Wednesday Morning, November 6, 2002

Homeland Security
Room: C-209 - Session HS-WeM

Plenary Session on Homeland Security
Moderator: R.J. Colton, Naval Research Laboratory

8:20am **HS-WeM1 Chemical and Biological Agent Decontamination of Civilian Facilities**, ***T. Carlsen***, Lawrence Livermore National Laboratory **INVITED**

The purpose of this presentation is to discuss the existing and emerging decontamination technologies for use following a chemical and/or biological weapons incident at civilian and/or public sector facilities. Additionally, the necessary requirements of these technologies to successfully decontaminate civilian facilities and the approach needed to obtain regulatory compliance will also be discussed. The types of decontamination methods likely to be most successful are different than would be most effective in response to a military and/or wartime incident. Current military decontamination techniques aimed at CBW agents are corrosive and/or toxic and can cause collateral damage to facilities and equipment. As a result of recent terrorist events, there is increased interest in decontaminating agents and their effectiveness for the civilian sector. The optimum technology would be non-toxic, non-corrosive, and easily deployable, thereby insuring effective use by first-line responders. Methods should allow for detoxification and/or degradation to environmentally acceptable components rather than necessitate complete destruction. Effective decontamination requires the use of reagents that can be dispersed as solids, liquids, and/or gases, depending on the particular scenario involved. Several technologies currently under development are aimed at meeting these requirements. however, there are some distinct scenarios for which current technology is still inadequate to respond in a rapid and effective manner. Effective decontamination also requires effective sampling and verification methods to demonstrate that cleanup goals have been attained. The final decontamination must be defensible to regulatory agencies and to an uninformed public. In order to accomplish this we must understand and even influence the answer to the question: "How clean is clean enough?" The level of decontamination required will influence the choice of these systems under consideration.

9:00am **HS-WeM3 Science and Technology for Combating Terrorism**, ***A.T. Hopkins***, Defense Threat Reduction Agency **INVITED**

This briefing describes the Defense Threat Reduction Agency's (DTRA) efforts to accelerate research and development programs for combating terrorism. DTRA is a combat support agency providing a unique blend of operational and technical expertise and experience to reduce weapons of mass destruction threats. DTRA's Technology Development portfolio includes programs in nuclear weapon effects technology, integrated systems applications that include advanced concept technology demonstrations, counterproliferation technology, and nonproliferation and arms control technology. Technology challenges include the detection of dispersed and non-dispersed nuclear, chemical and biological threats, remote detection of weapons of mass destruction, force protection technologies, microscale hazard prediction, information management, hard and deeply buried target defeat, and agent defeat.

9:40am **HS-WeM5 Basic Research Needs for Countering Terrorism**, ***T. Michalske***, Sandia National Laboratories **INVITED**

Improving our ability to counter threats of terrorism has become a high priority in the U.S. and many other countries around the world. While it is widely recognized that science and technology will play an important role in this effort, it must also be recognized that terrorism is a highly complex socio-political problem for which there are simply no "silver bullets" to easily solve the problem. This presentation summarizes key points and recommendations from a recent U.S. Department of Energy Workshop that involved experts familiar with counter-terrorism technologies, strategies, and policies. Direct connections between technology needs for countering terrorism and the underlying science issues are defined along with some specific examples that show how previous science investments have led to new approaches to counter terrorism threats associated with weapons of mass destruction.

10:20am **HS-WeM7 Panel Discussion: Science & Technology Issues for Homeland Security, T. HOPKINS, Defense Threat Reduction Agency; T. MICHALSKI, Sandia Nat. Labs; E. RABER, Lawrence Livemore Nat. Lab; M.J. SAILOR, UC, San Diego; D. WALT, Tufts Univ.; L.J. WHITMAN, NRL** **INVITED**

Wednesday Afternoon, November 6, 2002

Homeland Security
Room: C-209 - Session HS+SS+BI-WeA

Chemical and Biological Detection
Moderator: J.N. Russell, Jr., Naval Research Laboratory

2:00pm **HS+SS+BI-WeA1 Photonic Crystals Derived from Nanocrystalline Porous Si: Applications in Detection of Chemical Warfare Agents, Explosives, Pollutants, and Biochemicals**, ***M.J. Sailor***, University of California, San Diego **INVITED**

The optical properties of nanostructured porous silicon films are exploited for a variety of sensor applications. With appropriate modification of the electrochemical preparation conditions, multilayered structures can be generated that behave as photonic crystals. These structures can be encoded and used as remote sensors for chemicals. For example, small particles of nanoencoded microporous Si are used to detect chemicals by measurement of the intensity of reflected light from a remote laser probe. The particles contain a periodic porous nanostructure that defines the code. The periodic structure forms a Rugate reflector which 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 adsorption of vapors within the porous matrix. Using a 10 mW laser as an optical probe and telescope collection optics, detection of ethanol, acetone and toluene vapors has been achieved at a distance of 20 m. Control experiments using water vapor at comparable partial pressures show very little response, demonstrating selectivity towards the hydrocarbon analytes. Examples of irreversible detection and reversible sensing modes for explosives, nerve warfare agents, and various biochemicals will also be discussed. A catalyst can be incorporated into the nanomaterials to provide specificity for nerve warfare agents. For example, rapid detection of a fluorophosphonate is achieved by catalytic decomposition of the agent to HF and subsequent detection of the HF in the porous silicon interferometer. The catalyst system can be integrated on the silicon chip and consists of a TMEDA[Cu(II)] catalyst (TMEDA = tetramethylethylenediamine) encapsulated in cetyltrimethylammonium bromide (CTABr) micelles. An operational battery-powered unit has been constructed and tested on the live nerve warfare agent Sarin. These devices are all compatible with conventional Si microfabrication technologies.

2:40pm **HS+SS+BI-WeA3 Magnetic Labeling and Microarray Detection of Biomolecules**, ***L.J. Whitman***, Naval Research Laboratory **INVITED**

NRL is developing two novel biosensor systems using magnetic microbeads to probe for target biomolecules specifically bound to receptor-patterned surfaces, with an initial focus on detecting biological warfare agents.[1,2] The microbeads serve both as reporter labels and as force transducers to allow "force discrimination" - a technique developed at NRL that greatly reduces the background signal-enabling the identification of single biomolecular ligand-receptor interactions with high sensitivity and specificity. Assays using magnetic labeling and force discrimination have been developed for a variety of bacteria, viruses, and protein toxins (immuno-sandwich assays), and for oligonucleotide microarrays (hybridization assays). How the assays are incorporated into a practical sensor system depends on how the specifically bound beads are detected. We are currently perfecting two detection approaches, an optical system that images beads captured on a patterned nanoporous membrane, and a chip-based sensor system that directly detects beads using an array of giant magnetoresistive (GMR) magnetic field microsensors. The optical system has achieved sensitivities of 10 pg/ml for proteins, $10^{2.5}$ cfu/ml for bacteria, and 10^{3} pfu/ml for viruses. Using a single GMR sensor, we have successfully detected 1 fM of DNA in a 30 µL sample with only 15 min of hybridization. I will discuss how the interplay between surface chemistry, sensor design, and microfluidics determines the overall performance of our biosensor systems. Supported by ONR, the DoD JSTPCBD, and DARPA.

[1]Lee et al., Anal. Biochem. 287, 261 (2000).

[2]M. M. Miller et al., J. Mag. and Mag. Mat. 225, 138 (2001).

3:20pm **HS+SS+BI-WeA5 Optical Microarrays for Chemical and Biological Detection**, ***D.R. Walt***, Tufts University **INVITED**

We have used coherent imaging fibers to make fiber-optic chemical sensors. Sensors can be made with spatially-discrete sensing sites for multianalyte determinations. We are investigating the limits of our ability to create high-density sensing arrays containing thousands of microsensors and nanosensors. Micrometer- and nanometer-sized sensors have been fabricated by etching the cores of the optical imaging fiber to create wells and loading them with micro and nanospheres. Such arrays can be employed for making genosensors for bio-agent detection. We have also created optical sensors based on principles derived from the olfactory system. A cross-reactive array of sensors is created such that specificity is distributed across the array's entire reactivity pattern rather than contained in a single recognition element. The ability to use such information-rich assemblies for broad-based chemical sensing will be discussed.

4:20pm **HS+SS+BI-WeA8 Real-time Detection of TNT Using Microcantilevers with Microcyclic Cavitand Coatings**[1], ***N.V. Lavrik***, *T. Thundat, G. Muralidharan, P.G. Datskos*, Oak Ridge National Laboratory

Real-time detection of nitroaromatic aromatic explosive compounds in various environments is a highly significant task in forensics, anti-terrorist activities and global de-mining projects. In particular, ability to detect trace levels of trinitrotoluene (TNT) in air and soil could greatly reduce continued fatalities from land mines among civilians and be a measure in tracking and locating explosive materials. In our work, we address this challenge of detecting TNT vapors in gaseous environment by using an innovative, highly sensitive microcantilever transducer combined with a chemically sensitive molecular coating based on the macrocyclic cavitand of a calixarene family. We measured responses to vapors of TNT and its analogs, 0-mononitrotoluene and 2,4-dinitrotoluene vapors in the range of temperatures of 298 K to 318 K. Our results were used in order to estimate the limits of detection (LODs) for these compounds and optimize the temperature regime of the designed detection system. In the case of TNT, the steady state responses were large, however, the response kinetics was significantly elongated, which is consistent with an analyte depletion model. As compared to more traditional surface acoustic wave sensors with a proven potential for detection of TNT, our approaches offer a simpler, low-cost alternative without sacrificing the performance. The reported results together with these advantages of microcantilever based gas detectors clearly indicate a viable technological approach to mass produced detectors of explosive materials.

[1] This work was supported by the U.S. Department of Energy and Micro Sensor Technologies, Inc. Oak Ridge National Laboratory is operated for the U.S. Department of Energy by UT-Battelle under contract DE-AC05-96OR22464.

4:40pm **HS+SS+BI-WeA9 A New Nanoscale Platform for Gas Sensor Applications**, *A. Kolmakov, Y. Zhang, G. Cheng*, ***M. Moskovits***, University of California Santa Barbara

The application of metal and semiconductor nanowires as solid state gas sensors has been an area of tremendous promise currently limited by challenges related to nanowire growth and device fabrication. We present an approach for fabricating individual and arrays of nanowires of a variety of metals and metal oxides with tunable, uniform diameters and length in the range of 10-100 nm and 5-200 micrometers, respectively, configured for gas sensing application. The materials successfully employed include Pd, Ag, Cu, Pb, PbO, CuO and SnO_2. Arrays of nanowires were fabricated in hexagonal close-packed nanochannel alumina templates. Electrodes deposited on the surfaces of these nanostructures provides electrical contacts which with the incorporated heaters determines the device architecture. Based on this method we explored the electronic and structural properties of Pd and SnO_2 nanowires using HRTEM, XPS and Auger spectroscopy. Chemical reactivity and gas sensitivity toward hydrogen and carbon monoxide of individual and assemblies of ca 10^9 Pd and SnO_2 nanowires were assessed using conductivity measurements and TPD analysis. This approach constitutes a novel platform for micro- and nanosensor application.

5:00pm **HS+SS+BI-WeA10 Metal Phthalocyanine Thin Films as Gas Sensors**, ***L. Lozzi***, *S. Santucci*, INFM and University of L'Aquila, Italy, *C. Cantalini*, University of L'Aquila, Italy

Metal Phthalocyanine (MPc) thin films have shown interesting properties as gas sensor, in particular for NO2. The wide variety of different available molecules, changing both the central atom and/or the chemical structure of the outer benzene rings, allows a fine modulation of the film sensing properties. In this work we will present our result on the interaction between oxidating gases (O2 and NO2) and different MPc films. We have deposited thin films (about 50 nm thick) of Copper Phthalocyanine (CuPc) and Exadecafluoro-copper-phthalocyanine (F16CuPc) onto Si3N4 substrates, for the spectroscopic characterizations, and onto Pt interdigital circuits, for the gas sensing tests. These films have been analysed both as deposited and after different thermal annealing. The electrical sensing analyses have shown a sizeable decrease of the film resistivity during the film exposure to NO2, even at very low concentration (up to 100 ppb). We have studied the electronic structure by means of the X-ray and ultraviolet photoemission

spectroscopies (XPS-UPS) after the exposure to NO2 and O2 both at room and at higher temperature, in order to investigate the surface reactivity of these samples and in particular the preferential adsorption sites.

Thursday Morning, November 7, 2002

Biomaterials
Room: C-201 - Session BI+HS+SS-ThM

Biosensors and Biodiagnostics
Moderator: J. Hickman, Clemson University

8:20am **BI+HS+SS-ThM1 Surface Functionalization for Self-Referencing and Multi-Channel Surface Plasmon Resonance (SPR) Biosensors**, ***J. Ladd***, *C. Boozer, Q. Yu, J. Homola, S. Yee, S. Jiang*, University of Washington

Recently, a novel SPR sensor with on-chip referencing has been realized. In this sensor, one half of the gold sensing surface is covered with a high refractive index overlayer of tantalum pentoxide (Ta2O5). When polychromatic beam illuminates the sensing surface, surface plasmon resonance in the areas with and without the overlayer occur at different wavelengths. Therefore, the reflected light exhibits two dips associated with SPRs in those two areas. When functionalized properly, one of the areas can be used as a specific sensing channel for detection of specific bio-interactions and the other can act as a reference channel for compensation for background refractive index fluctuations. In this work we present a new functionalization approach for these mixed architecture chips. The gold side of the chip is functionalized with a mixed self-assembled monolayer of polyethylene oxide (PEO) and biotin terminated thiols whereas the Ta2O5 side is coated with PEO terminated silanes. The PEO terminated thiols and silanes serve as a protein resistant background, while the biotin-terminated thiols are used to bind streptavidin, which in turn immobilizes biotinylated antibodies. Hence, the gold side of the chip is used for the binding and detection of target analytes and the Ta2O5 side functions as a reference channel that monitors bulk refractive index changes and temperature drift. We have applied this functionalization to an SPR based biosensor and have studied two model systems: mouse IgG and human hCG. In addition, we have quantified and compared the protein resistance of the PEO thiols versus the PEO silanes. This information will help us better compensate for non-specific effects and improve robustness of SPR measurements.

8:40am **BI+HS+SS-ThM2 Chemical Sensing Using Ultra-Fast Micro-Boiling**, ***O. Thomas***, *R.E. Cavicchi, M.J. Tarlov*, National Institute of Standards and Technology

We report a novel liquid sensing method that exploits micro-boiling phenomena on the surface of rapidly heated thin film heaters. The heaters are thin films of platinum and gold-plated platinum that are approximately tens of micrometers in width and hundreds in length. The micro-heaters are immersed in solutions where they are rapidly heated to high temperature with short, 5 - 40 microsecond, square voltage pulses. The temperature-time responses of the micro-heaters are obtained by measuring their resistance during the application of the heating pulse. The bubble nucleation event associated with boiling is signaled in the temperature-time transient by an inflection point that results from a change in heat transfer when a vapor film forms on the heater. Because of the extremely high heating rates, superheating is observed where nucleation temperatures approaching 300°C have been measured for aqueous solutions. The bubble nucleation temperature and average heater temperature during the micro-boiling process have been found to be highly dependent on the surface wettability of the heater, as well as the presence of surfactant molecules. We will report on the use of alkanethiol self-assembled monolayers to investigate the effect of surface wettability on micro-boiling. We will demonstrate that temperature-time transients of hydrophobic SAMs are distinct from those of hydrophilic SAMs and that information on SAM stability can be gleaned from transient data. We will also present preliminary results on using the micro-boiling phenomenon to detect surface binding events such as DNA hybridization and biotin-avidin coupling.

9:00am **BI+HS+SS-ThM3 Nanofluidic and Biomimetic Bioanalytical Systems**, ***G.P. Lopez***, University of New Mexico **INVITED**

This talk will present recent progress on the development of hybrid nano-materials containing synthetic and biosynthetic components for use in bioanalytical applications including separation and biosensing. Examples include the development of mesoporous s ilica microbeads that incorporate functional biomolecular components (e.g., transmembrane proteins in lipid bilayer systems) and stimuli-responsive polymers for the formation of "cell mimics" that preserve biological function in a robust, deterministic, n onliving system. Microscopic beads can be used in a variety of bioanalytical system formats including suspension assays in flow cytometry and microfluidic assays and separations in affinity microcolumns. Several aspects of these bioanalytical systems will be explored including optimization of ligand-receptor pairs for direct transduction of biomolecular recognition, microfluidic considerations, and fluorescence detection principles.

9:40am **BI+HS+SS-ThM5 A Gold Nanoparticle Sensor to Interrogate Biomolecular Interactions in Real-time on a Surface**, *N. Nath*, ***A. Chilkoti***, Duke University

We present a label-free optical technique to study biomolecular interactions in real time on a surface that is based on particle surface plasmon resonance (PSPR). We demonstrate that the absorbance spectrum of immobilized gold nanoparticles on glass exhibits a red shift as well as an increase in the absorbance at peak wavelength as a function of binding of biomolecules at the solid-water interface. The results obtained with the absorbance sensor were compared with those obtained using conventional SPR for fibrinogen adsorption onto a COOH-terminated surface and for the binding of streptavidin to a biotin-functionalized surface. We have also examined the sensitivity and dynamic range of the sensor as a function of nanoparticle size, and found a threefold improvement in sensitivity as the size of the nanoparticles is increased from 13 to 50 nm. This sensor is attractive because of its simplicity: gold nanoparticles are easily prepared with high reproducibility, they can be readily immobilized on glass, and their absorbance spectrum can be easily measured using widely available UV-vis spectrophotometers. Furthermore, this technique should be easily amenable to the design of chips in an array format for application in high-throughput immunoassays and proteomics.

10:00am **BI+HS+SS-ThM6 Evaluation of Methodologies for Arraying a Porous Inorganic Bioassay Support**[1], ***C. Cole***, Nova Research, Inc., *D.B. Chrisey, R.J. Colton, H. Kim, B.R. Ringeisen*, Naval Research Laboratory, *C.R. Tamanaha*, Geo-Centers, Inc., *L.J. Whitman*, Naval Research Laboratory

A membrane-based immunosensor has been developed for the detection of eight biological agents with a response time of <15 minutes and a sensitivity ~3 orders of magnitude higher than conventional ELISAs. The Force Discrimination Biosensor[2] (FDB) uses generically functionalized 0.8 µm-diameter beads to label captured target; a magnetic field gradient removes nonspecifically bound beads, thus improving sensitivity by reducing both background and the incident of false positives. Already demonstrated for single analyte detection, methodologies to array the alumina ultrafiltration membrane for multiplexed detection have been evaluated. One of the biggest challenges is to array hydrophobic antibody conjugates onto porous hydrophilic PEG-biotin surfaces without losing pattern integrity due to lateral wicking. Patterning via a PDMS stamp or mask works reasonably well, but is too cumbersome for the patterning of the large number of membranes needed for practical applications. Instead, a pulsed laser transfer technique developed at NRL has been adapted to pattern antibody conjugates[3] onto PEGylated membranes. With an average element dimension of $(100\ \mu m)^2$ and 200 µm spacing between elements, a 10 x 10 array can be written in 3 mm^2. Such arrays can be patterned to give a single diagnostic for a variety of bacterial, viral, or protein agents without requiring the use of an additional membrane for positive/negative controls. Multiplexed assays for bacterial spores and cells, viruses, and protein toxins have been performed with these filters; results will be presented to demonstrate the application of pulsed laser writing to biosensor patterning.

[1] Supported by the Joint Service Technical Panel for Chemical and Biological Defense.

[2] Lee et al., Anal. Biochem. 287, 261 (2000).

[3] Ringeisen et al., Biomaterials 23, 161 (2002).

10:20am **BI+HS+SS-ThM7 DIOS-MS for Reaction Monitoring and Chemical Analysis**, *Z. Shen*, University of California, San Diego, *G. Siuzdak, M.G. Finn*, The Scripps Research Institute, ***J.E. Crowell***, University of California, San Diego

Desorption/Ionization On Silicon Mass Spectrometry (DIOS-MS) is a new mass spectrometry strategy based on pulsed laser desorption/ionization from a porous silicon surface. DIOS-MS is similar to matrix-assisted laser-desorption ionization mass spectrometry (MALDI-MS) in that it utilizes the same instrument; however, in DIOS-MS, porous silicon is used to trap analytes deposited on the surface and laser radiation is used to vaporize and ionize these molecules, without the presence of any matrix material. We have shown that DIOS-MS can be used for a wide range of small molecules as well as biomolecules at the femtomole and attomole level with little or no fragmentation. DIOS-MS offers many unique advantages including good sensitivity, low background ion interference, and high salt tolerance. We will demonstrate the application of DIOS-MS to small molecule quantitative analysis, high throughput screening, chemical reaction monitoring, enzyme-substrate reaction and inhibition characterization, drug

metabolism studies, and protein identification. We will also discuss aspects of the desorption and ionization mechanisms of DIOS.

10:40am **BI+HS+SS-ThM8 ToF-SIMS Analysis of PNA/DNA Hybridization on Thiolated Biosensor Chips**, ***M. Schröder***, Westfälische Wilhelms-Universität Münster; Germany, *J.C. Feldner, S. Sohn, H.F. Arlinghaus*, Westfälische Wilhelms-Universität, Germany

We have investigated a diagnostic method that uses peptide nucleic acid (PNA) biosensor chips to detect hybridization of unlabeled DNA. Using two different approaches, different PNAs were immobilized onto Au-coated spots with an approximate diameter of 100µm. One method was to immobilize thiolated PNA in a single-step reaction to the Au-surface via an Au-S-bond. The other method was to crosslink the N-terminal end of the PNA to a preformed layer of 11-mercaptoundecanoic acid (MUA) in a reaction consisting of two steps forming an amide bond. These layers were hybridized with complementary and non-complementary unlabeled single-stranded DNAs (ssDNA). Since the backbone of DNA, in contrast to PNA, contains phosphorous, it is possible to identify DNA-PNA-hybrids with time-of-flight mass spectrometry (ToF-SIMS) via DNA-specific phosphate-related ions at the masses 63 amu (PO_2^-) and 79 amu (PO_3^-). In addition to these signals, the deprotonated bases M-H$^-$ were detected in both immobilization approaches. In the case of the two-step-immobilization, it was possible to independently control the different steps by measuring characteristic peaks of MUA-fragments. Due to the manifold control-possibilities, especially variation of surface-density of the immobilized PNA and saturation of the remaining active Au-binding-sites with different thioles, it is possible to optimize hybridization conditions and suppression of uncharacteristic bonding of the ssDNA to the Au-surface. From the obtained data it can be concluded that both PNA immobilization approaches are very promising for designing PNA biosensors and that ToF-SIMS is a useful tool for identifying DNA-PNA-hybrids on these biosensor chips with good discrimination.

11:00am **BI+HS+SS-ThM9 Covalent Attachment and Hybridization of DNA Oligomers at Polycrystalline Diamond Thin Films**, *T. Knickerbocker, W. Yang, W. Cai,* University of Wisconsin-Madison, *J.N. Russell, Jr., J. Butler,* Naval Research Laboratory, *D.M. Gruen, J.A. Carlisle,* Argonne National Laboratory, *L.M. Smith, D. Van der Weide,* ***R.J. Hamers***, University of Wisconsin-Madison

Diamond has a number of unique properties, including a very wide range of electrochemical stability and very good electrical and thermal properties. These properties may make diamond a particularly attractive material to use as a substrate for biological sensors. We have explored the covalent bonding of DNA to several different types of diamond thin films, including free-standing polycrystalline films, thin films of microcrystalline diamond on silicon substrates, and ultrananocrystalline diamond thin films. Starting with H-terminated diamond, we prepared a homogeneous amine-terminated surface using a photochemical attachment processes, optimized using core-level photoemission spectroscopy. These amine-terminated diamond surfaces are then used as a starting point for subsequent attachment of DNA oligomers. The efficiency and selectivity of hybridization have been determined using conventional fluorescence measurements after the surface-bound oligomers are hybridized with fluorescently-tagged complementary and non-complementary oligomers. Our studies show that DNA-modified diamond surfaces show good hybridization properties and good selectivity. More importantly, the DNA-modified diamond surfaces show extremely good stability with repeated hybridizations, and retain this selectivity even after being dried and later reconstituted. This talk will discuss the fabrication of DNA-modified diamond surfaces for biosensor applications, and the differences and similarities between the various forms of DNA-modified diamond thin films.

11:20am **BI+HS+SS-ThM10 Direct Electronic Detection of DNA Hybridization at Surfaces**, ***W. Cai***, *J. Peck, D. Van der Weide, R.J. Hamers*, University of Wisconsin-Madison

We have explored the use of electrical measurements to detect DNA hybridization in a label-free manner at surfaces. Our work has emphasized materials that are compatible with microelectronics, including DNA-modified surfaces of silicon, gold, and diamond. While most previous studies have focused on detection via low-frequency measurements, our work has focused on measurements at high frequencies, from ~10 kHz up to 10 GHz. The use of radio- and microwave-frequencies brings with it reduction in 1/f noise, the possibility of constructing electrically resonant devices for enhanced sensitivity, and the ability to perform single-ended measurements based on reflection instead of transmission. At these high frequencies, the electrical properties are controlled by the capacitance of the electrical double-layer, with some possible contributions from the space-charge region of semiconducting substrates. Using electrochemical impedance spectroscopy, we find a small, but reproducible change in capacitance at the interface when DNA oligomers are hybridized with the complements. By comparing the responses generated when the surface-bound oligos are exposed to matched and mismatched sequences in solution, we can separate the changes in dielectric properties arising from hybridization from other possible sources of systematic error. To enable measurements to be performed with high sensitivity on very small areas, we have constructed a novel heterodyne reflectometer that allows us to measure the dielectric properties of very small interfaces in a manner that is essentially zero-background. To do this, we take advantage of the fact that the electric double-layer is intrinsically nonlinear, and that hybrization and other biological binding processes modify the dielectric properties of the double-layer region. This talk will discuss different schemes for direct electronic detection of DNA hybridization, with particular emphasis on the use of RF and microwave methods.

11:40am **BI+HS+SS-ThM11 Engineered Biointerfaces for Protein Biochip Applications**, ***H.B. Lu***, *M. Mariano, S. Schweizer, H.M. Tran, L.A. Ruiz-Taylor, H. Hong, H.H.J. Persson, R.L. Cicero, P. Kernen, P. Wagner*, Zyomyx, Inc.

Protein biochip technology promises breakthroughs in large-scale protein analysis. Measuring and analyzing protein activities in a highly efficient, miniaturized and parallel fashion requires advanced surface chemistries for reproducible protein immobilization and minimized non-specific adsorption. Controlling the solid-liquid interface of a miniaturized biochip becomes a key step for maintaining protein activity and integrating highly sensitive detection techniques. We present several reactive surfaces engineered for protein biochip applications at Zyomyx. Systematic efforts on designing organic layers on different substrates have been carried out to improve packing density, orientation, and functionality of immobilized capture reagents, as well as to minimize non-specific biomolecule adsorption in complex biological samples. The latter is particularly important for improving detection limits and obtaining meaningful results in multiplex protein assays. To reduce non-specific adsorption and optimize chip performance, we incorporated oligo- and poly-ethylene glycol (EG) molecules in our organic layers that are well known to reduce non-specific protein adsorption. Effects of substrate type, surface coverage, and molecular structure of the assembled organic layers on specific and non-specific interaction of biomolecules with the surfaces are presented. Specificity, loading capacity and detection sensitivity of protein immunoassays using high-density protein arrays configured with these surfaces are demonstrated and discussed.

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