SYMPOSIUM DD

Interfacial Aspects of Soft Biomaterials

April 24 – 26, 2000

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*Invited paper
SESSION DD1: surface modification and cellular response

8:30 AM *DD1.1 MODULATING THE ACTIVITY OF BIOLOGICAL SURFACES. Jeffrey A. Hubbell, ETH and Univ. of Zurich, Inst. for Biomedical Engr and Dept of Materials, Zurich, SWITZERLAND.

Cell-surface interactions play an important role in mediating a variety of healing responses, and biomaterials systems will be described in this talk with which to modulate those interactions, both between cells and tissue surfaces and between cells and the surfaces of biomaterials used as cell-growth matrices. Cell and tissue surfaces are net negatively charged. Correspondingly, copolymers (PEG-PLA) of polyethylene glycol (PEG) grafted to polylactic acid (PLLA) have been synthesized and explored to statically stabilize cell-cell and cell-matrix adhesion. The PEG backbone serves as the anchor domain, and the dangling PEG chains form a polymer brush at the cell or tissue surface that can sterically stabilize the approach of a potentially interacting cell. Polyamino acid moieties have been additionally grafted to the PEG backbone, to thereby strengthen the interaction of the anchor domain with the biological surface via crosslinking with sialic acid residues that terminate the branched oligosaccharides in glycoproteins. Using such approaches, it is possible to block high affinity biological interactions between cells and cell or tissue surfaces. In the context of three-dimensional cell-growth matrices, synthetic hydrogels have been developed consisting of tetrafunctional PEG tricarboxylic, cross-linked in situ with peptides that contain two reduced cysteine residues, where the cross-linking occurs via a Michael-type addition reaction. The peptide can be designed so as to contain a site for proteins that are produced by cells during the culture, allowing the cell to remodel the biomaterial as though it were natural extracellular matrix. Adhesion peptides can likewise be incorporated into the material as dangling structures. Such materials have been explored, successfully, in generation of ectopic bone in animal models, in conjunction with the release of the bone-inducing growth factor BMP-2.

9:00 AM DD1.2 BIODEGRADABLE POLYMER AMPHIPHILES FOR SURFACE MODIFICATION OF TISSUE ENGINEERING DEVICES. Rafal A. Mickiewicz, Pallibh Banerjee, Darrell J. Irvine, Anne M. Mayes, Catherine D. Reyes, Department of Materials Science and Engineering, and Linda G. Griffith, Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA.

Materials designed for specific control of cell behavior through cell surface receptor mediated signaling have useful applications in tissue engineering. Amphiphilic copolymers have been designed to limit non-specific protein adsorption, while at the same time allowing for cellular level control through chain end functionalization. A further requirement on tissue engineering scaffolds is that they be biocompatible once their function has been served. In light of this, a biodegradable copolymer based on poly(E-caprolactone) and poly(ethylene glycol) has been synthesized. This polymer may further be used in the development of biodegradable hydrogels for coating biomaterial surfaces. The ability of these coatings to regulate cell behavior and the stability of these surfaces in an aqueous environment has been studied. Control of the degradation and signaling properties of the substrate are necessary for the successful design of tissue engineering scaffolds.

9:15 AM DD1.3 SURFACE ENGINEERING OF POLY(LACTIC ACID): FOR USE IN BIOLOGICAL SYSTEMS. Robin Quirk, Martyn Davies, Saul Tendler, Kevin Shakesheff, Dept of Pharmaceutical Sciences, Nottingham University, UNITED KINGDOM.

Enhancing the surface properties of biodegradable polymers such as poly(lactic acid) (PLA) can prove difficult, due to the lack of suitable surface chemistry for coupling biologically-active molecules. We have developed a novel approach for modifying PLA, based on the physical entrapment of a secondary species at the polymer surface. The technique involves exposure of the polymer surface to a solvent/ non-solvent system. This partial solvent swells the interface, allowing the modification to diffuse into the loose network of PLA chains. The rapid addition of a PLL non-solvent results in the collapse of the surface and the immobilisation of the modifier. The successful incorporation of both poly(ethylene glycol) and poly(L-lysine) (PLL) have been demonstrated using this method. The amount of PLL immobilised may be controlled by varying process parameters such as solvent/non-solvent ratio or polymer/partial solvent contact time. XPS analysis suggests that surface coverages of the tagged species are in excess of those required for many applications. This includes the stimulation of integrin-mediated cell interactions, which we have demonstrated following conjugation of RGD peptide sequences to PLL nanoparticles. Results show that these nanomaterials can successfully promote cell spreading characteristic compared with unmodified PLA and thus offer potential in tissue engineering applications.

9:30 AM *DD1.4 INTERACTIONS BETWEEN PEG BRUSHES IN AQUEOUS MEDIUM: SOFT SURFACE MODIFICATION FOR IMPLANTS AND BIOMATERIALS. Uri Rappo, Pierre Laurent, Joseph Pey, Rafal Tadrous, Jacob Klein, Dept of Materials and Interfaces, Weizmann Institute of Science, Rehovot, ISRAEL.

Poly(ethylene glycol) (PEG) is a water soluble polymer compatible with the immune system of the human body. Thus it may be a good candidate to modify surfaces of artificial implants, or to serve as a soft spacer for modifying surfaces with different biomolecules. To examine this, direct measurement of the shear forces between two atomically smooth silica surfaces bearing functionalised PEG immersed in pure (conductivity) water have been carried out as a function of surface separation. PEG (Mw=3k) that has been functionalised on both ends, was introduced into water and adsorbed only at one end onto the micra surface. A monotonically-increasing forces distance law was indicated, beginning at surface separations of \(\approx 100nm\). This repulsion is shorter ranged than the conductivity water, due to the shorter Debye length in the presence of higher ion concentration. High repulsion forces starting at \(\approx 5nm\) are due to the extensive compression of the grafted polymer layers. The range of the high repulsion forces (5-50nm) and the AFM images indicate that the modified PEG molecules form a uniform monolayer on the surface. Shear motion was then applied between the surfaces, at separations from some tens of nanometers down to closest approach distance, and the lubricating properties of the layers were investigated. Results indicate that such PEG molecules can readily used for surface modification of implants as well as precurser for active biomolecules, will be presented at the meeting.

10:15 AM *DD1.5 IMAGING OF GFP-TAGGED CYTOSKELETAL PROTEINS IN LIVE CELLS PROVIDES A MEANS OF ASSESSING THE EFFECTS OF SURFACES ON CELL BEHAVIOR. Teng-Leong Cheek, Wendy A. Wolf and Benjamin H. Yost, Department of Biological and Molecular Biology, Northwestern University Medical School, Chicago, IL.

Interactions between cells and their environment represent an important focus for biologists and materials scientists interested in the development of biologically active or biocompatible materials. Our long-term goal is to develop a real time readout for the interactions between cells and the surfaces with which they interact. We are employing a combination of live cell imaging using digital microscopy, computer assisted image capture and processing and fluorescence tagged tagged elements of the cytoskeleton and cellular adhesion systems. The actin cytoskeleton and the cellular matrix myosin that associates with it are the principal force generating structure in cells. The organization of the actin cytoskeleton is greatly influenced by its interaction with the cellular adhesions on the surfaces on which the cells grow. Consequently the organization of the actin cytoskeleton may provide a direct readout indicating how cells react to different substrate environments. To monitor the organization of the actin cytoskeleton in living cells we have generated myosin regulatory light chain (RLC) tagged with green fluorescent protein (GFP). The GFP tagged myosin associates with bundles of actin filaments known as stress fibers-thought to be the primary contractile element in cells. The punctate pattern of GFP-RLC localization has allowed us to directly observe the contraction of stress fibers. In addition, we have observed the apparent treadmilling of the stress fibers, suggesting a new form of intracellular motility. This experimental system allows us to directly visualize changes in the actin cytoskeleton and the adhesion contacts to which it connects in response to the environment. We have also employed patterned surfaces to examine real time dynamic changes in the organization of the actin cytoskeleton in response to changes in surface hydrophobicity. This approach should provide materials scientists and biologists a powerful new tool for assessing the effects of surfaces on cellular behavior.

10:45 AM DD1.6 DEPOSITION OF NANO-SIZED POLYMER FILMS FOR IMPROVED CELL INTERACTIONS AND CONTROLLED RELEASE BIOHIMICAL APPLICATIONS. Andrew J. Fitz-Gerald, Rajiv Singh, University of Florida, Gainesville, FL.

To improve tissue interactions and for local delivery of anti-inflammatory and/or immunosuppressant drugs from implants devices such as stents, biodegradable poly(lactic acid) (PLLA), poly(lactic-co-glycolic acid) (PLGA), and poly(ethylene glycol) (PEG) coatings
were investigated. Recently, stainless steel stents, dip-coated into poly(lactic acid) solution with incorporated agents, showed reduced thrombogenicity. These findings suggest that an ex vivo human atherosclerotic plaque model can be used to study the effects of different coatings on the surface.

For preliminary evaluation of an improved method of applying biodegradable coatings on implant surfaces, nanometer-thin polymer films were formed using a Pulsed Laser Deposition (PLD) technique and characterized by SEM, GPC, IR, FTIR, and PLD. PLD coatings were applied using an excimer laser (248 nm) directed at a polymer target in a vacuum chamber, which is absorbed and expands from the surface in a plasma of polymer clusters that is directed over the surface of the polymer samples using SEM, FTIR, NMR, and GPC verified.

**11:00 AM DD17**

**ENHANCED ATTACHMENT AND PROLIFERATION OF HUMAN NEONATAL FIBROBLASTS ON EXPANDED PTFE SUBSTRATES MODIFIED WITH P-15. A SYNTHETIC PEPTIDE (AMERICAN LINEAGE) GROWTH FACTOR (ALGF),**

Rajendra S. Bhattachar, University of California, Berkeley and San Francisco, Joint Biotechnology Graduate Group, San Francisco, CA.

Expanded polytetrafluroethylene (e-PTFE) has numerous clinical applications ranging from blood vessel reconstruction to soft tissue augmentation but lacks adhesion properties due to its low surface energy. To enhance the surface reactivity of this fluoropolymer, e-PTFE sheets were functionalized by glow discharge followed by covalent immobilization of P-15, a synthetic peptide modeled after the putative cell binding region of human type I collagen. Surface-modified e-PTFE sheets were seeded with human neonatal dermal fibroblasts (HFFs), and at varying time points, specimens were characterized by metabolic labeling, stereomicroscopy, confocal laser scanning microscopy of the actin cytoskeleton, and scanning electron microscopy. After 24 hours in culture, a greater number of cells adhered to and displayed a spread morphology on the e-PTFE substrates modified with P-15. In contrast, few HFFs attached to control e-PTFE specimens, forming cell clumps which exhibited little spreading. After 3 days in culture, cells cultured on P-15-e-PTFE formed multiple layers with extensive actin stress fiber networks in parallel arrays, while controls showed fewer cells with a random orientation. In addition, HFFs appeared to adhere more strongly to P-15-e-PTFE than cells grown on control e-PTFE, which were observed to slough off and detach from the surface of the polymers. Finally, [3H]-thymidine labeling experiments confirmed that HFFs seeded on P-15-e-PTFE proliferated faster than those on control e-PTFE. Taken together, these findings suggest that P-15-e-PTFE materials may provide a more conducive environment for cell attachment and proliferation, important determinants of intact fixation and stability.

**11:15 AM DD18**

**SURFACE CHARGE, TOPOGRAPHY AND CHEMISTRY STUDIES OF HUMAN SKIN FIBROBLAST GROWTH ON SURFACE MODIFIED PTFE BIO-MEMBRANES.**

Ian Baeke, Biocurrents Research Centre, Marine Biological Laboratory, Woods Hole, MA.

Artificial Bio-Membranes such as functionalised micro porous PTFE have many applications involving cell growth and adhesion such as artificial skin and cell scaffolds. Key factors in promoting cell growth are the chemistry, topography and surface charge of the biomaterial. Here, several over looked parameters is the surface charge. Using a novel multi-tip Scanning Bio-Kinin Probe (SBKP)®, we have performed high resolution topographical and charge topographical characterisations of functionalised membranes prior to Human Skin Fibroblast growth. Using SBKP coupled with SEM and XPS, we have characterised the charge, topography and chemistry of surface modified bio-membranes prior to Human Skin Fibroblast (HFB) growth. Subsequent video-microscopy growth data indicates an extraordinary correlation between a regime of homogeneous negative surface charge profiles and confluent HFB films. We anticipate many applications of this technique in monitoring biomaterials/biological interfaces as it permits non-invasive charge imaging which dramatically affects bio-compatibility.


**11:30 AM DD19**

**SURFACE MODIFICATION OF NEURAL PROSTHETIC DEVICES BY CONDUCTING POLYMERS AND PP-Graft-COPOLYMERS COMPOSITES.**

Xinyan (Tracy) Cui, David C. Martin, Material Science and Engineering and Macromolecular Science and Engineering; David J. Anderson Electric Engineering and Computer Science, University of Michigan, Ann Arbor, MI.

Micromachined neural prosthetic devices facilitate the functional stimulation of and recording from the peripheral and central nervous system. However, when these devices are implanted into brain tissue for long term use, they lose their functional connectivity as a function of time and migrate from their intended position. There is a mismatch between the stiff, electrically conductive silicon - based metal electrode and the soft, ionically conductive brain tissue. In order to improve the electrical interface and improve the signal transmission, bioactive, electrically conductive polymer composites were coated onto the surfaces. Polypropylene combined with different high molecular weight acrylic acid monomers have been precisely deposited onto the functional sites of neural prosthetic probes by galvano-synthetic electrochemical deposition. Polyethylene/PSD (polyethylene sulfonate) composite was deposited out of 0.1M pyrrole aqueous solution, using 0.1 M PSSN as the dopant. The influence of current density, monomer concentration, and reaction time on the thickness, morphology, and electrochemical properties of the polypropylene films has been studied by Optical Microscopy (OM), Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), Electrochemical Impedance Spectroscopy (EIS), and Cyclic Voltammetry (CV). The roughness of the surface varied as the film grew. Rough surfaces give the electrode a much higher interfacial surface area, which is good for charge transfer at the interface. Polyethylene/PSSN films discovered the fractal characteristics of the films, which can be correlated to frequency - dependence of the impedance. The impedance of the film varied with film thickness and roughness. An optimum thickness exists in terms of the lowest impedance at the biologically - relevant frequency of 1 kHz. A reversible redox reaction shown by CV provides the film with a large capacity, which decreases the magnitude of electrode impedance.

In vivo acute recording tests in guinea pig cortex showed that strong neural signals can be detected through the polypropylene/PSD coated probes. To further improve the biocompatibility, the acrylic was replaced by bioactive molecules, such as collagen and synthetic protein SLFP, respectively. Collagen is well known as an extracellular matrix protein to cell culture media, and SLFP is a genetically synthesized silk-like protein polymer which contains a high concentration of the RGD amino acid sequence, the cell binding sequence of fibronectin. Microscopic IR data indicates that the bioactive molecules are well immobilized onto the polypropylene/PSD matrix. The biocompatibility of the polypropylene/bioactive molecule composites are being tested in cell culture. In vivo chronic tests of polypropylene coated neural recording probes are under way.

**11:45 AM DD1.10**

**NEURON PATTERNING BY ORGANIC SELF-ASSEMBLED MONOLAYERS.**

Cristian Ionescu-Zanecci, Yoko Nakamura, Physics Department, UC Santa Cruz, The Salk Institute, La Jolla, CA; Alain Lichte, Santa Cruz Institute for Particle Physics, Santa Cruz, CA; Lindsay Hinck, Biology Department, UC Santa Cruz, CA; Sue Carter, Physics Department, UC Santa Cruz, CA.

Understanding the function of neurons in connected networks has suffered from our inability to directly record changes in the membrane potential for a large neuronal ensemble. While new electrode arrays can be fabricated on the spatial scale of single neurons, the simultaneous recording of large numbers of interconnected neurons has yet to be achieved. The major obstacles have been patterning the neurons on top of the electrode arrays and controlling the neuron-electrode interface. Here we present work aimed at assembling organic monolayers on the active sites of the electrode arrays. Thiol chemistry is used to deposit a self-assembled monolayer (SAM) on the exposed platinum electrodes. Metal adhesion to the SAM molecules arranges the cultured neurons into ordered structures that match the array geometry, enabling efficient charge transfer between living neurons and the inorganic electrode arrays. The control of neuron placement on a recording array will be instrumental in the future development of biomimetic devices.

**SESSION DD2: LIPID MEMBRANES AND VESICLES**

Chair: Stella Y. Park
Monday Afternoon, April 24, 2000 Olympic (Argent)

**1:30 PM DD2.1**

**STIMULUS-RESPONSIVE LIPOPHER VESICLES FOR TRIGGERING PROTEIN AND POLYSACCHARIDE HYDROGEL FORMATION.**

Eric Westhues, Xiaoping Zeng, Bruce Losche, Nicole Eiberle and Philip B. Messersmith, Northwestern University Medical School and Department of Biomedical Engineering, Chicago, IL.

In nature, phospholipid assemblies (e.g. lipid bilayers) act as physical barriers that partition the aqueous phase into distinct cellular subcellular, and extracellular compartments that are chemically and functionally distinct. In our laboratory we are exploiting the barrier properties of phospholipid vesicles to entrap and isolate reactive chemical species of an aqueous suspension. The liposomes have been designed to release the entrapped species in response to an applied stimulus, such as light, temperature, pH, etc. Upon release, a chemical reaction ensues which culminates in the formation a semi-solid biomaterial. This bioinspired strategy represents a departure from the
traditional use of liposomes for intravenous delivery of drugs and
diagnostic agents, and could lead to new clinical materials for hard
and soft tissue reconstruction, wound healing. This self-assembly
process is driven by the use of liposomes for intravenous delivery of
drug and diagnostic agents, and could lead to new clinical materials for hard
and soft tissue reconstruction, wound healing. This self-assembly
process is driven by the traditional use of liposomes.
upon animal-derived materials also precludes the application of surfactant replacement therapy to children and adults, who are at risk for adverse immune responses to animal proteins. We have synthesized, purified, and performed in vitro testing of a new class of biomimetic spreading agents for lung surfactant replacements, based upon sequence-specific polymers called "polypeptides" or "nusblotated glycopolymers." We synthesize up to fifteen of an efficient, automated solid-phase synthesis that allows incorporation of diverse N-glycend sidechains (including proteinogenic sidechains) in a sequence-specific manner. Despite close similarity to polypeptides, polypeptides are more reliable substrates for proteins due to their lower molecular weight and hence are stable in vivo and less prone to immune system recognition.

We have shown that certain polypeptide sequences adopt stable helices in aqueous and micellar solvents. Our present aim is to develop functional, biomimetic spreading agents that control lipid phase behavior in a manner similar to natural surfactant proteins, that can serve as safe, reliable, bioavailable, and cost-effective additives to aqueous lung surfactant preparations. Additionally, we hope to gain detailed knowledge of interactions between surfactant proteins and lipids at the surface of the lung. Preliminary results using a Langmuir-Blodgett balance in conjunction with fluorescence microscopy show that polypeptide-based spreading agents have promising biophysical activity and surface morphologies in phospholipid monolayers.

4:30 PM *DD3.8 NEUTRON REFLECTIVITY TECHNIQUES FOR BIOMIMETIC BILAYER MEMBRANE STRUCTURAL CHARACTERIZATION. S. Krueger, N.F. Berk and C.F. Majkrzak, NIST Center for Neutron Research, Gaithersburg, MD. With C.W. Meaux and A.L. Plant, NIST Biotechnology Division, Gaithersburg, MD.

Neutron reflectivity measurement techniques are being developed to characterize structural properties of novel synthetic bilayers and phospholipid biomimetic systems, or hybrid bilayer membranes (HBM), which are formed on gold-coated single crystal silicon substrates, and which are in contact with aqueous solutions. Particular emphasis is being placed on designing a sample environment and experimental protocol that maximizes the reflected neutron intensity while still permitting in situ sample preparation and manipulation. In order to better interpret the reflectivity data, a model-independent fitting method for obtaining neutron scattering length density (SLD) profiles of the HBM structure perpendicular to the plane of the bilayer was developed. Most recently, experimental methods that permit direct inversion of the reflectivity data to SLD profiles, without the need for data fitting, have been successfully developed for the measurement of HBM SLDs. In addition, methods for measuring and interpreting the reflectivity data from patterned surfaces that are possible matrices for HBMs with transmembrane proteins are currently under investigation.

Discussion will focus on reflectivity measure ments made on HBMs consisting of a monolayer of thioether-phosphate ester derivatives 3(TEO), which contains an ethylene glycol moiety at the gold surface, and a monolayer of 3(TEO) covalently bonded to DMPG. Distributions of the DMPG DAB solution mixtures at 28°C, where the DMPG layer is in the fluid phase, both in the absence and in the presence of the membrane-active peptide, melitin, in the solution. Neutron SLD profiles of the HBM structure were obtained and compared to reflectivity measurements using both fitting and direct inversion experimental methods.

The reflectivity data and resultant SLD profiles will be discussed in terms of structural models for the HBM and the location of melitin in the bilayer. Results from measurements of other monolayers on patterned surfaces will also be discussed.

SESSION DD3: SURFACE MODIFICATION AND CHARACTERIZATION Chair: Anne M. Myers Tuesday Morning, April 25, 2000 Olympic (Argent)

8:30 AM *DD3.1 ENGINEERING A NEW CHEMICAL LANGUAGE ONTO CELL SURFACES. George Lemieux, Department of Chemistry, University of California, Berkeley, CA.

Cell surface glycoconjugates encode a wealth of information that dictates how a cell interacts with its extra-cellular environment. Our work has focused on introducing a new chemical language into cell surface glycoconjugates through carbohydrate metabolic pathways. By exploiting the intrinsic permeability of oligosaccharide biosynthetic pathways, orthogonally reactive, functional groups can be incorporated into cell surface oligosaccharides. We have utilized these engineered cell surfaces to induce specific cellular interactions with toxins, diagnostic probes, and viruses. In addition, we envision the application of this strategy to mediate specific cell-cell and cell-surface interactions which are a critical component of many biological events.

9:00 AM DD3.2 SELF-ASSEMBLY PROPERTIES OF CATIONIC LIPIDS ON MICA. Anne E. McKeehan, Timothy Rusto, Marjorie L. Longo, Department of Chemical and Biomolecular Engineering, Bioprocess Graduate Group, University of California, Davis, CA.

Supported lipids bilayers may serve as an ideal substrate for the formation of well-ordered biopolymers or DNA and protein arrays. The morphology of the bilayer, in particular inhomogeneities, such as domain formation and defects, may affect the layer properties of an adsorbed biopolymer. Therefore, understanding the structure of lipid domains and their ability to cause segregation in adsorbed layers will be useful in the production of biomaterials that utilize supported bilayers. Domain formation in micropatterned bilayers of DPTAP and DMTPA, fluorescently labeled with an NBD lipid was investigated with both fluorescence and atomic force microscopies. Hecting the bilayers above their acyl chain melting temperatures and varying the rate of cooling resulted in the appearance of fractal (DPTAP) and feather (DMTPA) domains of controllable sizes. These morphologies indicate that domain formation occurs via a diffusion-limited process. Atomic force microscopy (AFM) scans revealed that dark regions in fluorescent images were approximately 4 nm thick, indicating that a single bilayer was present on the mica. Height differences between dark and light regions were 1.4 nm (approximately double the reported monolayer steps in LE-LC coexistence) implying that two lipid tilted phases were present in the bilayer. The organization of the biomaterial was further investigated by adding CY5-labeled DNA to the NBD-labeled bilayer and imaging with confocal microscopy. Preliminary scans suggest that DNA prefers to adsorb to the more condensed dark domains rather than the more tilted light domains indicating that lipid density may be a factor in adsorption to supported lipid membranes.

9:15 AM DD3.3 RECOGNITION BIOSURFACES VIA SELF-ASSEMBLY AND AMINO ACID IMMUNOLOGIZATION: PREPARATION, CHARACTERIZATION, AND IN VITRO BIOLOGICAL ASSESSMENT. Buddy D. Warner, Sheng Pan and David G. Cramer, University of Washington, Departments of Chemical Engineering and Bioengineering, Seattle, WA.

Biospecific recognition surfaces were made by random immobilization of arginine (R), glycine (G), and aspartic acid (D) amino acids on well-defined self-assembled monolayer (SAM) surfaces. The surface reactions were systematically characterized by x-ray photoelectron spectroscopy (XPS) and time-of-flight secondary ion mass spectrometry (TOF-SIMS). The randomized amino acid derivatized surface demonstrated the ability to stimulate cell attachment and spreading on the surface without the presence of serum proteins. The biospecific recognition between the surface and the cell receptors was attributed to the presence of the appropriate chemical environment and the resulting pattern matching between the randomly distributed RGD domains and cell receptors. This observation may be useful in providing the basis for developing novel engineering strategies for biomaterial designs. The study also demonstrated the utility of SAMs as model surfaces for biointeraction studies.

9:30 AM *DD3.4 OPTICAL CHARACTERIZATION OF SINGLE MOLECULES AND SMALL DOMAINS IN ORGANIC THIN FILMS. Lori S. Goldner, Kenneth D. Weston, Jesseung Hwang, National Institute of Standards and Technology, Gaithersburg, MD.

This paper discusses recent innovations and progress in the optical characterization of thin organic films. Two techniques, near-field scanning optical microscopy (NSOM), and single molecule fluorescence detection using confocal microscopy will be discussed. With the application of new-field scanning optical microscopy (NSOM), it is possible to image thin films and surfaces with 20 nm resolution. In NSOM subwavelength light source is used as a scanning probe to achieve optical resolution beyond the diffraction limit. With the application of photometric techniques to NSOM we acquired quantitative information about local birefringence (strain) and dichroism. Eventually this may permit the imaging of domains and defects in very thin (single molecular layer) biomimetic films or coatings without the use of dye. Ordinary optical microscopy is limited by diffraction to a approximate thickness of half the wavelength of light. Nonetheless, single fluorophores can be detected and their properties (spectra, lifetime, diffusion, orientation) measured with confocal microscopy. We can measure the number, distribution, orientation, and re-orientation of...
10:30 AM DD3.5 CHARACTERIZATION OF SUPPORTED BIOMIMETIC FILMS USING BROADBAND VIBRATIONALLY RESONANT SUM-FREQUENCY GENERATION. Kimberly A. Brightman, Teresa P. Pescitelli, J. Robert Shepherd, John C. Stephenson, National Institute of Standards and Technology, Gaithersburg, MD.

Supported organic films have received considerable attention as both model biological membranes and biomolecular templates for the development of biomimetic devices. A complete characterization of these biomimetic films requires the application of in-situ techniques capable of probing fully hydrated systems. We have been exploring the potential of broadband vibrationally-resonant sum frequency generation (VRSFG) as an in-situ probe for the study of hybrid bilayer membranes (HBMs). Our novel broadband approach provides a complete SFG spectrum over a window of several hundred wavenumbers, combining interface sensitivity and molecular specificity with the advantages of short acquisition times and no need for wavelength tuning. We have characterized both alkane and thin-ether bilayer HBMs and self-assembled monolayer solid supports via VRSFG. Additionally, real-time, in-situ studies of the formation of phospholipid monolayers on these solid supports from flowing buffered vesicle solutions have been performed. A discussion of the formation kinetics and the stability of HBMs will be presented. 


10:45 AM DD3.6 NOVEL BIOMATERIALS THROUGH TAILORING OF SOLID SURFACES. Jürgen RHäse, Univ of Freiburg, Freiburg, Germany.

The modification of monolayers by monolayers of polymers which are covalently attached to the surface of the substrate is a very attractive way to improve the properties of solids in bio-oriented applications. We describe several new pathways for the synthesis of surface-attached ultrathin polymer films which carry functional groups relevant for biological or biomedical applications. The polymer molecules are either grown at the surface of the substrates in situ by using self-assembled monolayers of initiators or preformed polymers are photochemically attached to the material which is to be modified. Additionally, the formation of ultrathin, patterned networks of functional polymers will be described. An example for groups contained in the monolayers are peptide moieties, which could act as cell recognition ligands for the growth (patterned) outgrowth of cells on surfaces. The characterization of the monolayers, especially the swelling of these layers in an aqueous environment, will be described.

11:00 AM #DD3.7 CONTROL OF RECEPTOR-MEDIATED CELL BEHAVIOR USING SYNTHEtIC POLYMERS. Linda G. Griffith, MIT, Department of Chemical Engineering and Division of Bioengineering & Environmental Health, Cambridge, MA.

Virtually every aspect of cell behavior is governed at some level by interactions of receptor molecules on the cell surface with ligands in the extracellular environment. Molecular components involved in activation of receptors mediated signaling pathways which culminate in cell migration, differentiation, and growth are being identified at a rapid rate. Much overlap exists in signaling pathways activated by distinct classes of receptors; for example, ligand activation of growth factor receptors influences integrin-mediated processes of migration while integrin ligation is required for growth factor-induced proliferation of many cell types. Several strategies to induce intracellular signaling molecules are activated by both integrins and growth factors. How does the cell take information from such overlapping stimuli and process it to achieve different responses? In addition to the specific identification of the overall context of ligand presentation – relative concentrations, spatial organization, and kinetics – must be considered to understand how a cell integrates stimuli to achieve a precise response. In order to pursue how these factors contribute to overall innate and adaptive cellular response, we are developing approaches in which key variables can be systematically controlled by a combination of biochemical and physical means. This talk will focus on the physical aspects of this approach – designing new polymeric materials that can be applied to both tissue engineering and to fundamental studies of receptor-mediated phenomena. A specific interest is controlling signaling by the epithelial growth factor receptor (EGFR). For example, we have shown that mEGF stimulates both DNA synthesis and cytoskeletal changes when tethered to the cell culture substrate to that internalization is inhibited, and that EGF can serve as either a stimulatory or inhibitory regulator of cell migration speed depending on the cell-substrate adhesion characteristics. We are using these findings to inform the design of 3D scaffold materials for tissue engineering, including surface modification of degradable polymers as well as a new enzymatically crosslinked hydrogels for cell encapsulation.

11:30 AM DD3.8 DYNAMICS OF BOND BREAKING IN CONDENSED PHASE STUDIED BY CHEMICAL MICROSCOPY. Aleksandr Noy1, Salvador Zepedia1,2, Christiane A. Orme1, Yin Yeh2, James J. DeYoreo3. 1Department of Chemistry and Materials Science, Lawrence Livermore National Laboratory, Livermore, CA; 2University of California, Davis, CA.

Intermolecular forces underlie a variety of phenomena in chemical and in biological systems, such as colloidal stability, cell adhesion, protein folding and molecular recognition in ligand-receptor pairs. Understanding the dynamics of these interactions is critical for modeling and controlling these processes. The advent of ultra-sensitive force measurement techniques has enabled direct measurement of the bond strength on the relevant length scale. Recent measurements have pointed out the importance of kinetic factors in bond strength and pointed out the necessity to explore the whole energy landscape of a chemical bond. Still, little is known about the response of the bond strength to the environmental variables such as temperature. The analysis of this response provides a way to determine thermodynamic characteristics of the binding interaction. We used chemical force microscopy to measure the temperature dependence of the interaction forces in a well-defined system presented by a finite number of identical hydrogen bonds between the force microscope tip and sample surface in different solvents. The tip of the scanning probe microscope was modified with distinct chemical functionalities to give rise to the well-defined and uniform interactions with the sample surface. We also constructed a temperature stage that allowed rigorous control over the temperature in the microscope fluid cell over a wide range of temperatures. We will discuss the results of these measurements and the theoretical framework for their interpretation, as well as the relative importance of thermodynamic and kinetic factors affecting the bond strength in the presence of solvent medium. We also point out the differences in kinetics of bond breaking in single bond systems vs. multiple bond systems.

11:45 AM DD3.9 FIBEROPTICAL SPECTROSCOPY: NEW TOOL FOR BIOCOMPATIBILITY STUDIES. N. Anamayo, Dept of Physics, Univ of Nevada, Reno, NV; E. Bornscheuer, J. Bode, The Research Institute, The College of Juden and Samarin Ariel, ISRAEL; R. Bruch, S. Gammush, L. Weiser, Dept of Physics, Univ of Nevada, Reno, NV; A. Kazar, 1. Wasser, School of Physics and Astronomy, Tel Aviv Univ, Tel Aviv, ISRAEL.

The methods of vibrational spectroscopy have been applied to study of biocompatibility of polymer and crystal surfaces of implants with living tissue in vitro. The infrared (IR) spectral features of biomaterials' surfaces before implantation allowed us to create a quality control for the long-term biocompatibility of implants with eye and cardiac/vascular media. Spectral information regarding the biocompatibility and for biocompatibility of implants has been obtained from spectral features of specific molecular composition, surface structures and level of polymerization most appropriate for long-term compatibility in humans. Modified surfaces of implants have also been analyzed by means of vibrational spectroscopy. A new infrared interferometric method has been developed in conjunction with lowcost flexible optical fibers, sensors and probes. This combination of optical fibers and Fourier Transform (FT) spectrometers can be applied to many fields, including noninvasive medical diagnostics of cancer, other different diseases and physiological fluids in vivo. For example, this technique is ideal for testing of different types of polymer and crystal implants for their interaction with human tissue and body fluids. Such surfaces, as well as living tissue, have been investigated without sample preparation. Protection of silver halide optical fiber via thin film polymer coatings for studies of biological fluids allows developing and enhancing applications of optical fibers to the spectroscopic analysis. Coatings of optical fibers with biomaterial substrates could be used for long-term applications involving contact of a part of the sensor with tissue and biological fluids. Long-term monitoring of biocompatibility of implants at the medical level has been considered. Results on the vibrational spectral analysis of normal, pathological tissue, biological fluids and the interaction with implant surfaces in the region of 850-4000cm⁻¹ are presented.
SESSION DD4/FF4: JOINT SESSION: POLYEOLECTROLYTES AND PROTEINS AT SURFACES

Chair: Almgri Karim
Tuesday Afternoon, April 25, 2000
Metropolitan I (Argent)

130 PM *DD4.1/FF4.1

Adhesion, proliferation, differentiation and migration of cells in their native environment are critically dependent on their interaction with the surrounding extracellular matrix (ECM). Therefore, in order to promote bio-adhesion, cells must "belong" to the "at home". In the future, a better understanding of cellular processes between the ECM ligand proteins and the cell membrane receptors will give us tools to engineer the development of cell cultures (potentially human tissue constructs) that are more reproducible than those obtained from bioactive polymer surfaces. It is important to be able to control and maintain the conformation of immobilized ligand groups, since this has an effect on the surface-cell interaction. Surfaces prepared by coupling of ligands directly to the surface can exhibit reduced biological activity owing to steric hindrance or conformational changes. A spacer group between the matrix and the ligand may facilitate effective binding and shield the ligand from the surface to circumvent these problems as will be presented here.

2:00 PM DD4.2/FF4.2
BIOLUMINESCENCE: THE SHEAR OF ADSORBED POLY-ELECTROLYTES AND OF POLYMER BRUSHES. Jacob Klein, Xueyun Zhang, Alfred Wilke, Weizmann Institute of Science, Rehovot, ISRAEL.

The lubrication of mammalian joints takes place at the interface between articular cartilage layers as they rub past each other. To study and understand this effect at a microscopic level, we have used a surface force balance with unique sensitivity in measuring both normal and frictional forces to examine the friction between compressed layers of neutral, charged, and polyelectrolyte brushes. Our results reveal that entropic forces play a crucial role in reducing the frictional forces and may thus underlie the extremely efficient lubrication known to be active in biological joints. For the case of neutral surface-attached chains, configurational entropy of the polymer chains resulting from excluded volume effects leads to large osmotic repulsion between the compressed surfaces, and enables large loads to be borne with a very fluid interfacial layer as they slide past each other. For the case of charged chains - resembling the biological situation - there is the additional role of the counterions in solution, and in this case it is their translational entropy which leads to an osmotic repulsion between the mutually compressed neutral interfaces. We present recent results on this effect which reveal the remarkable effect of these entropic factors in reducing friction, and which may point to possible strategies for better design of artificial joint implants.

2:15 PM DD4.3/FF4.3
NOVEL MICROPOROUS BIO-INTERFACE MATERIAL PREPARED FROM POLYEOLECTROLYTE MULTILAYERS. James D. Mendelsohn, Anne M. Hayes and Michael F. Rubner, MIT, Department of Materials Science and Engineering, Cambridge, MA; Christopher J. Barrett, McGill University, Department of Chemistry, Montreal, CANADA.

A novel process has been developed to create large area, highly uniform macroporous bio-interface materials. The relatively new layer-by-layer (LbL) self-assembly process, whereby oppositely charged polymers are sequentially adsorbed from dilute aqueous solutions onto an immersed substrate, was used to fabricate hydrogel multilayer thin films from the polyelectrolyte polystyrene (PAA) and the polyanion polyallylamine hydrochloride (PAH). It has been found that a substantial, irreversible phase separation will occur on PAA/PAH multilayers assembled at pH conditions of 3.5-7.5, respectively, simply by briefly exposing the films to aqueous solutions of a pH of 2.2-2.5. AFM characterization shows that this pH-induced phase separation leads to a highly porous microstructure, with a 2D porosity of pores with pore sizes of 105 (50nm). While PAA/PAH multilayers have been used as a model system to investigate this pH-driven porosity phenomenon, efforts are currently underway to create macroporous films from charged biopolymers, the feasibility of incorporating charged drugs, enzymes, or other active biomolecules, e.g., cell adhesion molecules for specific bio-interface activity, into the multilayers will be investigated. The LbL method also advantageously enables the in situ inclusion of nanoparticles of silver, a known antimicrobial, into the films. The pH-dependent porosity and swelling in these multilayers allow for controlled drug release capabilities, and these porous films are also foreseen as dialyzer membranes and scaffold materials. Furthermore, this simple porosity transformation may lead to an alternative strategy to the polyelectrolyte complex conservation technology routinely used to encapsulate cells or drugs. Since it assembles into one molecular layer at a time with a nanoscale precision, the LbL technique, coupled with this unique pH-induced phase separation, could be a novel approach to synthesizing porous biomimetic with highly tunable features, including well-defined surface and interfacial properties.

2:30 PM DD4.4/FF4.4
POLYION-INDUCED STRUCTURAL REARRANGEMENTS IN NEGATIVE LIPOSOMAL MEMBRANES. Alexander Yaroshchuk, Viktor Kabanov, Moscow State Univ, School of Chemistry, Moscow, RUSSIA.

Permanently growing biomedical applications of synthetic polyelectrolytes require to study their behavior in biological environment and especially, their interaction with cells. In the latter case, spherical bilayer vesicles composed of lipid molecules can be used as cell mimetic objects. It is known that a cell membrane usually carries a net negative charge. Therefore, we focused on synthetic polyelectrons, interacting with neutral and negative vesicles. Interaction of polycationic species with liquid vesicles can be accompanied, in certain systems and under certain conditions, by lateral lipid segregation (microphase lipid separation), highly accelerated transmembrane migration of lipid molecules (polyion-induced flip-flop), incorporation of adsorbed species into the liposomal membrane, aggregation of vesicles and their disruption. If the system is strongly adsorbed polyelectrolyte, if not additionally anchored by an attached hydrophob, can be completely removed from the membrane surface by repelaction. The above mentioned phenomena were examined depending on structure and linear charge density of polyelectrolyte molecules, content of charged lipid, vesicle phase state and size, as well as ionic strength of solution. It is likely that the observations we made might be useful to interpret biological effects of polyelectrolytes and multicharged polymeric constructs.

3:15 PM *DD4.5/FF4.5
BIOFUNCTIONALIZATION OF SURFACES WITH PEPTIDE AMPHIPHILES. Matthew Timney, College of Engineering, University of California, Santa Barbara, CA.

Peptides carry enormous capacity and versatility for participating in specific ligand-receptor binding interactions. As small fragments of proteins, they offer the possibility of delivering a selected activity in constructing a biofunctionalized surface or interface, absent other, undesired activities present in the full protein molecule (e.g., immunogeneity). We have been exploring the self-assembly and cell recognition properties of peptide fragments (thus far derived from extracellular matrix fragments) that we have ligandized synthetically by attaching a phospholipid-mimic, double-chain, hydrocarbon tail. Lipidation confers interesting and selective binding properties on the molecules and enables the stable deposition of layers of peptide amphiphiles on surfaces. Specifically, we have been using peptide amphiphiles to functionalize surfaces with peptide fragments derived from collagen and fibronectin. Deposition of the molecules by Langmuir-Blodgett methods gives a very high degree of control over the density and orientation of the surface molecules. This in turn enables us to explore the effects on cell response of peptide density and molecular architecture variations with a great degree of precision. The principal results so far, which seem to have some generality for different kinds of peptides, are that there is an optimum peptide density for each kind of peptide fragment, and that the architecture of the peptide presentation is a very sensitive controller of bioactivity. Examples will be given of these effects.

3:45 PM DD4.6/FF4.6
POLYELECTROLYTE BRUSHES: SIMULATION AND SCALING THEORY. Christian Seidel, Felix S. Casajo, Roland R. Netz, Max-Planck-Institut for Colloids and Interfaces, Golm, GERMANY.

Polyelectrolyte brushes are important with respect to fundamental as well as applied research. However, both in experiment and in theoretical work, polyelectrolytes are a challenging subject with many unresolved problems. In this situation, computer simulations are a promising tool to validate established models, and to probe quantities and regimes which are not easily observable experimentally. We use stochastic molecular dynamics to study end-grafted polyelectrolytes for varying chain lengths, anchoring densities, degrees of ionization, counterion sizes and Bjerrum lengths. The model includes counterions explicitly, and the full Coulomb interaction is treated using a direct summation technique proposed by Lekker and modified by Sperb. At Bjerrum lengths slightly before the Manning condensation limit we obtain new collapsed phases for strongly charged chains. The brush
height scales linearly with grafting density, a behavior which is known for charged brushes in poor solvent. This is in disagreement with the accepted model for the osmotic regime, which predicts that the brush height becomes independent of grafting density. We believe that this is caused by strong counterion condensation effects. The new brush regimes can be understood by an extended scaling model which includes Coulomb interaction between charged monomers and counterions. For partially charged chains we obtain a broad cross-over between the scaling regimes given by theory. Reducing the counterion size we find the osmotic regime in agreement with our scaling theory; phase diagrams of the Bjerrum length we obtain a non-monotonic behavior of the brush thickness with a maximum at very small coupling where already a considerable part of counterions has left the brush.

4:45 PM DD4.10/FF4.30
PROTEIN INTERACTIONS WITH PDMS DURING INTERFACIAL PDMS RESTRUCTURING AND DEFORMATION. Feng Li and Maria Simoni, Lehigh University, Department of Chemical Engineering, Bethlehem, PA.

We report the influence of surface properties on the adsorption kinetics of immunoglobulin on modified PDMS (polymethyl silicone) surfaces. It was found that the hydrophobic surface of native PDMS has a high affinity for immunoglobulin, which adsorbs in abundance at the transport-limited rate. Correlation of PDMS yields a relatively hydrophilic surface with minimal affinity for immunoglobulin. In the ~100 hours following surface treatment, the hydrophilic nature of the surface recovers (as evidenced by contact angle evolution). The affinity, rate of adsorption, and ultimate coverage of immunoglobulin also increase, but not at the rate of the contact angle evolution. Starting the surface after treatment accelerates this recovery and increases protein adsorption. The recovery is attributed to oligomeric PDMS fragments that diffuse to the surface after its chemical treatment.

SESSION DD5: POSTER SESSION
SOFT BIOMATERIALS IN INTERFACES
Chair: Darrell J. Irvine
Tuesday Evening, April 25, 2000
8:00 PM
Metropolitan Ballroom (Argent)

DD5.1
SURFACE CHARGE AND POTENTIAL IMAGING OF POLYMER SYSTEMS. Ian Baikie, Biocurrents Research Centre, Marine Biology Laboratory Woods Hole, MA. Heriot-Watt University, Dept. of Applied Physics, Robert Gordon University, Aberdeen, UNITED KINGDOM.

A much overlooked feature of polymer systems is the remarkable variation in surface charge with surface treatments. The surface electric field gradients can be considerable, e.g. kV/m and the electrical nature of the surface can have a major effect on the performance of the material. Moreover, the adsorption of charged polymers e.g., polylysine. Further, to determine the influence of the spatial distribution of surface charge on the adsorption process, charge modulated SAMs were prepared using the micro-contact printing technique (Chemical Reviews, 111, 1081 (1996)) and polyelectrolyte adsorption on those modulated surfaces was investigated.

4:30 PM DD4.9/FF4.9
ENDOTHELIAL CELL GROWTH AND PROTEIN ADSORPTION ONTO HETEROGENEOUS SELF-ASSEMBLED INTERFACES. B.J. Turnasiewicz, Battelle Pacific Northwest National Laboratory, Richland, WA; J. Tizwell, B. Rotter, University of Washington, Seattle, WA; D. D. Allara, Pennsylvania State University, University Park, PA.

Biological interactions onto interfaces such as endothelial cell adhesion and growth are of great importance to medical technologies including artificial implants and tissue engineering. The success of a biomaterial depends largely on how well surfaces promote or inhibit protein and cellular responses. It is believed that protein adsorption onto surfaces and surface properties of the biomaterials play a significant role in many cell functions such as functional group density and surface structure have not been well studied. We report studies of endothelial cell adhesion and growth on tailored surfaces using tailored surfaces in studies of the effects of surface chemistry features such as interface and surface treatments are essential to provide confluent cell growth. We illustrate application of this device in correlating polymer surface topographies to cell growth, corrosion resistant films and potential bio-resistance properties in polymer based anti-fouling paints. [1] I. Baikie and P.J. Earl, Rev. Sci. Instrum, 69, 3902 (1998).

DD5.2
SELF-ASSEMBLING MOLECULES IN TISSUE ENGINEERING. Daniel A. Harrington, Peter L. Dezel, Julian J. Hwang, Samuel I. Stupp, Northwestern University, Dept of Materials Science and Engineering, Evanston, IL.

Cellular interaction with a biomaterial depends greatly on the material’s surface properties. Controlled modification of surfaces with self-assembling molecules allows for the presentation of selected chemistries which may alter or mediate cellular response. The synthesis and properties of a series of liquid crystalline biodegradable oligomers are reported. Our model biomaterial consists of a cholesterol moiety attached to oligo-(L-lactic acid) and an optional
biologically relevant headgroup. Variations of this design were
evaluated for their effect on cellular growth and application to
engineered tissue bioartificial organs. Bioartificial liver scaffolds
and surfaces improved cell adhesion and growth in two dimensions
as compared to uncoated poly-L-lactic acid (PLLA) surfaces. Surface
characteristics of three-dimensional poly-L-lactic acid scaffolds have
been coupled with oligomers and characterized using confocal
microscopy with fluorochrome-labeled molecules.

**DD5.3**

**SURFACE WETTABILITY OF MICROPOREOUS MEMBRANES AFFECTS THE METABOLIC BEHAVIOUR OF ISOLATED RAT LIVER CELLS**

S. Lascatola, R. Dharap, S. Bhat, A. Zeb, Department of Chemical Engineering, University of Illinois at Urbana-Champaign, Urbana, IL.

Microporous membranes are often used in bio-artificial organs as immunosieve barriers, to supply cells with oxygen and also as the substrate for the adhesion of anchorage-dependent cells (e.g., liver cells). Characterization of possible quantitative effects of membrane surface properties on cell metabolism may provide clues to the selection (vs. development) of cytocompatible membranes for bio-artificial livers (BALs). In this paper, we characterized the effect of surface wettability on the rate of oxygen consumption, ammonia elimination and urea synthesis by primary hepatocytes in two membrane concentrations. Membrane wettability of microporous polyethylene (PP) membranes was modified by treatment with ethanol-containing solutions and was characterized by dynamic contact angle (DCA) measurements. Rat liver cells were cultured on these membranes in a continuous-flow bioreactor whose fluid dynamics were optimized for the kinetic characterization of cell reactions, at 0.15 and 1.7 M ammonia. The treatment yielded membranes with lower DCA from 79 to 21 deg. Cells generally adhered and formed aggregates on all tested membranes. Rates of the metabolic reactions increased with increasing membrane wettability in a fashion dependent on ammonia concentration and exhibited a maximum at about 37 deg. DCA. Rate dependence on DCA changes with the investigated method and with methods used to fabricate the sensor devices. The sensor devices will be characterized using related analytical techniques. The research will also focus on the optimal detection of various biological antigens and antibodies using the fabricated piezoelectric sensors.

**DD5.4**

**ADSORPTION OF ISONIAZIDE ON COLLAGEN BIOMATERIALS**

E. Biswas, R. Bhat, A. Zeb

Polymers of plant and animal origins have been widely used in medicine for delivery of a number of drugs in therapeutic zone. In order to increase the efficiency of treatment, polymer has to bind firmly with the drug and to release slowly at infections sites. In this study, the microstructure of collagen has been used as an effective carrier of antitubercular drug of isoniazide. It has been determined the maximum degree of binding between isoniazide and collagen fibre in colloid solution takes place when pH of the solution correspond to an isoelectric point of collagen. The binding of isoniazide onto collagen particles has been found to follow a Langmuir type of adsorption until saturation. It has been established the binding of this drug was mainly governed by hydrogen interactions involved with the active sites of the surface of the drug. It has been observed that isoniazide is soluble at pH of the colloid system changes on more acidic or alkaline, the binding weakened. These results show that collagen particles are effective carrier for delivery of antitubercular drug of isoniazide.

**DD5.6**

**FREQUENCY SEPARATION OF TWO PHASE DEFORMABLE MEMBRANES**

J. Jiang, T. Lockman, A. Sueno, Chemical Engineering, University of California, Santa Barbara, CA.

Using a coupled-field Ginzburg-Landau model we study the dynamics of phase separation and accompanying shape deformation on a two-phase elastic membrane. We obtain an exact periodic wall solution for the equilibrium shape and phase ordering field. We observe preferential phase separation in regions of differing curvature on a variety of vestibules and estimate the degree of deformation of the membrane. We also investigate the effects of deformation on the domain growth kinetics and the interface velocity.

**DD5.7**

**FIBROGRADE BASED BIOSENSOR FOR IMMUNOLOGY APPLICATIONS**

A. Kumar, Department of Electrical Engineering, University of South Alabama, Mobile, AL.

The converse piezoelectric effect, in which an electric field applied across a piezoelectric material induces a stress in the material, has spurred many recent developments in mass measurement techniques. Advances in this field in the last few years have made it possible to determine mass changes that occur on thin films and surfaces under a variety of conditions. The low cost, procedural and conceptual simplicity allow for broad development of commercial and research applications. This work will focus on using quartz crystals coated with thin films of different materials. Proteins and antibodies will be attached to the surface of the thin film which will help in the detection of analytes, such as antigens. The pulsed laser deposition (PLD) and sputtering methods have been used to fabricate the sensor devices. The sensor devices will be characterized using related analytical techniques. The research will also focus on the optimal detection of various biological antigens and antibodies using the fabricated piezoelectric sensors.

**DD5.8**

**DEVELOPMENT OF AN OCULAR DRUG RELEASE SYSTEM**

C. Lee, B. T. Lee, Y. Lee, Bioengineering Program, Iowa State University, Ames, IA.

An erodible ring-shaped ocular insert containing an antibiotic (tylosin tartrate) has been developed for treatment of infections bovine keratoconjunctivitis (IBK). The ocular device is comprised of an outer cross-linked alginate matrix (Ca-Alginate), and an inner core of hydrogel drug-particles. It is capable of bioeroding in the environment of the eye without causing any adverse effect, and it contains an adequate amount of tylosin tartrate to treat IBK.

From several formulations tested, the material chosen for retention and release characteristics was a 75% weight % low molecular weight, 25% weight % high molecular weight alginate containing 7.5% Tween 80 platinizer. This was crosslinked in a 30% calcium chloride aqueous solution for 72 h at room temperature and with calcium alginate, and used to form a 10% hexahydrate aqueous solution for 1 h. The hydrogel was a copolymer of methyl methacrylate and 2-hydroxyethyl methacrylate. Each ocular insert contained 140 mg of hydrogel-drug particles of which 46 mg was tylosin tartrate. The sizes of the particles were equal to or smaller than 150 μm. A variety of rings, with outer diameters ranging from 37 to 52 mm, were able to accommodate a wide range of eye sizes from 31 to 43 mm in diameter. The ring size was taken to be X the side dimension of the pupilal fissure of the eye. The diameters of the cross section of the rings were 1.8 to 2.0 mm. In the retention test of the ring devices in eyes of normal calves, the erodible ocular insert had an average retention time of 3.92 ± 0.73 days. The average inter-suffix time of the ocular device ranged from 1 day to more than 6 days. Normally, from 50 to 70 % of ring devices remained in the eyes of animals for more than 3 days. In infected eyes, the erodible ocular insert had an average retention time of 2.1 ± 0.63 days. After 5 days, the drug release from the ring was reduced to 34 μg/hr, which was above the minimum release rate of 1.3 μg/hr.
required to treat HK. The medicated ocular device has the ability to suppress and reduce the number of bacteria in the eye to an undetectable level within four days after the rings are inserted. The bacteria levels in most of the eyes remained undetectable or low for the rest of the test period even though most medicated rings fell out of the eyes within 2 days after insertion. The eyes that received medicated ocular inserts tended to improve clinically within a few days.

SSNCE DD6: TISSUE ENGINEERING/PATTERNED BIOMATERIAL SURFACES
Chair: Buddy D. Ratner
Wednesday Morning, April 26, 2000 Olympic (Argent)

8:30 AM *DDG.1 SOFT BIOMATERIALS: ENGINEERING TISSUES FOR THE FUTURE. Joan Zehliger, Lee Landeck, Holly Alexander and Noshin Dunkelman, Advanced Tissue Sciences, Inc., La Jolla, CA.

Soft, synthetic or natural biomaterials, e.g., ePTFE or Dacron vascular grafts and processed xenograft or allograft valves, are typically unsupportive of host cell integration and formation of functional tissues. But will be presented demonstrating that by prescribing structural features of scaffolds (e.g., substrates for cell growth) one can potentially regulate the in vitro cellular responses in synthetic scaffolds to form tissue engineered vascular grafts. Likewise, porcine heart valve replacement conditions support human fibroblast integration. Synthetic Scaffolds: Human or animal dermal fibroblasts, arterial fibroblasts or arterial smooth muscle cells were cultured, radially or dynamically up to eight weeks on poly (glycolic acid), polyethylene terephthalate, or poly (caprolactone) scaffolds that differed by their features (e.g., dimensions, architecture, pore size, or void fraction) and fabrication (e.g., frozen, dried, or solvent cast sponges). Within the scaffolds of the various chemical formulations, cellular viability and distribution (depth and uniformity) and the construct morphology were influenced by both cell type and scaffold features as determined by quantitative measures for cell number and metabolic activity, glycosaminoglycan and collagen assays, and qualitative immunohistology and histology. Natural/Biologic Scaffolds: Tissue engineered aortic heart valves (BioXenoGrafts™) were developed by culturing human dermal fibroblasts onto decellularized, porcine valves up to eight weeks. Under static or dynamic conditions, the host cells remained metabolically active. Increases in fibroblast integration with time was shown histologically, immunocytochemically and by quantitative digital image analysis. Thymidine and proline radiolabeling showed that the fibroblasts were mitotic and synthesized extracellular matrix. Closing: Future devices will be likely tissue engineered medical products (TEMPs) that are precellularized or promote uniform formation of tissue functional and material properties. Scaffolds for TEMPs will be engineered to match the mechanical properties of the tissue replaced. More profoundly, these biomaterials must provide unrivaled biological compatibility. Development of standards for TEMPs and biomaterials will be discussed.

9:00 AM DDG.2 THE ATTACHMENT AND GROWTH OF BALB/c 3T3 FIBROBLASTS ON PATTERNED POLYLACTIC MEMBRANES. Zbigniew Gugala, Sylvester Gogolewski, Polymer Research, AO/ASIF Research Institute, Dnoo, SWITZERLAND.

The material surface topography, in addition to the surface chemical characteristics determines a great extent the cell-material interaction. Patterned implant surfaces promote oriented cell growth and potentially may enhance guided tissue and organ regeneration. In this study, Balb/c 3T3 fibroblasts were cultured on three types of biodegradable polylactic acid membranes prepared from poly(L,Lactide) (PLLA) 100%, with a viscosity-average molecular weight of 200,000 dalton. The membranes were cast from the polymer solution in nonchelating solvent and had the following surfaces: 1. a smooth, relatively smooth surface (surface roughness average Ra = 8.9 nm); 2. a porous rough surface (Rq = 18.1 µm); 3. a patterned surface created by hot-drawing of the porous membranes to various draw ratios. The cells cultured on all the membranes established a morphology typical for fibroblasts. The cells on the porous surfaces were attached to the pore walls and grew deeply into the pores while on the nonporous membranes they formed typical foci. On the patterned oriented surface the fibroblasts assumed a spindles-like shape. They were preferentially attached to the edge pores and highly elongated in the membrane drawing direction. The cells communicated with each other at the connection area of the pores edges. It can be appreciated that the stretching of the membrane led to a reorganization of both the surface texture, and the initial arrangement of the chemical groups at the membrane surface. The oriented growth of fibroblasts on these patterned surfaces seems to indicate that the cells are capable of sensing these different micrometer scale patterns. Guided orientation by patterned polylactic membranes could be exploited in ligament repair and in the regeneration of segmental bone defects.

9:15 AM DDG.3 TISSUE ENGINEERED SPINAL CORD. Martin Vocatí, Jack Leonard, Benjamin Dore, Lawrence Bommar, Yalin Cao, Stanley Schuman, Alan Farwell, Joseph Vocatí, Charles Vocatí, University of Massachusetts Medical School, Life Sciences Engineering, Worcester, MA. Massachusetts General Hospital, Department of Surgery, Boston, MA.

We report the generation of functional spinal cord tissue in surgically created spinal cord gaps in adult rats employing synthetic composite polymer scaffolds to deliver spinal cord progenitor cells isolated from adult rats. In vitro, the grafts were excised and the resulting gaps implanted with PGA 14 micron diameter filters of polyglycolic acid saturated with a 23% solution of Pluronic F127 seeded with 20 million stem cells/ml. Controls received cells alone, polymer alone, or nothing at all. Postoperatively, sensory and motor function was assessed using modified BBB scale. Animals were sacrificed and specimens evaluated using antibodies to specific neural antigens. Labeled cells were visualized microscopically by FITC epifluorescence. In vitro, the neural progenitor or cell marker, nestin, was expressed, as were the glial (GFAP) and neuronal (NF) markers. In vivo of 9 experimental animals recovered significant sensory and motor (including the ability to coordinate use all four limbs in ambulation) function below the transaction. Control animals remained paralyzed. Experimental implants consisted of new tissue containing abundant GFP+29 postnatal day, when examined using a dual FITC/Texas Red filter, demonstrated co-localization of the GFP+29 label and the cell-specific markers. These data confirm that the spinal cord progenitor cells suspended in the polymer composite were the source of the tissue. Control animals contained a disorganized array of bony spurs and scar tissue, without evidence of new neural tissue. These data suggest generation of new neural tissue to replace lost neural function may be accomplished by implantation of plastic neuroprogenitor cells associated with a composite synthetic polymer scaffolding.

9:30 AM *DDG.4 SYNTHETIC EXTRACELLULAR MATRICES FOR TISSUE ENGINEERING. David Mooney, University of Michigan, Depts. Biologic & Materials Sciences and Chemical Engineering, Ann Arbor, MA.

It is now possible to partially replace damaged or failing organs and tissues by the transplantation of cells on polymeric scaffolds. However, these engineered tissues often are not fully functional. We hypothesize that synthetic scaffolds designed to chemically and mechanically interface in a precise manner with cells will regulate tissue function at the cellular level. These polymers would mimic many functions of the native extracellular matrix of tissues. To test this approach, hydrogels have been synthesized which could, when examined using cells in cell adherence, to the polymer, and convey specific mechanical stimuli to the cells. The proliferation and differentiation of a number of cell types (e.g., smooth muscle, osteoblasts) is regulated by the specific adhesion ligand type and density presented to the cells from the polymer. The intrinsic mechanical properties of the scaffolds, and external mechanical stimuli (e.g., tensile loading) applied to the polymer can also be modulated to control cellular gene expression and overall tissue function. Strikingly, there is a significant interplay between the chemical and mechanical signaling pathways in these systems. The ability of cells to respond (e.g., upregulate proliferation and matrix synthesis) to external mechanical strain is regulated by the ligand to which they adhere to the scaffold. Altogether, these results suggest that the concept that engineered tissue function can be regulated by designating specific aspects of the cell-polymer interaction. This approach may ultimately lead to engineered tissues with utility to patients suffering from a variety of diseases.

10:00 AM *DDG.5 SELF-ASSEMBLY OF PROTEIN-RESISTANT TETHERED LIGAND SURFACES ON BIOMATERIALS. Darrell J. Irvine, Dept. of Materials Science and Engineering and the Division of Bioengineering and Environmental Health, Massachusetts Institute of Technology, Cambridge, MA.

Protein-resistant surfaces that present tethered protein or peptide ligands with controlled spatial distribution may enable greater control over cellular responses at the tissue - biodegradable polymer interface. Utilizing ligands distributed homogeneously on a substrate. We have prepared protein-resistant surfaces which allow ligands to be presented...
in a clustered array on length scales from a few nanometers to several microns, utilizing a comb polymer which controls the outermost surface structure. Other comb polymers have been studied as a coating for biomaterials, or as a self-assembling surface in blends with biodegradable materials. Bulk and surface properties of blends of poly(aryl) with the comb polymer have been thoroughly characterized in order to correlate cell responses with the materials structure. Clustering of ligands on nanometer length scales is achieved by the comb architecture while simultaneous larger length scale patterning and/or ligand clustering is controlled by the meso- or macroscopic scale of blends or inkjet patterning. Patternning is thus controlled by self-organization during processing and equilibration of the materials. Cell adhesion, adhesion strength, growth, and morphology of the comb clustered micro-patterned and nanoscale ligands have been studied and correlated with peptide surface display. We find that, in general, all of these aspects of cell behavior are affected by the spatial distribution of adhesion peptide and cell response can thus be tuned by appropriate design of the ligand. These phenomena will be discussed in the context of current and future directions in biomaterials, with an emphasis on the feasibility of recapitulating natural extracellular matrix-based cell signaling for the design of improved implants, in vitro assay and culture systems, and in vivo medical devices.


The control of spatial cell arrangement is a promising new tool for the improvement of bioartificial systems as bioreactors and biosensors as well as for tissue engineering. Micropatterned growth of adherent cells can be induced by chemical microstructures on various surfaces. There are different techniques available for the creation of chemical pattern in cellular dimensions. Only few of them are easily applicable to typical polymeric biomaterials. The development of commercially practicable techniques for surface patterning is still a challenging task. Here, a sequence of low-temperature gas discharge plasma steps is reported which creates regions of improved and suppressed cell adhesion on polymer substrates.

In a first step, the polymer surface is functionalized by a nitrogen containing reactive gas mixture which is mixed into the polymers surface enhance wettabillity and improve cell adhesion. In the second step a passivation containing hydrogen is applied for pattern transfer using a laser cut metal mask. Plasma passivation is characterized by a removal of functional groups introduced into the polymer surface enhance wettabillity and improve cell adhesion.

The temporal development of pattern recognition after cell seeding is investigated for different adherent cell lines and primary cells. Well-expressed cell patterns were obtained after a short recognition phase. The pattern recognition capacity can be correlated to type and size of the cells. Fluorescence labeling of ECM and cytoskeletal components was used to determine cell spreading and spreading of the cell attachment mechanism at the different surface regions. Finally, it was shown, that this gas discharge plasma based approach is applicable to a wide variety of polymeric biomaterials.

SESSION DD7/FF7: JOINT SESSION - MECHANICAL ASPECTS OF SOFT BIOMATERIAL INTERFACES
Chair: Samuel I. Stupp and Kenneth R. Shull
Wednesday, April 26, 2000
Metropolitan I (Argent)

1:30 PM *DD7.E/FF7.1 BIOADHESIVE POLYMER FORMULATIONS THAT PROLONG DRUG DELIVERY ACROSS MUCOSAL SURFACES. Alim Hoffman, Chad Brown, Masashi Nishikawa, Gochun Chen, and Yoshi Hayashi, Dept. of Biomedical Engineering, Univ. of Washington, Seattle, WA; Wayne Gomputz, Dean Pettit, Lotte Kreigler, and James Mansueto, Immunex Corp, Seattle, WA; Michael Roberts and Milton Harris, Shoreway Polymers, Huntsville, AL.

Bioadhesive polymers are often added to drug formulations in order to prolong the residence time on mucosal surfaces such as the eye, the nose, and the intestines. However, this does not necessarily result in prolonged drug release from such formulations, since the drug may still be released too rapidly as the formulation swells and dissolves. We have designed a family of polymeric formulations that combine bioadhesive polymers with additives or conjugates that cause gelation of the formulation. These formulations should be in the form of viscous gels at body temperatures, and should also be bioadhesive, lending to extended residence times on the mucosal surfaces, as well as to reduced diffusion of drug molecules through the gel. The synthesis, properties, drug loading and in vitro delivery profiles of several of these hybrid carrier systems will be described and discussed.

2:00 PM DD7.E/FF7.2 THE INFLUENCE OF INTERFACIAL MECHANICAL BEHAVIOUR UPON DEFORMATION AND FRACTURE OF COMPOSITE BIOPOLYMER GELS. K.P. Plucknett, V. Norman, S.J. Pomfret, D. Ferrari and W.J. Freeman, Unilever Research,
The large deformation mechanical behaviour of mixed biopolymer gel composites, which are potential structuring additives for foods, has been examined in both tension and compression. Composite gels were fabricated by phase separation from mixed biopolymer solutions, followed by gelatin, which results in discrete 'included' particles that are contained within a continuous matrix phase. This structure can also be inverted by reversing the volume fractions of the respective phases. Two systems were investigated, gelatin/maltodextrin and gelatin/aragrose. The mechanical response of these materials was primarily determined by the individual constituent behaviour and the interfacial fracture energy in the maltodextrin system, interfacial debonding was observed, which resulted in a pseudo-yielding response. A simple elastomer model was used to indirectly calculate an approximate interfacial fracture energy of ~0.25 J m$^{-2}$ for this good agreement between this value and that obtained directly by peel testing, where a gelatin layer was cast directly onto maltodextrin and subsequently peeled off. Conversely, debonding was not observed for the phase-separated gelatin/aragrose system. However, it was possible to conduct peel tests with a gelatin layer cast onto aragrose. The fracture energy obtained in this case was approximately 30 times greater than that for the gelatin/maltodextrin system. This dramatic increase in interfacial fracture energy for this system, relative to gelatin/maltodextrin, is believed to result in the lack of observed interfacial debonding noted for the actual composite structure.

2:15 PM DD7.5/F7.5
ADHESION OF INJECTABLE SEMI-INTERPENETRATING POLYMER NETWORKS. Ramee A. Sade, Kevin E. Healy, Northwestern University, Department of Chemical and Biomedical Engineering, Chicago, IL; Elizabeth Falbromski, Kenneth R. Shull, Northwestern University, Department of Materials Science and Engineering, Evanston, IL.

Neither polymer scaffolds nor tissue-engineered cartilage adheres to the native tissue lining cartilage defects which decreases the likelihood that integration will occur. Previously, we developed injectable poly(n-isopropylacrylamide-co-acryloyl N-acryloxysuccinimide) (PNAAc-AC) hydrogels that supported bovine articular chondrocyte viability and promoted the formation of cartilage-like tissue in vitro. The aim of our current work was to develop injectable semi-interpenetrating networks (semi-IPNs) comprised of (PNAAc-co-AC) hydrogels and linear peptide-functionalyzed P(AA) chains containing sequences that adhere to the extracellular matrix of articular cartilage. The primary objective of this study was to determine the effect of synthesis conditions on the material properties of the semi-IPNs. The solvent, the molar ratio of AA:NIPAAM in the hydrogel, and the molecular weight of the P(AA) chains were varied, and the injectability, the volume change when heated to 37°C, and the lower critical solution temperature (LCST) of the semi-IPNs were determined. P(NIPAAM-co-AC) hydrogels served as controls. The semi-IPNs demonstrated significantly smaller volume changes, as compared to P(NIPAAM-co-AC) hydrogels, due to the P(AA) chains. However, the P(AA) chains did not significantly affect the LCST. The molecular weight of the chains affected the injectability of the semi-IPNs, as matrices with higher molecular weight chains were more difficult to inject. Finally, the molar ratio of AA:NIPAAM significantly affected the LCST and volume change of the semi-IPNs. To assess adhesive properties of the matrices, asymmetric adhesion analyses were performed on thin (1 mm) layers of semi-IPNs using a custom-designed small scale adhesion test. We observed a time-dependent increase in adhesion energy/elastic modulus as a function of displacement, consistent with data reported previously for a model system. Experiments are underway using this methodology to study the effects of semi-IPN formulation and peptide sequence on adhesion to cartilage. These semi-IPNs may be useful in cartilage regeneration applications.

3:30 PM DD7.6/F7.6
ADHESION OF PRESSURE SENSITIVE ADHESIVES WITH APPLICATIONS IN TRANSDERMAL DRUG DELIVERY. Marc B. Tseh and Reinhold H. Draxlhardt, Dept of Materials Science and Engineering, Stanford Univ, Stanford, CA.

The growing use of transdermal devices for drug delivery, as well as the development of increasingly complex and novel patch designs, necessitates an understanding of the adhesion occurring between the device and the soft dermal layer. Pressure sensitive adhesives (PSAs) are used as the adhesive in this system due to their desired properties of good initial and long-term adhesion, clean removability, and skin and drug compatibility. In addition, their highly viscoelastic properties are necessary for removability from soft tissue. However, the adhesion of PSAs is not well understood with almost no reproducible test methods or quantitative adhesion data. This study utilizes a mechanical approach to quantify the adhesive properties of representative PSAs. Adhesion of PSAs is accompanied by cavitation in the PSA and the formation of an extensive cohesive zone. The presence of such large-scale bridging provides significant energy dissipation and increased resistance to detachment. The strain energy release rate (G) during debonding of a custom-freeze dried sample, containing at its midline a thin layer of PSA, was utilized to quantify the adhesion of the PSA. The analysis accounts for both the work of adhesion as well as the viscoelastic cohesive behavior of the soft viscoelastic adhesive layer. Effects of adhesive chemistry, layer thickness, and strain rate will be discussed.

3:45 PM DD7.7/F7.7
EFFECT OF PLASMA TREATMENT ON THE ADHESION OF AN ELECTROLESS SILVER FILM ON A BIOMEDICAL POLYMER. ETHAN. Joy E. Gray, P.R. Norton, K. Griffths, Dept of Chemistry, Univ. of Western Ontario, London, Ontario, CANADA.

Bacterial growth on medical implants and devices is a common source of infection. There is a great deal of interest in the surface modification of polymeric materials to decrease infection rates, without altering properties which affect their function. One possibility is to coat the material with a well known antibacterial agent such as silver. The adhesion of silver deposited on a biomedical polyurethane using a conventional electrospray plating technique has been studied. Air plasma treatment of the polyurethane surface prior to electros
phating results in exclusive chemical modification of the surface and has been shown to dramatically improve silver adhesion. X-ray photoelectron spectroscopy indicates an increase in oxygen functionalities at the surface. Contact angle goniometry shows a significant increase in wettability. The absence of surface roughening or abrasion has been confirmed by atomic force microscopy. The improved adhesion of the silver film following plasma treatment has been demonstrated using a standard tape test. Rutherford back-scattering spectrometry measurements show little change in the amount of silver on a plasma-modified polymer surface after the tape test. Tape test results in almost complete removal of the silver from an unmodified polymer surface. Atomic force microscopy has been used to study the structure of the silver films produced. An unmodified polymer surface shows silver in closely bound clusters while the plasma-modified polymer film results in complete silver coverage in a uniform film. This work demonstrates the importance of chemical surface modification in the role of metal/polymer adhesion.

4:00 PM DD7.8/FFT8
ADHESION AND MICROTOUGHNESS OF POLYETHYLENE GLYCOL COVERED SILICA SURFACES: Norma A. Kibler, Tanya L. Kuhl, Amy Stacy, Shag S. Aydil, Jacob N. Israelachvili, University of California, Dept of Chemical Engineering and Dept of Materials, Santa Barbara, CA.

A thin layer of polyethylene glycol (PEG) attached to a surface resist protein adhesion and biological attack. We have developed a direct method for chemically grafting low molecular weight PEG onto silica coated surfaces. The silica films are produced by plasma enhanced chemical vapor deposition (PECVD) and hydrolyzed by exposure to water plasma. The end alcohol group of the PEG chain reacts with the silanol group on the silica surface to form an ester linkage, (Si-O-C). The adhesion and tribological properties of these surfaces were determined using the Surface Forces Apparatus (SFA) with friction devices and bimorph slider. The measurements were conducted in dry air, 100% relative humidity and in bulk water. The presence or absence of water alters the frictional behavior from smooth sliding to stick-slip motion. We compare and discuss the differences between the friction, wear and lubrication properties of symmetric surfaces of PECVD deposited silica, hydrolyzed silica and PEG-grafted surfaces. Deposited silica surfaces have the highest friction and least resistance to wear. On the other hand, with PEG-covered silica surfaces the friction force dramatically increases with sliding velocity indicating possible “shear thickening” behavior under confined conditions.

4:15 PM DD7.9/FFT9
NANOINDENTATION EXPERIMENTS TO PROBE THE SURFACE MECHANICAL PROPERTIES OF PLASMA TREATED POLYETHYLENES: C.M. Klippaert, K. Komvopoulos, Department of Mechanical Engineering. Univ of California, Berkeley, CA and I. Pritz, Departments of Mechanical and Bioengineering, Univ of California, Berkeley, CA.

Low-temperature plasma treatments have recently emerged as a popular method for the surface modification of polymers for biomedical and load bearing applications. These surface treatments have been shown to affect the surface chemistry of the material. Crosslinking by plasma treatment is also possible and can result in enhanced mechanical properties of the polymer surface. Since the plasma treatment only affects the surface or subsurface to a depth of a few microns, it is not possible to use traditional bulk tests to evaluate the mechanical properties. In order to characterize the surface mechanical properties, nano- and micro-mechanical tests were performed with a conventional atomic force microscope modified with a force-displacement transducer that utilizes a diamond tip to apply nano- and micro-Newton forces to localized regions of the polymer surface. The elastic modulus and hardness was determined by analyzing the data from these experiments using the compliance method. Since the indentation depths achievable are on the order of hundreds of nanometers for soft materials, this test method allows probing of the mechanical properties of the treated surface layer in energetically treated or mechanically altered polymers. Polyethylene was chosen as the material for this study because of its clinical and industrial importance. Further, polyethylene can be produced with controlled morphology and molecular properties. This control provides a means for assessing the importance of these variables on both the surface properties and response to plasma treatment. Ultra-high-molecular weight (UHMWPE), high-density polyethylene (HDPE), and low-density polyethylene (LDPE) were treated in various low-temperature plasma environments. Indentations were made on all materials, and the resulting force-displacement curves were analyzed to determine the surface mechanical properties and adhesion behavior. The methods presented in this study provide a novel technique to study the surface mechanical properties resulting from controlled plasma treatments of polyethylene films with varying degrees of crystallinity, molecular weight, and crosslinking.

4:30 PM DD7.10/FF7.10
STRENGTH AND TOUGHNESS OF AN ORGANICALLY REINFORCED CARBONATED APATITE BONE MINERAL SUBSTITUTE: Victoria C. Jew, Reinhold H. Duschardt, Stanford University, Dept of Materials Science and Engineering, Stanford, CA.

Carbonated apatite materials resembling the mineral phase of bone have received considerable attention for biomedical applications. When formed at physiological temperature, they present significant potential for rapid bone repair, fracture fixation, and augmentation of load bearing hardware. To date, the strength and resistance to fracture of such apatites has been extremely low. This study investigates strategies to enhance the mechanical properties of a carbonated apatite bone cement, utilizing the addition of soft biological organic phases such as albumin, fetal bovine serum, collagen, and gelatin. The distribution of phases and the interface between the added phase and the apatite are characterized. The addition of soft organic phases is shown to have a marked impact on strength, reliability, and toughness of the bone mineral substitute. Microstructural examination of the inorganic-organic composite materials reveals a number of toughening mechanisms. Most significant is the bridging of cracks in the apatite by the organic phase. Micromechanical models have been developed to account for strengthening and toughening effects. Implications for the integrity and reliability behavior of such synthetic bone mineral substitutes in load bearing applications are considered.