SYMPOSIUM J

Biomimetic Polymers and Gels

November 28 - December 1, 2005

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* Invited paper

SESSION J1: Gels and Self-Assembly in Biopolymer Systems I
Chairs: Ferenc Horkay, Noshir Langrana and Bernard Yurke
Monday Morning, November 28, 2005
Room 201 (Hynes)

8:30 AM *J1.1
Symmetry, Equivalence and Self-Assembly. Jack F. Douglas[1] and Kevin Van Workum[2]; [1]Polymers Division, NIST, Gaithersburg, Maryland; [2]Chemistry Deparatment, US Naval Academy, Annapolis, Maryland, Maryland.

Molecular self-assembly is central to the formation of numerous biological structures and the emulation of this process through the creation of synthetic counterparts offers great promise for nanofabrication and nanometrology. Our approach to understanding the principles governing this type of self-organizattion process is inspired by the biological self-assembly of actin, tubulin, and icosahedral viral capsid and clathrin structures. Our Monte Carlo calculations show the self-assembly of chain-like, membrane-like, tubular, and hollow icosahedral structures upon cooling, depending on the symmetry of the particle potential. The particles leading to these different organizational patterns are characterized by directional (dipolar, or multipolar) interactions. Specifically, a dipolar potential having a continuous roatational potential gives rise to the formation of chains, while potentials having discrete rotational symmetries (e.g, square quadrupole or a triangular ring of dipoles having two and three-fold rotational symmetries, respectively) led to the formation of nanotube and icosahedral structures with some resemblence to tubulin and the icosahedral structures of viral capsids. These examples of self-assembly provide insights into how the symmetry properties of the particle potentials encode the symmetry properties of their counterpart organized structures. Our findings should be useful in the design of synthetic structures of prescribed geometry utilizing self-assembly.

9:00 AM J1.2
Designing Compliant Substrates to Regulate the Motion of Vesicles. Anna C. Balazs, Alexander Alexeev and Rolf Verberg; Chemical Engineering Department, University of Pittsburgh, Pittsburgh, Pennsylvania.

By integrating mesoscale models for hydrodynamics and micromechanics, we examine the fluid-driven motion of vesicles on compliant surfaces. The vesicles, modeled as fluid filled elastic shells, represent biological cells or polymeric microcapsules. We isolate mechanically and topographically patterned surfaces that transmit "stop" and "go" instructions, causing the vesicles to halt at specific locations on the substrate, and with an increase in the imposed flow velocity, to resume moving. For surfaces containing regular arrays of compliant posts, the substrates also affect the vesicles' gait, causing them to "crawl", "walk" or "jump". The latter behavior could promote the intermixing of reactants that are encapsulated within the microcapsules. Such control over vesicle dynamics can facilitate various biological assays and enable the fabrication of arrays of mobile micro-reactors.

9:15 AM J1.3
Electronic Control of F-actin Polymerization. Ian Y. Wong and Nick Melosh; Materials Science and Engineering, Stanford, Stanford, California.

Polymerization of G-actin monomers into F-actin filaments and bundles is essential for eukaryotic cell division and motility, and can form reversible hydrogels at higher weight percentages. The dynamic polymerization of these filaments in vivo is controlled by a complex network of proteins designed to modulate the monomer reactivity, however it is difficult to achieve similar dynamic control for in vitro systems where F-actin is polymerized by increasing the bulk concentrations of certain cations (Mg2+, K+) in solution. Here we demonstrate how an electronic chip can be used to direct the behavior of a biological or chemical system by exploiting the localized electrical field in the vicinity of the electrode surface. Polymerization of actin is induced by applying a negative bias to the electrode, locally increasing the Mg2+ around the electrode. Actin monomers in the concentrated Mg2+ regions become activated by complexation with the magnesium, and subsequently proceed to polymerize. In addition, patterning nucleation molecules such as ActA or VCA allows the spatial location of the actin growth to be controlled as well. The kinetics of this polymerization process is modeled by introducing a new electronically-controlled activation step before actin polymerization starts taking place. The rate of actin activation depends upon the voltage and frequency of the applied electrical signal. By interfacing this electronic control with optical fluorescence microscopy in a feedback mechanism, it may be possible to dynamically regulate F-actin growth and hydrogel formation near microfabricated devices. This mechanism also has interesting implications for controlling the local mechanical characteristics of multivalent ion-bridged hydrogels for highly localized drug release.

10:00 AM *J1.4
Clustering and Solvation in Model Polymer Solutions. Boualem Hammouda, National Institute of Standards and Technology, Gaithersburg, Maryland.

Model synthetic polymer systems are often used as templates for understanding basic interactions in biopolymers. Water-soluble polymers yield good insight into hydrophobic interactions, hydrogen bonding, aggregation and micelle formation. Poly(ethylene oxide) is the simplest water-soluble polymer. It has received much attention in basic research. Hundreds of papers have been published on PEO and PEO containing polymers. This research spans many areas including synthetic polymers and biology. PEO is often used in biology research because of its biocompatibility and constitutes a simple-enough (and therefore tractable) biopolymer template. The simple CH2CH2O monomer unit is characterized by both hydrophobic interactions around the CH2 groups and hydrophilic interactions through hydrogen bonding around the Oxygen groups (mediated by water molecules). The proximity of hydrophobic and hydrophilic interactions within the same monomer makes PEO a valuable system for understanding basic interactions that occur in molecular systems. Biological structure and function are often driven by such interactions. The technique of Small-Angle Neutron Scattering (SANS) is used to investigate PEO solutions in various solvents and experimental conditions. This technique is valuable because it can probe a size range from the near atomic to the near micrometer scales. The use of deuterated solvents helps enhance the SANS signal. When dissolved in water, PEO forms clusters (seen as large scale aggregation by SANS) but it dissolves rather well at the monomer level (seen as local chain solvation by SANS). This behavior has been investigated extensively by our group. We have found, for instance, that the large-scale clustering is due to hydrophobic interactions whereby hydrophobic groups cluster in order to shield interactions with water. On the other hand, the water solvation layer around the polymers is due to hydophillic interactions (hydrogen-bonding mediated through water molecules). PEO also dissolves in non-aqueous solvents such as benzene, toluene, methanol, ethanol, ethylene glycol, xylene, and chloroform. Semidilute solutions of PEO in such (deuterated) solvents have been investigated. SANS measurements in solvent-mixtures have shown that mixing solvents enhances the solvation process. This is due to the non-ideal mixing within the solvation layer around the polymers. We have also investigated another water-soluble polymer containing charges (polyelectrolyte). Poly(acrylic acid) is a useful template for DNA. PAA and DNA are characterized by the same SANS features when dissolved in water (semidilute solution regime). Both show a clustering signal at low-Q (low scattering wavenumber) and a polyelectrolyte peak at high-Q. More details will be included.

10:30 AM J1.5
Bilayers and Interdigitation in Block Copolymer Vesicles. Anthony J. Ryan and Guiseppe Battaglia; Department of Chemistry, The University of Sheffield, Sheffield, United Kingdom.

Amphiphilic block copolyethers assemble into membranes with thickness between 2.4 and 7.5 nm. The vesicular morphology is been confirmed by small angle x-ray scattering combined with electron microscopy for diblock copolymers and triblock copolymers of both architectures. The scaling of the membrane thicknesses with the length of the hydrophobic block is in good agreement with the strong segregation theory for block copolymer melts, indicating a mixed and stretched conformation of the hydrophobic chain inside the vesicle membrane. This result is in contrast to previous published results where the hydrophobic membranes were observed to have bilayer geometry and polymer chains that are relatively unperturbed from their ideal Gaussian dimensions. We question the usefulness of the nomenclature of bilayers and interdigitation when applied to block copolymer vesicles. The behaviour of block copolymer lamellae in the melt clearly shows that the two stretched brushes, emanating from the interfaces and comprising each domain, are mixed for entropic reasons. Obviously the relative lack of flexibility in a phospholipid chain can cause the bilayer morphology to be preferred, the configurational entropy does not necessarily drive layer mixing in this case, but there are no compelling reasons why two hydrophobic polymer brushes would separate, and this is borne out by the measurements presented here. The picture presented is not, however, an interdigitated membrane that leads to water exposure of every hydrophobic block at both the block junction and the other end of the PBO chain. Whilst this might be the case for interdigitated lipids, we suggest that block copolymer brushes are entangled with buried chain ends rather than being either a definite interdigitated monolayer or well separated bilayer. Furthermore the phospholipid description of the well-separated hydrophobic bilayer and the completely interdigitated monolayers are extreme boundary conditions and are

not always appropriate to describe the more subtle structure of block copolymer vesicles or polymersomes.

10:45 AM J1.6
The Formation of Multilamellar Tubules: Myelins.
Battaglia Guiseppe and Anthony J. Ryan; Department of Chemistry, The University of Sheffield, Sheffield, United Kingdom.

The complexity and the functionalities of biological membranes have been recently mimicked by synthetic amphiphilic copolymers. The entirely artificial nature of these polymeric membranes allows an extensive variety of chemistries to be applied in the design of mechanically and chemically enhanced micro- and nano-structures with a tunable range of dimensions and membrane thicknesses. As well as the biological membranes, polymer membranes have been found to generate more or less complex architectures. In particular, we present, a study of polymeric myelins formation using an artificial copolyether poly(ethylene oxide)-co-poly(butylene oxide) copolymer (E16-B22).. Myelins are very long (up to few meters) multilamellar tubules that connect together the neuronal cells and together with them make up the intricate network essential for the functioning of any nervous system. The polymeric myelin formation has been firstly studied at the copolymer/water interface and then reassembled into a dispersed phase forming sun-like structures made with complex multilamellar structure core and a corona made of short myelins. The myelin growth has been controlled by dilution ratio with water and the presence of an apolar solvent (chloroform). A model for myelin formation has been developed. The results show how control myelination and myelin formation. The slower kinetic of amphiphilic copolymers can be of benefit for the understanding of myelin growth. Furthermore, the beneficial effect of sdded solvent on myelination can be interpreted as a fluidification of the hydrophobic membrane. By analogy, cholesterol has the same effect on biological membranes, in particular, cholesterol is found in greater proportions in nerve cell membranes than in other biological membranes and has been shown to have a crucial role in myelination. Moreover the possibility of engineering controlled tubular structure can be of help for the design novel scaffolds for tissue engineering or using such morphologies for molecular electronics applications

11:00 AM J1.7
Hydrogels via β-Hairpin Peptide Self-Assembly: Reversible Stiffening Below a Peptide Fibril/Ion Complexation Transition Temperature. Bulent Ozbas[1], Karthikan Rajagopal[2], Joel P. Schneider[2] and Darrin J. Pochan[1]; [1]Materials Science and Engineering, Delaware Biotechnology Institute, University of Delaware, Newark, Delaware; [2]Chemistry and Biochemistry, University of Delaware, Newark, Delaware.

We study de novo designed β-hairpin peptides that intermolecularly self-assemble into rigid hydrogel networks after an intramolecular folding event that can be triggered by temperature, pH or ionic strength. The peptides are locally amphiphilic with two linear strands of alternating valine and lysine amino acids flanking a central tetrapeptide turn sequence. The irreversible folding transition of the β-hairpin molecule is around 25 'C at pH9. When the temperature is raised above the folding transition, the hydrophobic interactions dominate over the electrostatic repulsions between the lysine residues and the peptide arms are forced into a beta-sheet secondary structure by the turn sequence. This intramolecular folding event is followed by the intermolecular self-assembly of β-hairpins into semiflexible fibrillar structures with permanent, physical-crosslink points. As the folding and assembly proceeds the low-viscosity, dilute peptide solution changes into a self-supporting, soft-solid hydrogel. The rheological behavior of these hydrogels can be modulated with the arm length of the peptides that inherently dictates the cross-sectional diameter of the fibrils. These networks exhibit a second type of transition on cooling when boric acid is used as a buffer salt. This transition stiffens the hydrogel and leads to a more than an order of magnitude increase in storage modulus. Oscillatory measurements show that this transition is reversible and that the rigidity of the hydrogels increase with decreasing temperature below the transition point. These transitions can be tuned with peptide and borate concentration, pH and ionic strength. SANS and DLS data reveal that during this transition static structure is preserved while the dynamics of the network is slowed down significantly. These transitions are also observed with DSC and NMR techniques. Although it has been shown that the boric acid/borate ions form complexes with polyols and polysaccharides, rheological experiments with different peptide sequences suggest the formation of new type of complex with lysine residues.

11:15 AM J1.8
Using Di-Peptides to Produce Nano-Scaffolds by Self Assembly. Rein Vincent Ulijn, Vineetha Jayawarna and Julie E. Gough; School of Materials, University of Manchester, Manchester, merseyside, United Kingdom.

Molecular self assembly is a very powerful tool for the preparation of novel materials with well defined properties at the molecular level. Peptides are particularly interesting as building blocks for these materials and self assembled nano-wires, cages, fibres, sheets and tubes have all been described. A difficulty in the design of improved peptide materials is that little is understood about the rules that govern self assembly and much work has been based on trial and error. One aim of our work are to gain insight into some of these phenomena by studying the simples possible peptides that consist only of 2 amino acids. Using dipeptides allows us to vary the amino acids systematically and in this way we hope to gain insight into what determines the self assembled structures that arise. Peptide structures that arise are analysed by circular dichroism and imaged by cryo scanning electron microscopy. In addition we aim to apply self assembled peptide scaffolds to tissue engineering. We have succeeded in identifying a mixed di-peptide scaffold that is stable at pH 7 and has a gelation temperature of just over 40C. This scaffold was used for the 3D culturing of chondrocytes (cartilage cells).

11:30 AM J1.9
Synthesis and Self-assembly of Nanomaterials Using Genetically Engineered Viruses For Medical and Semiconductor Applications. Seung-Wuk Lee, Bioengineering & Chemistry, University of California, Berkeley, Berkeley, California.

A fundamental challenge in bio-nanoscience is to identify an active building block that can perform highly selective functions with remarkable precision based on specific recognition, programmable self-assembly, and non-toxic biocompatibility. Biological building blocks, such as DNA, peptides, and lipids, have been utilized to create vesicles, nanofibers, nanotubes, and two-dimensional synthetic hierarchical structures. By responding to external stimuli, artificial DNA conjugated with nanoparticles and peptide amphiphiles can self-assemble in reversible patterns to form hierarchical nanostructures and perform specific functions. However, their functions and precision are still not comparable to those of biological systems such as bones, brittle stars, abalone shells, and diatoms, which can orchestrate remarkable spatial and temporal control on both the nanometer and micrometer scales during the mineralization process. Identifying potential functional nanoscale basic buildings block from living systems is still challenging because of long encrypted peptides and genes. In my seminar, I will demonstrate that genetically engineered viruses can perform multiple processes, ranging from isolating basic building units to transforming into inorganic electronic components. These components can self-assemble into solid state device-like hierarchical structures that may be useful for next generation construction of nanometer scale devices, sensors, and machines. In addition, I will elucidate a molecular level understanding of bone mineralization using phage display. Short binding motifs screened against single crystal hydroxyapatite (HA) (inorganic part of bone) resulted in the identification of a collagen-like pseudo repetitive 12mer peptide. Similar to collagen, which is an organic scaffold of bone mineralization, the 12mer binding peptide directed the mineralization of HA. Control experiments using scrambled peptides and alanine-substituted peptides facilitated the investigation of the role of the amino acid residues in bone binding and mineralization.

11:45 AM J1.10
Interaction of Fibrinogen with the Synthetic Clay Langmuir Blogett Film. Ja Seung Koo, T. Koga, M. H. Rafailovich and J. C. Sokolov; Materials Science, Stony Brook University, Stony Brook, New York.

Fibrinogen, a protein extracted from human body, was adsorbed onto synthetic organoclay monolayers. To prepare the single clay platelet on the Si wafer Langmuir-Blogett technique was used. A solution of organoclay particles dissolved in xylene was spread at the air water interface. As the molecular area decreased, the surface was covered with monolayer clay platelets. At 38mN/m where the suface pressure increased rapidly, whole areas were fully covered by clay particles. X-ray reflectivity and atomic force microscope (AFM) and scanning electron microscope (SEM) were applied to provide the evidence for the formation of hybrid clay-organic monolayers. By using X-ray reflectivity, the total thickness of the layer was found to be 14 angstron which is in good agreement with AFM data. These Langmuir-Blogett clay films were plated into fibrinogen solution (0.1mg/ml) in PBS buffer to investigate the interaction the protein with clay monolayer. The results showed that the thickness of fibrinogen layer increased with the incubation time. Furthermore, the organo-surfactant will affect on the adsorption of the protein on the clay layer.

SESSION J2: Gels and Self-Assembly in Biopolymer Systems II
Chairs: Jack Douglas and George Pins
Monday Afternoon, November 28, 2005
Room 201 (Hynes)

1:30 PM *J2.1
Tuning the Elasticity of Biopolymer Gels for Optimal Wound Healing. Penelope C. Georges[1,2], Margaret McCormick[1], Lisa A. Flanagan[3] and Paul Janmey[1,2]; [1]Institute for Medicine and Engineering, University of Pennsylvania, Philadelphia, Pennsylvania; [2]Bioengineering, University of Pennsylvania, Philadelphia, Pennsylvania; [3]Pathology, University of California-Irvine College of Medicine, Irvine, California.

Soft polymer networks with large mesh size, not flat rigid surfaces, are the normal environment for most animal cells. Cell structure and function depend on the stiffness of the surfaces on which cells adhere as well as on the type of adhesion complex by which the cell binds its extracellular ligand. Most cell types, including fibroblasts and endothelial cells, switch from round to spread morphology as stiffness is increased between 1000 and 10,000 Pa. Coincident with the change in morphology are a host of differences in protein phosphorylation levels, expression of integrins, and changes in cytoskeletal protein expression and assembly. In contrast, other cells types such as neutrophils do not require rigid substrates in order to spread, and neurons extend processes better on soft (50 Pa) materials than on stiffer gels. We compare the stiffness sensing of neurons to that of astrocytes, a glial cell type derived from embryonic rat brain. Astrocytes switch from a round to spread morphology as substrate stiffness increases, but do so over a stiffness range 10 times softer than that over which fibroblasts alter morphology. In co-cultures of primary neurons and astrocytes the surface elasticity can be manipulated over a range to select for neuronal outgrowth while limiting astrocyte activation and proliferation. Stiffness-dependent morphologic changes observed from studies of cells grown on surfaces of protein-laminated polyacrylamide gels that have linear elasticity are also seen when cells are embedded in three-dimensional matrices of natural biopolymers such as fibrin. Biopolymer gels like fibrin can be formed with appropriate stiffness to optimize for neuronal cell survival, and may have utility for repair of damaged neural tissues. The complex non-linear rheology of fibrin and other gels formed by semi-flexible biopolymers that exhibit strain-stiffening and negative normal stresses provide additional mechanisms by which cells can respond to and actively remodel the mechanical features of their environment.

2:00 PM J2.2
Macro- and Micro-Scale Probing of the Mechanical Properties of DNA-Crosslinked Gels Using Embedded Inclusions. David C. Lin[1], Bernard Yurke[3], David I. Shreiber[2], Uday Chippada[1], Xue (Frank) Jiang[2], George Patrick Watson[3] and Noshir A. Langrana[1,2]; [1]Department of Mechanical and Aerospace Engineering, Rutgers University, Piscataway, New Jersey; [2]Department of Biomedical Engineering, Rutgers University, Piscataway, New Jersey; [3]Bell Laboratories, Murray Hill, New Jersey.

A class of biomaterials based on DNA-crosslinked hydrogels is investigated in this research. Hybridization chemistry and strand displacement mechanisms allow reversible assembly and shape change through the application of particular strands of DNA. Choice of base sequence allows for the design of gels that are degraded by particular restriction endonucleases or by particular messenger RNA strands. Altering the composition of the polymer, the length of the DNA strands, or the density of the crosslinks allows these materials to exhibit a wide range of biomechanical properties. Measurements of global and local mechanical properties of soft materials can be performed using a large number of established methods. Existing techniques, however, are difficult to adapt to situations requiring measurements coincident with some external influence. For instance, local changes to the stiffness of a cellular engineering substrate in response to traction forces exerted by motile cells would not be possible to measure using an atomic force microscope. In this work on DNA-crosslinked hydrogels, it was necessary to develop a nondestructive method of measuring changes in the global elastic moduli of the materials as specific DNA strands were introduced to alter the polymer network structures. The microliter-sized samples and experimental conditions imposed strict limits on materials handling, precluding the use of direct compression and indentation methods. In the new technique, embedded magnetic inclusions are deflected using an electromagnet. Recently, we showed that finite size effects of the medium can be accounted for to allow the use of spherical inclusions of relatively large size. Applying this technique using 0.8 mm diameter beads, the scaling behavior of the elastic modulus with crosslink density was determined. Additionally, it was shown that a threefold increase in stiffness was possible by generating prestress in the DNA-crosslinked gel network. In our ongoing work, we embed the gels with micro-fabricated nickel bars (0.5x1x5 and 0.5x1x10 μm) to locally measure elastic and shear moduli as well as Poisson's ratios. The single electromagnet is replaced with a four-pole magnetic tweezers system similar in concept to that introduced by one of the authors. The tweezers allow a magnetic force to be applied in any direction. Unlike a sphere, which only translates in a magnetic field, an oblong inclusion will also rotate about its center of mass. This behavior allows inference of Poisson's ratio in addition to the elastic modulus. Preliminary data clearly indicated that the magnitudes of rotation and translation are directly related to the stiffness or crosslink density of the gel. The nickel bars are used to quantify stiffness gradients generated in DNA-crosslinked gels by spatially controlling the crosslink density. We are also functionalizing the gel for cell attachment and using this technique to assess cell-substrate interactions.

2:15 PM J2.3
Directed Motion and Cargo Transport through Propagation of Polymer Gel Volume Phase Transitions. Ulrich Wiesner[1] and Lilit Yeghiazarian[2]; [1]Materials Science & Engineering, Cornell University, Ithaca, New York; [2]Biological Engineering, UCLA, Los Angeles, California.

One of the fundamental problems in biotechnology is the transformation of energy into directed motion and load transport on very small scales. Hybrid devices driven by molecular motors have been engineered but are often limited through required specific environmental conditions. Here a prototype position controlled synthetic soft device is demonstrate built from a thermosensitive polymer hydrogel for which motion is based on a mechanism different from those employed in earlier gel-based devices. The directional motion of cylinder-type hydrogels is generated by spatially controlled propagation of the volume phase transition along their length, demonstrating velocities of about 15 micrometer/sec for cylinder diameters of the order of a millimeter. The reason why directional motion of polymer gels is achieved lies in breaking the symmetry by spatial-temporal inhomogeneity of the induced volume phase transition. While on the local scale the relative change of the gel dimensions is isotropic, different segments of the gel along its length may be found in different phases in space and time. Similar phenomena are observed in nature, for instance, in the locomotion mechanisms of a variety of worms, including the common earthworm for which various segments of the gel are 'fat' or 'thin' at different points in time and space, and 'fat' segments provide anchor points in the burrow and allow for further extension of the 'thin' parts of the body. The moving synthetic gel of the present study is capable of transporting cargo and can be stopped and restarted at any time. Since gel volume changes are diffusion controlled, miniaturization to the micron scale can be expected to dramatically enhance gel speeds beyond what is currently observed in small scale devices. It is anticipated that this principle will be widely utilized in a variety of areas in biotechnology including microfluidics, robotics and drug delivery. Reference: L. Yeghiazarian, S. Mahajan, C. Montemagno, C. Cohen, U. Wiesner, Adv. Mater. (2005), in press.

3:30 PM *J2.4
pH-dependent Gelation of Gastric Mucin. Rama Bansil, Physics, Boston University, Boston, Massachusetts.

Mucin, a polymeric glycoprotein secreted by gastric epithelial cells is the major polymeric component responsible for the viscoelastic properties of gastric mucus which protects the stomach from being digested by the gastric juices that it secretes. In this talk I will present dynamic light scattering data to show that purified pig gastric mucin solutions form a gel under acidic pH. Microscopic DLS measurements of tracer particles incorporated in mucin provide estimates of its viscoelastic constants. Using tapping mode Atomic Force Microscopy in an aqueous medium was used to examine conformations of purified gastric mucin molecules as a function of pH and to obtain direct visual evidence of aggregation. AFM studies on human mucus will also be presented. A model of gelation based on the interplay of hydrophobic and electrostatic interactions will be discussed.

4:00 PM J2.5
Abstract Withdrawn

4:15 PM J2.6
Probe diffusion in concentrated polymer solutions and gels by fluorescence correlation spectroscopy. Ariel Michelman-Ribeiro[1,2], Ralph Nossal[1], Ferenc Horkay[1] and Hacene Boukari[1]; [1]Laboratory of Integrative and Medical Biophysics, National Institutes of Health, Bethesda, Maryland; [2]Physics Department, Boston University, Boston, Massachusetts.

The study of transport of macromolecules in concentrated solutions and gels is relevant to many technological and biological processes. In this talk we demonstrate how fluorescence correlation spectroscopy (FCS), a relatively non-intrusive optical technique, can be applied to

quantitate the diffusion of probe particles in polymer solutions and gels. In the case of Poly(vinyl-alcohol) (PVA, 85 kDa) polymers we measure characteristic diffusion times of various fluorescent probes (TAMRA(430 Da); dextran (10 kDa and 70 kDa); BSA protein (66 kDa)) in non-fluorescent -hence invisible- polymer solutions as a function of the polymer concentration and cross-link density. In the semi-dilute regime, the decrease of the diffusion coefficient with increasing polymer concentration (c) is analyzed with the universal scaling law ($\exp(-\alpha c^{\nu})$), which mainly yields the solvent quality (ν). Remarkably, the measurements indicate that when the size of the probe particles is smaller than the polymer-polymer mesh size, the particles appear to experience the single-chain viscosity rather than the solvent viscosity. Cross-linking of the solutions into gels slows down further the diffusion of probe particles. Moreover, the more the polymer chains are cross-linked, the slower the particles diffuse. We attribute this latter effect to the formation of superstructures by cross-linking of the PVA chains, which affect generally the elastic modulus of the gels. Here, we find a simple linear relation between the elastic modulus and the diffusion times. This emphasizes the importance of cross-link density as a relevant parameter to be included in the analysis of probe diffusion data in polymer gels.

4:30 PM J2.7
Water Flow through a Hydrogel during its Phase Transition.
Muneyuki Yoshikawa[1], Jun Matsui[2] and Atsushi Suzuki[1]; [1]Environment and Information Sciences, Yokohama National University, Yokohama, Kanagawa, Japan; [2]Mechanical Engineering, Yokohama National University, Yokohama, Kanagawa, Japan.

We report the experimental results on the water flow through a thermoresponsive hydrogel during its temperature-induced phase transition. The friction between the polymer network and water of poly(N-isopropylacrylamide) gel was measured by a newly designed simple apparatus where the hydrogel was mechanically constrained in a glass microcapillary. The velocity of water-flow depended on the length and the cross-section area of the gel and on the applied pressure to the solvent water at a constant temperature. The water-flow through the hydrogel in the vicinity of the transition temperature could be continuously controlled by more than ten times only by adjusting the temperature. These findings will be discussed in terms of the effective pore size and the fluctuations of the mechanically constrained polymer network during the phase transition.

4:45 PM J2.8
Thermoresponsive Behavior of Poly(*N*-Isopropylacrylamide) Hydrogels Containing Gold Nanostructures. Nolan Flynn, Frances Y. Pong, Michelle Lee and Jessica R. Bell; Chemistry, Wellesley College, Wellesley, Massachusetts.

Poly (*N*-Isopropylacrylamide) hydrogels are thermosensitive polymer networks that undergo a volume phase transition during which the gel network contracts and expels its contents into its surroundings. We report the changes in the poly(NIPAm) structure and phase transition when gold nanostructures are synthesized *insitu* within the hydrogel matrix. Cross-linked poly(NIPAm) hydrogels were synthesized using *N*-isopropylacrylamide and 0.00 - 3.50% (wt./wt.) of *N*, *N*′-methylenebisacrylamide (MBAm) and/or *N*, *N*′-cystaminebisacrylamide (CBAm) as cross-linking agents. The hydrogels were then soaked in potassium tetrachloroaurate ($KAuCl_4$) to introduce gold ions followed by reduction in a sodium borohydride ($NaBH_4$) solution. Infrared spectroscopy, UV-Visible spectroscopy, and equilibrium swelling were used to examine the structural/physical differences between gels of different composition; mass measurements were used to observe the kinetics and thermodynamics of the hydrogel phase transition. These studies revealed marked differences in the physical characteristics and phase transition behavior of hydrogels. The property differences are attributed to combination of (1) gel composition and (2) the presence or absence of gold. IR spectra of gold-containing hydrogels with CBAm revealed a peak at 1040 cm^{-1} not present in gels that do not contain both gold and CBAm. UV-Vis spectra of gold-containing hydrogels indicated that the spectral properties are strongly dependent on the cross-linker identity and concentration. Equilibrium swelling measurements revealed that hydrogels with high CBAm content and low MBAm are significantly larger than those with low CBAm content. Phase transition studies revealed that the kinetics and thermodynamics of the hydrogel samples were dependent on the hydrogel composition when gold was present but independent of composition in native hydrogels. The synthesis of gold nanostructures within the poly(N-isopropylacrylamide) hydrogel matrix thus serves as a method to tune the optical and thermoresponsive properties of these nanocomposites. The ability to control properties has potential use in fields ranging from sensing to drug delivery.

SESSION J3: Poster Session: Biomimetic Polymers and Gels
Chairs: Ferenc Horkay, Noshir Langrana and Bernard Yurke
Monday Evening, November 28, 2005
8:00 PM
Exhibition Hall D (Hynes)

J3.1
Novel polymersome, PICsome, from a pair of oppositely charged block copolymers as nanocontainer of biomacromlecules. Aya Koide[1], Kensuke Osada[1], Yuichi Yamasaki[1] and Kazunori Kataoka[1,2]; [1]Graduate School of Engineering, The University of Tokyo, Tokyo, Japan; [2]Graduate School of Medicine, The University of Tokyo, Tokyo, Japan.

Recently, polymersomes formed through a self-assembly of block copolymers have been paid much attention because of an encapsulation of substances, a high structural stability and the variety of molecular design. However, a driving force of conventional polymersomes formed by amphiphilic block copolymers is hydrophobic interaction, therefore it is difficult to give some functional properties such as permeability of hydrophilic reagents and to control their formation and dissociation. Here we designed a novel type of polymersomes as ePICsomef formed by polyion complex (PIC) formation. It was clarified that the PICsome was prepared in an aqueous solution through the electrostatic attraction between a pair of the oppositely charged block copolymers. Generally, the block copolymers, poly(ethylene glycol)-b-poly(aspartic acid) (PEG-PAsp) as polyanion and poly(ethylene glycol)-b-poly(5-amino pentyl aspartamide) (PEG-PeDA) as polycation, tend to form polymeric micelles in aqueous solutions. However, we could obtain the polymersomes by controlling the chain length of the PEG and the charged segments as well as preparing the block copolymers having exactly the same chain length distribution in order to form PIC in lamellar structure, which is necessary to assemble the PICsome. Formation of the PICsome with micrometer-size was suggested by a dark-field microscopy. Additionally laser confocal scanning microscopy images revealed an encapsulation of FITC-labeled macromolecules (MW 4,2000) into the inner phase of the PICsomes. The membrane composed by polyion complex had permeability of low molecular weight substances. The PICsome can be drug delivery carriers as well as containers of biomacromolecules because bioactive compounds such as enzymes are easily encapsulated without using any organic solvents. Thus the PICsome has a great feasibility as a novel type of biomaterials.

J3.2
Novel Approach for Biofouling-Release Materials with Interpenetrating Polymer Networks. Kenji Mori, Masanobu Naito, Takashi Nakai, Michiya Fujiki and Takuma Kawabe; Graduate School of Materials Science, Nara Institution of Sciense and Technorogy, Ikoma, Nara, Japan.

Marine fouling organisms, such as barnacles and blue mussels, have caused serious economic losses by attaching themselves to the hulls of ships, and to pipes of power plants. A highly effective method for preventing this adhesion is a self-polishing type antifouling paint, in which organotin compounds, such as tributyltinoxide (TBTO) or cuprous oxide are hydrolyzed and elute into the seawater to kill the marine fouling organisms. Environmentally friendly organic-inorganic hybrid materials with repellent activity against marine fouling organisms have been developed using interpenetrating polymer networks (IPNs), composed of a three-dimensional silica matrix of tetraethoxysilane (TEOS) and chain-like polymers, such as poly(methylmethacrylate) (PMMA) and poly(vinylacetate) (PVAc). The repellent activities of the IPNs were evaluated by an easy bioassay with blue mussel, Mytilus edulis galloprovincialis, and an anti-diatom assay with Navicula Ulvacea. The repellent activity of the IPNs reached a maximum of approximately 90% relative to that of TBTO. This antifouling approach based on IPNs would be a breakthrough in the development of non-metal-elution antifouling paints in the 21st century. The potential for long-term usage of optimized IPNs is currently being explored in field tests. The presentation will also include the relationship between surface properties, such as porosity and roughness, and repellent activities.

J3.3
Towards Low Cost Disposable High Throughput Screening Devices. Gerardo Antonio Diaz-Quijada[1], Regis Peytavi[3], Andre Nantel[2], Emmanuel Roy[1], Dominic Gagne[3], Michel G. Bergeron[3] and Teodor Veres[1]; [1]Industrial Materials Institute, National Research Council of Canada, Boucherville, Quebec, Canada; [2]Biotechnology Research Institute, National Research Council of Canada, Montreal, Quebec, Canada; [3]Centre de recherche en infectiologie, Laval University, Sainte Foy, Quebec, Canada.

Microarrays have become one of the most convenient tools for high throughput screening and this has led to major advances in genomics and proteomics. Other important applications can be found in medical diagnostics, detection of biothreats, drug discovery, etc. Integration of microarrays with microfluidic devices can be highly advantageous in terms of portability, shorter analysis time and lower consumption of precious biological analytes. Traditionally microfluidic devices have been constructed from glass, however, glass micromachining is a rather expensive process. As a consequence, there is considerable interest in employing polymeric materials as a low cost alternative for mass production. We inspected a number of commercially available thermoplastics for this purpose and identified poly(methylmethacrylate) and a Zeonor polycyclic olefin as promising candidates, for which we developed methods for surface modification and covalent immobilization of oligoDNA. In addition, we present proof-of-concept plastic based microarrays with and without integration with microfluidics.

J3.4

Engineered titanium surfaces for specific interactions with integrin receptors through poly (L-lysine)-g-poly (ethylene glycol) adlayers functionalized with collagen derived mimetic peptide. Peter Worbs[1], Salvatore Chessari[1], Samuele Tosatti[1], Milvia Lepre[2] and Marcus Textor[1]; [1]Materials, Swiss Federal Institute of Technology, Zurich, Switzerland; [2]Synthes AG, Oberdorf, BL, Switzerland.

Engineering surfaces for specific integrin-ligand interaction and signaling cascades provides a biomolecular strategy for optimizing cellular responses in biomaterials applications. The integrin ?2?1 recognizes a specific amino acid binding sequence that is present on type I collagen. Integrin recognition is entirely dependent on the triple-helix conformation of the ligand similar to that of native collagen[1]. This study focuses on engineering ?2?1-specific bioadhesive surfaces by immobilizing a triple-helical collagen-mimetic peptide, incorporating the specific binding sequence, onto model nonadhesive substrates. Metal oxide surfaces can be made protein-resistant through spontaneous assembly of poly-(L-lysine)-g-poly-(ethylene glycol) (PLL-g-PEG) grafted co-polymers. This copolymer is used as a basis for developing special surfaces with controlled specific biological properties[2], e.g. through grafting the binding sequence of type I collagen to part of the PEG-chains to induce a direct interaction of the peptide ligands at controlled surface density with cell receptors. The polymer functionalized surfaces were characterized by Optical Waveguide Lightmode Spectroscopy (OWLS), Ellipsometry and X-ray photoelectron spectroscopy (XPS). The peptide-modified polymers were adsorbed on TiO2 and preliminary tests with cells were performed. In particular Rat Calvarian Osteoblast and Human Fibroblast were used as substrate: the presence of the collagen-like functionalized polymer seems to induce a preferred cellular adhesion of Osteoblast with respect fibroblast, as compared to the control peptide-functionalized polymer, after 1 day of incubation; nevertheless more detailed experiment have to designed and performed to validate such results. References 1. Reyes, C.D. and A.J. Garcia, Engineering integrin-specific surfaces with a triple-helical collagen-mimetic peptide. Journal of Biomedical Materials Research Part A, 2003. 65A(4): p. 511-523. 2. Tosatti, S., et al., Peptide functionalized poly(L-lysine)-g-poly(ethylene glycol) on titanium: resistance to protein adsorption in full heparinized human blood plasma. Biomaterials, 2003. 24(27): p. 4949-4958.

J3.5

Electrohydrodynamic Processing of Starch Films and Coatings. Rajesh Pareta and Mohan J. Edirisinghe; Materials, Queen Mary, University of London, London, United Kingdom.

Starch is a naturally occurring polysaccharide. Starch films and coatings have various bio-medical applications. Starch films are non-toxic and bio-degradable, with the mechanical properties similar to plastic films. Starch films and coatings are used for the preparation of tablets in oral drug delivery. Starch-based materials offer an attractive alternative as nasal administration drug carriers. Starch-based microspheres have been also used for protein drug delivery. Starch films and coatings are traditionally prepared by solvent casting and extrusion. As the mechanical properties of films/coatings depend on thickness, it is of immense significance if thickness can be controlled. In this work, maize starch was chosen as an example to demonstrate a novel method for the rapid preparation of starch films and coatings with nearly linear control over the thickness with electrospraying time. A starch solution cannot be electrosprayed primarily due to its high viscosity and its tendency to retrograde from the solution. Therefore, a modified starch solution was tailored for this purpose. 5% starch was gelatinized in de-ionized water (w/v), and subsequently ethanol and a water-based acrylic polymeric dispersant were added. To prepare a stable solution for electrohydrodynamic processing ultrasonic disruption was utilized. The electrohydrodynamic atomization behaviour of this solution was studied in detail to determine the solution atomization modes at various conditions. The solution was then electrosprayed in stable cone-jet mode at an optimized flow rate and applied voltage of 3μl/min and 7 kV, respectively. Films were collected on a rotating conductive ground plate at various electrospraying times. This method resulted in an even distribution of starch solution droplets and therefore uniform films with a diameter of $\sim$40 mm were produced. Film thickness and integrity were investigated by electron microscopy. Starch films with thicknesses between 8 μm and 40 μm were prepared successfully using this novel method. Starch films and coatings are mostly prepared by solution casting, which usually takes day(s). Our method using electrohydrodynamic atomization of starch solution provides instantaneous films/coatings, as the solvent gets evaporated during the process, with good thickness control. This process provides an opportunity for further research to prepare drug-loaded films and micro-spheres of starch and starch-based biomaterials.

J3.6

Microparticles of Alginate Calcium Gel Modified by Chitosan for Pulsative Delivery Of Rifampicine. Rinat M. Iskakov, Erkesh O. Batyrbekov, Karlygash K. Kombarova, Aliya Tleumukhambetova and Bulat Zhubanov; Institute of Chemical Sciences, Almaty, Kazakhstan.

The aim of this work is the development of controlled delivery system immobilized by antimicrobial drug rifampicine on the basis of microparticles of alginate calcium gel, modified by natural polymer chitosan. Modified microparticles were obtained by syringed dropwise a solution of rifampicine in solution of sodium alginate was into a mixed solution of chitosan in calcium chloride. The obtained modified alginate microparticles were contained immobilized rifampicine and a surface layer of chitosan. Effects of chithosan concentration and exposure duration on the thickness of polymer coating were determined. For the determination of surface thickness a red congo dye has been used able to form a complex with chitosan. It has been established that with an increase in the concentration of a polymer from 0,3 up to 1,5 mass % the thickness of the modified layer increases from 5 up to 60 microns, and an increase of the time of gel exposition in a 2,5% solution of chitosan from 30 min to 24 h results in an increase in thickness of a layer from 5 up to 20 microns respectively. When studying an influence of pH of the medium upon an interaction of alginate and chitosan it was been observed a formation of a polyelectrolyte complex between a chitosan polycation and an alginate polyanion stabilized by ionic bonds. The release of rifampicine from the modified alginate gel particles into a physiological solution with different thickness of a chitosan coating were studied. It was shown that the characteristic maximums on the curve of release observe after 10, 30, 90 and 120 min for the samples without the coating and with the coating thickness of 55, 100 and 150 microns respectively. The data obtained shown a possibility of the regulation of the rate of rifampicine relase from the modified alginate particles by way of alternation of thickness of the chitosan coating.

J3.7

Segmented Polyurethane/Collagen Blends for Biomedical Application. Rinat M. Iskakov[1], Erkesh Batyrbekov[1], Gulsharat Esenalina[2], Aman Kurashev[2], Maria Kim[1] and Bulat A. Zhubanov[1]; [1]Institute of Chemical Sciences, Almaty, Kazakhstan; [2]Medical State Academy, Karaganda, Kazakhstan.

In the present study the preparation of biomedical devices and some biomedical application of implantable devices based on segmented polyurethane (SPU)/collagen blends have been described. SPU with different content of hard and soft segments were synthesised by a two-step polymerization using a number of polyethylene and propylene glycols and tolylene diisocyanate. The successful biomedical application of SPU/collagen blends as biomaterials at some fields of medicine has been shown. These blends were used for the fabrication of artificial esophageal prostheses for treatment of injures and diseases of esophagus such as chemical burns, cicatrical structures, total stenosis in children when standard technique of surgical bypass of the nonfunctioning esophagus can not be used. The SPU/collagen blends containing anticancer agents were used for treatment of sarcoma of the orbit. It was established that the anticancer effect against Rhabdomiosarcoma of implanted blends prolongs 17-20 days and the toxic effects decrease due to reduce a total therapeutic dose from 2,0 mg/kg to 1,4 mg/kg. Microparticles of SPU with diameter 200-500 microns were prepared with water-toluene interface emulsion polycondensation of toluene-2,4-diisocyanate and poly(ethylene glycol) of various molecular weight 400-2000. The current procedure allows to develop a series of microcapsulated drug delivery forms for respiratory therapeutic use. A method of exterior nose correction using a biocompatible SPU/collagen blend has been developed. The successful application of polyurethane films for reconstruction of the bridge and septum of nose in 15 patients was described.

J3.8
Heparin-Mimetic Peptides for the Production of Noncovalently Assembled Hydrogels for Protein Delivery.
Sung Hye Kim and Kristi L. Kiick; Materials Science and Engineering, University of Delaware, Newark, Delaware.

Heparin and heparan sulfates have been known as important mediators for many physiological and pathological processes, such as inflammatory responses and tumor cell metastasis; their broad scope of action is due to the variation of functional group placement in these glycosaminoglycans. Recently, heparin has also been employed in the production of physically crosslinked hydrogel systems formed via the interactions between heparin and heparin binding proteins and peptides. However, heterogeneity in the structure of natural heparins can cause difficulties in controlling the assembly and properties of these hydrogels, or in producing biomaterials for growth factor delivery. These difficulties have motivated the development of homogeneous heparin mimics via the use of *O*-sulfated oligosaccharides or sulfated peptides. In this study, the feasibility of employing sulfated peptides as heparin substitutes for the production of a noncovalently assembled network was investigated. Solid phase peptide synthesis facilitates control of molecular structure and spacing of side-chains, which may have important consequences on designing sulfated peptides for the above materials investigations. *O*-sulfated tyrosine-containing peptides were synthesized via standard solid phase synthetic protocols and purified via ion-exchange chromatography. Interactions between different sulfated peptides and heparin-binding peptides and growth factors were measured via affinity column chromatography and surface plasmon resonance techniques. The importance of spacing between the sulfate groups was indicated via comparisons of the binding properties of a poly-sulfated peptide with those of peptides with a lower density of sulfation. The binding affinities of heparin-binding peptides/proteins for the sulfated peptides were compared to those measured for LMWH. The results show that certain sulfated peptides bind to the heparin-binding peptides and proteins with similar affinities as LMWH, suggesting the potential application of the sulfated peptides for assembly of noncovalently assembled hydrogels.

J3.9
pH-sensitive Inverse Opal Hydrogels for Gene Delivery.
Yuhua Hu[1], Patrick S. Doyle[1] and Darrell J. Irvine[1]; [1]ChemEng, MIT, Cambridge, Massachusetts; [2]Material Science, MIT, Cambridge, Massachusetts.

Gene therapy has the potential to treat a broad range of diseases and provide a basis for protective vaccines. Synthetic carriers for gene delivery are of great interest due to their potentially increased safety and manufacturability relative to viral vectors. However, to date synthetic gene delivery vectors have met with limited success, due to the low efficiency of intracellular DNA delivery. One of the significant challenges in DNA delivery is to achieve efficient escape of DNA from acidic endosomal intracellular compartments, where DNA and carriers localize on internalization by cells. DNA carrier materials that respond to changes in pH could be useful for selective DNA release from these compartments. We are thus investigating the use of pH-sensitive hydrogels with an inverse opal microstructure as a novel gene delivery system, which could protect DNA from nucleases and exhibit pH-triggered DNA release. Our initial studies have focused on the fabrication and characterization of bulk pH-responsive hydrogel structures with templated, ordered submicron porosity, as a first step in this line of investigation. Inverse opal hydrogels were synthesized by polymerizing poly(ethylene glycol) monomethacrylate and diethylaminoethyl methacrylate (DEAEMA) within the interstitial space of a colloidal crystal template (formed from 1 or 5 micron diameter polystyrene microspheres), followed by template dissolution using tetrahydrofuran. The resulting 3D periodic porous structures were characterized by bright field microscopy, laser scanning confocal microscopy, and scanning electronic microscopy. Ionization of the amino groups of the gels' DEAEMA repeat units at reduced pH resulted in reversible swelling of the inverse opal hydrogel, which was evaluated by measurement of the volumetric swelling ratio (Qv) and microscopic characterization of the gel structure (inverse opal pore size and inter-pore window size changes) as a function of pH and gel composition. Fluorescence videomicroscopy tracking of nanoparticle diffusion through the templated porous gel structure indicated that the highly interconnected pore morphology of the templated gel structures provides pathways for constrained diffusion of large macromolecules (e.g., DNA) and nanoparticles. Particle transport through the ordered porous structure was rapid at pHs' where the gel was swollen and significantly reduced at pHs' where the gel de-swelled, due to direct changes in the pore morphology as a function of pH. The ability to create ordered porous scaffolds or hydrogel particles capable of controlled DNA molecules release rates may provide a means to enhance and regulate gene delivery, and in turn increase the utility of gene therapy.

J3.10
Electrochemical detection of bilirubin from a synthetic molecularly imprinted polymer thin film fabricated electrode chip.
Mei-Jywan Syu and Shih-Chieh Chang; Department of Chemical Engineering, National Cheng Kung University, Tainan, Taiwan.

A synthetic polymer membrane prepared from the molecular imprinting technique was applied to fabricate a sensing chip specifically for the detection of bilirubin. The polymer matrix was synthesized by imprinting bilirubin molecules as the templates into the poly(methacrylic acid-co-ethyl glycol dimethacrylate) (poly(MAA-co-EGDMA)) film. The imprinted polymer film was coated on the Au-electrode chip with a surface area of 1.0 x 1.0 or 0.5 x 0.5 cm^2. Before the imprinted polymer film was coated onto the eletrode, ally mercaptan was applied to pre-treat the Au surface so that the polymer film could be adhered on the Au layer firmly for a long period of operation. The surface condition as well as the film thickness was observed from SEM. A uniform film thickness of estimated to be 160 nm was inspected from the photo. Cyclic voltammetry (CV) profiles from bilirubin solution and background solution with the molecularly imprinted polymer (MIP) film coated electrode chip were compared. With a proper voltage determined by the CV, the detected currents of the MIP fabricated chip were investigated. The bilirubin solutions of different concentrations were applied as the working solutions for the electrochemical detection from the MIP chip. Excellent linear calibration result was obtained from the prepared MIP chip. The response currents of bilirubin from the bare Au-electrode, the MIP chip and the non-imprinted polymer (NIP) were compared. Significant current effect was comparably achieved from the MIP sensing chip. The bilirubin concentrations of less than 15 mg/dL corresponded to the response currents within the range of 10 μA. In addition, the pH of the bilirubin in different concentrations was also measured and the results indicated that there was only slight variation was observed. It is obvious that the solvent used to dissolve bilirubin did not cause significant current signals from a bare Au electrode, an MIP electrode and an NIP electrode. The sensitivity of bilirubin detected from the MIP fabricated chip was twice of the bare chip. The current change of bilirubin from the NIP chip was rather small. In conclusion, the MIP sensing chip for the detection of bilirubin within the range of approximately 15 mg/dL was successfully prepared. (The grant supported from ROC Ministry of Education Ex-91-E-FA09-5-4 on this work is appreciated.)

J3.11
Biocatalytic Activity of Polyethylene Imine Hydrogel Complexes with Transition Metal Ions.
Gulnara Amantaevna Bektenova, Nurzhan S. Chinibaeva and Essen Abikenovich Bekturov; Institute of Chemical Sciences, Almaty, Kazakhstan.

Nowadays researchers have paid much of their increasing attention to biomimetic problems. The studying object of biomimetic is considered to be the system which is imitating all the animate nature process, including various functions, such as biocathalytic ones. Special attention is given to the enzyme-like systems creation which is working according to the principles of metal-containing enzymes, including those ones which have almost the same characteristics on their activity and action selectivity. Therefore till now the researchers have been interested in studying processes of the model systems which are simulating catalase enzyme action and catalyzing the reaction of hydrogen peroxide decomposition. High-swelling polymer hydrogels are rather perspective in catalysis, since on the basis of such hydrogels it is possible to get the transition metal complexes with various structure and composition; more over the hydrogel ability to swelling process causes its high permeability for reagents, and a polymer net mobility can provide the realization process of the catalyst direction on a substrate. Polyethylene imine hydrohel complexes with various salts of bivalent and trivalent ferric iron have been received, and their biocatalytic properties in the reaction of hydrogen peroxide decomposition have been investigated. The given systems activity was determined by the permanganatometric method. Catalase activity of complexes depends on the salts nature, however, as a whole, the relative catalase activity of these complexes is rather low. The major interest is represented with threefold complexes, therefore we have received insoluble complexes of various composition: low-cross-linked polyethylene imine hydrogel - copper (II) nitrate - natrium dodecylbenzylsulfate. The role of the last one in acceleration of hydrogen peroxide decomposition reaction is that electrostatic interaction of polyethylene imine hydrogel - copper (II) complex with detergent leads to the macromolecules compactization process and to the active centers local concentration increasing in a macromolecular coil. Probably, the combination of groups with the enzymatic action and hydrophobic areas is one of the necessary conditions for the effective catalysts creation. It was shown that under the constant concentration of a substratum the increasing catalyst content leads to the increasing peroxide hydrogen decomposition degree. It is connected with the increasing of active centers in the reaction

mixture. Under the catalyst constant weight the reduction of substrate concentration is followed by the reduction of a substrate decomposition degree. The solution pH has less influence on the hydrogen peroxide decomposition at the beginning of the process.

J3.12
Microstructures of Cross-linked Polymeric Systems Replicated into Silica Matrix. Emiko Otsuka, Takanori Nakamura, Youhei Seto, Ken-ichi Kurumada and Atsushi Suzuki; Environment and Information Sciences, Yokohama National University, Yokohama, Kanagawa, Japan.

The network structures of polymer gels have been extensively studied by means of laser light scattering technique, confocal microscopy, and small angle x-ray or neutron scattering. Since the network of a polymer gels is continuously connected to form dilute three-dimensional solid in a liquid with a complicated structure, the nanoscopic structure has not been directly observed so far. In order to investigate the network structure in nanoscopic level,we replicated polymer gels into a silica matrix. For a template gel, we first used a cross-linked polymeric system of N-isopropylacrylamide (NIPA) and N,N?f-methylene-bisacrylamide (BIS). The transparent bulk silica was obtained by annealing the dried silica in the NIPA polymeric system at 873K for 5 hours to remove NIPA polymer. The pore size and its distribution were obtained by the nitrogen adsorption/ desorption measurements, and the max pore size and width of the distribution was found to increase with increasing the nominal amount of NIPA. The microstructure of the cleaved silica was also observed by TEM. The TEM micrograph indicated that there were thin channel-like pores ranging from 4 to 20 nm that connected each other and formed a structure something like a three-dimensional network. The size of the network structure depended not only on the nominal concentration amount of NIPA, but also on the dehydration conditions. These results indicated that the pore size and its distribution corresponded well to the microstructure of the NIPA polymeric system. In this paper, the effects of the nominal concentration amounts of NIPA and BIS on the pore size and its distribution of the silica, and the TEM micrograph will be presented. In addition, this technique was applied to the other polymeric systems crosslinked by BIS, such as N, N-diethylacrylamide, and acryloylmorpholine. The microstructure of the present polymeric systems will be discussed in terms of the phase separation of polymers depending on the polymerization parameters (temperature and dehydration condition) and of the density of polymers and/or cross-linker.

J3.13
Self Assembly of β-Hairpin Peptides into Rigid Hydrogels: Effects of Peptide Hydrophobicity. Tuna Yucel[1,2], Chris Michael Micklitsch[3], Joel P. Schneider[3] and Darrin J. Pochan[1,2]; [1]Materials Science and Engineering, University of Delaware, Newark, Delaware; [2]Delaware Biotechnology Institute, University of Delaware, Newark, Delaware; [3]Chemistry and Biochemistry, University of Delaware, Newark, Delaware.

Monomeric peptides have been designed to undergo reversible intramolecular folding with external stimuli such as pH, temperature, and salt concentration to form β-hairpins that consequently self assemble into a hydrogel network consisting of well-defined nanofibrils on the nanoscale rich in β-sheet. In the initial peptide design for Max 1, β-hairpins were composed of a central tetra-peptide turn sequence (V^DPPT) flanked by two extended strands containing alternating hydrophilic lysine (K) and hydrophobic valine (V) residues. The hydrophobicity of Max 1 has been altered through replacing all or part of the valine residues in the arms (see Table). Circular dichroism spectroscopy (CD) illustrated that the random-coil to β-sheet transition could be tuned from 65^oC (Max 3) to below 5^oC (Max 32 and Max 33) under basic conditions. Transmission electron microscopy (TEM) confirmed that the peptides self-assembled into a fibrilar network. Single fibril dimensions varied between 2 and 3 nm as measured using TEM and small-angle neutron scattering (SANS). These dimensions are consistent with folded β-hairpin that have undergone intermolecular self-assembly mechanism into nanofibrils. A direct correlation between fibril rigidity and consequent changes in the nature of junction points as observed by TEM, and the final gel rigidity as measured via small-deformation oscillatory rheology, was observed. Max 31 peptides assembled into rigid fibrils, which in turn, assembled hierarchically in the lateral direction to form laminates. Atomic force microscopy revealed that the laminates were c.a. 2-3 nm high, confirming the folded nature of the assembled β-hairpins. Max 32 fibrils were more flexible, forming intra-fibrilar loops and less rigid networks. At a temperature above their β-sheet transition, hydrogels of the latter were c.a. 5 times less rigid than the former. Overall, the extent of control over the gel supramolecular properties through tailoring the intramolecular folding and self-assembly kinetics as dictated by peptide design was demonstrated.

J3.14
Characterization of hierarchical components of squid reflective tissues. Wendy J. Crookes-Goodson[1], Ryan M. Kramer[2] and Rajesh R. Naik[2]; [1]Medical Microbiology and Immunology, University of Wisconsin, Madison, Wisconsin; [2]Materials and Manufacturing Directorate, MLPJ Biotechnology Group, Air Force Research Laboratory, WPAFB, Ohio.

Naturally-occurring reflective tissues such as those in aquatic animals are a source of inspiration for the design of nanostructured biomimetic optical devices. Reflective tissues of the squid *Euprymnascolopes* are composed of a hierarchical series of materials, each of which probably contributes to the optical activity of the overall tissue. We have used elemental analysis, NMR, circular dichroism, x-ray diffraction, and other spectroscopic techniques to characterize the biochemical and biophysical attributes of each component of this hierarchy. Highest in the hierarchy are flat platelets, thousands of which are stacked in the reflective tissue. Elemental analysis of the platelets showed that inorganics were associated with the platelets; these inorganics may contribute to the optical properties of the platelets. Next in the hierarchy is a very unusual protein family, called the reflectins, that composes each platelet. Reflectins are highly insoluble and have a skewed amino acid composition dominated by six amino acids. Full-length reflectin is composed of five repeating peptide domains, the last components of the hierarchy. The characteristics of a single synthetic reflectin repeat peptide (RRP) were assessed. Unlike native and recombinant full-length reflectins, RRP was soluble under aqueous conditions. RRP formed 3(10)-helices and alpha-helices depending upon the conditions of solubilization. The potential contributions of the biochemical characteristics of each structure in the hierarchy to the overall optical properties of the reflective tissue will be discussed.

J3.15
Size Tunable Vesicles via Self-Assembly of Uncharged Amphiphilic Block Copolypeptides. Jarrod Hanson[1], Kelly Hales[2], Darrin Pochan[2] and Timothy Deming[1]; [1]Bioengineering, UCLA, Los Angeles, California; [2]Materials Science, University of Delaware, Newark, Delaware.

Vesicles created by the self-assembly of amphiphilic block copolymers has become an increasingly important field in polymer materials. Vesicles serve to encapsulate potent drug molecules and deliver them to the desired target with minimal harm to the patient. Polymeric vesicles have garnered interest due to their added stability over lipid vesicles (liposomes), allowing increased drug loading and circulation times *invivo*. Being able to control polymer architecture and composition, much like nature does with many proteins, can give added control over the self-assembly of the polymeric materials. Proteins are able to perform very specific functions based upon their folded or self-assembled structure. To mimic some of the features of proteins, amphiphilic block copolypeptides were synthesized using the transition metal mediated polymerization of α-amino acid-*N*-carboxyanhydrides developed in our lab. These copolypeptides were found to self-assemble into vesicles with a range of diameters (50 – 500 nm). The key components for structure formation were the ethylene glycol modified lysine residues that make up the hydrophilic portion of the copolymer. The poly(ethylene glycol-modified lysine) chains, K^p, are nonionic and have stable α-helical secondary structures. Amphiphilic copolymers ${K^p}_x(rac\text{-leucine})_y$ were prepared by growth of a hydrophobic segment of racemic oligoleucine onto the K^p chains. Light scattering data as well as electron microscopy images showed that these copolymers self assembled in water to form vesicles with diameters that vary with chain length and composition. Vesicle diameter was found to scale roughly with the length of the hydrophilic domain. Modifications to the chain conformation of either domain were also found to cause significant alteration to the resulting assemblies. To illustrate the ability of our copolymer vesicles to encapsulate molecules, texas-red labeled dextran was encapsulated within the vesicles and retention ability was shown to correlate with vesicle size.

J3.16
Biomimetic Electrospun Nanofiber Conduit for Vascular Grafts. Sang Jin Lee[1], Joel Stitzel[2], Grace Lim[1], James J. Yoo[1] and Anthony Atala[1]; [1]Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Winston-Salem, North Carolina; [2]Department of Biomedical Engineering, Wake Forest University School of Medicine, Winston-Salem, North Carolina.

Cardiovascular disease, including coronary artery and peripheral vascular disease, is the leading cause of mortality in the United States. More than 1.4 million surgical arterial bypass procedures for coronary and peripheral atherosclerotic diseases are performed each year. Biological and synthetic vascular grafts have been widely used as a blood vessel substitute for cardiovascular bypass procedures. However, these grafts have shown several limitations such as donor site morbidity, immunogenic response and thrombosis.

Electrospinning technology offers a new potential for controlling composition, geometry and mechanical properties of electrospun nanofiber scaffolds. We investigated the feasibility of electrospinning to create vascular grafts biomechanically similar to native vessels and tested their biocompatibility and morphological features in vitro. In this study, we fabricated biomimetic vascular grafts using electrospinning method with polymer blends of collagen type I, elastin and various types of synthetic biodegradable polymers such as poly(D,L-lactide-co-glycolide) (PLGA), poly(L-lactide) (PLA), poly(ϵ-caprolactone) (PCL) and poly(D,L-lactide-co-ϵ-caprolactone) (PLCL). Collagen type I, elastin and synthetic polymer are mixed at a relative concentration by weight of 45% collagen, 40% polymer, and 15% elastin to mimic the native blood vessel. The solutes are dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol (HFP) in the concentration range from 5% to 20% (wt/vol). The resulting biomimetic nanofiber conduit scaffold possessed nano-scale and randomly oriented fibers. The fiber diameters of the electrospun scaffold increased with increasing solution concentration. The optimal concentration of the collagen/elastin/polymer blend solution was 10% (wt/vol). The average fiber diameters of the electrospun nanofiber conduits ranged from 477.35 ± 43.49 to 765.85 ± 175.42 nm. The biomechanical properties of resulting conduit were different depending on the compositions of blended polymers. The tensile strength of the electrospun nanofiber scaffolds increased in order of collagen/elastin/PLLA, collagen/elastin/PLCL, collagen/elastin/PLGA, collagen/elastin/PCL, and collagen/elastin alone. Addition of synthetic polymers to the collagen/elastin blend could improve and control the mechanical properties of the vascular grafts. Biocompatibility of the biomimetic nanofiber scaffolds was confirmed by cell viability and mitochondrial metabolic activity. There was no evidence of toxic effects of the biomimetic electrospun nanofiber conduits. In vitro studies revealed that the electrospun nanofiber scaffolds support adhesion and migration of sheep smooth muscle cells. These findings suggest that the nanofiber conduit scaffolds fabricated by electrospinning technology rendered a promising biomimetic material for vascular tissue engineering.

J3.17
Aqueous Synthesis and Properties of Interpenetrating (IPN) Nanogels. Xihua Lu[1] and Rishen Yao[2]; [1]Northwestern University, Evanston, Illinois; [2]Hefei University of Technology, Hefei, China.

Nanogels with diameters in the range of tens to hundreds of nanometers have attracted significant interest in the recent years. Relative to bulk hydrogels and due to their very small size, nanogels can show much faster response to microenvironmental stimuli such as temperature and pH. Smart nanogels have found important applications in the interface of nanotechnology and biotechnology, including controlled drug release, biomedical diagnostics, biosensor, and genetic and protein analyses. In this study, a new class of interpenetrating (IPN) monodisperse nanogels has been synthesized. This IPN nanogel consists of poly(N-isopropylacrylamide-co-2-hydroxyethylacrylate) (poly(NIPA/HEA))/poly(acrylic acid) (PAA). Poly(NIPA/HEA) was first synthesized at 650C using emulsion precipitation polymerization. After completion of polymerization, the polymerization system was cooled down to temperature well below the LCST of poly(NIPA/HEA) and then acrylic acid was added into poly(NIPA/HEA) dispersions. Under nitrogen protection, initiator ammonium persulfate was added to start polymerization and form IPN poly(NIPA/HEA)/PAA nanogels. Dynamic light scattering analysis showed that the size distribution of IPN nanogels is very narrow, less than 0.05. The phase transition behaviors of the nanogels were characterization by DLS and UV-vis spectrophotometer as a function of temperature and pH. The results showed that the LCST of the nanogels shifted to a lower temperature with a decrease of pH and that the volume of the ionized nanogels at pH=7.4 around the LCST exhibited a small change with an increasing composition of PAA in the IPN nanogels. Viscosity measurement demonstrated that the ionized IPN nanogels were thermo-gelling above the LCST. The thermo-gelling behavior may result from the inter-nanogel hydrophobic association of the pending poly(NIPA/HEA) polymer chains around the surface of the IPN nanogels and strong water absorbability of anionic COO- of PAA. IPN nanogels will find application in drug delivery system and nano-reactor for the synthesis of functional inorganic nanoparticles Furthermore, the IPN nanogels self-assembled into tunable colloidal crystals, correlating with a pH value. IPN nanogel colloidal crystals could be stabilized by physical thermo-gelation and chemical cross-links.

J3.18
Compositionally Modified Hydroxyapatite Nanocrystals for Polymer/Ceramic Scaffold Applications. Andrei Stanishevsky, Peserai Chinoda, Aaron Catledge, Vinoy Thomas and Derrick Dean; University of Alabama at Birmingham, Birmingham, Alabama.

Hydroxyapatite (HA) is the most commonly used bioceramic material due to its similarity to the major mineral component of the hard tissue. The biological behavior of HA is, among other factors, strongly affected by its crystallinity, presence of impurities, and surface morphology. It has been shown that a nanoscale grain size of synthetic HA and the presence of CO^{3-} and Mg^{2+} ions show further stimulatory effects on bone growth. We synthesized carbonated and Mg-modified HA nanocrystals with various concentrations of CO^{3-} and Mg^{2+} ions by chemical precipitation in the range of the process temperatures from 25 ^{o}C to 100 ^{o}C. The as-synthesized HA nanopowders were washed and redispersed in water, methanol, and hexafluoropropanol (HFP) for further use. The samples were characterized using FT-IR spectroscopy and X-ray diffraction. The size of HA nanocrystals is strongly affected by the process temperature. It increases from 10 to 80 nm with the temperature changing from 25 to 100 ^{o}C. The presence of Mg at concentrations up to 10 % in a room temperature process leads to smaller size of HA crystallites. There were no other crystalline phases detected in all samples within the range of tested compositions and used process parameters. The HA nanocrystals in HPF were mixed with collagen solution in HPF to fabricate nanofiber collagen/HA three-dimensional constructs by electrospinning with the HA loading up to 30 % by weight. Water based HA nanocrystal suspension was used for the loading prefabricated collagen nanofiber constructs. Mechanical properties of both types of constructs were investigated using nanoindentation technique. The effect of the constructs exposure to simulated body fluids on the collagen/HA ratio and the mechanical properties was studied.

J3.19
The fabrication of hydrogel as a microvalve in microfluidic system. Chehung Wei and Ray-hung Chen; Mechanical Engineering, Tatung University, Taipei, Taiwan.

The small volume of sample and fast response time are the primary features of micro fluidics system. It is essential for expensive sample. Microvalve is a key component in an integrated microfluidic system to regulate the flow movement. The working principle of conventional microvalves relies on its mechanical or electromagnetic properties. These valves are not biocompatible and are not suitable in bioassays. Stimuli-response hydrogels whose properties of efficient mode of energy conversion (chemical to mechanical), excellent biocompatibility and the combination of multiple function (sensing and actuation) have become the leading candidate as engineered microscale components. In this paper, we study the feasibility of thermo-sensitive hydrogel as a valve on the microchip. A metal resistor or peltier was used as the temperature regulator. The results show that the quality of the hydrogel miniaturization depends on many factors like the deposition surface (glass chip vs. PDMS chip), the volume of the hydrogel (the size of the valve) and the vacuum condition (the evaporation rate) and the content of the oxygen. The response time of the hydrogel valve strongly depends on the size of the hydrogel which varies from days to hours. It is shown that the hydrogel can be implemented as microvalve in microfluidic system.

J3.20
Injectable hydrogel blend for regeneration of infarcted myocardium. Yoon Yeo[3], Jason Burdick[4], Wenliang Geng[3] and Milica Radisic[2,1]; [1]IBBME, University of Toronto, Toronto, Ontario, Canada; [2]Department of Chemical Engineering and Applied Chemistry, University of Toronto, Toronto, Ontario, Canada; [3]Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts; [4]Department of Bioengineering, Univeristy of Pennsylvania, Philadelphia, Pennsylvania.

Conventional treatment options for myocardial infarction (MI) are limited by the inability of mature myocardium to regenerate after injury. Although functional improvements after injection of various cell types have been demonstrated, the clinical utility of this procedure has been hampered by poor cell localization, low survival rate, high diffusibility of injected angiogenic factors and the absence of local structure suitable for injection. We propose a novel therapeutic approach for the treatment of MI through the use of an injectable photocrosslinkable hydrogel (a blend of chitosan and Acryloyl-poly(ethylene glycol)-RGDS (Acr-PEG-RGD)) for delivery of cells and angiogenic factors thus enabling an independent control over protein release (via chitosan) and cell attachment (via RGD). Chitosan was modified with photoreactive azidobenzoic acid to make an in situ photocrosslinkable hydrogel. Acr-PEG-RGD was synthesized by reacting Tyr-Arg-Gly-Asp-Ser (YRGDS, 1 mg/ml) with an equimolar amount of acryloyl-PEG-N-hydroxysuccinimide (3400 Da). For injection and encapsulation each polymer was dissolved in Di-H2O and pH was adjusted to 6.4 Our preliminary studies showed that C2C12 myoblasts proliferated and differentiated on the surfaces of the hydrogel blend with 5mM Acr-PEG-RGD, but not on the chitosan alone (20mg/ml). In vitro, photoencapsulation prevented rapid diffusion of VEGF, as evidenced by the 84% retention

of loaded VEGF(165) for 24 days. Ex vivo, we were able to localize the hydrogel on the surface of an adult rat heart or in the ventricle wall by brief (2min) UV light crosslinking at cytocompatible intensity (4mW/cm2). Live/dead staining of neonatal rat heart cardiomyocytes encapsulated into the chitosan/Acr-PEG-RGD hydrogel indicated that most of the cells survived the UV cross-linking for 3min when cast into tissue culture plates. In the future studies, the envisioned strategy for MI regeneration will be tested vivo in a rat model.

SESSION J4: Drug and Gene Delivery
Chairs: Eric Amis and Kristi Anseth
Tuesday Morning, November 29, 2005
Room 201 (Hynes)

8:30 AM *J4.1

Exploding Microcapsules. Bruno Gerard De Geest[1], Stefaan De Smedt[1], Christophe Dejugnat[2], Gleb Sukhorukov[2] and Joseph Demeester[1]; [1]Ghent University, Ghent, Belgium; [2]Max Planck Institute for Colloids and Surface, Potsdam, Germany.

Due to recent advances in biotechnology, an increased amount of macromolecular drugs such as proteins, oligonucleotides, etc. becomes available. Compared to traditional sustained release where the therapeutics are delivered at a more or less constant rate, it could be advantageous to have a pulsed release pattern. Especially in those cases where a biological tolerance is developed when the drugs are present in the body at a constant level, a pulsatile release pattern would be beneficial. Here we report on the synthesis of 10 mμ sized polyelectrolyte capsules made by coating biodegradable dextran-hydroxyethyl methacrylate (dex-HEMA) microgels with biopolymers using the layer-by-layer technique. Briefly, the layer-by-layer technique is based on the sequential adsorption of oppositely charged species onto a charged substrate. This technique, only recently introduced, has shown great potential in the fabrication of thin films and hollow capsules due to its easiness and multifunctionality of the compounds which can be incorporated into the multilayers. Upon degradation of the dex-HEMA microgels the swelling pressure increases and at the end of the degradation process finally ruptures the polyelectrolyte coating, leading to the release of encapsulated species. We also show that depending on the choice of polyelectrolytes exploding capsules or intact hollow capsules can be obtained.

9:00 AM J4.2

Flexible worm micelles as drug nano-carriers for controlled release. Younghoon Kim, Paul Dalhaimer, David Christian and Dennis Discher; Department of Chemical & Biomolecular Engineering, University of Pennsylvania, Philadelphia, Pennsylvania.

Flexible nano-sturucures such as polymeric worm micelles offer a new and promising method for the delivery of therapeutics. Worm micelles prepared as blends of degradable polylactic acid (PLA) and inert block copolymer are shown provide a controlled release of their hydrophobic encapsulant. Degradation of PLA by hydrolysis leads to the self-shortening of worms and a clear transition toward spherical micelles, correlating with the release of hydrophobic dyes. The typical loading and release profile of a hydrophobic dye from degrading worm micelles show that the release time can be tuned by the blend ratio of degradable to inert copolymer. Also presented here is the study of the transport of worm micelles through tortuous, nanoscale environments, which reveals that worm micelles are able to penetrate this environment where 100nm sized vesicles could not. These studies were done with the hope of creating a vehicle capable of delivering agents to tissue with nanoscale porosity.

9:15 AM J4.3

Microstructure, Mechanical Properties and Drug Release Behavior of Solutions and Hydrogels of Poly (lactide)-Poly (ethylene oxide)-Poly (lactide) Triblock Copolymers. Sarvesh Kumar Agrawal[1], Naomi Sanabria-DeLong[2], Gregory N. Tew[2] and Surita R. Bhatia[1]; [1]Chemical Engineering, University of Massachusetts, Amherst, Amherst, Massachusetts; [2]Polymer Science and Engineering, University of Massachusetts, Amherst, Massachusetts.

Biodegradable and biocompatible polymers made from poly(lactide)-poly(ethylene glycol)-poly(lactide) have attracted attention recently because of their property to form hydrogels, which has potential applications in drug delivery and tissue engineering. We have performed for the first time a complete structural characterization of PLA-PEO-PLA in the solution and hydrogel states. Previous studies on hydrogels of these polymers have shown that these gels have excellent mechanical properties suitable for possible application in tissue engineering and drug delivery. To obtain further insight into the structure-property relationships for these materials, we have performed small angle neutron scattering (SANS) to understand the self-assembly of these polymers in aqueous solution with change in the block length and stereospecificity of the PLA block. A significant difference in structure and association behavior was seen between the polymers made from amorphous D/L-lactide as compared to those with crystalline L lactide blocks. In the former case spherical micelles were seen to form whereas the latter forms nonspherical polydisperse micellar assemblies. Despite the difference both polymers were seen to form an associative network structure leading to gelation at high concentration. The size of structural moieties formed was also comparable and was about 7-14 nm in both cases. The PLA block length was also seen to directly influence the sizes and association number of the nanodomains forming the hydrogels. This difference in microstructure has important implications for use of these polymers in biomedical applications. We also performed ultra small angle x-ray scattering (USAXS) and confocal microscopy on these polymer gels to look at their structure from nanometer to micron length scales. Polymers made from both D/L lactide and L-lactide blocks show the presence of large-scale fractal aggregates in the hydrogels with water channels running between them. Also, the fractal structure was denser for the D/L lactide series polymers as compared to the L-lactide series polymers. These results show that we can tune the microstructure and thereby the mechanical strength of these gels depending upon the specific application we need it for. The value of elastic moduli of these gels is in the same range as several soft tissues, making these materials excellent candidates for a variety of tissue engineering applications. We also show profiles for release of common drugs (e.g. sulindac, tetracaine) from 5 weight% solutions of these polymers in phosphate buffer solution. The profiles follow an almost zero order release behavior that continues slowly and steadily over several days and is found to be strongly dependent on the crystallinity and chemistry of the PLA block. Thus, by modification of two simple parameters, we can engineer the required release rate of drugs from these materials.

10:00 AM *J4.4

Shape-memory Effects in Polymer Networks for Medical Application. Andreas Lendlein, [1]Institute for Technology and Development of Medical Devices, D-52074 Aachen, Germany; [2]GKSS Research Center, Institute of Chemistry, D-14513 Teltow, Germany.

Shape-memory polymers have the capability of changing their shape upon exposure to an external stimulus [1]. The shape-memory effect is a functionality resulting from a combination of the polymer's chemical structure and programming/processing technology. Such polymers possess a high innovation potential in minimally invasive surgery, e.g. stents or smart sutures. Their shape-memory capability enables bulky implants to be placed in the body through small incisions or to perform complex mechanical deformations automatically. This paper describes thermally-induced as well as light-induced shape-memory polymers. Thermo-responsive polymer networks were prepared from poly(ϵ-caprolactone)dimethacrylates by photo-crosslinking. The switching temperatures T_{trans} of these materials can be adjusted between 30 °C to 50 °C by the molecular weight of the macrodimethacrylates used as educts in synthesis and by controlling the crystallization process. It was possible to alter the mechanical properties of the polymer networks in a wide range, e.g. elongation at break ϵ_R at room temperature between 18% to 210%. In cyclic, thermomechanical tensile tests the photoset materials showed excellent shape-memory properties with values for strain recovery between 92% and 97% and average values for strain fixity between 86% and 97% after five cycles. [2] By introduction of the comonomer n-butylacrylate, a polymer system with an AB-polymer network structure has been obtained. The weight content of comonomer is the molecular parameter allowing adjustments of the mechanical properties in the temporary shape. [3] In contrast to these semi-crystalline photosets, a series of copolyester-urethane networks were amorphous and biodegradable. The cooligoester segments consisted of oligo[(*rac*-lactide)-*co*-glycolide]. The crosslink points were introduced by ring-opening polymerization with hydroxyfunctional initiators resulting in trifunctional or tetrafunctional netpoints. [4] Light-induced shape-memory polymers are photo-responsive polymer systems the shape of which can be switched by application of ultraviolet light having specific wavelengths. Polymers containing photo-reactive groups, e.g. cinnamic acid (CA), can be deformed and fixed in predetermined shapes such as elongated films or arches by ultraviolet light illumination. These new shapes are stable for long time periods, even when heated to 50 °C, and they can recover their original shape at ambient temperatures when exposed to ultraviolet light of a different wavelength.[5] [1]A. Lendlein, S. Kelch, Angew. Chem. 2002, 114, 2138-2162. [2]A. Lendlein, Michael Schroeter, Annette M. Schmidt, Robert Langer J. Polym. Sci. A: Polym. Chem. 2005, 43, 1369-1381. [3]A. Lendlein, A. M. Schmidt, R. Langer, Proc. Natl. Acad. Sci. U. S. A. 2001, 98(3), 842-847. [4]A. Alteheld, Y. Feng, S. Kelch, A. Lendlein, Angew. Chem. Int. Ed. 2005, 44, 1188-1192. [5]A. Lendlein, H. Jiang, O. Juenger, R. Langer, Nature 2005, 434, 879-882.

10:30 AM J4.5
Molecular Imprinting of Peptides for Therapeutic Delivery Systems. Elizabeth Hunter Lauten[1] and Nicholas A. Peppas[1,2,3]; [1]Biomedical Engineering, University of Texas at Austin, Austin, Texas; [2]Chemical Engineering, University of Texas at Austin, Austin, Texas; [3]Pharmaceutics, University of Texas at Austin, Austin, Texas.

Angiotensin II is an octapeptide hormone which is critical in vasomotor function and, when present in increased levels, has been implicated in the development of atrial fibrosis. Ultimately it would be beneficial to be able to reduce the levels of this and other overexpressed peptides and proteins. We have therefore designed a new recognitive polymeric system that would allow for such reduction of circulating peptides in the blood. The new synthetic recognitive biomaterials have been designed to mimic biological recognition. We have used configurational biomimesis which produces polymeric surfaces or polymeric recognitive networks that have three dimensional, stereospecific binding cavities based on a given template molecule. We are now attempting to impart the therapeutic effect of peptide destruction by incorporating biodegradable components which can be hydrolytically cleaved at ester bonds. Upon degradation, an acidic microenvironment is created. It is this environment which has catastrophic effects on peptides such as angiotensin II. Imprinted polymer networks were prepared by fast, UV-initiated, free radical polymerization reactions of acrylamide as the functional monomer, poly(ethylene glycol) dimethacrylate as the crosslinking agent, and angiotensin II as the template molecule. In order to examine the efficiency of the imprinting process, recognitive/binding studies were conducted and then analyzed by HPLC. The imprinted polymers had a 20% higher selectivity for angiotensin II than for the peptide derivatives. In order to optimize the repeated recognition (rebinding) of angiotensin II, the molar ratio of template to functional monomer was varied. The various ratios experimented with were 1:8, 1:16 and 1:32. The cross-linking ratio was also varied from 10% to 80%. To determine the integrity of the three dimensional binding cavities, dynamic swelling studies were performed with polymer disks under physiological conditions of 37°C and pH of 7. Ultimately the networks were then analyzed by scanning and transmission electron microscopy. We are now investigating the acidic degradation effects on the polymer structure and the peptide using FTIR and mass spectroscopy.

10:45 AM J4.6
Photopolymerized Multilaminate Composite Hydrogels for Tailored Drug Delivery. Andrew Watkins[1], Stephanie Southard[1] and Kristi Anseth[1,2]; [1]Chemical and Biological Engineering, University of Colorado, Boulder, Colorado; [2]Howard Hughes Medical Institute, Boulder, Colorado.

Multilaminate hydrogel composites composed of poly(ethylene glycol) 550 dimethacrylate and 2-hydroxyethyl methacrylate were photopolymerized to create drug delivery vehicles with highly controllable release profiles. The spatial and temporal control of the photopolymerization allows facile synthesis of composites with spatially varying properties and/or loading. By varying the initial loading and diffusional properties in each layer, the magnitude and rate of the initial dosing, or burst effect, could be readily tuned or even eliminated. Additionally, this technique was utilized to construct devices with quasi-steady state release rates. In this work, low molecular weight fluorescent probes (e.g., Oregon Green 488 and Texas Red sulfonyl chloride) were encapsulated as model drugs to enable the use of confocal laser scanning microscopy (CLSM) to non-invasively monitor three-dimensional dye distributions within the multilaminate constructs in real-time. In conjunction with experimental work, a theoretical release model was developed for comparison and to provide guidance in the construction of multilaminates. The model employs the Crank-Nicholson finite difference method to solve Fickian diffusion equations, incorporating spatially varying diffusion coefficients and initial loading profiles. Release experiments were conducted with multilaminate composites of 2-5 layers. During release, dye distribution within the constructs and fractional release were monitored simultaneously. For all release studies in this work, experimental data compared favorably to the theoretically predicted Fickian profiles. Measured dye diffusion coefficients ranged from 10^{-8} to 10^{-10} cm^2/s, depending on dye size and the crosslinking density of the gel.

11:00 AM J4.7
Biomimetic Recognitive Polymer Networks for Ocular Delivery of Anti-Histamines. Sid Venkatesh, Stephen P. Sizemore and Mark E. Byrne; Biomimetic & Biohybrid Materials, Biomedical Devices, and Drug Delivery Laboratories, Chemical Engineering, Auburn University, Auburn, Alabama.

Enhanced drug partitioning in hydrogels can be achieved by configurational biomimetic imprinting (CBIP) techniques which involve the formation of pre-polymerization complexes between template molecules and functional monomers with specific chemical structures designed to interact with the template by non-covalent chemistry. This new class of recognitive intelligent materials is designed by incorporating motifs with structural and molecular homology to biological receptors. This work addresses the unmet need for the controlled release of histamine antagonists such as ketotifen fumarate on the surface of the eye to treat allergic conjunctivitis. Mast cell and eosinophil degranulation occurs due to the IL-4 driven TH2 cell response to allergens and the subsequent IgE secretion. This prompts the release of inflammatory mediators such as histamine, which binds to the H1-receptors. Pharmacological downregulation is possible by the local delivery of H1-antihistamines, resulting in decreased vascular permeability, bronchodilation and decreased exudation of effector cells. Treatment options for seasonal and perennial allergic conjunctivitis primarily consist of oral antihistamines (which provide only partial and delayed relief with potential systemic side effects) and topical treatments. Since ocular bioavailability of topical drugs is very poor (typically less than 7% is absorbed by the eye), a high dosage is needed which prohibits contact lens use. Controlling and tailoring the release of anti-histamines via novel recognitive contact lenses with significantly enhanced partitioning can solve these problems with increased bioavailability, less irritation to ocular tissue, and reduced ocular and systemic side effects. Controlled release by conventional soft contact lenses typically does not work due to a lack of sufficient drug loading. Analysis of the transmembrane domains of H1 receptors revealed the critical amino acids for histamine binding. Acrylate and methacrylate based copolymers, with varying monomer compositions, were synthesized with relevant functionalities to mimic G-protein coupled receptors for histamine. 1H-NMR and 13C-NMR titrations confirmed the non-covalent interactions and binding stochiometries, which aided the rational design of gels with optimized drug-polymer complexation. Polymer networks were synthesized in a temperature controlled non-oxidative environment using free-radical UV photopolymerization. Equilibrium binding isotherms demonstrated enhanced loading with a factor of 2 to 6 times increase in the partitioning of drug compared to conventional networks depending on polymer formulation and polymerization conditions. Dynamic binding studies showed that within 15 to 20 hours gels could re-load a significant percentage of maximum drug capacity. Dynamic release profiles under physiological conditions demonstrated that a viable therapeutic concentration of drug can be delivered at a constant rate for extended periods.

11:15 AM J4.8
Synthesis of virus-mimetic hydrogel particles in an aqueous two-phase system for coincident antigen and activation signal delivery to immune cells. Siddhartha Jain[1], Woon Teck Yap[1] and Darrell John Irvine[1,2]; [1]Biological Engineering, MIT, Cambridge, Massachusetts; [2]Department of Material Science and Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts.

Materials that effectively deliver protein antigens together with activating ligands to antigen presenting cells (particularly dendritic cells) and B cells are sought for improved non-viral vaccines. To this end, we synthesized protein-loaded poly(ethylene glycol) (PEG)-based hydrogel particles, by cross-linking PEG within the polymer-rich submicron emulsion droplets formed by a poly(ethylene oxide-b-propylene oxide-b-ethylene oxide) triblock copolymer in saturated aqueous salt solution. When a model protein antigen ovalbumin (ova) was included in the emulsion, hydrogel particles (500 nm diameter) containing high levels of encapsulated protein (∼75% of dry mass) were formed. The encapsulated protein was selectively released by proteolytic enzymes normally present in the phagosomal/endosomal compartments of dendritic cells (DCs). For co-delivery of cellular activation signals, gel particles were surface-modified by sequential electrostatic adsorption of polyarginine and DC-activating CpG oligonucleotides. DCs pulsed with CpG-bearing, protein-loaded particles were activated to secrete inflammatory cytokines (IL-12, IL-6, and TNF-a) at ∼10-fold lower total doses of oligonucleotide compared to soluble CpG oligonucleotide, and surface receptors of DCs (CD80, CD86, CD40, and MHC class II) were upregulated in response to CpG-modified gel particles. Particle-loaded dendritic cells in turn activated naive CD4+ and CD8+ T cells ∼10-fold more efficiently in vitro than DCs incubated with soluble protein. In vivo, mice immunized with CpG-coated particles had high anti-ovalbumin IgG titers in serum, and IgM was observed in serum as early as one week; soluble ovalbumin control immunizations elicited no humoral response. Based on these findings, this organic solvent-free strategy for protein encapsulation within submicron-sized hydrophilic particles may be attractive for macromolecule delivery to a variety of phagocytic and non-phagocytic cells.

11:30 AM J4.9
Design, synthesis, and testing of a new class of modular gene delivery systems based on linear-dendritic hybrid polymers. Kris C. Wood, Robert Langer and Paula T. Hammond; Chemical

Engineering, MIT, Cambridge, Massachusetts.

Ideally, the next generation of nucleotide delivery systems will be nontoxic, non-immunogenic, and made from building blocks that are versatile to allow for optimal delivery to a range of cells or tissues of interest. Here, for the first time, we present the design, synthesis, and testing of a unique family of hierarchically structured linear-dendritic hybrid polymers that self-assemble with DNA to form stable nanoparticles with a series of concentric, functional "shells" possessing independently-tunable properties necessary for effective targeted delivery. These systems demonstrate serum stable, receptor-mediated delivery to a range of targeted cell and tissue types (both in vitro and in vivo) with transfection efficiencies exceeding the most efficient commercially available polymer, poly(ethylenimine) (PEI) and low toxicity at concentrations one to two orders of magnitude higher than those at which PEI is toxic. These systems may find utility in the clinic as in vivo gene delivery systems for DNA or RNA-based therapies.

11:45 AM J4.10
Neurotrophin Releasing Hydrogels for Improved Electrode-Cell Electrical Contacts in the Retinal Implant.
Jessica Winter[1], Stuart F. Cogan[2] and Joseph F. Rizzo[1,3]; [1]Center for Innovative Visual Rehabilitation, VA Hospital Boston, Boston, Massachusetts; [2]EIC Laboratories, Norwood, Massachusetts; [3]Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard University, Boston, Massachusetts.

One of the most pressing issues in neural prosthetics is increasing device resolution. Electrode size is limited by the amount of electrical current density that may be safely applied to the electrode-tissue interface. Unfortunately, required currents in many situations are high because anatomical and surgical constraints prevent close electrode proximity to target structures. This is particularly true in the retinal implant, where several hundred microns of native and scar tissue may be present between target neurons and the prosthesis. To provide intimate contact between target cells and electrodes additional strategies are needed. Here we discuss our initial studies to increase neuron-electrode interactions by promoting neuronal growth to the device surface. Our system is composed of biodegradable poly(ethylene glycol)-poly(lactic acid) hydrogels (PEGPLA), that may be designed to release a number of neurotrophins through their degradable ester linkages. Additionally, PEG has been shown to reduce cell adhesion and may limit the invasion of scar tissue and glial cells at the implant site, enhancing biocompatibility of the implant. Gel degradation controls drug release rates, and also limits the gel interference on electrode electrical properties. We synthesized PEGPLA polymers of varying molecular weight using previously published methods. Liquid PEGPLA precursors were placed on electrode surfaces of a subretinal visual prosthesis consisting of 15 - 400 micron diameter (1.3 x 10-3 cm2) gold electrode sites coated with iridium oxide. Gels were crosslinked in situ using UV radiation. Hydrogel degradation and drug release were evaluated using a model protein, bovine serum albumin. Electrochemical properties were evaluated using cyclic voltammetry and impedence spectroscopy over the course of hydrogel degradation. Additionally, we investigated PEGPLA hydrogel biocompatibility and ability to induce neurite outgrowth in cell culture. Future gels are being optimized for release of retina-active neurotrophins (e.g., BDNF, CNTF), and will be tested in animals with normal and diseased retina to characterize the extent of neurite extension in vivo.

SESSION J5: Functional Biomimetic Systems I
Chairs: Boualem Hammouda and David Shreiber
Tuesday Afternoon, November 29, 2005
Room 201 (Hynes)

1:30 PM *J5.1
Nanomechanics and Mechanobiology of Cartilage Biopolymeric Networks and Macromolecules.
Alan J. Grodzinsky[1,2,3], Delphine Dean[1], Laurel Ng[3], Lin Han[4] and Christine Ortiz[4]; [1]Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, Cambridge, Massachusetts; [2]Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts; [3]Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts; [4]Department of Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts.

Cells in articular cartilage synthesize an extracellular matrix (ECM) of proteoglycans, collagens, and other non-collagenous proteins to create a dense biopolymeric tissue network that can withstand joint loading *invivo*. At the same time, mechanical forces acting on chondrocytes *invivo*, and in tissue explants and tissue engineering constructs *invitro*, can differentially regulate the gene expression and biosynthesis of these macromolecules, as well as their precise nanomolecular structure. Such changes in molecular fine structure can affect their ability to perform their biomechanical function within the tissue matrix. This mechano-biological feedback is critical for maintenance of healthy cartilage, and for the success of cartilage tissue engineered constructs being developed for the repair of cartilage defects and diseases such as osteoarthritis. Studies suggest that there are multiple regulatory pathways by which chondrocytes can sense and respond to mechanical forces, including upstream signaling and changes in protein gene transcription, translation, and post-translational modifications such as the glycosylation of proteins. An important example is the 2-3 MDa proteoglycan, aggrecan, a highly charged comb biopolymer made by chondrocytes and secreted into the ECM, where supramolecular aggregates of aggrecan (200-300 MDa) are then formed extracellularly by association with newly synthesized hyaluronan and link protein. The resulting aggregate helps cartilage to resist compressive loads due to electrostatic repulsion interactions between the negatively charged chondroitin sulfate (CS) glycosaminoglycan (GAG) chains that are added to the aggrecan core protein and sulfated intracellularly just prior to secretion. Previous studies have shown that mechanical loading of intact cartilage tissue can alter intracellular biosynthesis of aggrecan, including GAG length, sulfation (charge density), and GAG spacing along the aggrecan core protein; each of these post-translational modifications can significantly affect the nanomechanical properties of aggrecan and the resulting tissue-level biomechanical properties of cartilage. To understand the relation between aggrecan molecular structure and the nanomechanics of aggrecan and aggrecan layers, we have measured and modeled intermolecular forces between CS-GAGs and between aggrecan proteoglycans. Multiscale modeling of these interactions extends from the tissue level down to a coarse grained GAG model from an all-atom description of a GAG disaccharide. Experiments have utilized atomic force microscopy, high resolution force spectroscopy, and GAG- and aggrecan-functionalized substrates and probe tips. Together, these experimental and modeling results highlight the role of electrostatic interactions in the mechanical properties of these macromolecules and molecular-based tissue matrices.

2:00 PM J5.2
Separation of DNA of different conformations on flat and nanopatterned surface.
Bingquan Li[1], Xiaohua Fang[1], Youngsoo Seo[1], Haobing Luo[1], Vladimir Samuilov[1], Dilip Gersappe[1], Jonathan Sokolov[1], Miriam Rafailovich[1] and Benjamin Chu[2]; [1]materials science, stony brook university, stony brook, New York; [2]chemistry, stony brook university, stony brook, New York.

We have previously shown that it is possible to separate linear double stranded DNA by using surface interactions rather than topological constraints [1-3]. Since this technique functions by inducing a change in the chain conformations on surface, we postulated that separation could be achieved not only between chains of same lengths, but also between chains of different internal structures. In order to test this hypothesis, we measured the mobility of DNA chains of similar number of base pairs, but in linear, supercoiled, and circular conformations. The magnitude of the mobility was greatest for supercoiled, linear and circular respectively. On the other hand, the scaling relationship of the mobility,μ , for the supercoiled DNA with N number of base pairs, was found to be similar to that of linear molecules on homogeneous Si surfaces ($\mu \sim N^{-0.26}$). We also studied the influence of different buffer concentrations. The buffer concentration mostly affected the chains by varying the chain stiffness or the persistence length. We found that the influence of the buffer concentration was the greatest on the circular and least on the supercoiled DNA. These results are consistent with the circular chains being most relaxed. The introducing of a nanopattern on the surface seemed to improve the dispersion relationship for both linear and supercoiled DNA, where the scaling relationship proved to $\mu \sim N^{-0.33}$.
[1]. N. Pernodet, V. Samuilov, K. Shin, J. Sokolov, M.H. Rafailovich, D. Gersappe, B. Chu, Phys. Rev. Lett., 85 (2000) 5651-5654. [2] Y.-S. Seo, V.A. Samuilov, J. Sokolov, M. Rafailovich, B. Tinland, J. Kim, B. Chu, Electrophoresis, 23 (2002) 2618-2625. [3] Y.-S. Seo, H. Luo, V. A. Samuilov, M. Rafailovich, J. Sokolov, B. Chu, D. Gersappe, Nano Lett., 4, 2004, 659-664.

2:15 PM J5.3
Amphiphilic Star-Like and Scorpion-Like Macromolecules for Treating Atherosclerosis.
Jinzhong Wang[1], Nicole Plourde[2], Evangelia Chnari[2], Prabhas V. Moghe[2] and Kathryn E. Uhrich[1]; [1]Chemistry and Chemical Biology, Rutgers University, Piscataway, New Jersey; [2]Department of Chemical and Biochemical Engineering, Rutgers University, Piscataway, New Jersey.

Amphiphilic scorpion-like macromolecules (AScMs) and star-like macromolecules (ASMs) are nanoscale polymers with similar structures designed for drug delivery applications. AScMs are comprised of a hydrophobic part with four-alkyl chains pendant to a

central linear sugar (mucic acid) moiety and a poly (ethylene glycol) (PEG) tail. In ASMs, the core parts of four mucic acid alkyl derivatives are covalently connected via a multi-functional core. In aqueous solutions, the AScMs aggregate to form micelles at very low concentrations below 1 μM while ASMs behave as unimolecular micelle. The micelle sizes of AScMs and ASMs are between 15 to 30 nm through dynamic laser scattering studies, small enough to avoid rapid clearance by reticuloendothelial system (RES). AScMs and ASMs with available carboxylic acid groups are of interest for treating atherosclerosis. First, carboxylate groups on the polymers can mimic the charge properties of glycosaminoglycans and potentially sequester low-oxidized low-density lipoproteins (LDL), as we found through particle size studies. Second, carboxylate groups can block surface scavenger receptors on macrophages and smooth muscle cells that play a role in highly oxidized LDL binding and uptake. Last, polymer micelles can encapsulate and subsequently release hydrophobic anti-oxidant vitamin E into the vascular intima to prevent LDL oxidation. We addressed the use of carboxylates by specifically generating carboxylate groups at the PEG tails and hydrophobic core parts. These polymers are being assessed for abilities to sequester low oxidized LDL and block scavenger receptors.

3:30 PM *J5.4
Probing cartilage constituents at different length scales.
Peter Basser and Ferenc Horkay; NICHD, NIH, Bethesda, Maryland.

Cartilage swelling is essential for effective load bearing and joint lubrication. Its osmotic properties allow it to resist applied compressive loads and to regulate fluid expression during loading necessary for lubrication. Cartilage swelling behavior is also exquisitely sensitive to structural and biochemical changes that occur in development, disease, degeneration, and aging. Previously, we showed that controlled swelling of cartilage could be used to measure functional properties of both its collagen network and proteoglycan (PG) phases. This entailed modeling the extracellular matrix (ECM) as a composite medium in which the collagen network dialyzed a proteoglycan solution trapped within it. "Pressure-volume" curves for the collagen network and PG phases were measured in tandem. Shortcomings of this experimental approach, however, are that it requires many person-days to analyze a single tissue specimen and relatively large amounts of tissue to make these measurements. We recently invented and developed a new micro-osmometer that addresses these problems. This device will eventually permit us to obtain a profile of the osmotic compressibility or stiffness of multiple cartilage specimens simultaneously as a function of depth from the articular surface to the bone interface. It will also allow us to quantify the contributions of individual components of the ECM, e.g., aggrecan and hyaluronic acid (HA), to the total osmotic pressure. Moreover, it should allow us to assess the osmotic compatibility and mechanical integrity of developing tissues and of tissue-engineered cartilage for implantation. However, micro-osmometry is a macroscopic technique that does not provide information about the underlying molecular motions and interactions that produce the osmotic pressure. To elucidate these effects we resort to high-resolution techniques (e.g., small-angle neutron scattering) that provide conformational and structural information at the molecular and macromolecular length scales. Scattering measurements reflect molecular architecture. This knowledge is essential to understanding how the organization of PGs and collagen fibrils affect functional properties of cartilage. We have studied the structural organization of aggrecan in a length scale range between 1 and 500 nm, and have found that the conformation of aggrecan/HA aggregates is exceptionally insensitive to calcium ion concentration. We have also applied these experimental methodologies to a variety of biomolecular and biomimetic model systems (e.g., synthetic gels, polyelectrolye solutions, DNA gels, tissue-engineered specimen), and believe that this biopolymer physics approach is applicable to study water-ion-biopolymer interactions in a wide range of applications.

4:00 PM J5.5
Hybrid Gels as Medical Diagnostic Tools. P. K. Jha, S. Y. Gadre and P. I. Gouma; Material Science, State University of NY at Stony Brook, Stony Brook, New York.

This paper discusses the synthesis and characterization of active hybrid gels for medical diagnostic applications. The hybrid organic-inorganic gel consists of enzymes entrapped within the pores of an active metal oxide matrix. The enzymes were found to retain their biochemical activity to catalyze a specific reaction with the target analyte. The choice of enzyme and thus reaction was such that a gaseous product was released (e.g use of urease to detect urea through the production of ammonia). The matrix is a selective gas sensitive element, so these hybrid gels can be used as novel bio-sensors for rapid monitoring of analytes(e.g. urea, glucose) the concentration of which in body fluids is an indicator of diseases. The effect of various processing parameters on the structure of gel was determined using a range of analytical techniques, including TEM, BET and FTIR.Examples of such sensor prototypes are discussed.

4:15 PM J5.6
Reflectins: Characterization of Nature's Optical Material.
Ryan Michael Kramer, Joseph Slocick, Lawrence Drummy, Wendy Crookes-Goodson and Rajesh R. Naik; Materials and Manufacturing Directorate, Air Force Research Laboratory, Wright-Patterson AFB, Ohio.

Several evolutionary adaptations in biology that manipulate and interact with light have been demonstrated in a number of different terrestrial and aquatic organisms. The apex of this dynamic light interplay has been reached in cephalopods to include squid, octopi, and cuttlefish, which use a host of physiological adaptations in concert to dynamically alter light. One such adaptation, which can be found throughout this family, is the nanofabrication of reflective elements that results from a cumulative Bragg reflection of multiple thin plates of alternating refractive indexes. A recent report by Crookes et. al. showed that the major composition of these reflective layers is proteinaceous and is composed of a family of closely related proteins termed reflectins. These proteins have an extremely unusual and rare amino acid composition and represent a unique optical material whose properties are inherently important for static, and perhaps, dynamic light reflection. Here we characterize a repeat region within these proteins using NMR, x-ray diffraction, circular dichroism, and combination of different spectroscopies. These short repeat regions can be precipitated to form broad wavelength reflective materials. We also perform elemental analysis of native squid nanostructures and have discovered a subset of inorganic materials that may have a role in altering refractive indexes of the proteinaceous material. Finally, we have recombinantly expressed a genetically optimized reflectin protein and have characterized the recombinant reflectin protein using x-ray diffraction and small angle x-ray scattering.

4:30 PM J5.7
Charged Polypeptide Vesicles with Controllable Diameter.
Eric Peter Holowka[1], Darrin Pochan[2] and Timothy J. Deming[3]; [1]Materials Engineering, University of California Santa Barbara, Santa Monica, California; [2]Materials Science, University of Delaware, Newark, Delaware; [3]Bioengineering, University of California Los Angeles, Los Angeles, California.

The transition metal mediated living polymerization of α-amino-N-carboxyanhydrides (NCA) has allowed for the synthesis of copolypeptides with a high degree of chain length control and incorporation of a wide variety of natural and unnatural pendant functionalities. Amphiphilic block copolymers have been used to form unilamellar vesicles as a more stable alternative to lipid vesicle systems for encapsulation of drug molecules. In order to increase their applicability to living systems, these block copolymers typically have an amino acid functionalized outer block. A purely peptidic block copolymer amphiphile, however, additionally benefits from its ability to tailor polymer structure using amino acids that form known secondary structures, which allow for nanoscale ordering via self-assembly into supramolecular structures. We found lysine-block-leucine amphiphilic diblock copolypeptides having less than 100 residues show dramatically different self-assembly behavior (fiber, membrane, micelle, vesicle) depending on the hydrophobic and hydrophilic block compositions. Specifically, the vesicles showed dynamic properties indicating fluidity in the formed bilayer structure. These properties were highlighted by vesicle size modification through extrusion, reversible response to osmotic pressure, assembly response to ionic media, and stability over a range of temperatures. Despite the fluidic behavior of these vesicles, they remain stable for an extended period (12 weeks) after extrusion, which indicates a distinct advantage over lipid vesicles. Extrusion was also utilized as a means to encapsulate dextran in a series of vesicles of different sizes. Modification of the copolypeptide by substituting oppositely charged glutamate has yielded glutamate-block-leucine vesicles, which behave similarly to the lysine-block-leucine vesicles. These vesicles remain stable in the presence of buffer and serum-containing cell culture media.

4:45 PM J5.8
Biocatalytic Polymerization of Naturally Occurring Catechins for Anticancer Applications. Subhalakshmi Nagarajan[1,2], Ramaswamy Nagarajan[2], Ferdinando F. Bruno[4], Jayant Kumar[1,2], Donna McIntosh[3], Susan J. Braunhut[3], Klaudia Gorski[3] and Lynne A. Samuelson[4]; [1]Departments of Chemistry and Physics, University of Massachusetts, Lowell, Lowell, Massachusetts; [2]Center for Advanced Materials, University of Massachusetts, Lowell, Lowell, Massachusetts; [3]Department of Biological Sciences, University of Massachusetts, Lowell, Lowell, Massachusetts; [4]Nanomaterials Science Team, Natick Soldier Center, US Army RDECOM, Natick, Massachusetts.

Catechins are polyphenolic compounds found in the leaves of green tea that have been known to exhibit anti-carcinogenic, anti-oxidant

and anti-inflammatory properties. Among these catechins, Epigallocatechin gallate (EGCG) has been reported to exhibit chemoprotective and therapeutic properties and is considered to be a potent inhibitor of human breast cancer cell proliferation. However, EGCG has poor stability and loses activity within a few hours of solubilization. To address these limitations, oxidative polymerization of catechins catalyzed by enzymes such as Horseradish peroxidase (HRP) have been carried out, however the resulting polymeric products have limited solubility, thus restricting their compatibility with biological systems. Here we report a unique enzymatic approach for the synthesis of water-soluble poly(catechins) with enhanced stability and anti-cancer activity. Various stereoisomers of catechin [(+), (-), (±)] and (-)-epicatechin have been biocatalytically polymerized using HRP in ethanol/buffer mixtures. This one-pot oxidative polymerization is carried out in ambient conditions yielding water-soluble poly(catechins). The starting materials, intermediates and the products obtained are completely biocompatible and therefore do not have any harmful effects to human life/environment. The non-toxic nature of the process and aqueous solubility of the poly(catechins) facilitates the ease of deliverability of these materials into biological systems. These synthesized poly(catechins) were tested in-vitro for the anti-tumorigenic activity on commercially available normal and cancerous human breast cell lines. The poly(catechins) exhibit greater growth inhibitory effects than monomers as well have higher specificity towards highly metastatic cells as opposed to normal cells thus achieving a high therapeutic ratio. Further, this new class of synthetic water-soluble polycatechins surpasses EGCG, in its selectivity and stability. The synthesis, characterization and the growth inhibitory effects of these novel water-soluble poly(catechins) will be presented.

SESSION J6: Design, Synthesis and Characterization of Biomaterials
Chairs: Stefaan De Smedt and Ferenc Horkay
Wednesday Morning, November 30, 2005
Room 201 (Hynes)

8:30 AM *J6.1
Combinatorial Methods for Structure, Properties, and Biological Responses to Dental Materials. Eric J. Amis[1], Nancy J. Lin[1], LeeAnn O. Bailey[1], Sheng Lin-Gibson[1], Forrest A. Landis[1] and Peter Drzal[2]; [1]Polymers Division, NIST, Gaithersburg, Maryland; [2]Materials and Construction Research Division, NIST, Gaithersburg, Maryland.

Combinatorial and high-throughput methods have been developed for investigations of the effects of co-monomer composition and reaction irradiation time on the structure, properties, and biological responses of model two-component dimethacrylate dental resin blends. The approaches allow preparation of gradients of composition and reaction time and evaluation of degree of methacrylate conversion by near infrared spectroscopy, mechanical properties by nanoindentation, and cellular response by fluorescence microscopy studies of viability of Raw 264.7 macrophages. Excellent correlation was observed between the reaction conversion and mechanical properties for the cross-linked networks with methacrylate conversion ranging from 40 % to 85 % and the mechanical properties increasing over two orders of magnitude. Cell viability stains demonstrated that decreased viability as resin conversion decreased.

9:00 AM J6.2
Matrix Assisted Pulsed Laser Evaporation (MAPLE) Thin Film Processing of Biopolymers: Mussel Adhesive Protein Analogs. Anand Doraiswamy[1], C. Jin[1], R. J. Narayan[1], C. Dinu[2], R. Cristescu[3], N. Mihailescu[3], S. Stafslien[4], J. Wilker[5], R. Modi[6] and D. B. Chrisey[6]; [1]Bioengineering Program, School of Materials Science and Engineering, Georgia Institute of Technology, Atlanta, Georgia; [2]Max-Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany; [3]Plasma and Radiation Physics, National Institute for Lasers, Bucharest-Magurele, Romania; [4]North Dakota State University, Fargo, North Dakota; [5]Department of Chemistry, Purdue University, West Lafayette, Indiana; [6]US Naval Research Laboratory, Washington, District of Columbia.

Mussel adhesive protein analogs are biologically-derived materials that possess unique adhesion properties. We have demonstrated thin film growth of mussel adhesive protein analog: a dihydroxystyrene copolymer with selective DOPA components, using a novel approach termed as Matrix Assisted Pulsed Laser Evaporation (MAPLE). The protein analog is developed into thin films using an excimer laser (193 nm ArF) on different substrates using a variety of solvent matrices. The deposited films are characterized using various techniques including FTIR, XPS, and AFM to demonstrate the deposition of high quality thin films. Contact angle and de-lamination studies of these films show properties similar to natural mussel adhesive protein. Antifouling studies using marine relevant bacterias demonstrated improved resistance to biofouling in these MAPLE deposited protein analog thin films. These novel polymer thin films have numerous medical, electronic, and marine applications.

9:15 AM J6.3
Novel Self-Assembling Template Directed Sol-Gel Polymerisation of Nanostructured Silicas. Jonathan Meegan[1,2], Richard Ansell[2], Amalia Aggeli[2] and Neville Boden[2]; [1]Atomic Weapons Establishment, Reading, United Kingdom; [2]Chemistry, University of Leeds, Leeds, United Kingdom.

Organisms such as bacteria or diatoms are capable of forming amorphous silica shells from naturally occurring silica in the environment. In the case of diatoms these silica shells are often very complex and ordered nanoscale structures comprising of atomically amorphous silica. The intricate nature of their silica shells and their ability to precipitate and mineralise silica nanostructures (biomineralisation) has meant that diatoms in particular have been the subject of extensive studies in recent years. Biomolecules such as proteins, peptides and also other naturally occurring biomimetic or synthetic self-assembling systems (as analogues of naturally occurring species or polymers containing unnatural amino acids) can be used as organic templates for silica deposition. The use of such templates allows for synthesis of nanostructured materials over a wide pH range and through careful choice or design of the template can provide a unique way of understanding the processes involved in silica biomineralisation. The term sol-gel applies to systems in which a colloidal suspension (a sol) is converted into a viscous gel (a semi-solid colloidal system consisting of a solid dispersed in a liquid) and ultimately a solid material. The processes involved in the sol-gel synthesis of a siliceous material can be broken down into several stages; 1) Hydrolysis of precursor 2) Condensation of hydrolysed species 3) Gelation of sol 4) Ageing of gel 5) Drying of gel The concerted way in which the steps occur means that the concentration of hydrolysed precursor within the system can, through careful manipulation of the pH be kept at a constant low level. This allows for careful control of the condensation and gelling steps, providing a neat way of controlling the properties (particle size, porosity and pore chemistry) of the final material.. Sol-gel precursors are often volatile compounds and can be purified by distillation or sublimation and if a high purity mixed material (a semiconductor for example) is required the precursors can be readily homogenised prior to reaction resulting in high quality materials. In this abstract we hope to briefly run through our existing published work and describe new and exciting developments using rationally designed peptides and novel synthetic molecules as templates for silica deposition.

10:00 AM *J6.4
Modifying the Properties of Collagen Scaffolds with Microfluidics. David I. Shreiber[1], Harini G. Sundararaghavan[1], Minjung Song[1] and Kathryn E. Uhrich[2,1]; [1]Biomedical Engineering, Rutgers, the State University of New Jersey, Piscataway, New Jersey; [2]Chemistry and Chemical Biology, Rutgers, the State University of New Jersey, Piscataway, New Jersey.

It is now well accepted that the mechanical properties and cell adhesion profile of 2D and 3D extracellular matrix molecules combine to dictate cellular fate processes, such as differentiation, migration, proliferation, and apoptosis, through a process generally known as 'mechanotransduction', or the conversion of mechanical signals into a cellular response. The stiffness and adhesion density combine to affect the force balance that exists between an adherent cell and the surrounding substrate. We have established BioMEMS, microfluidic technology to alter the mechanical properties and cell adhesion profile of collagen scaffolds. Using soft lithography, we fabricate elastomeric networks that serve as conduits for the controlled mixing of type I collagen solutions. Our technology enables us to generate reproducible, controlled homogeneous and inhomogeneous microenvironments for 3D cell culture, assays of cell behavior in 3D, and the development of bioartificial tissue equivalents for regenerative and reparative therapies. The adhesivity of collagen is modulated by covalently grafting peptides (such as RGD) or proteins (such as laminin) to soluble collagen molecules with 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide (EDC), a hetero-bifunctional coupling agent. EDC activates the carboxylic group of collagen and forms an amine bond with the grafting molecule. The grafted collagen self-assembles into a fibrillar gel at physiological temperature and pH with no measurable changes in rheological properties compared to controls. A solution of peptide-grafted collagen is then mixed in microfluidic networks with unaltered collagen to form controlled gradients or other patterns of the two solutions, which immobilize upon self assembly. Separately or in the same network, the mechanical properties of the collagen gel can be altered regionally by the microfluidic delivery a solution of a cell-tolerated crosslinking agent. We use genipin, which has the unique property of generating crosslinks that autofluoresce. The intensity of the fluorescence correlates with

the degree of crosslinking (and thus the mechanical properties) enabling us to monitor and measure changes in mechanical properties dynamically and non-invasively. Lastly, though it requires constant delivery or recirculation, the same networks can be used to impose gradients of soluble factors, such as growth factors and cytokines. Thus, we have developed a platform to examine the response of cells to simultaneous chemotactic, haptotactic, and durotactic gradients in a 3D environment. We are employing this technology to examine the response of neural cells to gradients of biomaterial properties to optimize cues for spinal cord regeneration. Supported by the New Jersey Commission on Spinal Cord Research (03-3028-SCR-E-0), Rutgers NSF IGERT on Integratively Engineered Biointerfaces (DGE 033196), and a collaborative agreement with Lucent Technologies through the New Jersey Nanotechnology Consortium.

10:30 AM J6.5
Microfluidic Immunoassay: Development of a Fluorescence-based Heterogeneous Immunoassay in a Cyclic Polyolefin Microfluidic Device. Arpita Bhattacharyya, Bekah Gensure and Catherine Klapperich; Biomedical Engineering, Boston University, Boston, Massachusetts.

The development of a polymeric lab-on-a-chip device for microfluidics-based surface immunoassay is described in this paper. Immunoassay is a powerful biochemical analysis method and is widely applied in the field of medical diagnostics. Miniaturization of this analytical method offers significant advantages over traditional techniques in terms of reaction kinetics, sample/reagent consumption, parallel analysis and ease of automation. Moreover, fabricating the microdevices in plastic makes it a more cost-effective system and enables it to be used as disposable, hand-held devices for immunoassay applications at the point-of-care. Earlier studies reported in the field of microfluidic immunoassay were based on Enzyme-linked Immunosorbent Assay (ELISA), which have several disadvantages in terms of colorimetric quantification of the immune reactions occurring in the microchannels. The goal of this work was to develop a fluorescence detection-based immunoassay in a polycycloolefin microfluidic device. The microchip was made by hot-embossing with a silicon master. The master itself was made using photolithographic techniques and Deep Reactive Ion Etching (DRIE). The immunoassay process was electrokinetically-controlled and geared towards diagnosis and monitoring of infectious diseases. Preliminary proof-of-principle testing of the device was performed by immobilizing the target antigens in the reaction channels through passive adsorption. This was followed by successively reacting the primary antibodies and the fluorescently tagged secondary antibodies in the microchannels. Fluorescent signal resulting from the antigen-antibody reaction scheme was detected with a fluorescent microscope. The paper also describes the surface modification techniques applied to optimize the physisorption of the analyte (target antigen) to the polycycloolefin surface. We have also studied the performance of the immunoassay at different flow velocities and surface densities of the target antigens. The strategies explored to optimize the assay towards maximum sensitivity and faster performance will further the development of microfluidic immunoassay in a plastic microchip.

10:45 AM J6.6
High-Porosity Nanoporous Silica via Nanocasting Template of Hydrogels. Takanori Nakamura, Naoki Umeda, Ken-ichi Kurumada and Atsushi Suzuki; Environment and System Sciences, Yokohama National University, Yokohama, Kanagawa, Japan.

We report here the study of novel method to generate high-porosity nanoporous silica using hydrogels as a nanocasting template. These nanopores were controllable between 4nm to 20nm with increasing concentration of the gel moiety to silica. The highest porosity we generate in this way was over 80%, and the max nitrogen adsorption value was more than 1500ml/g. Therefore, this nanoporous bulk silica was expected to be 3-dimentional carriers for atoms and molecules for many possible applications, such as the drug delivery system. We used N-isopropylacrylamide (NIPA) gel for the template gel, and N,N'-methylene bisacrylamide (BIS) was used as the crosslinker of acrylamide series at molar ratio 1/81. N,N,N',N'-tetramethylethylenediamine (TEMED) and 1wt% APS were used as polymerization accelerator and polymerization initiator, respectively. Silica sol was obtained by hydrolysis of tetraethyl-orthosilicate (TEOS) in acidic condition with HCl (PH 4∼5). The pre-gel solution and silica-sol were mixed and vigorously stirred for the simultaneous polymerization and gelation followed by slow dehydration process. Finally, the dehydrated samples followed by calcinations at 873K for 5 hours to obtain the nanoporous bulk silica samples. The effect of different gel templates and the effect of concentration of the gel moiety to silica were examined expecting that it can give a variation in the nanopores and their sizes. Pore size distribution of the nanoporous bulk silica was calculated by nitrogen adsorption/desorption measurements, and we verified the channel-like pores clearly by Transmission Electron Microscope (TEM). By increasing the concentration of the gel moiety to silica, NIPA gel trended to segregate their polymer network structures, and the partial overlap of NIPA chains increased the average pore size, which was confirmed by TEM images. On the whole, the results of nitrogen adsorption/desorption corresponded with the TEM images, and it can be concluded that the pore sizes of the present silica prepared by the nanocasting of hydrogel template was easily controlled by increasing the concentration of the gel moiety to silica.

11:00 AM J6.7
Nanohydrogel Protein Arrays. Ishtiaq Saaem[1], Vasileios Papasotiropoulos[2], Tongsheng Wang[2], Patricia Soteropoulos[2] and Matthew R. Libera[1]; [1]CBME Dept., Stevens Institute of Technology, Hoboken, New Jersey; [2]Center for Applied Genomics, Public Health Research Institute, Newark, New Jersey.

Protein microarrays rely on a highly structured interface between a biosynthetic surface and a physiological system. Like DNA arrays, they involve the surface immobilization of bioreagents - typically proteins or antibodies - which are then hybridized with a solution containing target molecules such as oligonucleotides, antibodies, other proteins, or drug candidates. However, proteins are chemically and physically heterogeneous, have a three-dimensional structure that is critical to their function, and have no analogous amplification technique. Many proteins are also known to lose activity when bound to a solid surface, and most will adsorb nonspecifically to commonly used substrate materials. Therefore, protein arrays are challenged by: (1) the lack of amplification methods such as PCR, which limits the availability of needed protein-based bioreagent; (2) the susceptibility of proteins to denature upon binding to a solid substrate and consequently alter their function; and (3) non-specific adsorption of most proteins to traditionally-used substrate materials that creates high background noise. We have been developing nanohydrogels as a means to simultaneously address all of these issues. We use focused electron beams to create nanohydrogels - ∼ 200 nm in diameter - from amine-terminated poly(ethylene glycol) [PEG] by radiation crosslinking. The swelling properties can be controlled by the electron dose and swell ratios as high as 15 can be achieved. The nanohydrogels can be surface patterned on glass or silicon at submicron spacing, and we can pattern ∼7500 nanohydrogels in a 100 micron diameter area in ∼10 seconds. This is an areal density 10,000 times greater than that of a modern DNA chip. After patterning, we treat the surface with a triblock (PEO-PPO-PEO) copolymer to minimize background noise from non-specific protein adsorption. We have covalently bound fibronectin and laminin to different arrays of nanohydrogels, and, using anti-laminin and anti-fibronectin antibodies, we show that these proteins maintain their biospecificity with high fidelity. Using a nucleic acid binding protein (NBP), we created protein arrays by attaching the NBP to the nanohydrogel surface following two different strategies: (1) directly attaching the NBP to the nanohydrogel and (2) attaching a specific antibody first and then the NBP. We then hybridized the protein with a 55mer oligonucleotide substrate to examine whether the protein would remain functional. We compared the performance of these two formats to equivalent arrays produced using state-of-the-art spotting technologies on nitrocellulose, epoxide, and amino-silane substrates. The nanohydrogel array format demonstrates both a higher peak fluorescent signal as well as the best signal-to-background ratio. Our current work is focused on the single molecule functionalization of individual nanohydrogels.

11:15 AM J6.8
Cholesterol-MIP Fabricated by Sol-gel Method for Application in Polar Solution. Chun-Wei Hsu and Ming-Chang Yang; Department of Chemical Engineering, National Cheng Kung University, Tainan City, Taiwan.

Cholesterol-imprinted polymers (Cholesterol-MIPs) have been synthesized with various functional monomers and crosslinkers. Methacrylic acid (MAA) is the most common functional monomer for cholesterol-MIPs, and the adsorption is usually carried out in apolar solutions, e.g., cyclohexane. Cholesterol and bile acid esters can be used to synthesize monomers for the fabrication of cholesterol-MIPs for application in polar solution (methanol/H2O = 95/5). These two methods in fabricating MIPs involve monomers with an acrylic functional group. A sol-gel method is also applied for MIP fabrication to give lower uptake than acrylic-type MIP, with remarkably lower nonspecific binding toward propranolol. In our research, we synthesized cholesterol-MIP for application in a polar solution. Cholesterol was used to synthesize a functional monomer to provide hydrophobic interaction for cholesterol binding. Tetraethyl orthosilicate (TEOS) was a crosslinker to fabricate sol-gel type of cholesterol-MIP. The synthesized polymer was ground by ball mill followed by sieving. The template of cholesterol was extract from the polymer powder with methanol. In the rebinding experiment, target molecule and interference was rebound to polymer powder in a mixture of methanol and H2O (methanol/H2O = 95/5). The experimental results showed that the MIP synthesized with MAA

monomer does not have more amount of binding in polar rebinding solution than non-MIP. However, most cholesterol-MIPs using MAA as monomer did give more amount of binding in the apolar solvent than non-MIP. It implied that the hydrophobic interaction was strong for cholesterol-MIPs in polar system. This might be due to a large hydrophobic segment in cholesterol molecule. Although the MIP fabricated by sol-gel method had lower uptake than the MIP synthesized with monomer containing acrylic functional group, it also had lower nonspecific binding capacity. As a result that the selectivity of sol-gel MIP was higher with more hydrophilic interference, e.g., testosterone, and was lower with more hydrophobic interference, e.g., stigmasterol. Other properties of this type of MIP will be reported. (Financially supported by the Ministry of Education in Taiwan, A-91-E-FA09-5-4)

11:30 AM J6.9
Reactive polymer coatings made by chemical vapor deposition polymerization. Hsien-Yeh Chen, Himabindu Nandivada and Joerg Lahann; Chemical Engineering and Materials Science and Engineering, University of Michigan, Ann Arbor, Michigan.

Future biomedical implant devices and microfluidic bioassays will use advanced surface engineering technologies to actively modulate tissue integration. Towards this goal, vapor-based polymer coatings have been interesting candidates for the coating of implant devices, because of their advanced processibility and their excellent intrinsic biocompatibility. For instance, a specific vapor-deposited polymer (parylene) is already used in FDA approved drug-eluting stents. The commercially available coatings lack, however, anchor groups for further modification and therefore do not allow for immobilization of biomolecules or the implementation of protein-resistancy. Recently, we established a surface modification technique based on the chemical vapor deposition (CVD) polymerization of substituted [2,2]paracyclophanes to prepare a diverse class of functionalized poly-p-xylylenes with a wide variety of functional groups such as amines, esters and alcohols that can be used for covalent binding of biomolecules. Advantages of the CVD technique include control of the composition and architecture of the films, high coating accuracy, solvent-free environments, and excellent adhesion. We now demonstrate the usefulness of the CVD polymerization process to prepare a novel aldehyde functionalized poly-p-xylylene, poly(4-formyl-p-xylylene-co-p-xylylene), which is suitable for the immobilization of polysaccharides. The chemical composition of the resulting polymer thin films has been confirmed by infrared spectroscopy (IR) and X-ray photoelectron spectroscopy (XPS). The availability of the aldehyde functionalities on the surface of the polymer films is studied by means of chemical conversion with hydrazides to yield hydrazone linkages. Moreover, tethering model sugars to the reactive surfaces has been demonstrated. By moving from the aldehyde group to a benzoyl group, a photodefinable polymer can be prepared via CVD polymerization. Based on XPS and IR analysis, the polymer films has been characterized to be poly[4-benzoyl-p-xylylene-co-p-xylylene]. This photodefinable coating has a wide range of applications with respect to patterned substrates. As an example, we demonstrate its potential for surface modification by preventing non-specific protein adsorption on different substrates including silicon and polydimethylsiloxane as measured by fluorescence microscopy. Fibrinogen and albumin have been studies as model proteins. More importantly, 3-D patterns are created within polymer-based microfluidic channels; establishing spatially controlled, bioinert surfaces. The herein reported method addresses a critical challenge with respect to surface modification of microfluidic devices, namely the fabrication of discontinuous patterns within microchannels.

SESSION J7: Scaffolds for Cell and Tissue Engineering
Chairs: Peter Basser and David Shreiber
Wednesday Afternoon, November 30, 2005
Room 201 (Hynes)

1:30 PM *J7.1
Hydrogel Niches Designed to Promote Mesenchymal Stem Cell Function. Charles Nuttelman, Danielle Benoit and Kristi Anseth; Chemical and Biological Engineering, University of Colorado and HHMI, Boulder, Colorado.

Hydrogels provide a unique, largely aqueous environment for 3D cell culture, and when locally modified with appropriate signaling molecules, these synthetic niches can facilitate the regeneration of tissues. While the gel environment is often >90% water, the microscopic architecture and chemistry play an important role in dictating cell morphology, gel degradation and erosion, and the secretion and distribution of extracellular matrix molecules. In this work, hydrogels were synthesized to present local signals to human mesenchymal stem cells (hMSCs) that induce osteogeneis, maintain cell function, and promote mineralized tissue formation. While a significant amount of research has focused on the differentiation of hMSCs in monolayer culture, very little is known about their differentiation potential when cultured in a three-dimensional environment. In particular, results will demonstrate approaches to modify the structure and chemistry of hydrogel hMSC carriers to facilitate osteogenic differentiation. Hydrogels were synthesized by the photoinitiated polymerization of multivinyl macromolecular monomers, based on poly(ethylene glycol). This general approach to fabricate covalently crosslinked gels provides a robust platform to directly encapsulate cells under cytocompatible conditions and examine the influence of the gel structure and chemistry on cell differenitation and tissue evolution. First, the survival of hMSCs was investigated as a function of the gel chemistry. hMSC viability dropped to lower than 15% when cultured in pure PEG gels; however, osteopontin sequestering PEG gels were synthesized that contained phosphate pendant group, and results demonstrate greater than 97% viability after 4 weeks of in vitro culture. In addition to the design of PEG gels that permit hMSC 3D culture and expansion, osteogenic promoting hydrogels were synthesized that locally present dexamethasone through a degradable linker that controls the kinetics of release, and ultimately, the differentiation of hMSCs to osteoblasts. The kinetics of the dexamethasone release was studied, especially with respect to the effect of the linker length on the release profile. Thereleased dexamethasone was biologically active and influenced the expression of osteogenic genes (e.g., alkaline phosphatase and cbfa1), as measured using real-time RT-PCR, in a degradation-dependent manner. Finally, single and multiphoton imaging was used as a non-invasive technique to explore living cell behavior, especially differentiation of hMSCs, as a function of the local gel chemistry and delivery of osteogenic factors.

2:00 PM J7.2
Electrospun 3D Hyaluronic Acid (HA) Hydrogel Nanofibrous Scaffold: A Novel Material for Tissue Engineering. Yuan Ji[1], Kaustabh Ghosh[2], Xiaozheng Shu[3], Glenn D. Prestwich[3], Richard A. F. Clark[2], Jonathan Sokolov[1] and Miriam Rafailovich[1]; [1]Materials Science and Engineering, SUNY at Stony Brook, Stony Brook, New York; [2]Biomedical Engineering, SUNY at Stony Brook, Stony Brook, New York; [3]Medicinal Chemistry, The Uinversity of Uath, Salt Lake City, Utah.

A unique 3D hyaluronic acid (HA) hydrogel nanofibrous scaffold was successfully fabricated to mimic the architecture of natural extracelluar matrix (ECM) using the electrospinning technique. Poly (ethylene oxide) was added into the aqueous solution of a thiolated HA derivative at a 1:1 weight ratio to facilitate the fiber formation during electrospinning. The electrospun HA/PEO blend scaffold was crosslinked by Poly (ethylene glycol)-diacrylate (PEGDA) within 15 minutes. PEO was then extracted in deionized water to form an electrospun HA hydrogel nanofibrous scaffold. SEM was used to investigate the morphology change of the electrospun scaffold before and after PEO extraction. The electrospun scaffold still maintained the 3D nanofibrous architecture while the average fiber diameter increased from 80nm to 150nm due to the dissolution of HA during PEO extraction. FT-IR was employed to confirm the absence of PEO after extraction. DSC and TGA experiments show that the thermal degradation temperature of the HA hydrogel nanofibrous scaffold increased about 20K after crosslinking. Cell seeding experiment shows that the electrospun HA hydrogel nanofibrous scaffold significantly improved the attachment and spreading of the 3T3 fibroblasts. The 3T3 fibroblasts migrated into the scaffold and showed a dendritic morphology which is much different from the typical flattened morphology on 2D surfaces. These results demonstrate that the electrospun HA hydrogel nanofibrous scaffold is an ideal biodegradable ECM for tissue engineering and wound healing. Supported by NSF-MRSEC.

2:15 PM J7.3
Biomimetic Hydrogel/apatite Nanocomposite Scaffolds for Bone Regeneration. Esmaiel Jabbari, Chemical Engineering, University of South Carolina, Columbia, South Carolina.

Bone matrix is a composite material consisting of aqueous and inorganic phases. The aqueous component gives bone its form and contributes to its ability to resist tension, while the inorganic, or mineral, component primarily resists compression. Recent studies demonstrate that there is a significant physical and chemical interaction between the aqueous and mineral phases of the bone matrix. The aqueous phase of the bone matrix, even though it constitutes only 15% of the matrix, plays a central role in maintenance of matrix integrity. In this work, we describe synthesis, characterization, and fabrication of hydrogel/apatite nanocomposite scaffolds for bone regeneration. Poly(lactide-ethylene oxide-fumarate) (PLEOF) unsaturated terpolymer was synthesized by condensation polymerization of low MW PLA and poly(ethylene glycol) (PEG) with fumaryl chloride (FuCl) and triethylamine (TEA) as the

catalyst. PLEOF macromers were synthesized using PEG with Mn ranging from 1 to 5 kD and PLAF with Mn ranging from 1 to 7 kD. The structure of PLEOF macromer was characterized by 1H-NMR and FTIR. Hydrogel/apatite porous scaffolds were prepared using PLEOF as the degradable macromer, methylenebisacrylamide (MBIS) as the crosslinking agent, a neutral redox initiation system, and sodium chloride crystals as the porogen. The redox system consisted of ammonium persulfate (APS) and tetramethylethylenediamine (TMEDA), respectively. HA based on total weight of the hydrogel was added to the polymerizing mixture, transferred to a 5 mm diameter x 3 mm height Teflon mold and placed in an oven to facilitate crosslinking and the porogen was leached out by soaking in distilled water for 2 days. The pore morphology was studied with an ESEM equipped with an electron backscattered detector and an integrated x-ray energy dispersive analysis system. Macropores created by the porogen and micropores created by the partial phase separation of hydrophilic (PEG) and hydrophobic (PLA) domains of PLEOF hydrogel were observed in the ESEM micrographs. Scaffolds were seeded with bone marrow stromal (BMS) cells isolated from Wistar rats and incubated for 48 h to study cell attachment. Attached cells were fixed and permeabilized. Cell nucleus was stained with DAPI or SYTOX Green and counterstained with Texas Red-X Phalloidin. When the nanocomposite scaffold was treated with collagen type I, having integrin binding RGD domains, cells adhered to the surface and had extended morphology with focal point adhesion. The cell morphology was further examined by SEM, demonstrating strong attachment of the BMS cells to the scaffold surface mediated by the integrin binding sequences on the collagen fibrils. Our results demonstrate that hydrogel/apatite nanocomposites are an attractive alternative as a biomaterial for hard tissue regeneration.

3:30 PM *J7.4
Designing Collagen Scaffolds to Enhance Tissue Regeneration. George D. Pins, Biomedical Engineering, Worcester Polytechnic Institute, Worcester, Massachusetts.

Using biomimetic design strategies and novel fabrication processes, we developed three-dimensional constructs that emulate native tissue architecture and cellular microenvironments. We use these scaffolds to characterize the roles of extracellular matrix (ECM) cues and topographic features in modulating cellular functions, including adhesion, migration, proliferation, differentiation and tissue remodeling. One study in our laboratory focuses on using microfabrication techniques to create collagen membrane-based basal lamina analogs that emulate the complex interdigitated topography at the interface between the dermal and epidermal layers of skin. When keratinocytes are seeded on the surfaces of these basal lamina analogs, and grown in culture for 7 days, they form a differentiated and stratified epidermis that conformed to the features of the microtextured membrane. Morphometric analyses of these immunostained skin equivalents indicate that the rates of keratinocyte stratification and differentiation increase as channel depth increases and channel width decreases. This trend is most pronounced in channels with the highest depth-to-width aspect ratios (i.e., 200 μm deep, 50 μm wide). Ultimately, we anticipate that the results of these studies will provide us with design parameters to fabricate basal lamina analogs that will increase the structural and mechanical integrity of bioengineered skin substitutes. A second study in our laboratory is investigating the development of bioactive collagen scaffolds for tendon/ligament regeneration. Towards this goal, our laboratory is developing a series of experimental techniques to assess the capacity of individual collagen threads to facilitate tissue regeneration by measuring cell attachment, proliferation and migration in vitro. Recently, we developed a novel method for self-assembling solutions of collagen molecules into threads that exhibit mechanical properties and aligned fibrillar substructure comparable to native tendon structures. To characterize cellular responses to the surfaces of these collagen threads, we developed an in vitro fibroblast migration assay. Fibroblast migration rates are determined by measuring the distances that cells travel along the lengths of the various thread types as a function of time. Threads self-assembled from type I collagen are found to have migration rates similar to native tendon threads while crosslinking by severe dehydration decreases the rate of cell migration. We anticipate that this in vitro model system will be a valuable tool for measuring contact-guided cell migration from a wound margin onto biomaterials with precisely engineered surface topographies and extracellular matrix compositions. Furthermore, this assay will allow us to identify design parameters that will be most effective for enhancing the rate of tissue ingrowth on fiber-based collagen scaffolds for soft tissue regeneration.

4:00 PM J7.5
Self-Assembling Bioactive Nanofiber Systems for Neural Regeneration. Krista Lynne Niece[1], Catherine Czeisler[3], Stephen Soukasene[1], John A. Kessler[3] and Samuel I. Stupp[1,2,3]; [1]Materials Science & Engineering, Northwestern University, Evanston, Illinois; [2]Department of Chemistry, Northwestern University, Evanston, Illinois; [3]Feinberg School of Medicine, Northwestern University, Evanston, Illinois.

Our laboratory demonstrated previously the formation of nanofibers through self-assembly of peptide amphiphiles (PAs). In one example nanofibers have been shown to trigger rapid and selective differentiation of neural progenitor cells into neurons. In this work we present experimental data on nanofibers containing two neuro-active epitopes and study the internal distribution of these biological signals within the fiber. In this context we examine PAs bearing the laminin epitopes IKVAV and YIGSR and simplified model systems with similar charge distributions but optimized for more accurate characterization. Two PAs of opposite charge form fibers of mixed composition, and NMR evidence suggests the existence of a repeating domain structure motif. In contrast, similarly-charged PA mixtures appear to phase separate into fibers largely composed of a single epitope. When cultured on these materials in two or three dimensions, progenitor cells survive and differentiate into neurons.

4:15 PM J7.6
Morphological Control of Mineralization via Complex Coacervation. Brandon John McKenna[1], J. Herbert Waite[2,3] and Galen D. Stucky[1,4]; [1]Chemistry and Biochemistry, University of California Santa Barbara, Santa Barbara, California; [2]Marine Science Institute, University of California Santa Barbara, Santa Barbara, California; [3]MCDB, University of California Santa Barbara, Santa Barbara, California; [4]Materials, University of California Santa Barbara, Santa Barbara, California.

Coacervation is a spontaneous phase separation resulting from competing electrostatic attraction and hydration effects of oppositely-charged chemical entities, producing polymer-rich, liquid-like colloids that may coalesce into a single coacervate phase. We have published examples of polymers combined with small, multivalent ions to effect coacervation, which in turn triggered silica condensation to yield hollow inorganic microspheres. In this work we synthesized coacervates from divalent metal ions and higher concentrations of polyanions than those typically used in biomineralization studies. We show the resulting phase can nucleate mineralization of biologically relevant minerals (calcium carbonate, calcium phosphate). This method provides morphological tunability of materials by temporarily preserving amorphous mineral as a precursor within a liquid phase. We suggest that coacervation may contribute to the common observation of spherical synthetic calcium carbonate by demonstrating the shape-directing ability of the coacervates with examples of new and unique structures.

4:30 PM J7.7
Acidic Macromolecules as Process-Directing Agents- Relevance to Biomineralization. Lijun Dai and Laurie B, Gower; Materials Science & Engineering, University of Florida, Gainesville, Florida.

The acidic macromolecules associated with biominerals have long been thought to regulate the formation of the biomineral crystals, as well as influence the final properties of the bioceramic composite. Our in vitro studies have led us to propose that the way in which this is accomplished is through the use of acidic proteins which serve as process-directing agents, in which we have shown that mimetic polypeptides can induce liquid-liquid phase separation in the crystallizing medium, which transforms the traditional crystallization process into an amorphous precursor process. An important aspect of the acidic macromolecules is the level of hydration water that is integrated into the amorphous precursor, which imparts fluidity to the precursor phase, and this has important consequences with respect to the molding and shaping of the crystals. Non-equilibrium crystal morphologies can be generated which mimic many biomineral features, such as the deposition of thin tablets and films, extrusion of crystal fibers, patterning and templating of crystals, and intrafibrillar mineralization of collagen to mimic the nanostructure of bone. Given the strong likelihood that this process plays a fundamental role in the morphogenesis of calcific biominerals, we have been examining the crystallochemical mechanism involved in this polymer-induced liquid-precursor (PILP) process, to determine if there are general concepts related to this non-specific process which can ultimately be adapted to a variety of inorganic crystallization systems. A variety of mimetic polypeptides have been synthesized with varying acidic domains and examined with respect to their ion binding potential and hydration capacity, to determine how this impacts the overall compositional changes that occur within the precursor phase as it transforms from an amorphous gel to a solid mineral phase. Interesting structural features result from the means by which this transformation occurs, many of which are relevant to the defect textures observed in biominerals.

4:45 PM J7.8
A Bladder Submucosa Matrix (BSM) derived Bio-Organic Composite Material for Bone Tissue Regeneration.
Grace Jeong Lim, Sang Jin Lee, Mark Van Dyke, James Yoo and Anthony Atala; Regenerative Medicine, Wake Forest University, Winston Salem, North Carolina.

Background: Numerous synthetic and naturally derived biomaterials have been used as bone tissue substitutes, however, none has shown to be entirely satisfactory. Recent advances in tissue engineering and regenerative medicine have introduced a new concept of using cells for bone formation in vivo. Creation of bone tissue using cells requires a scaffold that serves as a cell carrier, which would provide adequate structural support until bone tissue forms in vivo. Although many biomaterials have been proposed as scaffolds for bone tissue engineering, none has shown to possess the ideal characteristics. The ideal scaffolds for bone tissue engineering should be biocompatible and possess adequate mechanical stability, a controlled degradation rate, hydrophilic surface chemistry, and an appropriate porosity for cell accommodation. Objective: In this paper, we aimed to develop an ideal bio-organic hybridized composite scaffold for bone regeneration that would meet these criteria by hybridizing bladder submucosa (BSM) as a natural biological material with synthetic organic PLGA polymers. Materials and Methods: BSM, which is, composed of type I and type III collagen, elastin fibers and various proteins was selected for their biocompatibility, hydrophilic nature and biological activities to induce cell proliferation. However, BSM alone is not suitable for bone graft applications due to their small pore size, poor interconnectivity and inability to maintain structural integrity. To overcome these limitations, we introduced organic PLGA polymer to make a natural-synthetic hybrid scaffolds that would possess an interconnected network of pores, and adequate mechanical and physicochemical properties. Cellular interactions of the BSM-PLGA composite scaffold were tested by using cell viability and mitochondrial metabolic activity (MTT assay) using both primary mature osteoblasts and stem cells. We characterized the surface properties and mechanical stability of the composite scaffold. Results: This study demonstrated that the BSM-PLGA composite scaffolds are biocompatible, biodegradable, easily fabricated and provide adequate structural support with abundant pores and good interconnectivity. The fabrication of composite scaffold with an appropriate pore size, porosity and surface hydrophilicity resulted in abundant cell accommodation with increased cell proliferation. In addition, BSM has shown to enhance cell proliferation due to the embedded bioactive molecules such as growth factors and cytokines. Conclusion: We successfully fabricated a novel bio-organic composite material composed of BSM and PLGA that possesses ideal characteristics required for bone tissue regeneration. The use of this bio-organic composite system with cells may enhance the formation of bone tissue for therapeutic regeneration.

SESSION J8: Functional Biomimetic Systems II
Chairs: Noshir Langrana and David Lin
Thursday Morning, December 1, 2005
Room 201 (Hynes)

8:30 AM J8.1
Post-gelation Functionalization of Degradable Thiol-Ene Biomaterials.
Amber E. Rydholm[1], Nicole L. Held[1], Christopher N. Bowman[1,2] and Kristi S. Anseth[1,3]; [1]Chemical and Biological Engineering, University of Colorado, Boulder, Boulder, Colorado; [2]Restorative Dentistry, University of Colorado Health Sciences Center, Denver, Colorado; [3]Howard Hughes Medical Institute, University of Colorado, Boulder, Boulder, Colorado.

Degradable networks formed from the photopolymerization of multifunctional monomers are an important class of biomaterials with unique advantages related to the ability to process these materials under physiological conditions in the presence of tissues, cells, and even DNA. Unlike many other photopolymeric scaffolds which are formed through chain-growth polymerizations, thiol-ene photopolymers are formed through radically initiated step-growth reactions. There are a number of advantages that make polymers formed via this alternative reaction mechanism very attractive as biomaterials, including improved control of the polymer's mechanical properties and degradation behavior. Additionally, the step-growth reaction mechanism can be used to create pendant reactive sites throughout the crosslinked network that are available for further functionalization post-polymerization. The thiol-ene photopolymers pendant reactive site concentration is controllable through variations in the reaction conditions and initial monomer formulation. To demonstrate this experimentally, tetrathiol (e.g. pentaerythritol tetrakis(3-mercaptopropionate)) and diacrylate (e.g. poly(ethylene glycol) diacrylate, M_n =1000) monomers were combined to form monomer mixtures containing 0, 40 and 50 mol% thiol functional groups. These mixtures were printed onto glass slides using a microarray spotter and polymerized using 15mW/cm^2 of 365 nm light to form 400 μm polymer dots with pendant thiol functional groups. The pendant thiols were then modified through either photo-induced coupling or Michael-type addition reactions with vinyl ether and acrylate terminated poly(ethylene glycol) molecules or an acrylated fluorescein. Two-dimensional modification gradients were generated by varying the light exposure during photo-coupling. The thiol concentrations in the monomer, polymer, and modified polymer dots were determined from the FTIR absorbance peak between 2610-2480 cm^{-1} and the amount of fluorescein coupled to the polymer dots was determined using a DNA slide reader. Future work will highlight the advantages of having a photopolymer capable of being modified after the network has gelled rather than through the incorporation of functionalized molecules in the initial monomer mixture. For example, this procedure enables fundamental cell-material interactions to be easily probed through the generation of two-dimensional gradients, allows intricately patterned devices that control where various cell-material interactions are encouraged or prohibited, and is an excellent platform from which individualized or highly specialized diagnostic devices can be fabricated.

8:45 AM J8.2
Capturing Protein Activity in Simple Synthetic Polymers: Designing Novel Antimicrobial Agents.
Greg Tew, University of Mass-Amherst, Amherst, Massachusetts.

Learning to mimic the essential physiochemical properties of natural macromolecules, like proteins and RNA, would foster unprecedented properties in synthetic polymers and facilitate next generation materials. Our approach to this problem has been to mimic a large class of protein interactions in which the overall physiochemical properties and architecture of the protein are more important than any single residue or amino acid. The first target of these studies has been a class of membrane active peptides, commonly referred to as host defense peptides that display broad spectrum antimicrobial activity and are non-toxic to mammalian cells. This class of natural molecules grabbed our attention for a variety of reasons including their rather unique architecture which is a facially amphiphilic (FA) structure in which positively charged polar (P) and non-polar (NP) groups extend from opposite sides of the structure. This occurs regardless of whether the structure is a simple alpha-helix or a more complicated tertiary fold like that of a defensin peptide. We initiated a program to study cationic, FA polymers in order to combine the essential features of the natural host defense peptides with the conformational rigidity and optical properties of this backbone. Extended conformations were expected here by positioning P and NP groups at the appropriate location along the polymer backbone. Previous Langmuir data confirmed this FA architecture and antimicrobial assays showed that these polymers were reasonably active against several bacteria. During the course of our studies we discovered a series of molecules that showed extremely potent and broad spectrum activity as well as significant selectivity so that it was ~100 times more active toward bacteria than mammalian red blood cells. Detailed studies show these are membrane active. This talk will highlight our recent results include insight into the interactions with bacteria.

9:00 AM J8.3
Synthesis of Protein Polymers for Enzymatic Hydrogel Formation.
Nicolynn E. Davis[1], Yuri Zimenkov[2], Phillip B. Messersmith[2] and Annelise E. Barron[1]; [1]Department of Chemical and Biological Engineering, Northwestern University, Evanston, Illinois; [2]Biomedical Engineering Department, Northwestern University, Evanston, Illinois.

Genetic engineering and bacterial expression were used to create high-molecular weight protein polymers that can be enzymatically crosslinked into hydrogels with viscoelastic properties. The synthesis of protein polymers by genetic engineering allows for precisely controlled protein length (monodispersity) and specifically tailored amino acid sequence (controlled reactivity), which affect the properties of the resulting hydrogels. "Controlled cloning"[1] was used to produce highly repetitive DNA templates, encoding the amino acid sequences $(GKGTGA)_n$ and $(GKAGTGSA)_m$ with lengths n = 40, 80 and m = 30, 60, and 120, respectively. The proteins were expressed in *E.coli* with a 10X His-tag for Ni affinity chromatography purification. Target proteins were released from the His-tag by CNBr cleavage and purified by cation exchange chromatography. In this designed family of protein polymers, the number of potential enzymatic crosslinking sites is controlled by lysine spacing. The goal of the study is to utilize the reactive lysine residues for chemical grafting of short transglutaminase (TG) substrate peptides (Ac-EGGGQQQLQ-NH_2 and Ac-EGGGFKG-NH_2)[2] to produce a comb-like protein polymer conjugate that can be enzymatically crosslinked by TG. Rheological studies are planned to quantitatively determine the loss and storage moduli of the resulting hydrogels. 1) J. Won, A. E. Barron,

Macromolecules **2002**, *35*, 8281. 2) B. H. Hu, P. B. Messersmith, *J.Am.Chem.Soc* **2003**, *125*, 14298

9:15 AM J8.4
Using the fluorescent monomer ZnPP to synthesize the imprinted poly(ZnPP-co-MAA) for the binding investigation of creatinine. Wei-Chi Chen and Mei-Jywan Syu; Department of Chemical Engineering, National Cheng Kung University, Tainan, Taiwan.

Molecular imprinting known as one of the molecular recognition techniques was applied to the binding of creatinine. It is expected that from the success of the approach, further specific detection of creatinine clinically could be achieved. In addition to the above-mentioned technique, to increase the binding stability and sensitivity of the material, ZnPP (Zn(II) protoporphyrin), a fluorescent compound, was chosen as one of the functional monomers. It contains a Lewis acidic binding site Zn that could stabilize the binding with creatinine via the formation of a coordinated complex. The more stereo-effect was thus established as well. With two functional monomers, ZnPP and MAA (methacrylic acid), copolymerization was carried out with creatinine as the template for imprinting and EGDMA (ethyl glycol methacrylate) as the crosslinker. To increase the temperature of the copolymerization, not only the reaction time could be shorten therefore, but also the imprinting effect could be improved. The imprinted polymer prepared from higher proportions of MAA monomer and EGDMA crosslinker could achieve better performance evaluated from the aspects such as imprinting effect, binding ability and selectivity. The imprinted poly(ZnPP-co-MAA), the imprinted poly(ZnPP) and the imprinted poly(MAA) and the corresponding non-imprinted ones were compared. The imprinting factors, defined as the specific adsorbed amount of creatinine by the imprinted polymer divided by the one by the non-imprinted polymer, were 5.24 $\pm$ 0.02, 3.83 $\pm$ 0.49 and 1.50 $\pm$ 0.02, respectively. In addition, superior selectivity was observed from the imprinted poly(ZnPP-co-MAA) regarding the binding experiments from different mixture solutions comprised of creatinine, creatine, N-hydroxysuccinimide and 2-pyrrolidinone. In fact, to utilize ZnPP alone as the monomer resulted in, as expected, wore specific binding amount and selectivity in any occasion from the imprinted poly(ZnPP). It could be realized from its merely single coordination compared to the possible interaction forces such as hydrogen bonds, which might occur for other imprinted polymers. The fluorescent quenching from the imprinted poly(ZnPP-co-MAA) particles after the up-take of creatinine was also measured. Normally, it was excited at 423 nm and emitted at 590 nm. Compared to the other compounds such as creatinine, N-hydroxysuccinimide and 2-pyrrolidinone, the imprinted poly(ZnPP-co-MAA) after applied with creatinine showed more significant quenching effect. In summary, the creatinine imprinted copolymer via the incorporation of the fluorescent monomer ZnPP demonstrated its binding ability from a variety of aspects, which was believed to be the altogether contribution of both ZnPP and MAA.

10:00 AM J8.5
Development of Carbon Nanotube/Collagen Fiber Nanocomposites for Orthopaedic Implants. Souheil Zekri[1], Douglas Pringle[2], Thomas Koob[2] and Ashok Kumar[1]; [1]Mechanical Engineering, University of South Florida, Tampa, Florida; [2]Skeletal Biology, Shriners Hospital, Tampa, Florida.

One of the remaining and still significant challenges for orthopaedic surgery is to insure competent bonding between implants and the surrounding musculoskeletal tissues. While there is no doubt that new materials and techniques will emerge to replace existing orthopaedic hardware, the challenge still remains of how to bond these materials into the biological system. Furthermore, skeletal implants have the added challenge of conforming to similar mechanical characteristics to their biological component they are replacing. The first generation orthopaedic implants did not take into account certain surface characteristics of the interface such as grain size and wear resistance. Although much improved in performance, today s orthopaedic implants and surface coatings applied to these implants still use materials with grain sizes varying in the micro to meso scale (1 to 104 micrometer). This scale does not match the biological scale. There is a growing realization that integration of and attachment between artificial orthopaedic devices and native tissues can be optimized by using a rapidly emerging class of materials in the nanometer size range. The grain size of nanomaterials could be tailored to match the surrounding biological environment, which is expected to facilitate post surgical osteointegration. As a result, we propose a novel nanocomposite that could be tailored to serve as a tendon or ligament implant. The nanocomposite is composed of single wall carbon nanotube (SWCNT) and Nordihydroguaiaretic acid (NDGA) crosslinked collagen. Preliminary results show good SWCNT dispersion in the collagen solution without need for additional solvents. Furthermore, a 31% stiffness increase in the nanocomposite fiber has been observed with 5% SWCNT content. Due to the inherent partial biodegradability of the collagen fibers it is expected that the carbon nanotubes will play a mediation role in new bone formation around the implant, thereby increasing the mechanical strength of the interface. Furthermore, we expected to use the ability to tailor the stiffness of the nanocomposite to develop bone-like mechanical properties that can be used for bone augmentation and replacement. The properties of this composite can be adjusted by varying the relative proportions of the constituents and the fiber formation processes.

10:15 AM J8.6
Protease Responsive Polymer Hydrogel Beads.
Rein Vincent Ulijn, School of Materials, University of Manchester, Manchester, merseyside, United Kingdom.

Smart, intelligent or responsive polymer hydrogels respond to applied stimuli such as temperature, ionic strength, solvent polarity, electric/magnetic field or light by changes in their physical properties. Application of the appropriate stimulus results in the swelling or collapse of the macroscopic structure and dramatic changes in the molecular accessibility of the hydrogel are observed. Future applications of these materials are anticipated increasingly in biomedical settings, with potential applications in drug delivery, wound dressings or as implant coatings where the hydrogels selectively release or remove agents into or from the biological environment (smart biomaterials). The stimuli that are mentioned above are all rather non-selective and fluctuating temperature, pH, ionic strength, and solvent polarity can disrupt biological interactions. Many existing smart materials are therefore not ideally suited for applications in biomedical settings. Hence, there is a requirement for polymers that respond to stimuli that are truly compatible with biological conditions. The use of enzymes as selective stimuli to trigger phase transitions opens up new avenues: (a) enzymes are uniquely chemo-, regio-, and enantioselective. (b) Enzymes naturally work under mild conditions (aqueous, pH 5-8). (c) many enzymes catalyse reactions near surfaces1 and are therefore well equipped to catalyse reactions at interfaces. (d) enzymes play key roles in biological functions and disease states, there is scope for the development of hydrogels that respond selectively to these disease markers. In this communication we describe a new class of enzyme responsive polymers based on enzyme compatible poly ethylene glycol acrylamide (PEGA) hydrogel beads.2 These beads can be programmed to respond to certain enzymes only by attaching enzyme cleavable peptide sequences to the PEGA polymers. Molecular accessibility of these polymer beads can then be controlled selectively by polymer collapse in response to enzymes present in the biological environment. Since protease play key roles in various diseased states this approach has potential for selective removal of harmful macromolecules in response to disease specific enzymes. References: Halling, P.J., Ulijn, R.V., Flitsch, S.L. Curr. Opin. Biotechnol. 2005, in press. Doeze, R.H.P., Maltman, B.H., Egan, C.L., Ulijn, R.V., Flitsch, S.L., Angew. Chem. Int. Ed. 2004, 43, 3138-3141.

10:30 AM J8.7
Biomimetic approach to drug design: Potent polyvalent inhibitors of anthrax toxin. Amit Joshi[1], Kunal Gujraty[1], Saleem Basha[1], Arundhati Saraph[1], Jeremy Mogridge[2] and Ravi S. Kane[1]; [1]Chemical and Biological Engineering, Rensselaer Polytechnic Institute, Troy, New York; [2]Pathobiology and Laboratory Medicine, University of Toronto, Toronto, Ontario, Canada.

Nature has designed a way of strengthening inherently weak interactions through the phenomenon of polyvalency. This phenomenon, in which multiple receptors on one biological entity simultaneously bind to multiple ligands on another, enables orders of magnitude increase in binding affinity as compared to a monovalent interaction. We have used this principle to design inhibitors of anthrax toxin. Since this toxin is responsible for symptoms and death in anthrax, it is a prime target for therapeutic intervention. We have identified peptides that bind to proteins that are implicated in various steps of the intoxication pathway. In particular, we have targeted the heptameric cell-binding subunit of anthrax toxin, as well as the cellular receptors for the toxin. Polyvalent display of these peptides on a linear polymeric scaffold enhances their potency by several orders of magnitude. We have also developed a novel method to synthesize activated polymers of controlled molecular weight. We are using the resulting polymers to understand the relationship between the dimensions of a polyvalent inhibitor and its potency. We have also designed inhibitors based on a biocompatible scaffold. These studies will help in developing a potent antidote for anthrax toxin, which would complement antibiotic therapy, thereby offering an effective remedy.

10:45 AM J8.8
Enhancing Oxygen Supply in Polymeric Biomaterials Using Perfluorcarbons. Kyuongsik Chin, Surita R. Bhatia and Susan C.

Roberts; Chemical Engineering, University of Massachusetts Amherst, Amherst, Massachusetts.

In tissue engineering devices, cell viability and functionality is highly dependent on dissolved oxygen levels. Hypoxic or hyperoxic conditions can have detrimental effects on cell survival. In cell encapsulation systems, oxygen transport is often limited due to the presence of additional barriers. Consequently, encapsulated cells/tissues can easily suffer from oxygen deficiency. Perfluorocarbons (PFCs) have been utilized as oxygen vectors both in vivo (e.g., blood oxygenation during surgery) and in vitro (e.g., increase media dissolved oxygen levels in bioreactors). However, most studies address oxygen transport by freely moving PFC emulsions. Few studies have focused on enhancement of oxygen transport using embedded PFC droplets in cell encapsulation matrices (e.g., hydrogels). In previous studies, we have demonstrated enhancement of cellular metabolic activity through inclusion of PFCs in alginate encapsulation devices. In this study, we have developed a simple cubic model to predict oxygen diffusivity in alginate/PFC composite systems. Inclusion of PFCs had a positive effect on oxygen diffusivity as compared to alginate alone. PFC content and droplet size are key factors in controlling diffusivity. A diffusion-reaction model using Michaelis-Menten kinetics with theoretically obtained oxygen diffusivities was developed. This model was verified through experimental measurements of oxygen profiles in alginate/PFC devices and oxygen uptake rates using a perfusion reactor developed in our laboratory. Oxygen profiles were obtained using a ruthenium complex (Ru(dpp)3Cl2,tris(4,7-diphenyl-1,10-phenanthroline) ruthenium(II) dichloride) incorporated in the encapsulation matrix that allowed for visualization and quantification of dissolved oxygen levels via fluorescence microscopy. Additionally, we have collected metabolic data using the liver HepG2 cell line (e.g., glucose consumption, lactate production) to demonstrate enhancement of aerobic metabolism due to the presence of PFCs. All of these data taken together suggest that inclusion of PFCs in cell encapsulation/tissue engineering devices can have a positive impact on cellular function.

11:00 AM J8.9
Mechanical Characterizations of Multiphase Biogenic Polymer Blends from Poly(L-lactide) and Poly(methyl methacrylate). Kim-Phuong N. Le[1], Richard L. Lehman[1], Kenneth VanNess[2] and James D. Idol[1]; [1]Materials Science and Engineering, Rutgers University, Piscataway, New Jersey; [2]Physics, Washington and Lee University, Lexington, Virginia.

Melt processing of binary immiscible polymer systems has been a focus of our group as an economical and scalable route to achieve blends with synergistic or superior mechanical properties at and around the co-continuous region without the need of compatibilization. System of poly(L-lactide) (PLLA) and poly(methyl methacrylate) (PMMA) was selected to target bio-related applications, including load-bearing implants and cell scaffolds, where the biodegradability of PLLA will enable the integration of native tissue into the implants over time. Binary blends of PLLA and PMMA have been prepared and characterized over a large range of compositions. Tunable properties such as morphology, interconnectivity, resorbability and interfacial bonding control the long-term integrity of the material and influence the cell-material interaction. Thermal extrusion of the two polymers produced multi-phase blends with average domain size ranging from 10 to 25 microns, whereas blends prepared from thermal molding has much larger domain size (average 100 microns). Imaging (SEM and optical) and dynamic mechanical analysis (DMA) demonstrated immiscible behavior, at least in a metastable sense, and regions of co-continuity were identified. Such regions exhibit a well interconnected structure that ensures controlled release of resorbable PLLA. Modulated differential scanning calorimetry (MDSC) detected a broad and unexpected transition between 70 ^{o}C and 100 ^{o}C. The magnitude of this transition is greatest within co-continuous regions, suggesting the presence of a complex or other derivative of the two primary phases. This complex appears to provide a degree of compatibilization between the phases, thus inducing mechanical property synergism.

11:15 AM J8.10
Adhesion Properties between Swollen Hydrogels in Air. Daisuke Sakasegawa[1], Takaya Sato[1], Motoaki Goto[2] and Atsushi Suzuki[1]; [1]Environment and Information Sciences, YoKohama National University, Yokohama, Japan; [2]Saitama Daiichi Pharmaceutical Co., Ltd, Kasukabe, Japan.

Hydrogel refers to a chemically- or physically- crosslinked network of linear polymers immersed in water. Such structures have been shown to exhibit unique properties related to the super water absorbents. Many researches concerning the functional properties have been reported in various fields. However, systematic studies on the adhesion properties have not been extensively studied until now. Especially, the mechanism of the adhesion between gel/gel interfaces is still missing. In this paper, the adhesion properties between swollen hydrogels were studied on poly(sodium acrylate) (PSA) hydrogels that were physically crosslinked by aluminum ions. This hydrogel has been widely used in the medical fields, such as anti-inflammatory analgesic cataplasm. The PSA gels with different cross-linking densities were prepared by changing the amount of aluminum ions at gelation. For the measurements, a simple apparatus to obtain the adhesion properties was newly designed for the soft matters, where the adhesive force of the spot contact between the swollen hydrogels and the total energy to separate the contact were measured using the springs (phosphor bronze sheets) with strain gauges. The surface adhesion between swollen hydrogels was studied by this simple technique under the several different conditions in air at room temperature. In the present experiment, the adhesion force and the separation energy were measured under the three experimental parameters; the waiting period prior to the separation, the separation velocity and the normal load. In addition, the main constituent of the polymer networks of gel was partly replaced by poly(aclylic acid) (PAA) and the effects of PSA/PAA ratio on the adhesion properties were also examined. The adhesion force and the separation energy were found to depend on not only the experimental parameters but also the cross-linking densities and the PSA/PAA ratio. These results will be discussed in terms of the surface molecular interaction and the viscoelastic properties. Moreover, the effects of the dehydration on the adhesive properties will be also presented.

11:30 AM J8.11
Influence of Modulus Shift on the Performance of Hydrogel Actuators. Geoffrey M. Spinks[1], Gordon Wallace[2], Philip Whitten[2], Seon Jeong Kim[3], Su Ryon Shin[3] and Sun Il Kim[3]; [1]School of Mechanical, Materials and Mechatronic Engineering, University of Wollongong, Wollongong, New South Wales, Australia; [2]University of Wollongong, Wollongong, New South Wales, Australia; [3]Hanyang University, Seoul, South Korea.

Hydrogels have long been studied for possible application as artificial muscles, or actuator materials. The impressive volume change occurring in these materials (as stimulated by a change in pH, for example) is a very attractive feature for actuators. Efforts in recent times have focussed on improving response times by micro or even nano fibers. In this paper we consider the load-bearing response of hydrogel actuators. To be practically useful, the actuator material must be able to generate a volume (or shape) change when an external force is applied. Previous work has shown that if the actuator volume change is accompanied by a change in the material's elastic modulus, then the actuator strain changes with applied load. In most cases, the strain decreases with an increasing applied load. Our work has concentrated on chitosan gels stimulated by pH changes. When acidified the gels typically expand. A PVA/chitosan gel blend was found to expand less when acidified at high tensile stresses. Surprisingly, however, the same gel contracted when acidified under a (constant) compressive stress. Analysis of the mechanical behaviour of the gel during tension and compression provides a possible explanation for the unexpected behaviour. Results of other gel systems will also be presented in the paper.