SYMPOSIUM DD

Interfacial Aspects of Soft Biomaterials

April 24 – 26, 2000

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* Invited paper

SESSION DD1: SURFACE MODIFICATION AND CELLULAR RESPONSE
Chair: Annelise E. Barron
Monday Morning, April 24, 2000
Olympic (Argent)

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 Matls, 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-ingrowth matrices. Cell and tissue surfaces are net negatively charged. Correspondingly, copolymers (PEG-g-PLL) of polyethylene glycol (PEG) grafted to polylysine (PLL) have been synthesised and explored to sterically stabilise cell-cell and cell-tissue adhesion. The PLL backbone serves as the anchor domain, and the dangling PEG chains form a polymer brush at the cell or tissue surface that can sterically stabilise the approach of a potentially interacting cell. Phenylboronic acid moieties have been additionally grafted to the PLL backbone, to thereby strengthen the interaction of the anchor domain with the biological surface via complexation with sialic acid resides 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-ingrowth matrices, synthetic hydrogels have been developed consisting of telechelic three-arm PEG triacrylates, 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 proteases that are produced by cells during cell migration, 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
BIODEGRADEABLE POLYMER AMPHIPHILES FOR SURFACE MODIFICATION OF TISSUE ENGINEERING DEVICES. Rafal A. Mickiewicz, Pallab Banarjee, 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 signalling have useful applications in tissue engineering. Amphiphilic comb 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 bioresorbable once their function has been served. In light of this, a biodegradeable comb copolymer based on poly(E-caprolactone) and poly(ethyleneglycol) has been synthesized. This polymer may further be used in the preparation of biodegradeable latexes for coating biomaterials 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 signalling 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 modifying material to diffuse into the loose network of PLA chains. The rapid addition of a PLA 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 material 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 entrapped 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 amine moieties. Results show these surfaces to greatly enhance cell-spreading characteristics 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 Raviv, Pierre Laurat, Joseph Frey, Rafael Tadmor, 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 measurements of the normal and shear forces between two atomically smooth mica surfaces bearing functionalised PEG immersed in pure (conductivity) water have been carried out as a function of surface separation. PEG (Mw=3.4k) that has been functionalised on both ends, was introduced into water and adsorbed only at one end onto the mica surface. A monotonically-increasing force-distance law was indicated, beginning at surface separations of ~100nm. This repulsion is shorter ranged than in the conductivity water, due to the shorter Debye length in the presence of higher ion concentration. High repulsion forces starting at ~5nm are due to the extensive compression of the grafted polymer layers. The range of the high repulsion forces (3-5nm) 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, which suggests that such PEG molecules can be 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 Chew, Wendy A. Wolf and Rex L. Chisholm, Dept. of Cell 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 bio-compatible 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 fluorescently tagged elements of the cytoskeleton and cellular adhesion systems. The actin cytoskeleton and the molecular motor myosin that associates with it are the principal force generating structure in cells. The organization of the actin cytoskeleton is greatly influenced by its association with the cellular adhesion complexes with 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 produced a 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 behaviors.

10:45 AM DD1.6
DEPOSITION OF NANO-THIN POLYMER FILMS FOR IMPROVED CELL INTERACTIONS AND CONTROLLED-RELEASE BIOMEDICAL APPLICATIONS. James D. Talton, James Fitz-Gerald, Rajiv Singh, University of Florida, Gainesville, FL.

To improve tissue interactions and for local delivery of anti-inflammatory/anti-thrombogenic drugs from implanted devices such as stents, biodegradable poly(L-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 in a human ex vivo human stasis model compared to uncoated stents. For prelimanary 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, 1H-NMR, and FTIR. 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 plume of polymer clusters that is directed over the implant surface. Analysis of the polymer samples using SEM, FTIR, NMR, and GPC verified

11:00 AM DD1.7
ENHANCED ATTACHMENT AND PROLIFERATION OF HUMAN NEONATAL DERMAL FIBROBLASTS ON EXPANDED PTFE SUBSTRATES MODIFIED WITH P-15, A SYNTHETIC PEPTIDE ANALOGUE OF COLLAGEN. Steven B. Nicoll, Ynes Montoya, Rajendra S. Bhatnagar, University of California, Berkeley and San Francisco, Joint Bioengineering Graduate Group, San Francisco, CA.

Expanded polytetrafluoroethylene (e-PTFE) has numerous clinical applications ranging from blood vessel reconstruction to soft tissue augmentation but lacks adhesive 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 began to display a uniform alignment on 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 and 7 days, 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, [3-H]-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 implant fixation and stability.

11:15 AM DD1.8
SURFACE CHARGE, TOPOGRAPHY AND CHEMISTRY STUDIES OF HUMAN SKIN FIBROBLAST GROWTH ON SURFACE MODIFIED PTFE BIO-MEMBRANES. Iain Baikie, Biocurrents Research Centre, Marine Biological Laboratory, Woods Hole, MA.

Artificial Bio-Membranes such as functionalised microporous 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 and topography of the surface, however a much overlooked parameter is that of the surface charge. Using a novel multi-tip Scanning Bio-Kelvin Probe (SBKP)*, we have performed high resolution surface potential and charge topographies 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 (HSF) growth. Subsequent video-microscopy growth data indicates an extraordinary correlation between a regime of homogeneous negative surface charge profiles and confluent HSF 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.
*I. Baikie, P.J.S. Smith, D.M. Porterfield and P.J. Estrup, Rev. Sci. Instrum, 70, 1842 (1999).

11:30 AM DD1.9
SURFACE MODIFICATION OF NEURAL PROSTHETIC DEVICES BY CONDUCTING POLYMER POLYPYRROLE 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 recording tests, they lose electrical 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 mediate interfacial differences and improve the signal transport, 3 bioactive, electrically conductive polymer composites were coated onto the surfaces. Polypyrrole combined with different high molecular weight anions have been precisely deposited onto the functional sites of neural prosthetic probes by galvanostatic electropolymerization. Polypyrrole/PSS (polystyrene sulfonate) composite was deposited out of 0.1M pyrrole aqueous solution, using 0.1 M PSSNa as the dopant. The influence of current density, monomer concentration, and reaction time on the thickness, morphology and electrochemical properties of the polypyrrole 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 grows. Rough surfaces give the electrode a much higher interfacial surface area, which is good for charge transport at the interface. Power Spectrum Density method 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 decrease the magnitude of electrode impedance.
In-vivo acute recording tests in guinea pig cortex showed that strong neural signals can be detected through the polypyrrole/PSS - coated probes. To further improve the biocompatibility, the anion PSS was replaced by bioactive molecules, such as collagen and synthetic protein SLPF, respectively. Collagen is well known as an extracellular matrix protein that is often added to cell culture medium. SLPF 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 indicated that the bioactive molecules are incorporated into the polypyrrole films. The bioactivities of the polypyrrole/bioactive molecule composites are being tested in cell culture. In-vivo chronic tests of polypyrrole coated neural recording probes are under way.

11:45 AM DD1.10
NEURON PATTERNING BY ORGANIC SELF-ASSEMBLED MONOLAYERS. Cristian Ionescu-Zanetti, Yuko Nakazawa, Physics Department, UC Santa Cruz, CA; Fred Gage, The Salk Institute, La Jolla, CA; Alan Litke, 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 now 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 of 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. Neuron 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 biomedical devices.

SESSION DD2: LIPID MEMBRANES AND VESICLES
Chair: Stella Y. Park
Monday Afternoon, April 24, 2000
Olympic (Argent)

1:30 PM *DD2.1
STIMULI-RESPONSIVE LIPID VESICLES FOR TRIGGERING PROTEIN AND POLYSACCHARIDE HYDROGEL FORMATION. Eric Westhaus, Xiaoping Zeng, Bruce Lee, Nicole Eberle and Phillip 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, and local drug delivery. The use of this approach will be illustrated by examples in which calcium and other metal ions, when released from lipid vesicles upon application of an appropriate stimulus, catalyze a reaction to form polysaccharide or protein-based hydrogels. Finally, to address the important issue of interfacial adhesion between these biomaterials and hard/soft tissues, our initial efforts to develop synthetic adhesive macromolecules will be described. These macromolecules are being designed to combine bioadhesive characteristics with the ability to undergo a sol-gel transition via a liposome-mediated mechanism.

2:00 PM DD2.2
SMECTIC PHASE OF FLUID MEMBRANES DECORATED BY AMPHIPHILIC COPOLYMERS. Francisco Castro-Roman, Gregoire Porte and Christian Ligoure, GDPC, University Montpellier 2, Montpellier, FRANCE.

We have investigated by small angle neutron scattering techniques, the physical properties of a lyotropic lamellar phase, whose membranes are decorated by amphiphilic copolymers: this system provides a simple experimental model to study the interactions between grafted polymers and biological lipid bilayers. We show that the polymer layers modify both the elastic properties of the individual membranes and the interactions between membranes. (i) They decrease the bending rigidity of the bilayers. (ii) They thin the bilayers: this effect can be quantitatively explained by bilayer's thinning due to the competition between stretching of the polymer brush in the smectic direction and stretching of the membrane in the lateral direction. It provides a new simple and universal method to measure the area stretching modulus of fluid membranes. (iii) They strongly enhance the repulsive interaction between membranes: by a careful analysis of the shape of the scattering patterns, we show that this interaction is of Helfrich's type: the polymer layers simply increase the collision's thickness of the bilayers. Two different regimes have to be considered: the mushroom's regime, at low polymer concentration, where the polymer layers are inhomogeneous and the brush regime in the opposite case: a simple model is built up to describe the two situations, which nicely meet the experimental results. The competition between electrostatic and polymer-mediated interactions are also investigated .

2:15 PM *DD2.3
LIPOSOMES AS REACTION VESSELS. Clyde Wilson, Stanford Univ, Dept of Chemistry, Stanford, CA; Daniel Chiu, Harvard Univ, Dept of Chemistry, Cambridge, MA; Anette Stromberg, Frida Ryttsen, Owe Orwar, Goteborg Univ, Dept of Chemistry, Goteborg, SWEDEN; Richard N. Zare, Stanford Univ, Dept of Chemistry, Stanford, CA.

We have demonstrated that the electrofusion of synthetic lipsomes containing different reagents is a means of initiating a chemical reaction within a femtoliter volume (Chiu et al., Science, 1999). With the aim of making this process quantitative, we have developed pipettes with a tip morphology conducive to holding vesicles one to ten microns in size, and a pressure control system for stable suctioning capable of holding vesicles on the pipette tip for an hour. We will discuss the main issues involved with mechanically manipulating micron-sized vesicles and present our progress in using them to carry out biorelevent femtochemistry.

2:45 PM DD2.4
THE LIQUID-CRYSTALLINE PHASE BEHAVIOUR OF NATURALLY OCCURRING CEREBROSIDES. G.H. Mehl, J.W. Goodby, Department of Chemistry, Centre for Organic and Biological Chemistry, Liquid Crystals Research Group, University of Hull, Hull, GREAT BRITAIN.

Cerebrosides are a class of glycolipids which occur widely throughout biological systems. Gluco- and particularly galacto-cerebrosides have been found in most animals and in humans. Various medical disorders have been connected to variations in their structure and predominance, some have been identified as membrane receptors of various pathogenous agents, thus making these systems interesting objects of research. We have investigated the liquid-crystalline phase behaviour of a series of materials where the carbohydrate group and the length and the structure of the alkyl-chains were varied. The materials investigated exhibit thermotropic and lyotropic liquid-crystalline behaviour. Due to their chemical structure the liquid crystalline phase behaviour is to be due to supramolecular arrangements of the molecules. The mesomorphic structures depend on the number and length of the attached hydrocarbon chains present in the molecules, with compounds having two alkyl chains per hydrocarbon core exhibiting columnar phases. We report the results gained from optical polarising microscopy studies, differential scanning calorimetry and X-ray diffraction in the liquid-crystalline state.

3:30 PM *DD2.5
OPTIMIZATION OF KEY PARAMETERS FOR NON-VIRAL GENE DELIVERY: TOWARDS A UNIVERSAL DESCRIPTION OF TRANSFECTION EFFICIENCY. Nelle L. Slack, Alison Lin, A. Ahmad, Heather M. Evans, C.X. George, C.E. Samuel, C.R. Safinya, University of California Santa Barbara, Departments of Materials, Physics, and Biochemistry and Molecular Biology, Santa Barbara, CA.

The use of cationic lipids as carriers of genes for delivery in cells is a promising alternative to viral-carriers for gene therapy. In order to develop an optimal cationic lipid carrier, more knowledge regarding interactions and structures of cationic lipid: DNA complexes (CL:DNA) is required. Using x-ray diffraction and biological assays, we show key parameters for optimizing gene transfer that are mediated by properties of the lipid. Previous work on CL:DNA non-viral carriers has shown that in systems containing univalent cationic lipids mixed with neutral lipids the overall structure of the carrier and the membrane charge density may be important variables for designing an efficient carrier[1]. We have found that cationic liposomes complexed with supercoiled plasmid DNA in solution self-assemble into a lamellar or an inverted hexagonal structure depending on lipid composition. Transfection efficiency, determined by X-Gal and Luciferase assays which measure protein synthesized as a result of reporter gene expression, shows the inverted hexagonal structure enhances gene transfer in complexes of low membrane charge density while structure is not an important variable for complexes of high membrane charge density. Results from complexes containing multivalent cationic lipids show that transfection efficiency dependence on membrane charge density and lipid geometric packing shape may be universal in vitro.
Supported by NIH R01-GM59288-01 and R37-AI12520-24, UC Biotechnology Research and Education Program (97-02), NSF-DMR-9972246.
1. J. Raedler, I. Koltover, T. Salditt, C.R. Safinya, Science 275, 810 (1997); Koltover, T. Salditt, J. Raedler, C.R. Safinya, Science 281, 78-81 (1998); A.J. Lin, N.L. Slack, A. Ahmad, I. Koltover, C.X. George, C.E. Samuel, C.R Safinya, Journal of Drug Targeting (to appear).

4:00 PM DD2.6
UNRAVELING DNA COMPLEXATION PROCESSES BY TIME RESOLVED MULTI-ANGLE LIGHT SCATTERING. Eva Lai, Johns Hopkins University, Dept of Chemical Engineering, Baltimore, MD; John H. van Zanten, North Carolina State University, Chemical Engineering Dept, Raleigh, NC.

Non-viral gene therapy is capable of treating genetic and acquired disorders at the molecular level with minimal immune response. Recent literature on characterizing non-viral gene delivery systems is primarily focused on structural details. The formation of these DNA complexes is equally important. This self-assembly process is driven mostly by electrostatic interactions of negatively charged DNA with positively charged vectors such as peptides, polymers, or lipids. The positively charged vectors enhance the delivery of DNA to cells by (1) reducing the repulsion between DNA and cell surface, and (2) compacting the size of DNA for cellular uptake. However, the kinetics and mechanisms of the complexation process remain relatively unknown. Therefore, an understanding of the DNA complexation process is crucial to the success of non-viral DNA delivery systems. In this study, we attempt to elucidate the governing parameters by using time resolved multi-angle light scattering to probe the kinetics and mechanisms of DNA-poly-L-lysine and DNA-liposome complexation processes. This convenient and non-invasive technique offers invaluable insights for the design of other non-viral DNA delivery systems, including polymer, peptide, and lipid-based vectors.

4:15 PM DD2.7
NON-NATURAL, SEQUENCE-SPECIFIC POLYPEPTOIDS DESIGNED TO MIMIC SURFACTANT PROTEINS AT THE AIR-LIQUID INTERFACE OF THE LUNG. Cindy W. Wu, Annelise E. Barron, Northwestern University, Dept of Chemical Engineering, Evanston, IL; Ka Yee Lee, University of Chicago, Dept of Chemistry, Chicago, IL.

Delivery of functional lung surfactant is necessary for the rescue of premature infants with Respiratory Distress Syndrome. Although lung surfactant is composed primarily of phospholipids, small amounts of the surface-active proteins SP-B and SP-C are necessary for the biophysical functioning of lung surfactant in vivo. These amphipathic surfactant proteins interact with phospholipid molecules on the surfaces of the alveoli, controlling lipid phase behavior at the air-water interface and enabling easy breathing. At present, the surfactant proteins are extracted from animal lungs for use in premature infants, introducing the risk of viral transmission. Reliance

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 "polypeptoids" or N-substituted glycine polymers. We synthesize up to 50mers by an efficient, automated solid-phase synthesis that allows incorporation of diverse N-pendant sidechains (including proteinogenic sidechains) in a sequence-specific manner. Despite close similarity to polypeptides, polypeptoids are essentially invulnerable to protease degradation and hence are stable in vivo and less prone to immune system recognition. We have shown that certain peptoid sequences adopt stable helices in aqueous and organic 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 exogenous 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-Wilhelmy balance in conjunction with fluorescence microscopy show that peptoid-based spreading agents have promising biophysical activity and surface morphologies in phospholipid monolayers.

4:30 PM *DD2.8
NEUTRON REFLECTIVITY TECHNIQUES FOR BIOMIMETIC BILAYER MEMBRANE STRUCTURAL CHARACTERIZATION. S. Krueger, N.F. Berk and C.F. Majkrzak, NIST Center for Neutron Research, NIST, Gaithersburg, MD; C.W. Meuse and A.L. Plant, NIST Biotechnology Division, NIST, Gaithersburg, MD.

Neutron reflectivity measurement techniques are being developed to characterize the structure of novel synthetic alkanethiol and phospholipid biomimetic systems, or hybrid bilayer membranes (HBMs), which are formed on gold-coated single crystal silicon substrates, and which are in contact with aqueous solution. Particular emphasis has been 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 HBMs. 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 thiahexaethyleneoxide octadecane (THEO), which contains an ethyleneoxide moiety at the gold surface, and a monolayer of d_{54}-DMPC. Data were obtained in D_2O/H_2O solution mixtures at 28°C, where the DMPC layer is in the fluid phase, both in the absence and in the presence of the membrane-active peptide, melittin, in the solution. Neutron SLD profiles of the HBM structure have been obtained from the 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 HBMs and the location of melittin in the bilayer. Results from measurements of THEO monolayers on patterned surfaces will also be discussed.

SESSION DD3: SURFACE MODIFICATION AND CHARACTERIZATION
Chair: Anne M. Mayes
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 been focused on introducing a new chemical language into cell surface glycoforms through carbohydrate metabolic pathways. By exploiting the intrinsic permissivity of oligosaccharide biosynthetic pathways, orthogonally reactive, foreign 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. Ariane E. Mc Kiernan, Timothy Ratto, Marjorie L. Longo, Department of Chemical Engineering and Material Science, and Biophysics Graduate Group, Division of Biological Sciences, University of California, Davis, CA.

Supported lipid 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 dewetting, may affect the layer properties of an adsorbed biopolymer. Therefore, an understanding of the generation 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 mica supported cationic bilayers of DPTAP and DMTAP fluorescently labeled with an NBD lipid was investigated with both fluorescence and atomic force microscopies. Heating the bilayers above their acyl chain melting temperatures and varying the rate of cooling resulted in the appearance of fractal (DPTAP) and feathery (DMTAP) 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 organizing properties of the bilayer itself were 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 less tilted and 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 IMMOBILIZATION: PREPARATION, CHARACTERIZATION, AND IN VITRO BIOLOGICAL ASSESSMENT. Buddy D. Ratner, Sheng Pan and David G. Castner, 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, even 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 statistical pattern matching between the randomly distributed RGD domains on the surface and cell receptors. This observation may be useful in providing the basis for developing novel engineering strategies for biomaterials design. 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, Jeeseong 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 near-field scanning optical microscopy it is possible to image thin films and surfaces with 20 nm resolution. In NSOM a subwavelength light source is used as a scanning probe to achieve optical resolution beyond the diffraction limit. With the application of polarimetric techniques to NSOM we acquire 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 dyes.
Ordinary optical microscopy is limited by diffraction to a resolution of approximately 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

dynamics of a fluorescently tagged biomolecule on or in an otherwise non-fluorescent material. This provides a tool for studying in detail, for example, binding sites on cellular scaffolding materials. In addition, the details of molecular diffusion or spectra often depend on the local environment (within 0.1-10 nm) of the molecule. It is therefore possible to use single molecule fluorescence or diffusion as a probe of local chemical or physical properties (i.e., strain and viscosity).

10:30 AM DD3.5
CHARACTERIZATION OF SUPPORTED BIOMIMETIC FILMS USING BROADBAND VIBRATIONALLY RESONANT SUM-FREQUENCY GENERATION. Kimberly A. Briggman, Teresa P. Petralli-Mallow, Lee J. Richter, Anne L. Plant and 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 (VR-SFG) as an *in-situ* probe for the study of hybrid bilayer membranes (HBMs). Our novel broadband approach[1] 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 alkanethiol and thia-(ethylene oxide) alkane self assembled monolayer solid supports via VR-SFG. 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.
[1]Vibrationally resolved sum-frequency generation with broad-bandwidth infrared pulses, Opt. Lett. 23 1594 (1998).

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

The modification of materials 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 pre-formed polymers are (photo-)chemically 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 sites for the (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 receptor-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 process of migration while integrin ligation is required for growth factor-induced proliferation of many cell types. Several common 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 identity of molecules involved, 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 parse how these factors contribute to the overall integrated cell 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 which can be applied to both tissue engineering and to fundamental studies of receptor-mediated phenomena. A specific interest is controlling signaling by the epidermal growth factor receptor (EGFR). For example, we have shown that mEGF stimulates both DNA synthesis and cytoskeletal changes in primary hepatocytes when tethered covalently to the culture substrate so 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 adapting these basic findings to 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 FORCE MICROSCOPY. Aleksandr Noy[1], Salvador Zepeda[1,2], Christine A. Orme[1], Yin Yeh[2], James J. DeYoreo[1]. [1]Department of Chemistry and Materials Science, Lawrence Livermore National Laboratory, Livermore, CA, [2]University of California, Davis, CA.

Intermolecular forces underlie a variety of phenomena in chemical and in biological systems, such as colloid 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 scales. 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 presenting 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 BIO-COMPATIBILITY STUDIES. N. Afanasyeva, Dept of Physics, Univ of Nevada, Reno, NV; E. Bormashenko, J. Reichlin, The Research Institute, The College of Judea and Samaria Ariel, ISRAEL; R. Bruch, S. Gummuluri, L. Welser, Dept of Physics, Univ of Nevada, Reno, NV; A. Katzir, I. Wasserman, 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 analysis of artificial surfaces before implantation allowed us to create a quality control for the long-term biocompatibility of implants with eye and cardiac/ vessels media. Spectral information regarding the bioinertness and/or bioactivity 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 low-loss 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 studying 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 biocompatible elastomers 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 molecular 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 850-4000 cm-1 are presented.

SESSION DD4/FF4: JOINT SESSION:
POLYELECTROLYTES AND PROTEINS AT SURFACES
Chair: Alamgir Karim
Tuesday Afternoon, April 25, 2000
Metropolitan I (Argent)

1:30 PM *DD4.1/FF4.1

GRAFTED POLY(ACRYLIC ACID) BRUSHES FOR CELL-SURFACE INTERACTIONS. Jöns Hilborn, B. Gupta, L. Garamzeigy, A. Laurent, Polymer Lab, Dept Materials Science, Swiss Federal Inst Techn, Lausanne, SWITZERLAND; I. Bisson, P. Frey, Pediatric Surgery, Centre Hosp du Canton de Vaud, Lausanne, SWITZERLAND; J. Hedrick, IBM ARC, San Jose, CA.

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 biointeraction, cells must "believe" they are "at home". In the future, a better understanding of cellular processes beetween the ECM ligand proteins and the cell membrane receptors will give us tools to engineer the developing of cell cultures (potentially human tissue) to give desirable properties. For the development of bioactive polymer surfaces, it is important to be able to control and retain 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

BIOLUBRICATION: THE SHEAR OF ADSORBED POLY-ELECTROLYTES AND OF POLYMER BRUSHES. Jacob Klein, Xueyan Zhang, Manfred Wilhelm, 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 polymer brushes and of charged polyelectrolytes. Our results reveal that entropic factors 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 arising 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 and sliding surfaces. 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 POLYELECTROLYTE MULTILAYERS. Jonas D. Mendelsohn, Anne M. Mayes 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 microporous 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 polyanion poly(acrylic acid) (PAA) and the polycation poly(allylamine 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 $\approx$ 2.3-2.5. AFM characterization shows that this pH-induced phase separation leads to a highly microporous morphology (up to a 2/3 volume of pores) with pore sizes of 100-500 nm. While PAA/PAH multilayers have been used as a model system to investigate this pH-driven porosity phenomenon, efforts are currently underway to create microporous films from charged biopolymers; the feasibility of incorporating charged drugs, enzymes, or other bioactive molecules, 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 dialysis membranes and scaffold materials. Furthermore, this simple porosity transformation may lead to an alternative strategy to the polyelectrolyte complex coacervation technology routinely used to encapsulate cells or drugs. Since it assembles one molecular layer at a time with nanoscale precision, the LbL technique, coupled with this unique pH-induced phase separation, could be a novel approach to synthesizing porous biomaterials with highly tailorable features, including well-defined surface and interfacial properties.

2:30 PM DD4.4/FF4.4

POLYCATION-INDUCED STRUCTURAL REARRANGEMENTS IN NEGATIVE LIPOSOMAL MEMBRANES. Alexander Yaroslavov, 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 polycations, 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 (polycation-induced flip-flop), incorporation of adsorbed species into the liposomal membrane, aggregation of vesicles and their disruption. Electrically adsorbed polycation, if not additionally anchored by an attached hydrophob, can be completely removed from the membrane surface by recomplexation with polyanions. The above mentioned phenomena were examined depending on structure and linear charge density of polyelectrolyte molecules, content of charged lipids, 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 Tirrell, 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., immunogenicity). We have been exploring the self-assembly and cell recognition properties of peptide fragments (thus far derived from extracellular matrix fragments) that we have lipidated synthetically by attaching a phospholipid-mimic, double-chain, hydrocarbon tail. Lipidation confers interesting amphiphilic and self-organization 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 these 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 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. Csajka, Roland R. Netz, Max-Planck-Inst of 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 theoretical 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 Lekner and modified by Sperb. At Bjerrum lengths slightly below 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 uncharged brushes in poor solvent. This is in disagreement with the accepted scaling law for the osmotic regime, which states 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 correlation 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 diagram. Varying the Bjerrum length we obtain a non-monotonic behavior of the brush thickness with a maximum at verry small coupling where already a considerable part of counterions has left the brush.

4:00 PM DD4.7/FF4.7
ADSORPTION OF HYDROPHOBIC POLYELECTROLYTES (PSS) ONTO NEUTRAL SURFACES. O. Théodoly, R. Ober, C. Williams, Collëge de France, Paris, FRANCE.

We are interested by the adsorption of strongly charged polyelectrolytes (Polystyrene sulfonate with rate of sulfonation between 30 and 90 %) on *neutral and hydrophobic* interfaces. The case of solution/air interface is investigated by Langmuir trough measurements, ellipsometry and X-ray reflectivity. The low adsorption rate, common for most polyelectrolytes, is also observed here and is explained by an *electrostatic barrier* effect. A maximum of adsorption with the rate of sulfonation is observed. We invoke a *conforma- tional barrier* effect to explain this phenomenon: chains with a low charge content are collapsed and form isolated globules which are repelled by a neutral surface. After rinsing adsorbed layers with pure water, the desorption is only partial, showing the existence of *a barrier that prevents complete desorption*. The existence of these energetical barriers leads to strong hysteresis phenomena and the state of an adsorbed layer in contact with a solution strongly depends on its history. Concurrently, adsorbed layers at the solid/liquid interface have been studied by a new technique of high-energy *X-ray reflectivity across water*. adsorbed layers are always very thin ($\approx 20\AA$) confirming the fact that the layers are monomolecular.

4:15 PM DD4.8/FF4.8
PROTEIN ADSORPTION ONTO CHARGE-REGULATED SELF-ASSEMBLED MONOLAYERS. Stella Y. Park, Anne M. Mayes, Michael F. Rubner, Massachusetts Institute of Technology, Dept. of Materials Science and Engineering, Cambridge, MA; Paula T. Hammond, Massachusetts Institute of Technology, Dept. of Chemical Engineering, Cambridge, MA.

Anomalous adsorption of poly(acrylic acid) onto charge-regulated self-assembled monolayers (SAMs) has been observed in recent experiments (Barrett and Mayes, submitted). In those studies, the charge density of the surfaces was changed through variations in the pH. The thickness of the adsorbed layer was observed to change abruptly from $25\AA$ to $5\AA$ over a narrow pH range. Here we extend the investigation to include the adsorption of charged biopolymers *e.g.*, poly(lysine). 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 (Clark et al., Advanced Materials, **11**, 1031 (1999)) 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. Tarasevich, Battelle Pacific Northwest National Laboratory, Richland, WA; C. Tidwell, B. Ratner, University of Washington, Seattle, WA; D.L. 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 proteins adsorb onto surfaces and then mediate interactions with cells via specific interactions between protein domains and integrin cell membrane receptors. The role of the surface in controlling responses, however, is not well understood. The effects of surface chemistry features such as functional group density and surface structure have not been well studied largely due to lack of availability of well controlled and characterized surfaces. We report studies of endothelial cell adhesion and growth and serum protein adsorption onto tailored chemically heterogeneous self-assembled interfaces composed of thiols on gold containing mixtures of COOH:OH and COOH:CH3 functional groups. Surface composition and site arrangement was studied using x-ray photoelectron spectroscopy (XPS) and time-of-flight secondary ion mass spectroscopy (TOF-SIMS). We found that endothelial cell growth was maximized onto mixed functionality surfaces compared to single component surfaces. There were differences in cell growth between the two mixture types which we attribute to higher degrees of phase segregation in the COOH:CH3 compared to COOH:OH mixtures. The adsorption and elutability of albumin (Alb), vitronectin (Vn) and fibronectin (Fn) varied with mixed SAM surface composition. Cell growth was maximal on mixed surfaces which exhibited the highest surface fraction of adhesive proteins and the highest Vn elutabilities (i.e. decreased Vn binding strength). These results suggest that the mixed surfaces control the composition and binding strength of proteins in the adsorbed protein layer which affects cell receptor interactions and mitogenic activity.

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

We report the influence of surface properties on the adsorption kinetics of immunoglobin onto modified PDMS (polydimethyl siloxane) surfaces. It was found that the hydrophobic surface of native PDMS has a high affinity for immunoglobin, which adsorbs in abundance at the transport-limited rate. Corona treatment of PDMS yields a relatively hydrophilic surface with minimal affinity for immunoglobin. In the $\sim$100 hours following surface treatment, the hydrophobic nature of the surface recovers (as evidenced by contact angle evolution). The affinity, rate of adsorption, and ultimate coverage of immunglobin also increase, but not at the rate of the contact angle evolution. Stretching the surface after corona 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 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. Iain Baikie, Biocurrents Research Centre, Marine Biological Laboratory, Woods Hole, MA; Bert Lagel, 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 profiles. 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. However on highly insulating surfaces this can be an extremely difficult parameter to measure. We have developed a novel Scanning Kelvin probe[1] which produces very high resolution surface potential/ surface charge profiles of thin polymer films in a non invasive fashion. The SKP allows interpretation of complicated charge topographies in terms of contamination or interfacial effects, furthermore it allows direct imaging of surface 2D charge transfer properties which could not be imaged using other techniques. We anticipate many applications of this technique in monitoring polymer interfaces as it permits non-invasive charge imaging which can dramatically affects polymer performance. For example polymer surfaces such as microporous PTFE are of considerable interest as substrates in artificial skin. However the base material displays poor cell adhesion and surface treatments are essential to provide confluent cell growth. We illustrate application of this device in correlating polymer surface charge topographies to cell growth, corrosion resistant films and potential bio-resistance properties in polymer based anti-fouling paints.
[1] I. Baikie and P.J. Estrup, Rev. Sci. Instrum, 69, 3902 (1998).

DD5.2
SELF-ASSEMBLING MOLECULES IN TISSUE ENGINEERING. Daniel A. Harrington, Peter L. Drzal, Julia 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 cholesteryl moiety attached to oligo-(L-lactic acid) and an optional

biologically relevant headgroup. Variations of this design were examined for their effect on cellular growth and application to engineered three-dimensional scaffolds. Cholesteryl-lactide coated surfaces improved cell adhesion and growth in two dimensions as compared to uncoated poly-(L-lactic acid) (PLLA) surfaces. Interior surfaces of three-dimensional poly-(L-lactic acid) scaffolds have been coated with these oligomers and characterized using confocal microscopy with fluorophor-labeled molecules.

DD5.3
SURFACE WETTABILITY OF MICROPOROUS MEMBRANES AFFECTS THE METABOLIC BEHAVIOUR OF ISOLATED RAT LIVER CELLS. Loredana De Bartolo, Research Institute on Membranes and Modelling of Chemical Reactors, CNR, Rende, ITALY; Claudio Della Volpe, Dept of Materials Engineering, University of Trento, Trento, ITALY; Gerardo Catapano, Dept of Chemical and Materials Engineering, University of Calabria, Rende, ITALY.

Microporous polymeric membranes are often used in bio-artificial organs as immunoselective barriers, to supply cells with oxygen and also as the substratum for the adhesion of anchorage-dependent cells (e.g., liver cells). Characterisation of possible quantitative effects of membrane surface properties on cell metabolism may provide guidelines to the selection (vs. development) of cytocompatible membranes for bio-artificial organs, and particularly for bio-artificial livers (BALs). In this paper, we characterised the effect of surface wettability on the rate of oxygen consumption, ammonia elimination and urea synthesis by primary hepatocytes at two ammonia concentrations. Surface wettability of microporous polypropylene (PP) membranes was modified by treatment with ethanol-containing solutions and was characterised by dynamic contact angle (DCA) measurements. Rat liver cells were cultured on these membranes in a continuous-flow bioreactor whose fluid dynamics were optimised for the kinetic characterisation of cell reactions, at 0.15 and 1.7 mM ammonia. The treatment yielded membranes with recession 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 recession DCA of 30 deg. Rate dependence on recession DCA changed with the investigated metabolic pathway and with ammonia concentration. Differences in cell behaviour on different membranes were more evident at 1.7 mM ammonia. Cells cultured on collagen-coated membranes consistently exhibited the highest metabolic rates in spite of the presence of hydrophobic domains, suggesting that the chemical nature of the substratum plays an important role in cell-membrane interactions. These results indicate that surface properties of membranes used in BALs should be carefully evaluated and their effect on the relevant hepatocyte metabolic reactions should be accounted for in BAL design.

DD5.4
ADSORPTION OF ISONIAZIDE ON COLLAGEN BIOMATERIALS. Erkesh O. Batyrbekov, Rinat M. Iskakov, Bulat A. Zhubanov, Institute for Chemical Sciences, Almaty, KAZAKSTAN.

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 efficient of treatment, polymer has to bind firmly with the drug and to release easily at infectious sides. In this study the nature polypeptide of collagen has been used as a efficient carrier of antituberculous 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 with the active sides on surface of the collagen fibres. It has been found if pH of the colloid system changes on more acid or alkaline, the binding weakens. These results show that collagen particles are effective carrier for delivery of antituberculous drug of isoniazide.

DD5.5
INTERACTION OF DIBLOCK COPOLYMER VESICLES WITH SURFACTANTS. Maria Santore, Lehigh University, Department of Chemical Engineering, Bethlehem, PA; Daniel Hammer and Dennis Discher, Department of Chemical Engineering, University of Pennsylvania, Philadelphia, PA.

Polymersomes are vesicles made from synthetic diblock copolymers, in this case polyethylene oxide (PEO) - polyethylethylene (PEE). This material was previously shown to form large (5-25 micron diameter) unilamellar vesicles of sufficient integrity to survive months in sugar solutions and to be amenable to study via micropipette manipulation, similar to their liposome analogs. The current work explores the interaction of these polymersome vesicles with Pluronic surfactants, as a means to further engineer their mechanical properties, permeability, and as an avenue towards their controlled rupture. It was found that in the extreme, the most hydrophobic Pluronics completely disrupt the polymersomes, while polymersomes can survive indefinitely in solutions of the more hydrophilic Pluronics. Pluronics of intermediate hydrophobicity incorporate into the polymersome membrane, altering the mechanical properties without destroying the vesicle structure. This talk addresses the timescales of Pluronic incorporation, and the extent to which equilibrium is achieved for mixed systems.

DD5.6
PHASE SEPARATION OF TWO-PHASE DEFORMABLE MEMBRANES. Y. Jiang, T. Lookman, A. Saxena, Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM.

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 domain wall solution for the equilibrium shape and phase ordering field. We observe preferential phase separation in regions of differing curvature on a variety of vesicles 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
PIEZOELECTRIC BASED BIOSENSOR FOR IMMUNOLOGY APPLICATIONS. Ashok 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 twenty years now make it possible to determine mass changes that occur at 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 FOR CATTLE. Thomas Q. Dinh, Biomedical Engineering Program, Iowa State University, Ames, IA (current address: Medtronic, Corporate Science and Technology, Minneapolis, MN), Raymond T. Greer, Biomedical Engineering Program and Department of Aerospace Engineering and Engineering Mechanics, Iowa State University, Ames, IA; Ricardo F. Rosenbusch, Department of Veterinary Microbiology and Preventive Medicine, Iowa State University, Ames, IA.

An erodible ring-shaped ocular insert containing an antibiotic (tylosin tartrate) has been developed for treatment of infectious bovine keratoconjunctivitis (IBK). The ocular device is comprised of an outer crosslinked alginate membrane (Al-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 drug release characteristics was a 75 weight % low molecular weight, 25 weight % high molecular weight alginate containing 7.5% Tween 80 plasticizer. This was crosslinked in a 30% calcium chloride aqueous solution for 72 h and then in a 10% aluminum chloride 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 outside diameters ranging from 37 to 52 mm, were available to accommodate a wide range of eye sizes from 31 to 43 mm in diameter. The ring size was taken as 1.2 X the side-to-side dimension of the palpebral 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 $\pm$ 1.73 days. The overall retention 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 device had an average retention time of 2.1 $\pm$ 1.63 days. After 5 days, the drug release rate in vitro still ranged from 4.3 to 34 μg/hr, which was above the minimum release rate of 1.3 μg/hr

required to treat IBK. The medicated ocular device has the ability to suppress and reduce the number of bacteria in the eye to an undetectable or negligible level within a short time (1 to 2 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.

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

8:30 AM *DD6.1
SOFT BIOMATERIALS: ENGINEERING TISSUES FOR THE FUTURE. Joan Zeltinger, Lee Landeen, Holly Alexander and Noushin 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 unsupporting of host cell integration and formation of functional tissues. Data 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 valves can, under specific processing conditions, support human fibroblast integration. Synthetic Scaffolds: Human or animal dermal fibroblasts, arterial fibroblasts or arterial smooth muscle cells were cultured statically or dynamically up to eight weeks on poly (glycolic acid), poly(ethylene terephthalate), or poly(ϵ-caprolactone) scaffolds that differed by their features (e.g., dimensions, architecture, pore size, or void fraction) and fabrication (e.g., felted, braided, 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 immunostaining and histology. Natural/Biologic Scaffolds: Tissue engineered aortic heart valves (BioXenoGrafts^{TM})were developed by culturing human dermal fibroblasts onto decellularized, porcine valves up to eight weeks. Under static or dynamic conditions, the human cells remained metabolically active. Increases in fibroblast integration with time was shown histologically, immunocytochemically and by quantitative digital image analyses. Thymidine and proline radiolabeling showed that the fibroblasts were mitotic and synthesized extracellular matrix. Closing: Future devices will likely be tissue engineered medical products (TEMPs) that are precellularized or promote uniform formation of structured, functional tissues after implantation. Biomaterials 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 DD6.2
THE ATTACHMENT AND GROWTH OF BALB 3T3 FIBROBLASTS ON PATTERNED POLYLACTIDE MEMBRANES. Zbigniew Gugala, Sylwester Gogolewski, Polymer Research, AO/ASIF Research Institute, Davos, SWITZERLAND.

The material surface topography, in addition to the surface chemical characteristics determines to 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 bioresorbable membranes prepared from poly(L/DL-lactide) 80/20% with a viscosity-average molecular weight of 200.000 dalton. The membranes were cast from the polymer solution in nonchlorinated solvent and had the following surfaces: 1. a nonporous, relatively smooth surface (surface roughness average R_a= 8.9 nm); 2. a porous rough surface (R_a=18.1 μm); 3. a patterned surface created by hot-drawing of the porous membranes to various draw ratios. The cells cultured on all three surface types revealed 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 spindle-like shape. They were preferentially attached to the pore edges and highly elongated in the membrane drawing direction. The cells communicated with each other at the connection areas of the pore edges. It can be appreciated that the stretching of the membrane leads to the 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 differences. Guided cell growth on the patterned polylactide membranes could be exploited in ligament repair and in the regeneration of segmental bone defects.

9:15 AM DD6.3
TISSUE ENGINEERED SPINAL CORD. Martin Vacanti, Jack Leonard, Benjamin Dore, Lawrence Bonassar, Yilin Cao, Stanley Stachelek, Alan Farwell, *Joseph Vacanti, Charles Vacanti, University of Massachusetts Medical School, Department of Tissue 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*, cells were infected with neural cell specific p29 Green Fluoroescent Protein chimera (GFPp29), as a label and studied. Full thickness segments, 3-4 mm in length, of spinal cord were excised and the resulting gaps implanted with PGA 14 micron diameter fibers 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 a 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 cell marker, nestin, was expressed, as were the glial (GFAP) and neuronal (NF) markers. *In vivo* 8 of 9 experimental animals recovered significant sensory and motor (including the ability to coordinate use all four limbs in ambulation) function below the transection. Control animals remained paralyzed. Experimental implants consisted of new tissue containing abundant GFPp29 positive cells; which, when examined using a dual FITC/Texas Red filter, demonstrated co-localization the GFPp29 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 pleiotrophic neural progenitor cells associated with a composite synthetic polymer scaffolding.

9:30 AM *DD6.4
SYNTHETIC EXRACELLULAR 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 polymer 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 control the mechanism of cell adhesion 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 findings validate the concept that engineered tissue function can be regulated by designing 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.

10:30 AM *DD6.5
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 cell responses at the tissue-materials interface than is possible using 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 of modified biomaterials. The comb polymer has 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(lactide) 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 morphology of blends or latex coatings. Patterning is thus controlled by self-organization during processing and equilibration of the materials. Cell adhesion, adhesion strength, growth, and migration on clustered adhesion ligand surfaces 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 display of the ligand. These results 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 ex vivo medical devices.

11:00 AM DD6.6
MICROSTAMPING OF BIOLOGICAL LIGANDS ON ACTIVATED POLYMER SURFACES. Ashutosh Chilkoti, Zhongping Yang, Duke University, Department of Biomedical Engineering, Durham, NC; Anna Belu, Physical Electronics, Eden Prairie, MN.

We report a new methodology, which enables biological ligands and proteins to be patterned onto the surface of polymers. This method, microstamping onto activated polymer surfaces (MAPS) is a multistep procedure: first, the surface of a polymer is derivatized to introduce a reactive group of interest. An elastomeric stamp, inked with a biological ligand containing a complementary terminal reactive group, is subsequently brought into contact with the activated surface of the polymer. This results in spatially resolved transfer and coupling of the biological ligand to the activated polymer surface. To demonstrate proof-of principle, we micropatterned COOH-derivatized poly(ethylene terepthalate) with an amine-terminated biotin-ligand. Periodic 10 μm biotin squares were created by MAPS, and incubated with Alexa 488 labeled streptavidin. Fluorescence microscopy showed that the streptavidin spatially-localized onto the biotin micropattern, with an average contrast ratio between patterned regions and background of 200:1. Imaging time-of-flight secondary ion mass spectrometry enabled unambiguous identification and mapping of the spatial distribution of the molecular species patterned on the surface of COOH-derivatized PET. The biotin pattern was imaged by mapping the distribution of CN^- in negative ion mode. In contrast, the substrate was identified by mapping the molecular anion, $C_6F_5O^-$, which arises from activation of the carboxyl groups in derivatized PET by reaction with pentafluorophenol. The contrast inversion in the images clearly indicated that the biotin ligand was spatially localized in the 10 μm square contact regions. Similarly, the image of the m/z = 70 cation, which is unique to streptavidin, showed the spatial localization of streptavidin, and revealed that streptavidin binds selectively to the biotin pattern. In summary, our results demonstrate that biomolecular patterns with a spatial resolution of at least 10 μm, high contrast, and good reproducibility can be fabricated on flat polymer films over a large area ($\sim$1 cm^2) by MAPS.

11:15 AM DD6.7
INVERTED CELL GROWTH ON PLASMA-PATTERNED SURFACES: AN EFFECTIVE APPROACH TO ISOLATING CELL CULTURES. Michael E. Salmon, Peter J. Yancey, Brian M. Robin and Richard J. Spontak, Department of Materials Science & Engineering, North Carolina State University, Raleigh, NC.

Recent developments in drug research demand that thousands of chemical and biological modifications (drug compounds and gene therapies) be screened expediently to discern their effects on living cells. Traditionally, this has been achieved through the use of conventional cell culture techniques in which cells are grown on the surface of a flask or multi-well plate and immersed in a nutrient bath. Current testing and screening procedures require a growth surface of about 0.3-0.5 sq. cm, along with an individual volume of nutrient media, for each cell colony. Physical isolation of small cell colonies into organized arrays within a single volume of media has attracted tremendous attention in recent years as an approach that lends itself to automation. Patterned cell culture surfaces have thus far been realized using self-assembled monolayers, photolithography techniques and cell-surface protein linkages. While these methods all show good initial confinement, decreased adhesion of mitotic cells tends to promote inter-colony contamination during media changes. To circumvent this problem, we have developed a novel cell culture device that employs inverted cell growth on patterned surfaces generated by plasma-enhanced chemical vapor deposition (PECVD). The surface is produced from a combination of HMDSO and nitrogen precursors and is superhydrophobic, exhibiting static contact angles in excess of 130 degrees. Effective seeding of the cells into isolated colonies is initially achieved by patterning this superhydrophobic surface. The efficacy of this patterned surface has been tested and compared with respect to geometric edge effects, surface chemistry and surface inversion. Results from these approaches have been analyzed and synergistically unified to create the design of a cell culture device demonstrating definitive cell isolation after repeated exchange of a single volume of nutrient media.

11:30 AM DD6.8
PREPARATION OF CHEMICALLY PATTERNED POLYMERIC BIOMATERIAL SURFACES BY GAS DISCHARGE PLASMA PROCESSES AND CHARACTERIZATION BY CELL CULTURES. Karsten Schröder, Dorit Keller, Asmus Meyer-Plath, Andreas Ohl, Inst. für Niedertemperatur-Plasmaphysik, Greifswald, Daniel Briem, Alexander Katzer, Univ.-Krankenhaus Eppendorf, Chirurg. Klinik, Univ. Hamburg, Bettina Husen, Dept. Reproduktionsbiologie, Deutsches Primatenzentrum, Göttingen, GERMANY.

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 technologies 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 plasma. Functional groups introduced into the polymers surface enhance wettability and improve cell adhesion. In the second step a passivation plasma containing hydrogen is applied for pattern transfer using a laser cut metal mask. Plasma passivation is characterized by a removal of functional groups and polymer crosslinking without generation of morphological textures. The cell adhesion in the passivated (hydrophobic) regions is suppressed.
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 quality can be correlated to type and size of the cells. Fluorescence labeling of ECM and cytoskeletal components was used to characterize temporal differences in 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
Chairs: Samuel I. Stupp and Kenneth R. Shull
Wednesday Afternoon, April 26, 2000
Metropolitan I (Argent)

1:30 PM *DD7.1/FF7.1
BIOADHESIVE POLYMER FORMULATIONS THAT PROLONG DRUG DELIVERY ACROSS MUCOSAL SURFACES. Allan Hoffman, Chad Brown, Masashi Nakakura, Guohua Chen, and Yoshi Hayashi, Dept of Bioengineering, Univ of Washington, Seattle, WA; Wayne Gombotz, Dean Pettit, Lotte Kreilgard and James Matsuura, Immunex Corp, Seattle, WA; Michael Roberts and Milton Harris, Shearwater 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 or the intestines. However, this does not necessarily lead to prolonged drug release from such formulations, since the drug may still be released too rapidly as the formulation swells and dissociates. 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, leading to extended residence times on the mucosal surfaces, as well as to retarded diffusion of drug and prolonged duration of drug release. 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 DD7.2/FF7.2
THE INFLUENCE OF INTERFACIAL MECHANICAL BEHAVIOUR UPON DEFORMATION AND FRACTURE OF COMPOSITE BIOPOLYMER GELS. K.P. Plucknett, V. Normand, S.J. Pomfret, D. Ferdinando and W.J. Frith, Unilever Research,

Colworth Laboratory, Sharnbrook, Bedfordshire, UNITED KINGDOM.

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 gelation, 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/agarose. The mechanical response of these materials was primarily determined by the individual constituent behaviour and the interface fracture resistance. For the gelatin/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 $\sim$0.25 J.m^{-2} for this system. There was 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/agarose system. However, it was possible to conduct peel tests with a gelatin layer cast onto agarose. 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 DD7.3/FF7.3
INTERFACIAL ADHESION OF BIOPOLYMER GELS MEASURED USING THE PEEL TEST. S.J. Pomfret, K.P. Plucknett, V. Normand, W.J. Frith, Unilever Research Colworth, Bedford, UNITED KINGDOM.

The adhesion between layers of biopolymer gels has been measured using the 90 degree peel test. Gel bilayers, including gelatin, agarose, maltodextrin and kappa-carrageenan, were prepared in several ways - simple contact between two pre-gelled layers; layers being cast on top of one another; and phase separation into bilayers. The force required to separate these layers was measured and the results allow the interfacial properties to be compared as a function of gel type, preparation method used, and layer contact time. The expression that describes the force required to peel two layers apart includes terms to account for alternative methods of energy dissipation, such as peel arm extension, that occur in addition to interfacial fracture. Preliminary attempts have been made to evaluate these terms and hence allow determination of the interfacial fracture energy of the systems involved. The value of approximately 0.2 J/m^2 for the interfacial fracture energy of a maltodextrin/gelatin interface, formed by casting gelatin on maltodextrin, is in good agreement with values indirectly observed from particle/matrix debonding experiments performed on composite systems.

2:30 PM DD7.4/FF7.4
pH-DEPENDENT SWELLING BEHAVIOR OF HYDROPHILIC GEL WITH POLYSACCHARIDE. Xiaowei He, Jian Xiong, Nuo Lei, Faxing Luo, Liansheng Yang and Xiong Fu, South China University of Technology, College of Food Engineering & Biotechnology, Guangzhou, PR CHINA.

It was known that charged polymeric networks have been recognized as useful matrices for delivering drugs because of their volume change in response to pH variation. However, most of the synthetic polymers gels so far studied have poor bio-intermiscibility and probably have side effect when they are applied to human body as a biomaterial. On the other hand, polysaccharide, which is natural polymer, has good bio-intermiscibility. Therefore, the gel with polysaccharide can be expected as a novel material like to biopolymer gels. In this study, the graft of polysaccharide and acylonitrileStarch-g-PAN gel were prepared and also, the swelling behaviors of the gel with poly- saccharide in an aqueous with different pH values were discussed. The response of the graft gels was investigated by the pH-dependence of weight swelling ratio. In a lower pH regionpH=4,the swelling ratio of the graft gel glucose group in starch: AN, 1; 6; molar ratio was almost constant. In a pH range above pH=4.0,the swelling ratio increased strikingly with pH up to pH=6.0, and showed a maximum at pH=7.0. Swelling and deswelling of the graft gel were induced by changing pH. For example, the swelling ratio of the graft gel decreased when the gel was immersed in water of pH=4.0 and then increased when it was performed in water of pH=7.0. The swelling ratio change for the graft gel could be reversibly repeated many times by switching the pH values of 4.0 and 7.0 Also, experimental data indicated that the deswelling and swelling behavior was sharp and quick in the stage and then, became slow in the late stage. This is due to different mechanisms during the overall process of both deswelling or swelling. Also, the discussion of the aggregation structure-pH responsive property relationships of the graft gel with polysaccharide will be presented.

3:15 PM DD7.5/FF7.5
ADHESION OF INJECTABLE SEMI-INTERPENETRATING POLYMER NETWORKS. Ranee A. Stile, Kevin E. Healy, Northwestern University, Departments of Biological Materials and Biomedical Engineering, Chicago, IL; Elizabeth Fabbroni, 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-acrylic acid) [P(NIPAAm-co-AAc)] 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 P(NIPAAm-co-AAc) hydrogels and linear peptide-functionalized P(AAc) 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-IPN. The solvent, the molar ratio of AAc:NIPAAm in the hydrogel, and the molecular weight of the P(AAc) 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-AAc) hydrogels served as controls. The semi-IPNs demonstrated significantly smaller volume changes, as compared to P(NIPAAm-co-AAc) hydrogels, due to the P(AAc) chains. However, the P(AAc) 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 solvent and the molar ratio of AAc:NIPAAm significantly affected the LCST and volume change of the semi-IPNs. To assess adhesive properties of the matrices, axisymmetric adhesion analyses were performed on thin (1 mm) layers of a semi-IPN using a coated hemispherical glass indenter. 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 tissue. These semi-IPNs may be useful in cartilage regeneration applications.

3:30 PM DD7.6/FF7.6
ADHESION OF PRESSURE SENSITIVE ADHESIVES WITH APPLICATIONS IN TRANSDERMAL DRUG DELIVERY. Marc B. Taub and Reinhold H. Dauskardt, 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, necessitate 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 desirable properties of good initial and long-term adhesion, clean removability, and skin and drug compatibility. In addition, their highly viscoelastic properties are necessary prerequisites for attachment to 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 mechanics 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 delamination. The strain energy release rate (G) during debonding of a cantilever-beam 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 constitutive behavior of the soft viscoelastic adhesive layer. Effects of adhesive chemistry, layer thickness, and strain rate will be discussed.

3:45 PM DD7.7/FF7.7
EFFECT OF PLASMA TREATMENT ON THE ADHESION OF AN ELECTROLESS SILVER FILM ON A BIOMEDICAL POLYURETHANE. Joy E. Gray, P.R. Norton, K. Griffiths, 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 electroless plating technique has been studied. Air plasma treatment of the polyurethane surface prior to electroless

plating 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 sample surface. Contact angle goniometry shows a significant increase in wettability. The absence of surface roughening or ablation 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. The 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 loosely bound clusters while the plasma modified polymer film results in complete silver coverage as a uniform film. This work demonstrates the importance of chemical surface modification in the role of metal/polymer adhesion.

4:00 PM DD7.8/FF7.8
ADHESION AND MICROTRIBOLOGY OF POLYETHYLENE GLYCOL COVERED SILICA SURFACES. Norma A. Alcantar, Tonya L. Kuhl, Amy Stacy, Eray 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 hydroxylated by exposure to water plasma. The end alcohol group of the PEG chain reacts with the silanol group on the silica surfaces 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 device 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, hydroxylated 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/FF7.9
NANOINDENTATION EXPERIMENTS TO PROBE THE SURFACE MECHANICAL PROPERTIES OF PLASMA TREATED POLYETHYLENES. C.M. Klapperich, K. Komvopoulos, Department of Mechanical Engineering, Univ of California, Berkeley, CA and L.Pruitt, 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 polyoelefins 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. Dauskardt, 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.