detection technique involves no labelling of the molecules by fluorescent, magnetic or radioactive markers and bulky detection schemes like laser scans, CCD imaging or radiography are avoided. The majority of the cantilever based sensing experiments reported to date have been based on the optical leverage method used in atomic force microscopy. This method is very accurate but for many applications it would be an advantage to have a more compact read-out mechanism that requires less adjustment and alignment. A readout integrated on the cantilever would also greatly facilitate operation of arrays of cantilevers and work in liquid. For monitoring changes in surface stress we have developed various types of micromachined silicon based cantilever devices with integrated piezoresistive read-out and built-in reference cantilevers. Arrays of up to 10 cantilevers have been integrated in micro-channels offering a method to develop compact biosensors with a simple read-out scheme. Recently we have realised cantilever sensors in the polymer SU-8, which is a negative resist with excellent mechanical, thermal and chemical properties. The use of polymer makes the fabrication process simple, cheap fast and flexible. Moreover, the polymer technology opens up for completely new ways of detecting cantilever bending, 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 realised silicon-based nanocantilevers with integrated capacitive read-out and electrostatic 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 ag/Hz has been deduced.

10:30 AM *HH7.3

Thin Films for Nanostructured Gas Sensors. Pietro Siciliano, Institute for Microelectronics and Microsystems IMM-CNR, Lecce, Italy.

The gas-sensing performance of solid-state chemoresistive thin film devices are strongly influenced by the structure and the morphology of the active material. In particular, the response itself as well as the response time of the sensor are known to be enhanced by decreasing the grain size of the active material. This effect is related to an enhanced depletion of the charge carriers in small crystalline grains upon the interaction of the sensor with adsorbed oxygen species and, hence, to remarkable and fast changes of the electrical properties of the sensor in contact with the target species. It is then important the possibility of preparing active materials characterized by typical nano-size of the crystal grains. In this sense, the use of chemical approaches in the preparation of active materials may be particularly useful in controlling the material microstructure beyond its morphology. Such techniques as the sol-gel process and other related solution-chemistry approaches are intrinsically advantageous in providing very thin (> 100 nm) films characterized by a small (< 10 nm) grain size, with added useful features as the possible introduction in the starting solution and, hence, in final structure, of various additives (molecules, ions, nanoparticles etc.) and the control of the film morphology by tuning the synthetic parameters. Further key issues are the cost of the precursors, the stability of the solutions and the compatibility of the chemical deposition process with standard

microelectronic processes in the preparation of the final device. The complex, multi-step procedure required for arriving at the final device will be reviewed referring to the results achieved concerning the synthesis of various single and mixed oxide thin films (starting from SnO₂, In₂O₃, MoO₃, WO₃, TiO₂ etc.) and their following processing until the complete microdevice. Results will be presented summarizing the gas-sensing performances of the single micro-devices and in arrays configuration for Electronic Nose.

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 microfabricated structures, 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 transformation, 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 functions [8] and surface-specific cell interactions [9] can be achieved. A cell force sensor based on nanofabricated, standing cantilevers, is used to evaluate cell force patterns [10]. Nanofabrication and evaluation of optically tailored nanoparticles and other nanostructures, which exploit so called nano-particle plasmon resonances, have potential for, e.g., biosensing [11-12]. The shark skin mimic is an example of so biomimetic materials science [13]. References: [1] B. Kasemo, Surface Science 500 (2002) 656, and references therein. [2] C. A. Keller and B. Kasemo, Biophysics. J., 75 (1998) 1397. [3] C. A. Keller, K. Glasmaestor, V. P. Zhdanov, and B. Kasemo, Phys. Rev. Lett. 84 (2000) 5443. [4] E. Reimhult, F. Hook, and B. Kasemo, Langmuir 19 (2003) 1681-1691. [5] M. Rodahl, F. Hook, A. Krozer, P. Brzezinski and B. Kasemo, Rev. Sci. Instrum. 66 (1995) 3924. [6] M. Zaech and B. Kasemo, to be published. [7] A.-S. Andersson, K. Glasmaestor, D. Sutherland, U. Lidberg and B. Kasemo, J. of Biomedical Materials Res. 64A (2003) 622-629. [8] F. Hook, A. Ray, A., B. Norden and B. Kasemo, Langmuir, 17, 8305 (2001). [9] D. Dahlborg, Julie Gold et al, to be published. [10] S. Petronis, J. Gold et al, Journal of Micromechanics and Microeng. 13 (2003) 900-913. [11] P. Hanarp, M. Kaell, and D. S. Sutherland, Journal of Physical Chemistry B 107 (2003) 5768-5772. [12] L. Gunnarsson, E. J. Bjerneld, H. Xu, S. Petronis, B. Kasemo, B. and M. Kaell, Appl. Phys. Lett. 7 (2001) 802. [13] H. Rapp, B. Kasemo and I. Zoric, to be published.

SESSION HH8: Applications

Chair: Yvan Bruynseraede

Thursday Afternoon, March 31, 2005

Room 3014 (Moscone West)

2:00 PM *HH8.1

Converging Technologies for Bioelectronic Applications. S. Borghs, 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 or as diagnostic tools for proteomics. 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 more intimate interaction between biological elements and micro-electronics will take place. I will discuss the status of our research of a neuro-electronic junction based on micro-electronic Si-chip that allow real-time interaction with electrical and chemical neuronal communication on the scale of individual neurons. Some aspects of long term and sensitive neuro-electronic interfacing 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 *HH8.2

Development of Nanomechanical Biosensors for Environmental Control and Functional Genomics.

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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 $\sim 1000 \text{ nm}^2$, 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.