SYMPOSIUM K
Biological and Bio-Inspired Materials and Devices
March 29 - April 1, 2005

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* Invited paper
The Structures and in width, and is composed of three related proteins known as serine hydrolases, which show significant assembly Hydrogen Bonding and structure of regulatory silaffins. Recently, we have characterized the silaffins from the diatom Thalassiosira pseudonana, a species exhibiting porous biosilica morphology. These approaches are facilitating our understanding of the process of cell wall formation in the diatom Thalassiosira pseudonana both structurally and genetically. Using light and electron microscopy, we identified intermediates in the formation of the diatom cell wall. We suggested that there are at least two distinct steps in this process. Using a proteomic approach, we identified proteins associated with an enriched cell wall fraction, and mass spectrometry was performed on this fraction. We have focused on two aspects of cellular metabolism related to silification: polyanmine synthesis and vesicle trafficking. Using known inhibitors of polyanmine synthesis, we have been able to modify the resulting silica structure, in a manner consistent with the two-step process seen by electron microscopy. These approaches are facilitating our understanding of the process of silica structure formation in diatoms, and constitute the first steps in manipulation of structure.

9:00 AM *K1.1
Biosilica Nanofabrication in Diatoms: The Structures and Properties of Regulatory Silaffins. Nils Kroeger1 and Nicole Poulsen2 1Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia; 2Biochemistry 1, University of Regensburg, Regensburg, Germany.

Diatoms are a large group of unicellular microalgae encased by silica cell walls that exhibit species-specific, mostly porous micro- and nanopatterns. Recently, unique proteins (silaffins) and unusually long polyanamines have been identified and implicated in silica morphogenesis. Based on the data obtained from work on the diatom Cyclotella nana, it has been suggested that diatom silica morphogenesis may generally require at least two components: LCPA, which accelerates silicic acid polycondensation, and regulatory silaffins that modulate the activity of LCPA. However, the architecture of C. fusiformis silaffins is rather unusual being mainly composed of long non-porous bands. Therefore, it has been unclear, if general conclusions about the mechanism of biosilica morphogenesis can be derived from studies on single species. Furthermore, elucidating the role of silaffins in biosilica morphogenesis has been hampered by the lack of structural and functional data of silaffins from other diatom species. Recently, we have characterized the silaffins from the diatom Thalassiosira pseudonana, a species exhibiting porous biosilica nanopatterns. It is demonstrated that this organism contains LCPA as well as regulatory silaffins, which drastically influenced silica formation in vitro. These results clearly support the hypothesis that silaffins play a key role in diatom biosilica nanofabrication. Chemical characterization of T. pseudonana silaffins and isolation of the corresponding genes enabled unprecedented insight into the structure of regulatory silaffins.

9:30 AM *K1.3
Control of Nanoparticle Assembly using DNA-Modified Diatom Templates. Nathaniel Long Rex, Emma Kate Payne, Shad Thaxton and Chad A. Mirkin; Chemistry, Northwestern University, Evanston, Illinois.

Microorganisms have been shown to be versatile templates for the organization of functional materials into larger scale functional architectures. An ideal biological template would be one that could be chemically modified in a versatile manner using conventional bench-top methods so that the interaction between the template and the nanoscale materials could be understood and easily controlled. To this end, we have investigated using diatoms as templates for the assembly of pre-fabricated nanoparticles. Specifically, we show that diatom cell walls can be covalently functionalized with DNA and then used as templates for the sequence-specific assembly of DNA-functionalized nanoparticles. We further demonstrate that the use of DNA can program the assembly of multiple layers of nanoparticles onto the template. This is a potentially powerful method for producing intricately ordered, hierarchically assembled macroscopic structures whose properties can be tuned at the nanoscale.

9:45 AM *K1.4
Blue Luminescent Biogenic Silicon-Germanium Oxide Nanocomposites. Shuhong Liu1, Clayton Jefferys1, Gregory L. Rorrer1, Chih-hung Chang1, Jun Jiao1 and James A. Hedberg2 1Chemical Engineering Department, Oregon State University, Corvallis, Oregon; 2Physics, Portland State University, Portland, Oregon.

Marine diatoms are a class of microalgae that possess cell walls composed of silica nanoparticles. These organisms actively assimilate silicic acid Si(OH)4 from seawater, polymerize silicic acid to silica nanoparticles by a protein-mediated precipitation process, and then assemble the silica nanoparticles into intricate patterns that constitute the cell wall microarchitecture (consists of around 30nm of SiO2 nanoparticles) of the diatom frustule. The biomineralization capacity of marine diatoms, Nitzschia, has been harnessed to biologically manufacture silicon oxide / germanium oxide nanocomposite materials. Germainium was incorporated into living diatom cell mass by a two-stage cultivation process. The micro- and nanostructures of biogenic oxide nanocomposites before and after post processing were characterized by electron diffraction, HR-TEM with EDX, and XRD. Photoluminescence (PL) measurements were performed on these biogenic oxide nanocomposites with the aim of elucidating the role of the organics. Strong blue photoluminescence was observed from samples treated with H2O2 and oxygen plasma. A clear blueshift was observed from the biogenic oxides with the addition of germanium. It is believed that self-trapped excitons affected by quantum confinement effect is responsible for the PL from these biogenic oxide nanocomposites. This research is supported by National Science Foundations Bioengineering and Environmental Systems program under grant number 09040648.
condensation of silicon alkoxide precursors into silica glass (SiO₂) and spatially direct deposition of the silica around the axial filament. Fiber diffraction studies demonstrate the long-range order that component proteins are arranged in a helical assembly. However, it is unclear how silicatein proteins organize into a filament or how the filament structure might influence inorganic product formation. Recent studies demonstrate that silicatein subunits self-assemble in vitro into filamentous structures, thereby recapitulating the biological process. In vitro assembly is influenced by temperature, pH and ionic strength, and has been investigated using static and dynamic light scattering and transmission electron microscopy to characterize assembly intermediates and kinetics. These experiments suggest a mechanism in which silicatein subunits assemble into 15 nm spheres that align in a linear arrangement to form protofilaments; these further assemble into higher order filamentous structures. Sequence differences between the silicatein and cathepsins, a family of well-characterized soluble cysteine proteases, reveal the presence of unique hydrophobic regions on the surface of silicatein. This suggests that unlike soluble non-enzymatic cathepsins, silicatein monomers associate via hydrophobic protein-protein interactions. A detailed understanding of the self-assembly mechanisms of the silicatein filament may provide new opportunities for nanofabrication through silicious biotechnology.

11:15 AM K1.5
Biologic Silification of 3-D Polyelectrolyte Scaffolds Assembled by Direct Writing. Mingjie Xu1, Eric Duoss2 and Jennifer A. Lewis2,1; 1Chemical & Biomolecular Engineering, University of Illinois at Urbana-Champaign, Urbana, Illinois; 2Materials Science and Engineering, University of Illinois at Urbana-Champaign, Urbana, Illinois.

We have developed a novel approach to patterning 3D polyelectrolyte scaffolds by direct-write assembly (DWA). Central to our approach is the creation of covalently bonded polyelectrolyte scaffolds that flow through fine deposition nozzles and then "set" almost instantaneously to facilitate shape retention as they span gaps in underlying layers. By tailoring ink composition, we have patterned polyaniline-rich scaffolds that, when introduced to silicic acid, will undergo silicification under ambient conditions. This mineralization process, which mimics diatom formation, yields high-resolution inorganic replicas of the filament or how the filament structure might influence inorganic product formation. Recent studies demonstrate that silicatein subunits self-assemble in vitro into filamentous structures, thereby recapitulating the biological process. In vitro assembly is influenced by temperature, pH and ionic strength, and has been investigated using static and dynamic light scattering and transmission electron microscopy to characterize assembly intermediates and kinetics. These experiments suggest a mechanism in which silicatein subunits assemble into 15 nm spheres that align in a linear arrangement to form protofilaments; these further assemble into higher order filamentous structures. Sequence differences between the silicatein and cathepsins, a family of well-characterized soluble cysteine proteases, reveal the presence of unique hydrophobic regions on the surface of silicatein. This suggests that unlike soluble non-enzymatic cathepsins, silicatein monomers associate via hydrophobic protein-protein interactions. A detailed understanding of the self-assembly mechanisms of the silicatein filament may provide new opportunities for nanofabrication through silicious biotechnology.

11:30 AM K1.6
Sol-Gel Syntheses on Single-CeS Scaffolds: Applying Complex Chemistry to Nature’s 3-D Nanstructured Templates. Michael Weatherspoon, Christopher Gaddis, Shawn Allan, Ye Cai, Michael Huisken, Robert Snyder and Kenneth Sandhage; Materials Science and Engineering, Georgia Institute of Technology, Atlanta, Georgia.

Intense global activity to produce advanced micro-to-nanoscale devices has led to increased biologically-inspired interest in nanoparticle structures. Certain micro-organisms are adept at assembling three-dimensional (3D) biomimetalized (bioclastic) micro-structures with precise shapes and fine (nanoscale) features. An exceptional variety of intricate 3-D structures are generated by aquatic micro-algae known as diatoms. Diatoms are single-celled organisms that assemble microshells (frustules) comprised of silica nanoparticles. While multifarious frustule shapes exist for potential use in applications, the range of potential device applications are limited by their ability to manipulate the chemistry of such 3-D assemblies, without altering the shape and fine features of the original bio-scaffolds, endows these structures with a much broader range of properties than are displayed by silica. Potential applications for such chemically-tailored, biologically-assembled structures will be discussed.

11:45 AM K1.9
Small-angle X-ray Scattering, FTIR and SEM Characterization of New PVA/TEOS Hybrids by Chemical Crosslinking. Herman Sauder Mansur and Alexandra Piscitelli Mansur; Metallurgical and Materials Engineering, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil.

In the present work, novel hybrid nanostructured composite materials were produced to be used in many potential applications such as biomedical, drug delivery systems, tri-dimensional scaffolds for biomaterials, biomechanical and tissue engineering, biomembranes and optical devices and others. Hybrids were synthesized by reacting poly (vinyl alcohol) (PVA) in aqueous solution with silicon alkoxide tetraethoxysilane (TEOS). PVA/TEOS hybrids were also modified in the nanometer-scale by crosslinking with bi-functional aldehyde, glutaraldehyde (GA) during the synthesis involving hydrolysis and policondensation of PVA/TEOS. The characterization of hybrids was carried out by using Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FTIR) and Small Angle X-ray Scattering (SAXS) techniques. FTIR spectra have showed major vibration bands associated with organic-inorganic chemical groups (OH, C=O, C-H, Si-O, Si=O) present in the hybrid composite PVA/TEOS. Also, typical absorption bands related to glutaraldehyde alkyl chain have indicated the crosslinking reaction of the hybrid network with glutaraldehyde (PVA/TEOS/GA). Small-angle X-ray scattering results have indicated different nanometer-size dispersions for PVA, PVA/TEOS hybrid and PVA/TEOS/GA chemically crosslinked hybrid. SEM photomicrographs have clearly identified quite different morphologies from chemically crosslinked polymer network dispersed to PVA hydrogel samples without glutaraldehyde reaction. The SAXS and FTIR spectroscopy characterizations have confirmed that hybrid materials were successfully obtained based on the combination of PVA and TEOS with glutaraldehyde crosslinked nanometer-scale network.

SESSION K2/L2: Joint Session: Functional Biomaterials and Biomimetis
Chairs: Trevor Douglas and William J. Landis
Tuesday Afternoon, March 29, 2005
Room 3002 (Moscone West)

1:30 PM *K2.1/L2.1
Biomimetic Silicification of 3-D Polyelectrolyte Scaffolds by Direct Writing. Mingjie Xu1, Eric Duoss2 and Jennifer A. Lewis2,1; 1Chemical & Biomolecular Engineering, University of Illinois at Urbana-Champaign, Urbana, Illinois; 2Materials Science and Engineering, University of Illinois at Urbana-Champaign, Urbana, Illinois.

The lamellar structure of bone is widespread, especially among the mammals. It was first identified by van Leeuwenhoek in 1691, and is still not fully understood. The basic motif resembles that of plywood, with parallel arrays of mineralized collagen fibrils arranged in layers with different orientations in a two-dimensional plane. Within the collagen fibril, are layers of very small plate-shaped crystals of carbonated apatite. Adjacent fibrils tend to have their layers aligned, but there is a progressive rotation of the fibrils from one surface plane of an individual lamella to the next. Here we confirm and amplify aspects of this structure using a Schottky FEG SEM with in-lens SE detector, and also show that there is a third structural element with mineralized collagen fibrils aligning the canaliculi, and hence being aligned perpendicular to the main lamellar plane. These fibrils originate from the main lamellar structure, but describe a 90 degree rotation to align themselves orthogonally to the lamellar plane. They may well fulfill a “pinning” function, by firmly bonding adjacent lamellae. Lamellae are often initially deposited as parallel arrays, but as a result of remodeling, reform as cylindrical secondary osteons. The elastic properties of lamellar bone are for the most part due to the lamellar structure, whereas the fracture properties are profoundly influenced by the cylindrical osteonal structure. Careful comparisons of lamellar bone types measured in water under tension and compression using electronic speckle pattern interferometry (ESPI), reveal new insights into the structure-mechanical properties of lamellar bone. Supported by grant DE006954 from the NIDCR to SW.

2:00 PM *K2.2/L2.2
Mechanisms Governing the Inelastic Deformation of Bone. Anthony Evans, Materials, UCSB, Santa Barbara, California.

To understand the inelastic response of cortical and trabecular bone, a three-part investigation has been conducted. In the first, a flexural test protocol has been designed and implemented that monitors the axial and transverse strains on both the tensile and compressive surfaces of cortical bone. The results are used to assess the relative contributions of dilatation and shear to the inelastic deformation. Unload/reload tests have characterized the hysteresis and provided

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Evidence from Atomic Force Microscope indentation, pulling and imaging together with evidence from macroscopic testing and enzymatic digestion suggests that collagen fibrils and mineral plates are not the only components of bone with a mechanical role. Therefore, it appears to be "glue" that binds mineralized collagen fibrils to other mineralized collagen fibrils. Order of magnitude calculations show that less than 1% by weight of this "glue" can have profound effects on the fracture resistance of bone, because it involves a remarkable natural toughening and strengthening system: sacrificial bonds and hidden length. The sacrificial bond-hidden length system can dissipate large amounts of work against entropic forces while stretching out the hidden length that is exposed when sacrificial bonds break. This apparent load-sharing between mineralized collagen fibrils is torn apart and slid relative to each other during bone fracture. In bone, this system depends on the presence of multivalent positive ions such as calcium ions. This dependence allows us to follow the involvement of the sacrificial bond-hidden length system right up to macroscopic fracture testing. Many bone matrix proteoglycans and glycoproteins have negatively charged groups at physiological pHs that could be bound together into sacrificial bonds by multivalent positive ions, and thus natural candidates for this "glue". We cannot, however, rule out a possible involvement of nonfibrillar collagen. Further research will be necessary to determine precisely which candidates or candidates are involved.

Evidence for a Possible Mechanical Role of Bone Matrix Proteoglycans and Glycoproteins. Paul Hansen, Georg Fantner, Johannes Knittl, Philipp Thurner, Leonid Pechenik, Marquesa Pinch, Peterin Turner, Georg Schütte, Blake Ericsson, Zachary Schirock, Laura Star Golde, Erik Strong and Simcha Frieda Udwin; Physics, University of California, Santa Barbara, Santa Barbara, California.

Evidence from Atomic Force Microscopy indentation, pulling and imaging together with evidence from macroscopic testing and enzymatic digestion suggests that collagen fibrils and mineral plates are not the only components of bone with a mechanical role. Therefore, it appears to be "glue" that binds mineralized collagen fibrils to other mineralized collagen fibrils. Order of magnitude calculations show that less than 1% by weight of this "glue" can have profound effects on the fracture resistance of bone, because it involves a remarkable natural toughening and strengthening system: sacrificial bonds and hidden length. The sacrificial bond-hidden length system can dissipate large amounts of work against entropic forces while stretching out the hidden length that is exposed when sacrificial bonds break. This apparent load-sharing between mineralized collagen fibrils is torn apart and slid relative to each other during bone fracture. In bone, this system depends on the presence of multivalent positive ions such as calcium ions. This dependence allows us to follow the involvement of the sacrificial bond-hidden length system right up to macroscopic fracture testing. Many bone matrix proteoglycans and glycoproteins have negatively charged groups at physiological pHs that could be bound together into sacrificial bonds by multivalent positive ions, and thus natural candidates for this "glue". We cannot, however, rule out a possible involvement of nonfibrillar collagen. Further research will be necessary to determine precisely which candidates or candidates are involved.


The interface between biology, chemistry, and materials science has motivated biomimetic approaches to the formation of inorganic nanomaterials. Biomolecules (proteins, peptides) and biomolecular architectures are being used as templates for the synthesis of inorganic nanomaterials. Our research efforts have been directed at not only understanding how biological organisms control nucleation and growth of inorganic materials, but also how this activity can be controlled in vitro. Biomolecular or biomimetic architectures can be used as building blocks in the bottom-up fabrication of inorganic structures. I will cover our efforts using biomolecules for growing inorganic structures and to exploit self-assembling structures for material synthesis by engineering desired functionalities into the self-assembling biomolecules for bottom-up fabrication.


Evidence for a Possible Mechanical Role of Bone Matrix Proteoglycans and Glycoproteins. Paul Hansen, Georg Fantner, Johannes Knittl, Philipp Thurner, Leonid Pechenik, Marquesa Pinch, Peterin Turner, Georg Schütte, Blake Ericsson, Zachary Schirock, Laura Star Golde, Erik Strong and Simcha Frieda Udwin; Physics, University of California, Santa Barbara, Santa Barbara, California.
K3.1 Synthesis and Structural Characterization of Silica Gels Prepared with Amino and Polyamine Cationic, Katy DePal1 and Nita Sara2,1; 1Chemistry, University of Wisconsin, Madison, Wisconsin; 2Geology and Geophysics, University of Wisconsin, Madison, Wisconsin.

Diatom and sponge proteins implicated in biogenic silica formation contain amine and polyanine moieties that have been shown to be necessary for protein catalytic activity. Previously, we have shown that simple amines and polyanines, chosen for their similarity to the moieties found in silica-precipitating proteins, can catalyze organosilicate hydrolysis and condensation at near-neutral pH. In this study, we examine the influence of these same catalysts on the formation of silica gels from tetraethylorthosilicate. We characterize the influence of amine type and pH on gelation time. In addition, we use light scattering techniques coupled with electron microscopy to determine how the choice of catalyst and pH condition can be used to tailor the resulting gel and precipitate morphology.

K3.2 Development of a Biocompatible Ink for Thermal Inkjet Printing. Helen E. Smith1, 2, Larry L. Brott 2, and Rajesh R. Kates3; 1Electrical Engineering, Marine Science Institute, Santa Barbara, California; 2Faculty of Physics, University of Santiago de Compostela, Spain; 3Faculty of Physics, University of Santiago de Compostela, Spain.

The increasing demand for patterned biomolecules requires a new method for such patterning which is less harsh than the current methods involving the utilization of photolithography, and UV processing. One possible alternative involves the use of ink jet printing technology, a fluid with vast potential and increasing application. The development of a water-based, biocompatible ink formulation for use with thermal ink jet printing will be discussed. The deposited ink adheres to diverse substrates while retaining the biocompatibility of the biomolecules. Additionally, a silica precipitating peptide dissolved in an aqueous solution can be patterned utilizing this technique, allowing for the formation of patterned silica nanoparticles on a flexible substrate.

K3.3 Polychaete Worm is an Expert Sand Mason. Hua Zhao, Chengjun Sun and Herbert Waite; Dept. of Mol Cellu and Dev Biology, Marine Science Institute, Santa Barbara, California.

The marine polychaete Phragmatopoma californica cements together building materials in its habitat such as sand and shell to construct its dwelling tubes in a manner closely resembling stone masonry. The cement is intriguing, first because so little is used, and second, because it solidifies rapidly from a liquid emulsion reminiscent of a complex coacervate. Several lines of evidence strongly suggest that phosphoserine-rich proteins are the dominant proteins in this cement. In this paper, we present two serine-rich precursor protein cDNA sequences which were isolated from the cDNA library constructed from the cement gland in the thorax of P. californica. Both cDNA encoded sequences consist of repeated motif (SinY, where n=3-12). Based on the deduced sequence, the amino acid composition of the two proteins is up to 60 mol% and 90 mol% serine, with almost 10 mol% tyrosine also present in both. These are the highest serine-containing proteins found so far in nature and, following phosphorylation, account for the high level of bound Mg and Ca in the cement.

K3.4 Elasticity and Piezoelectricity in Biological Systems on the Nanoscale: From Bones to Butterflies. Brian J. Rodriguez1, Alexei Gruverman2, and Sergei V. Kalinin1; 1Physics, North Carolina State University, Raleigh, North Carolina; 2Materials Science and Engineering, North Carolina State University, Raleigh, North Carolina; 3Condensed Matter Sciences Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Functional properties of biological systems are determined by an intricate set of mechanical and electromechanical interactions on the length scales that span several orders of magnitude: from macro to nano. Electromechanical coupling is a universal property of biological systems that was not observed when Luigi Galvani observed the effect of "animal electricity" in a frog leg. Understanding the inherently intertwined mechanical and electromechanical properties, such as elasticity and piezoelectricity, in living systems can provide an insight into the functionality of biomaterials and understand the biological relevance of these properties. Here, we present a scanning probe microscopy based approach for elastic and electromechanical imaging and spectroscopy of biological systems - from imaging the elasticity map in butterfly wings to differentiation of elastic and piezoelectric properties in enamel and dentine layers of human tooth to measuring the electromechanical response of a collagen-molecular bundle. This allows us to repeat Galvani's experiment on the nanoscale - more than two centuries later and with a million times higher resolution. Research performed as a Eugene P. Wigner Fellow (SVK), AG acknowledges financial support of the National Science Foundation (Grant No. DMR02-55629).

K3.5 Comparison of Piezoresistive and Optical Read-Out Methods for Microcantilever-Based Biosensor Fabricated by Surface Micromachining Technique. Kwang-Ho Na1, Hyung Do Kim1, Kyung Ah Yoo2, C. J. Kang1 and Yong-Sang Kim1; 1Electrical Engineering, Myongji University, Yongin, South Korea; 2Physics, Myongji University, Yongin, South Korea.

The widespread availability of inexpensive microfabricated cantilever in renewed interest in biosensor-based. Molecular recognition on the cantilever surface results in a mechanical response, that produces a microcantilever bending of few nm and a shift of the resonant frequency. The most common method is measuring the deflection of a cantilever because it is not sensitive to the damping in the liquid environment, in which only a single side is coated with receptor. Commonly the most wide spread detection technique, used in most commercial AFMs, is the optical leverage method that had advantage of high resolution. However it has many disadvantage in biosensor. It difficult to make it portable because external optical devices such as laser diode and photodiode are needed and measurements in opaque liquids is impossible. If the piezoresistive readout in biosensor is used to measure the deflection of the microcantilevers, the upper drawback will eliminate because of direct measurement without optical devices. We investigated the characteristics of piezoresistive and optical read-out methods after measuring the binding of microcantilever-based biosensor at the same time. The microcantilever-based biosensors fabricated by surface micromachining technique. The polysilicon piezoresistor was used for piezoresistive read-out and deposited by low pressure chemical vapor deposition (LPCVD) with a thickness of 300 nm. The microcantilever is bending from the difference of the surface stress caused by the formation of a glutaraldehyde/cystamine ditydroxychloride bilayer on the gold-coated microcantilever. The fluid cell for liquid flow was fabricated using PDMS and glass. The liquid flow was driven by gravity and the flow rate of 12-14μl/min was kept constant during the whole measurement. In order to evaluate the characteristics of the microcantilever, the cystamine terminated with thiol was covalently immobilized on the gold-coated side of the cantilever and glutaraldehyde that was attached with amine group in the cystamine was injected subsequently. This process was characterized by measuring the deflection of the cantilever in real time monitoring. The deflection of the cantilever was measured both by piezoresistive method and by optical read-out method at the same time for the analysis of the sensitivity and the resolution.

K3.6 Influence of the Crosslinked Chitosan Sphere and Films on the Calcium Carbonate Crystallization. Andronic David Neira-Carrillo1,2, Francisco Martinez2, Jaime Retorter1,2, Maria Soledad Fernandez1,3 and Jose Luis Arias1,2; 1Biology and Veterinary Science, University of Santiago, Santiago, Chile; 2Center for Advanced Interdisciplinary Research in Materials, CIMAT, Santiago, Chile; 3Faculty of Physics and Mathematics, University of Chile, Santiago, Chile.

Biomineralization is the process by which living forms influence the precipitation of mineral materials and leads to the formation of precisely controlled inorganic-organic composites, in which the minute organic component exerts substantial control on the mineralization process, which results in the formation of particles of uniform size, novel crystal morphology, specific crystallographic orientation and interesting properties. Crystal growth is typically heterogeneous crystallization and occurs in association with surfaces and occurs in a constrained volume. In nature, the living forms produce a geometrically well defined microenvironment, controlling not only the addition of the functionalized organic macromolecules but also variables such as localization and velocity of ions flux and the ions concentration in the constrained volume. In order to investigate the influence of the crosslinked chitosan sphere and films on the CaCO3 crystallization in vitro in a constrained volume, we have prepared sphere of chitosan in NaOH solution and compared with films. The crystallization method
X-ray Absorption Spectroscopy (XAS) has been used to characterize the structural evolution of bio-inspired crystallization systems. We present an XAS investigation of calcite growth on carboxyl-terminated alkanethiol self-assembled monolayers (SAMs) prepared on Au(111) substrates. In the natural world, bio-organisms utilize surface matrices of organic molecules to control the mode of mineral crystallization from solution. Elaborate, hierarchical inorganic assemblies are often generated, which can exhibit architecture on the sub-micron scale. Such precise engineering of crystal structure and shape, therefore, provides a direct application in the fabrication of inorganic components for optical and electronic devices. Hence, an understanding of the underlying physical processes is required to aid development of novel material growth technologies. Self-assembled monolayers of w-substituted alkanethiols serve as templates for patterned crystallization and, as such, mimic the natural processes of biomineralization. In addition, these systems offer a relative simplicity of structure. As a consequence, they represent useful models from which to characterize the interaction between organic and inorganic phases during crystal nucleation and growth. This interaction resides at the heart of biomineralization processes. XAS provides ideal capabilities for the investigation of structural development at the organic/inorganic interface during crystallization. Due to the chemical specificity of the technique, atoms at the buried interface can be probed directly. Furthermore, the X-ray Absorption Near Edge Structure (XANES), the first component of the X-ray absorption spectrum, allows for the determination of the coordination chemistry and bonding of specific elements in a sample. The amount of Ca2+ ions with the Fusarium sp. produces cruciform-shaped calcite crystals shows different morphologies and were related to the concentration of organic templates. Furthermore, a functionalized sulfate derivative of CaC03 with different morphologies was introduced into the blood stream, collagenous tissue that normally forms around the blood vessels and cell culture scaffolds. There are various techniques using plasma treatment, chemical vapor deposition, and graft copolymerization for surface modification of polymers. In particular, ozone treatment with UV light treatment can easily be carried out in various gases, solvent and solution media at room temperature without vacuum system and is suitable for heat unstable polymers. We have investigated the surface modification of polysulfone (PS) film using ozone treatment (O3/UV treatment) aiming at biomedical applications of the modified film. We confirmed that hydroxyl (OH) and carbonyl (C=O) groups are introduced on the PS film surface by the treatment in distilled water. In addition, the treatment in aqueous ammonia solution (O3/UV treatment) aims at biomedical applications of the modified film. These additional groups on the polymer surface are needed for protein immobilization. O3/UV treatment for polymer surfaces can be utilized to generate functional groups on the surface for modification with various biomolecules and living cells without any chemical treatment that causes contamination. In the present study, we have examined the immobilization of glucose oxidase (GOD; EC 1.1.3.4) as model enzyme on the PS film surface treated by O3/UV in water or aqueous ammonia solution and the relation between the enzyme activity and treatment media. Immobilization of GOD on PS films was carried out by the following method: PS films were placed in water or aqueous ammonia solution and aerated using ozone gas with irradiation of UV light. The films treated in water (W-PS) and in aqueous ammonia solution (A-PS) were immersed in an aqueous GOD solution (30 mg/mL) at room temperature for 24 hr. The total amount of GOD immobilized on the films was determined by the dye-binding method. The activity of GOD on the film was evaluated by decrease in the glucose concentration during the reaction between aqueous glucose solutions and GOD-immobilized film. The amount of GOD immobilized on W-PS was approximately 2 times higher than that on A-PS, which indicates that W-PS is better than A-PS for GOD immobilization. The glucose concentration over A-PS was lower than that over W-PS. Thus, the concentrations over W-PS and A-PS reduced from 28 mM to 25 mM and 23 mM, respectively. The activity of GOD on A-PS was higher than that on W-PS and a portion of GOD on W-PS became inactive. Hence, A-PS was concluded to be better than W-PS for making functional surface with GOD immobilized on it. The activity of GOD was found to depend on treating medium (water or aqueous ammonia solution) in O3/UV treatment.

K8.7
X-ray Absorption Spectroscopy Characterization of Crystal Growth on Organic Templates. Jonathan Lee1, Tony van Buuren1, Robert W. Meulenberg1, Trevor M. Willey1, Louis J. Terminello1, Robert W. Meulenberg1, Trevor M. Willey1, Louis J. Terminello1, Robert W. Meulenberg1, Trevor M. Willey1, Louis J. Terminello1

K8.10
Enhanced Biocompatibility of GPC by MeV ion Bombardment. Robert Zimmerman1, I. Gurhan1, C. Muntele1, S. Sarkisov1, M. Rodriguez2 and D. Ilia3, Daejin University, Normal, Alabama; 2Ege University Faculty of Engineering, Ismail, Turkey; 3University of Sao Paulo, Ribeirao Preto SP, Brazil.

Glycol Polymeric Carbon (GPC) is completely biocompatible and is widely used as a material for artificial heart valves and in other biomedical applications. Although it is ideally suited for fluid flow in the blood stream, collagenous tissue that normally forms around the mechanical parts of a GPC heart valve loses adhesion and embolizes downstream. We have shown that moderate fluence of MeV ions, especially oxygen ions, increases the surface roughness of GPC on a scale appropriate for enhancing tissue adhesion. Ion bombardment also increases the surface hardness of GPC to an extremely hard material. In vitro biocompatibility tests have been carried out with model cell lines to demonstrate that MeV ion bombardment can favorably influence the surface of GPC for biomedical applications.

K8.11

Hydroxyapatite (HAP) coating has been studied to improve biocompatibility of Ti or Ti-alloy implants. Micro-arc process (MAP) is an electrochemical route applicable for the HAP coating and the porous HAP films strongly bonded to Ti surface can be achieved. Also, it allows precision and easy coating on complicate implant parts. In this study amorphous calcium phosphate films with ~20 mm thickness were coated on Ti using MAP. The coated films were immersed in a buffer solution containing 0.78 ppm ions. The temperature and time period of the solution treatments were controlled for the crystallization kinetics study. X-ray diffraction (XRD) analysis on the films showed crystallinity of ~92% after the solution treatment at 40 °C for 12 h. The volume fraction values of

K8.9
Surface Treatment of Polystyrene with Ozone / UV in Water and Aqueous Ammonia Solution and Enzymatic Activity of Surface-Immobilized Glucose Oxidase. Ken Yasunaga1, Takuro N. Murakami1, Yoshitaka Hirono, Yoshihito Tokuoka1, Mitsuhiro Takahashi2 and Norimichi Kawashima1, 1Biomedical Engineering, Toin University of Yokohama, Yokohama, Kanagawa, Japan; 2Chemical Science and Engineering, Tokyo National College of Technology, Hachioji, Tokyo, Japan.

In recent years, the controlling of adsorption and adhesion of biomolecules, medicines, or cells on the polymer surface has attracted considerable attention in bioengineering due to the complexity of the biodegradable polymers and the influence on the surface of biological blood vessels and cell culture scaffolds. There are various techniques using plasma treatment, chemical vapor deposition, and graft copolymerization for surface modification of polymers. In particular, ozone treatment with UV light treatment can easily be carried out in various gases, solvent and solution media at room temperature without vacuum system and is suitable for heat unstable polymers. We have investigated the surface modification of polysulfone (PS) film using ozone treatment (O3/UV treatment) aiming at biomedical applications of the modified film. We confirmed that hydroxyl (OH) and carbonyl (C=O) groups are introduced on the PS film surface by the treatment in distilled water. In addition, the treatment in aqueous ammonia solution (O3/UV treatment) aims at biomedical applications of the modified film. These additional groups on the polymer surface are needed for protein immobilization. O3/UV treatment for polymer surfaces can be utilized to generate functional groups on the surface for modification with various biomolecules and living cells without any chemical treatment that causes contamination. In the present study, we have examined the immobilization of glucose oxidase (GOD; EC 1.1.3.4) as model enzyme on the PS film surface treated by O3/UV in water or aqueous ammonia solution and the relation between the enzyme activity and treatment media. Immobilization of GOD on PS films was carried out by the following method: PS films were placed in water or aqueous ammonia solution and aerated using ozone gas with irradiation of UV light. The films treated in water (W-PS) and in aqueous ammonia solution (A-PS) were immersed in an aqueous GOD solution (30 mg/mL) at room temperature for 24 hr. The total amount of GOD immobilized on the films was determined by the dye-binding method. The activity of GOD on the film was evaluated by decrease in the glucose concentration during the reaction between aqueous glucose solutions and GOD-immobilized film. The amount of GOD immobilized on W-PS was approximately 2 times higher than that on A-PS, which indicates that W-PS is better than A-PS for GOD immobilization. The glucose concentration over A-PS was lower than that over W-PS. Thus, the concentrations over W-PS and A-PS reduced from 28 mM to 25 mM and 23 mM, respectively. The activity of GOD on A-PS was higher than that on W-PS and a portion of GOD on W-PS became inactive. Hence, A-PS was concluded to be better than W-PS for making functional surface with GOD immobilized on it. The activity of GOD was found to depend on treating medium (water or aqueous ammonia solution) in O3/UV treatment.
HAp crystal formation in the amorphous films were obtained using a quantitative XRD analyses. Johnson-Mehli-Avrani (JMA) analyses were performed on a high-volume film density. The X-ray scattering exponent (u) value was determined from the slopes of JMA plots. From Arhenius plots the activation energy value was determined, and the nucleation and growth mechanism was considered for the HAp crystallization. Transmission electron microscopy (TEM) analyses were performed on the partially crystallized calcium phosphate films and compared to the results from JMA kinetics analyses.


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Material researchers have been interested in Nano-particles (NPs) because of their potentials to be used as nanotechnology key components. Metal or semiconductor NPs are small enough for the electron energy level to become separated as quantum dots. Magnetic NPs make it possible to produce high density storage media. Therefore, a lot of methods to produce NPs have been studied including the chemical synthesis, Laser ablation, and biological methods. We adopt a cage-shaped protein, apoferritin, to synthesize inorganic NPs in its internal cavity and propose a new process which utilizes the iron molecules to build nano-electronics devices. A key component (1). Apoferritin, the cellular iron-storage protein, is a spherical hollow shell composed of 24 polypeptide subunits and has the ability to encapsulate ferritin oxide in the cavity. The inner and outer diameters of the protein shell are about 7 nm and 12 nm respectively. There were preceding reports of metal complex NPs synthesis in the apoferritin cavity. We also succeeded to synthesize the FeNPs in the apoferritin cavity, for example, Co, Ni, Cr NPs (1). Besides these NPs, semiconductor NPs synthesis in the apoferritin cavity have been desired. However, there was only one report describing semiconductor CdS (3) and CdSe NPs synthesis (4) in the apoferritin cavity. To make compound semiconductor and ZnSe NPs in the apoferritin cavity, we designed a new chemical synthesis system which makes the chemical reaction of compound semiconductor element ions dramatically slow, so that the semiconductor NPs can be synthesized inside the apoferritin cavity. By altering reaction parameters, the ZnSe NPs are efficiently produced. These NPs were characterized by high resolution TEM, HRXRD, EDX, and BEELS analysis and they are proved to be ZnSe NPs. Furthermore, we employed some mutant apoferritins to study the difference of formation ratio (CFR) and to understand the mechanism of ZnSe NPs synthesis in the apoferritin cavity. From these results, three factors are proved to be important. (i) 3-fold channel; selective introduction of Zn ion into apoferritin cavity, (ii) apoferritin internal potential; Zn ion accumulation in the apoferritin cavity and (iii) the ferrocyanide center; Zn ion binding and then making the ZnSe nuclei at internal apoferritin cavity. The application of these obtained NPs as the key components of nano-electronics devices is in progress.


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Inorganic materials of nanometer order attract attention from application point of view. Many methods for fabrication of nano-inorganic materials were developed including physical and chemical methods. Inorganic materials required for the fabrications to be ordered as two-dimensional crystal as a first step for making the nanometric functional structures. We propose biological method to synthesize nano-inorganic materials and make two- or three-dimensional material of them. Ferritin is a spherical protein with a diameter of 12 nm. It has a cavity, 7 nm in diameter, surrounded by 24 polypeptide subunits. It is known that there are hydrophilic channels which penetrate the protein shell and are considered to be the pathway for the natural apoferritin. The cavity size consists of two types of subunits, H and L chains, the relative ratio of which varies with the type of biological species and organ. The H-subunit has a ferroxidase catalytic site at the interior surface where Fe(II) is oxidized to Fe(III) and was the L-subunit which has no ferroxidase activity. Under physiological conditions, apoferritin stores iron in the cavity as ferric-hydrate. Artificial biomaterialization of some other materials in the cavity has been reported. Despite its lack of ferroxidase activity, recombinant L-apolferitin, which consists of only L-subunits, can accumulate iron in the cavity. Recombinant L-apolferitin is known to crystallize two- or three-dimensionally by forming the cadmium sulfide (CdS) and selenium (Se) NPs through the incubation and drying process. Here, we report that iron streng protein recombinant L-apolferitin can accumulate nanosize indium oxide in the apoferritin internal cavity. The indium cores are formed in the recombinant L-apoferritin cavities by incubating indium and indium oxide in the apoferritin solution around pH 2.8 at room temperature for more than 24 h. The final concentration of each material were 0.1mg/ml recombinant L-apolferitin, 40mM HCl, 200mM monobasic sodium phosphate, 16 mM indium and 10mM indium oxide. Almost all incubated recombinant L-apolferitin formed indium oxide cores. The elements of obtained cores were determined by energy dispersive X-ray analysis (EDX). The EDX spectra show two indium peaks. High resolution TEM image showed the clear lattice lines which correspond Indium oxide crystal. These results indicate that recombinant L-apolferitin formed indium oxide core in the cavity.

K3.14 Metal-peptide Nanoassemblies: Combining the Principles of Supramolecular Coordination Chemistry with De Novo Protein Design. Michael Y. Ogawa, Mihail Tsurkan and Fei Xie; Department of Chemistry and Center for Photochemical Sciences, Bowling Green State University, Bowling Green, Ohio.

Our group is developing methods to exploit the directional bonding properties of coordination compounds to orient synthetic α-helical polypeptide domains in ways that can allow for the formation of novel nanostructured materials. The current approach utilizes both non-covalent and disulfide crosslinked coiled-coils as bridging ligands to join together Pt(II) coordination complexes in geometries that are dictated by the metal-dendrimer nanostructure centers, where each metal dendrimer is a Pt-peptide complex. The peptide sequences employed in this study were based on the IEALEGK heptad repeat which has been repeatedly used by our group to prepare a variety of metal-substituted, two-stranded α-helical coiled-coil peptide nanotubes. However, in this work the non-natural amino acid 4-pyridylalanine (Pal) was placed at position 14 of the sequence, which is the most solvent-exposed position of the second heptad repeat.

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K3.15 Selective Deposition of DNA-functionalized Gold Nanoparticles into Surface Nanopores. Angela J. Nieuw1, Krisann Bandyopadhyay1, 2, Eric Tsai1, Lin Ho1, Annie Tsao2 and Shenda M. Baker1, 2.

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We report the optimization of a novel approach for depositing individual DNA-functionalized gold nanoparticles into hexagonal arrays of surface nanopores generated from diblock copolymer thin films. These self-assembled DNA nanopore arrays can be used as scaffold to direct the ordered and selective secondary self-assembly of other...
DNA-functionalized nanoscopic entities, and are applicable in the development of novel biosensor surfaces. Deposition of individual DNA nanosphere arrays on the surface mimics the nanopore/s bottom SiOx surface while minimizing non-specific sticking between the two entities. We have obtained arrays of surface nanopores from hexagonally ordered thin poly(styrene)-b-poly(methylmethacrylate) (PS-PMMA) diblock copolymer films of sub-nanometer thickness, including silicon and quartz and glass. Nanoporous templates with pore diameters of 17±3 nm, 31±5 nm and 40±5 nm were fabricated through use of diblock copolymers of different molecular weights. Similarly, we have synthesized DNA-functionalized gold nanoparticles ranging from 0.5 to 15nm diameter colloidal gold. We will discuss how the relative sizes of these two nanoporous units affect the self-assembly process. To enable deposition of negatively charged DNA nanoparticles into the surface nanopores, we have functionalized these nanoporous templates with a variety of positively charged amine-containing silanes. We employed several approaches to achieve selective and effective functionalization of the nanoparticles on the silicon surface to minimize unwanted non-specific DNA interactions with the nanoporous walls. We further utilized electric fields to obtain more effective surface deposition of DNA nanospheres. These DNA nanosphere arrays have been characterized using atomic force microscopy (AFM) and X-ray photoelectron spectroscopy (XPS). We will also present preliminary studies on the use of these DNA nanosphere arrays for the controlled secondary self-assembly of other DNA-functionalized nanoscopic entities, on the integration of this system with a novel nucleic acid amplification technology, and on the detection of the immobilized DNA nanospheres using AFM as well as electronic methods.

K3.16
Nanostructure of β-Sheet Fibrils Constructed by Peptide Self-Assembly. Matthew S. Lamm1, Karthikan Rajagopal2, Joel P. Schneider3 and Darrin J. Pochan1; 1 Materials Science and Engineering, University of Delaware, Newark, Delaware; 2 Chemistry and Biochemistry, University of Delaware, Newark, Delaware.

A 20-residue peptide consisting of alternating valine and lysine residues flanking a tetra-lysine turn sequence has been shown to self-assemble via differing pathways into dramatically different materials. The primary structure of the turn sequence is critical in defining the different self-assembly pathways. Under appropriate solution conditions (pH, high temperature, and (or) strength), peptides with turn sequences designed to adopt a type I′ turn intramolecularly fold into β-hairpin conformations leading to the reversible assembly of β-sheet rich hydrogels. Alternatively, almost identical peptides differing in only the chirality of one turn sequence amino acid (L vs. D proline) do not fold into a β-hairpin but instead adopt an extended β-sheet conformation and reversibly assemble into fibrillar structures. These fibrillar structures are similar to classic β-sandwich or prion fibrils. Fibrils are formed by lateral association of individual β-sheet filaments providing an untwisted, un-branched and Darrinado hairpin (L vs. D proline) do not fold into a reversible assembly.

K3.18
Energy Transfer in Dendrimers. Jeffrey L. Krause, Quantum Theory Project, University of Florida, Gainesville, Florida.

We present a theoretical analysis of the dynamics of energy transfer in dendrimers. In one example, energy transfer occurs between donor groups on the periphery of the molecule and an acceptor group in the core. Detailed structural studies show that comparativeness rare events, in which the peripheral groups wrap to the core, dominate the energy transfer rates. Coarse-grained models, in which the rates are expressed in terms of an average constant, fail to capture the relevant dynamics. In a second example, energy transfer occurs via a series of independent steps down an energy gradient. We find that the venerable Förster model, which describes the Coulombic interaction in terms of point dipoles, is inadequate to determine the transfer rates. We employ an alternative method based on transition density cubes to analyze the effects of dynamics and temperature. The implications of our results for on-going ultrafast pump-probe experiments are discussed.

K3.19
Synthesis and Characterization of Multivalent Artificial Glycoproteins. Ying Wang1,2 and Kristi L. Kiick1,2; 1 Department of Materials Science and Engineering, University of Delaware, Newark, Delaware; 2 Delaware Biotechnology Institute, Newark, Delaware.

A family of alanine- and glutamine-rich artificial proteins, which contain glutamic acid residues at specific distances targeted to match the receptor spacing of certain toxins and lectins, have been synthesized via expression in E. coli. Previous work has demonstrated that the purified proteins form highly helical structures in aqueous solution, and the degree of helicity can be modified via alterations in solution conditions. Subsequent modification of these proteins with saccharides has been conducted via coupling of amine-functionalized saccharides with the glutamic acid functional groups of the protein polymer. Specifically, 1-amino-deoxy-b-D-galactose has been coupled to protein polymers of the type (AAAQAAQAQAAAEAAAQAAQAQ)6, via amide bond formation in the presence of the coupling reagent HBTru. The position of the glutamic acid residues in this sequence, coupled with their modification with galactose, was chosen to allow optimization of binding of the artificial glycoprotein to cholera toxin. The successful modification of the protein polymer with galactose was established via mass spectrometry, NMR spectroscopy, SDS-PAGE, and photometric measurements. Measurement of the photometric properties of the modified protein polymer via circular dichroism spectroscopy show that the glycosylated protein maintains a highly helical structure. Enzyme-linked immunosorbent assays suggest the avid binding of these glycopeptides to cholera toxin.

K3.20
Fabrication of Magnetic Hollow Silica Nanostructures for Bio-Applications. Weilie Zhao1, Lei Shao1,2, Daniela Cruntu1, Jianfeng Chen2 and Charles J. O'Connor1; 1 Advanced Materials Fabrication of Magnetic Hollow Silica Nanostructures for Bio-Applications. Weilie Zhao1, Lei Shao1,2, Daniela Cruntu1, Jianfeng Chen2 and Charles J. O'Connor1; 1 Advanced Materials
In this presentation, we report a successful synthesis of magnetic hollow silica nanospheres (MHSNS) that were functionalized with one step covalent attachment of PQQ and cystamine. The MHSNS were characterized by SEM, TEM, and SQUID. SEM and TEM results demonstrated that 1:100 ratio of PQQ to cystamine adsorbed within the first minute of the reaction. The cystamine adsorbed within the first minute of being adsorbed and was also stable during rinsing. This thylakoid-PQQ-cystamine-Au nanolayer stack allows the transfer of electrons generated by photosynthetic thylakoid membranes immobilized onto a gold substrate functionalized by self-assembled monolayers (SAMs) of cystamine and pyrrolodiquinoline quinone (PQQ) as part of our efforts to fabricate MEMS photosynthetic solar cells (PSC) and biosensors [1]. Thylakoid membranes are sub-cellular plant structures with an electricity generation capacity that can be used to detect biochemical agents such as herbicides that are essential for plant growth. The immobilization of thylakoids onto SAMs using carbodiimide chemistry was described. The kinetics of the SAMs and thylakoids were studied using the Sauerbrey equation, which relates the change in resonant frequency of the crystal to changes in mass attached to the crystal surface, including bound water. This approach can be used to study the interaction of thylakoids with SAMs and to develop biosensors for detecting bioactive molecules. The use of thylakoids as an electron donor for device engineering to induce partial COX activity is important for medicine and pharmacology. In particular, the design of biocompatible synthetic surfaces to control the interaction between a living system and an implanted material remains a major theme for biomaterials applications in medicine. The novel and low-cost electrostatic self-assembly (ESSA) technique provides an effective approach to fabricate various biomaterials on substrate surfaces, and gives great opportunity to develop unique biocompatible materials with well-organized interfaces. The incorporation of various ceramic biomaterials, water-soluble polymers and other materials such as heparin into self-assembled thin films can provide the opportunity to develop unique biocompatible materials with well-controlled interfaces. We have been successfully fabricated such biocompatible thin films on various substrates, including polymers and tubing's by the ESA process. The protein adsorption and hemocompatibility tests, including LDH, cell adhesion and clot mass, of the thin films have provided many interesting results. The thin films fabricated with biomaterials by ESA processing will have broad applications in tissue engineering, such as bone implants, anti-restenosis coating on medical devices (stents), and scaffolds to restore damaged organ structure.
novel materials and structures for a wide range of applications, including nanoelectronic and nanomechanical systems. Hierarchical structures that are assembled on a single nanometer scale, and independent control of each step are highly desirable since they offer flexibility in their design and versatility for applications.

In this talk, we describe the self-assembly of such hierarchical structures using Watson-Crick hybridization. The process begins with the construction of a 2D scaffold from a set of 21 synthetic oligonucleotides that are designed to hybridize to oligonucleotides bound to nanocomponents, resulting in rows of closely spaced hybridization sites. The extended feature used in this study is a 5′-(dA)15 sequence. After the formation of this DNA scaffolding, the 2D DNA scaffold is attached to a mica surface, thereby providing a template for later nanocomponent assembly. The prototype nanocomponents used in this study are composed of 6-nm Au nanoparticles functionalized with multiple strands of DNA (≈30 N). The strands are designed to hybridize to N thymine bases in the strands forming the inter-row spacing of 64 nm. In order to investigate the relationship between N (the number of thymine bases in the strands forming the nanocomponent shell) and the spacing between the Au particles along the rows, the self-assembly was studied for N over the range of 2 to 15. Characterization of the arrays by atomic force microscopy and transmission electron microscopy show that high-yield 2D arrays are formed for N in the range of 7 to 15. Arrays did not form for N less than 7, possibly because of aggregation of the components under the hybridization conditions. The spacing between components within the rows scale with N over the range of 7 to 15, with a corresponding gap between the Au particle cores of 2 to 15 nm. These results demonstrate the hierarchical self-assembly of nanocomponent arrays in which the inter-row spacing is controlled by the DNA scaffolding design and the spacing between components is controlled by the number of bases in the nanocomponent’s DNA shell.


There has been an intriguing suggestion that Staphylococcus aureus α-hemolysin (α-HL), a stable heptamer transmembrane protein pore, might be of use as the sensor element in a rapid, post-mortem single-molecule DNA sequencing process. This unnatural utilization of the protein has been the focus of intense work in the past few years. One fundamental requirement that had not been fully assessed is the pores sensitivity to single base pair mismatch. In this talk, we will show that α-HL can recognize ss-DNA with an apparent single nucleobase resolution. DNA strands that contain hairpin at one end are introduced at the cis side of a lipid bilayer containing a single oriented α-HL pore. DNA threading protocol and positive transmembrane holding potentials, formation of an α-HL-DNA pseudorotaxane is signified by the reduction in ion channel conductance caused by the presence of the ss-DNA inside the pore. Streptavidin binding to the biotinylated strand-edge at the trans side complete Rotaxane formation. Homopurine based rotaxanes and pseudorotaxanes are shown to possess significantly smaller current than homopyrimidine based structures. Series of adenine (a purine based nucleotide) DNA block copolymers and cytosine (a pyrimidine based nucleotide) DNA block copolymers and cysteine homopolymers with position-specific single-nucleotide adenine substitutions are used to discover and locate a specific nucleotide position responsible for the measured current, twenty nucleotides away from the hairpin. The pore location at which detection occurs is found to be near the trans entrance. The discovery that α-HL can recognize ss-DNA with an apparent single nucleobase resolution strengthens the case for its utility in rapid single-molecule DNA sequencing.

8:30 AM K3.4 Building from Bottom up: Fabrication of Materials using Peptide Motifs. Shaguang Zhang, Center for Biomedical Engineering NE417-379, Center for Bits & Atoms, Massachusetts Institute of Technology, Cambridge, Massachusetts.

Materials science has generally been associated with metallurgy, alloy ceramics, composites, polymer science, fiber spinning, coating, thin film, industrial surfactants and block copolymer development. That is about to change. Materials science will also expand to discovery and fabrication of biological and molecular materials with diverse structures, functionalities and utilities. The advent of nanobiotechnology and nanotechnology accelerated this trend. Similar as construction of an intricate architectural structure, diverse and numerous structural motifs are used to assemble a sophisticated complex. Nature has selected, produced and evolved numerous molecular architectural motifs over billions of years for particular functions that can now be used to fabricate the materials from the bottom up. Materials science will begin to harness nature's enormous power to benefit other disciplines and society.

9:00 AM K4.4 Cell Biology and Biochemistry of Coccolithophore Biominalization. Elina L. Gonzalez, Ecology and Evolutionary Biology, Univ of California-Los Angeles, Los Angeles, California.

The calcifying coccolithophore (Haptophyta) assembles a mineral and organic structure of exquisite design in a subcellular space while using a tool-kit comprised of only proteins, lipids and polysaccharides. These proteins are assembled by a cell membrane that defines this coccolith vesicle (cv). The cv maintains the conditions and carriers sufficient to import the raw materials (Ca2+ and CO32-) for calcite formation and, furthermore, to initiate self-assembly. The coccolith membrane, and its protein/enzyme component, is derived from the trans-Golg apparatus. The shape, size and structure of the organo-mineral complex are heritable. The mechanistic aspects of coccolith assembly are virtually unknown. How does calcium arrive at the cv? What is the identity of the carbon species taken up by the cv? How are Ca2+ and carbon species taken up into the cv? Is the calcification reaction exothermic or endothermic? How is the calcium ion released from the coccolithosome particle? One direction of inquiry has led to a proton-pumping ATPase, one of the protein complexes of the cv membrane. This calcium-stimulated proton pump is a multi-subunit enzyme. We have cloned and sequenced one of its components, the membrane-spanning subunit c, and found its amino acid sequence to be highly similar to that of the corresponding ATPase subunit from a wide range of taxa, including fruit flies and fish. We have proposed that the proton-pumping ATPase of the cv is involved in pH maintenance.


The development of self-assembled nanoscopic materials for controlled bottom-up fabrication of biomolecular devices is of current interest. In this regard, the self-assembly and the three-dimensional well-ordered structures of biomolecules could be used as excellent construction tools for the assembly of electronic devices. Along this line, several groups have demonstrated that amyloid fibrils can be used to create templates for metal nanowires, where metals were assembled to the amyloid fibril structures post-self-assembly of the fibrils. We have taken a different route and generated self-assembling electroactive bio-organic nanowires with 10 nm (widths) and lengths up to 10 μm. The nanowires are based on protein amyloid fibril co-assembled with conjugated oligoelectrolytes with a thiophene backbone. The nanowires are formed in acidic environment (pH 1.6) and at moderately elevated temperature (65° C). The luminescent oligomers were integrated into the fibril, which was evident from intensity and spectral distribution of the photoluminescence from the morphology of supramolecular structures in the form of bundled nanowires. The electro-optical properties of the wires are demonstrated with reversible electrochemical doping induced fluorescence quenching, thus demonstrating both power and transport and electroactivity. We suggest that this self-assembly method can be used for several types of electroactive organic materials. The possibility to synthesize and design amyloid forming peptides and proteins can be used in the formation of wires or carbon nanotubes can further be designed with address functions for anchoring of the wire to electrodes or other wires. Furthermore, changes in optical properties of the conjugated oligoelectrolytes can be used to probe amyloid fibril formation. As stated above, electroactivity of the wires can be present during amyloid fibril formation or be added to pre-formed fibrils, which results in a different spectral distribution. The conformation changes of the protein results in alterations in the geometry and the electronic structure of the oligoelectrolyte chains, which have been monitored with absorption and emission spectroscopy. This principle has lately been shown when conjugated polymers (CPs) were used as optical probes to monitor conformation changes[1] and calcium-induced conformational changes in calmodulin[2]. References: (1) Nilsson, K. P.; Rydberg, J.;

10:15 AM K4.6
Fabrication of Hierarchical Structures using Protein Cages as Building Blocks. Michael T. Klem1,3,4, Eric Gillilite2,3,4, Peter Sue1,3,4, Mark Allen1,3,4, Mark Young2,3,4 and Trevor Douglas1,3,4; 1Chemistry & Biochemistry, Montana State University, Bozeman, Montana; 2Materials Science, Montana State University, Bozeman, Montana; 3Center for Biophores NanoMaterials, Montana State University, Bozeman, Montana; 4Thermal Biology Institute, Montana State University, Bozeman, Montana.

Biomimetic approaches to materials chemistry have provided a new avenue for the synthesis and assembly of nanomaterials. There is growing interest in materials chemistry to take advantage of the physical and biological properties of proteins for designing the next generation of nanoscale materials. Protein cages exist in a variety of sizes and shapes and the protein surfaces can be used as synthetic platforms for chemical modification. The ability of some protein cages to form self-assembled arrays on a variety of substrates is of significant interest as possible precursors to interesting nanomaterials such as magnetic semiconductors. This work makes use of chemical and genetically modified spherical protein cages like the Cowpea Chlorotic Mottle Virus (CCMV) that self assemble into hierarchical structures by design on length scales approaching microns in 2 or 3 dimensions. A solid phase synthetic approach was adopted to generate protein cages with an asymmetric presentation of selected functional groups. Construction of protein cages with differing presentations of functional groups allow for the formation of larger structures through a "lock and key" mechanism. The incorporation of magnetic nanoparticles was also performed generating 2- and 3-dimensional materials. The resulting structures were then characterized by a variety of techniques including TEM, AFM, IR, magnetometry, and dynamic light scattering. This work highlights three important concepts. First, through a combination of genetic and chemical modification we can engineer chemical functionality to symmetry related sites on the exterior protein cage surface. Second, through a solid phase synthesis approach, we can selectively block functional groups in a spatially controlled manner, thereby breaking the symmetry of the protein cage with asymmetric functional groups can impart the ability to form hierarchical structures in 2- or 3-dimensions.

10:30 AM K4.7
Self-Assembled Material Nanostructure Defined By The Secondary Structure Of Amphiphilic Diblock Copolyptides. Lisa M. Potter1, Darrin J. Pochan1, Timothy Denning1, Eric Holowka2 and Andrew Nowak3; 1Materials Science and Engineering, University of Delaware, Newark, Delaware; 2Bioengineering, University of California, Los Angeles, Los Angeles, California.

Diblock copolyptides consisting of a hydrophilic lysine (K) block and a hydrophobic leucine (L) block were designed to self assemble due to their amphiphilic nature and the defined secondary structure of the hydrophobic block. In aqueous solution, these copolyptides assemble into diblock hydrogels at low volume fractions of polymer (vol. fraction poly peptide >0.5 wt%). The micro and nanoscale morphology of the hydrogels has been well characterized using laser scanning confocal microscopy (LSCM), cryogenic transmission electron microscopy (cryo-TEM), and ultrasmall and small angle neutron scattering (USANS and SANS). The microscopy and scattering data revealed the formation of membranes on the nanoscale that interconnect to create an innately porous network on the nano microscale. Altering the molecular design, such as hydrophobic to hydrophilic block ratios and overall polypeptide chain length, affected the overall hydrogel rigidity, determined rheologically, with very weak hydrogels being formed from chains with <10 mol% hydrophobic content and with degrees of polymerization above 350 and below 120. Decreasing the polypeptide chain length to below a degree of polymerization ~100 resulted in vesicle formation on the microscale without disrupting the nanoscale morphology. Alterations to the assembly pathway resulted in the formation of twisted fibrils or hexagonal single crystals. In all assemblies, regardless of the resulting structure, the secondary structure of the hydrophobic block remains an a-helix, and the hydrophilic cilia on the surface indicate the nanoscale assembly of these polypeptides into membranes is intrinsic to this class of molecules whereas any hierarchical, microscale assembly can be controlled through the assembly environment and molecular design.

10:45 AM K4.8
Biomimetic Nanotechnology: Exquisite Control Over Self-Assembly of Polypeptide Multilayer Nanofilms. Bingyun Li, Yang Zhong and Donald T. Haynie; Louisiana Tech University, Ruston, Louisiana.

This work describes the development of a novel methodology for the fabrication and stabilization of multilayer peptide nanofilms. The specific approach involves the exceptionally versatile technique of nanomanufacturing known as electrostatic self-assembly (ESA) of oppositely-charged polyelectrolytes. The polyelectrolytes of greatest interest here are designed peptide chains. The amino acid cysteine is introduced as it permits reversible disulfide bond formation (chemical cross-linking) between peptide chains. The role of solution pH, ionic strength, and adsorption of designed S-DSS peptides has been investigated in detail using a combination of physical techniques. Moreover, we have studied the role and importance of disulfide bond formations in stabilizing ESA multilayer nanofilms. Our results show that the ESA process can be exquisitely controlled, and substantially increased stability of S-DSS films is achieved by disulfide cross-linking. Unlike other cross-linking methods (e.g. glutaraldehyde treatment), disulfide bond formation is "peptide-inherent" and is transferable. The resulting film forms a basis for applications of biologically inspired polypeptide films with desired properties and superior stability. This is expected to lead to broader applications of ESA nano-assembly in biotechnology and biomedicine.

11:00 AM K4.9
Bio-inspired Design of Modular Multi-domain Polymers for Advanced Biomaterials. Zhibin Guan, Jason T. Roland, Dora Guzman and Jane Z. Bai; Chemistry, University of California, Irvine, California.

Native load-bearing proteins, such as the muscle protein titin, exhibit a remarkable degree of combined toughness, strength, and elasticity which have yet to be matched by synthetic materials. Single molecule nanomechanical studies on titin and other modular proteins suggest that these exceptional properties arise from a modular elongation mechanism. The sequential unfolding allows modular biopolymers to sustain a large force over the whole extension of the chain, which makes the polymer strong, along with a large area under the force-extension curve, making it tough as well. In addition, when the external force is removed, the unfolded domains of modular proteins will refold automatically, making them elastic. Inspired by nature, one research effort in my group is aimed at designing synthetic molecules that form high order structures by programming non-covalent interactions into polymer chain. The goal is to achieve synthetic biomaterials with combined strength, toughness and elasticity. Three classes of well-defined modular polymers have been synthesized in our laboratory: (1) using quasihydrogen-bonding motif f2-ureidon-4-pyrimidone (Upy) to direct the formation loops along a polymer chain (J. Am. Chem. Soc. 2004, 126, 2058); (2) using a peptidomimetic beta-sheet based double-closed loop (DCL) as module (J. Am. Chem. Soc. ASAP); and (3) an engineered protein G domain III as module. Single molecule force-extension experiments revealed the sequential unfolding of the loops or domains as these modular polymers are stretched, resulting in sawtooth-pattered curves similar to those seen in titin and other biopolymers. In this talk, we will discuss our designs, syntheses and single-molecule studies of polymers having modular domain structures.

11:15 AM K4.10
Synthesis of Transient Amorphous Calcium Carbonate, and Its Transformation to Oriented Calcite Crystals. Yong-Jin Han1,2, Kwang-Sup Song1,2, Guo-Jun Zhang2, Hitoshi Kato3,4 and Joanna Aizenberg1,5; 1Materials Research Department, Bell Laboratories, Lucent Technologies, Murray Hill, New Jersey; 2Lawrence Livermore National Laboratory, Livermore, California.

The ability of biological systems to exert precise control over the shape, size, orientation and hierarchical ordering of inorganic materials is of great interest to chemists and materials scientists, who are beginning to recognize its potential in the development of new synthetic pathways and in the improvement of existing materials. Amorphous calcium carbonate (ACC), one of many polymorphs of calcium carbonate but highly biologically organized, is often observed in biology, with somewhat enigmatic function, ranging from the structural support to the storage of calcium and carbonate ions for future precipitation in a more stable crystalline form. In this presentation, we report our experimental results on ACC crystal synthesis using the latter biological strategy. We form transient ACC film on a specially designed self-assembled monolayer (SAM) and use it to induce ACC into oriented calcite crystals. The results show that oriented calcite crystals are then induced by the nucleation site into the system without additional calcium or carbonate ions. The mechanism of phase stabilization and recrystallization as well as its implication in biomimetic fabrication will be discussed.

11:30 AM K4.11
The Characterization of a Novel DNA Immobilization on Diamond by Carboxyl Aromatic Amidation. Junghoon Yang1,2, Kwang-Sup Song1,2, Guo-Jun Zhang2, Hiroshi Kato3,4 and Joanna Aizenberg1,5; 1Materials Research Department, Bell Laboratories, Lucent Technologies, Murray Hill, New Jersey; 2Lawrence Livermore National Laboratory, Livermore, California.
Since diamond has excellent electrical and chemical properties such as wide potential window, chemical-physical stability, biocompatibility and so on, diamond is expected as a suitable material for electrochemical and biological applications. In case, H-terminated diamond surface are directly functionalized with DNA oligonucleotides were immobilized on the micro-structurally patterned diamond surfaces. The novel immobilization method by the surface functionalization is more effective on diamond surface than on other materials. First, the space between the binding sites of probe DNA has to be considered for hybridization efficiency because the excess density of probe DNA decreases the probability of hybridization. The partially aminoated diamond surface is not necessary to space due to control density of amino function, directly. In addition, amine bindings between aminoated-diamond surface and CAC or probe DNA and CAC are more stable than van der walls binding because carboxylic group have been included unshared electron more than aldehyde group. Therefore, direct immobilization method can overcome this disadvantage, weak interaction between probe DNA and other functional groups. For the surface-functionalized by DNA, aminoated diamond surface was formed in ammonia gas on H-terminated diamond surface by UV. Then, all of aminoated-diamond surface except for the masked micropatterns by gold has been reserved in order to improve signal-to-background ratio. The immobilization specificity was evaluated by means of 5 amino-modified oligonucleotides labeled with Cy-5 at its 3’ end attached onto microstructured patterns treated different CAC (EDC for formation of carbonyl bond). We confirm that probe DNA oligonucleotides were immobilized on diamond substrate and hybridized with target DNA. Also, Fluorescence intensity increased when target DNA was hybridized on carboxylated diamond surface with both trimesic acid and terephthalated diamond surface because the different density of carboxylic function. The fluorescence intensity increased by a factor of 1.7, which reflected the fact that the carboxylated binding-site of terephthalated diamond surface as high amount of trimesic acid. The 0.3 difference is due to steric effect between immobilized probe DNA.

Metallic Pd and Pt Nanoparticles on S-layer Proteins Studied by Small Angle X-ray and Neutron Scattering.

Barbara Aichmayer 1,2, Michael Mertig 1, Alexander Kirchner 1, Oskar Paris 3, Ingoen Jaeger 1,2 and Peter Fratzl 3; 1Department of Material Physics, University of Leoben, Leoben, Austria; 2Erich Schnrid Institute of Materials Science, Austrian Academy of Sciences, Leoben, Austria; 3Department of Biomaterials, Max Planck Institute of Colloids and Interfaces, Potsdam, Germany; 4Mxс-Bergmann-Center of Biomaterials, University of Technology, Dresden, Germany.

Pd and Pt nanoparticles were produced using isolated S-layer proteins (crystalline bacterial surface layers which form regular two-dimensional arrays) as templates. After adsorption of the precursor material (dissolved K2PdCl4 or K2PtCl4), either a chemical reducing agent or exposure to synchrotron radiation led to the formation of monodisperse metallic nanoparticles with radii from 1.5 to 8 nm depending on the reaction conditions. In order to study the metalization process and the interplay between the metal loading and the protein template, we characterized the S-layers as well as the size and arrangement of the metal particles by means of small angle x-ray and neutron scattering. In-situ investigations of the synchrotron radiation induced formation of Pd nanoparticles on the S-layers of S. solonosovica ureae showed that the protein templates were indeed capable of stabilizing particles with radii of 1.2-1.5 nm. We did not observe any coarsening during our investigations. The small angle scattering studies were complemented by UV/Vis spectroscopy and transmission electron microscopy investigations which showed that the metal particles were preferentially formed in the pores of the periodic protein structure. From our results we conclude that S-layer proteins are suitable templates to produce stable arrays of metallic Pd and Pt nanoparticles. We acknowledge the financial support of the EU project BIO-CAT (European Union grant number GRD1-2001-40424).
DNA using the nucleotide sequence and hybridization as address tags and as recognition events may be possible for more advanced applications. In addition to the use of tagged oligonucleotides, DNA hybridization techniques are used to determine the complex formation between biological and luminescent conjugated polyelectrolytes - a surface plasmon resonance study, Biosensor and Bioelectronics, In Press. [2] K. P. R. Nilsson and Ole Inganas, Chip and solution detection of DNA hybridization using a luminescent switerring polystyrene derivative, Nature Materials 2, 419-424.

2:15 PM K5.5
Bio-Evolved Inspiration of Zinc Oxide-based Materials
Directed by Amino Acids and Peptides: Joachim Bill, Peter Gerstel, Rudolf Hoffmann and Fritz Alldinger; Max-Planck-Institut fuer Metallfororschung/INAM, University of Stuttgart, Stuttgart, Germany.

Zinc oxide represents a promising material for functional applications, e.g. as a phosphor or a transparent and conductive oxide. Due to these applications, the elucidation of dynamic processes of zinc oxide-based materials and devices is a challenging research item. For that purpose, the deposition from aqueous media basically provides an effective means. However, in the case of zinc oxide the deposition behavior is strongly controlled by the tendency to form elongated micron-sized crystals that make the formation of smooth homogeneous nanostuctures impossible. Recently, the preparation of zinc oxide-based nanostructured films was reported [1]. This method involves macromolecular organic additives like graft copolymers and homopolymers, which are added to the aqueous deposition medium. Owing to the interaction of these polymers with zinc oxide in solution the growth of elongated films is hindered and organic/inorganic hybrid nanostructures are formed. The subsequent assembly of these particles can be controlled by organically modified surfaces and yields nanostructured films with luminescent properties. Living systems also apply a variety of organic molecules that interact with metal ions. One example is the zinc finger, which is made of amino acid units. These units built up a configuration of a DNA-binding protein that resembles a finger and contains usually histidine and cysteine, binding a zinc ion. Within this paper the suitability of amino acids and oligopeptides as structure-directing agents is discussed. According to that bioinspired approach these biomolecules were investigated in a combinatorial way with respect to the evolution of zinc oxide-based architectures. Whereas the before mentioned macromolecular organic additives mainly support film formation these small molecules are able to trigger the morphology in general, dependent on the kind and sequence of the amino acid units. It will be shown that this approach opens up pathways for nanomanufacturing as well as for the deposition of a variety of morphologies ranging from grain-like via two up to three dimensional features. Besides morphological aspects the structural characterization of these solids by means of X-ray diffraction, electron and atomic force microscopy as well as photoelectron and infrared spectroscopy will be discussed in order to extract the function of the biomolecules with regard to the formation of the inorganic phases. In addition, functional properties of these wettability, thermal and biological behavior, will be treated. [1] see e.g. R. C. Hoffmann, S. Jia, J. Bill, M. R. De Guire, F. Alldinger, “Influences of Additives on the Formation of ZnO Thin Films by Forced Hydrolysis”, J. Ceram. Soc. Jpn, Supplement 112 (2001).

2:30 PM K5.4
Biomimetic Synthesis of Metal Oxides using Protein Cages as Receptors: Wieland, J. Mark Allen, Mark Young and Trevor Douglas; Chemistry and Biochemistry, Montana State University, Bozeman, Montana; 3Center for Bioinspired Nanomaterials, Montana State University, Bozeman, Montana.

Supramolecular proteins that assemble into cage like architectures have been used for nanomaterials synthesis. Specifically ferritin and ferritin like proteins can be used as size constrained reaction vessels that encapsulate materials that have sizes that are determined by the internal dimensions of the protein cage. These include minerals, metal nanoparticles, and inorganic materials and have been used in a number of applications for controlled synthesis. It has been shown that the cavity of ferritin like proteins can be used to control the formation of frustrated complexes that are only stable at the molecular level. For example, ferritin is the protein that encapsulates the superparamagnetic properties found in natural magnetite. However, when the same material is prepared inside the ferritin cage using synthetic methods, the resulting magnetic behavior is that of a para-magnetic material. In contrast, the use of a similar ferritin like protein, Listeria innocua, the resulting behavior is superparamagnetic at room temperature. However, the same material is prepared inside the Listeria cage, the resulting magnetic behavior is that of a ferromagnetic material as determined by ac magnetic susceptibility measurements and vibrating sample magnetometry. This illustrates the utility of using protein cage architectures for materials synthesis where size dependent magnetic properties can be tuned by choice of the protein cage.

2:45 PM K5.5
Biotemplate-Based Nanostructuring and Metallization: Mark Allen, Sinan Balci, Anan Kadri, Fabian Boes, Alexander M. Bittner, Christina Wege, Holger Jesko and Klaus Kern; 1Exp. II, Max-Planck-Institut MSP, Halle, Sachsen-Anhalt, Germany; 2Nanostructure science, Max-Planck-Institut FKF, Stuttgart, Germany; 3Molekulare Biologie und Virologie der Pflanzen, University of Stuttgart, Stuttgart, Germany.

Ordered structures in the nanometer scale become more and more important in research and applications. Our group has been using biomolecules as self-assembled templates with intrinsic order, e.g. biomolecules. We present a biochemical approach to surface structuring and metallization on the nanoscale. The templates we use are Tobacco mosaic virus (TMV) and Potato virus X (PVX), nanotubular plant viruses that consists of self-assembled RNA strands and proteins. The immobilization of the viruses is attained on well-defined inorganic surfaces. We work with bare and chemically modified substrates or with self-assembled monolayers. In this way we achieve a fine tuning of the chemical properties of the surface in order to address the chemical groups on the viral surface. For the approach to ordered structures of TMV on surfaces we use the method of micro contact printing. Scanning probe microscopy, especially non-contact AFM. For the metallization we employ the technique of electron deposition of metals. By making use of the metal cation binding properties of certain amino acid moieties we are able to deposit small clusters of gold, nickel, cobalt either on the outer surface or inside the nanoscale virus channel. With this method nanowires of nickel and cobalt with 3 nm diameter and up to 600 nm lengths can be achieved. The metallization is investigated with a transmission electron microscope.

3:30 PM K5.6
Molecular Chaperones for Stimuli-Responsive Nanomachines: Takuzo Aida and Kazuhi Kimbara; Department of Chemistry and Biotechnology, The University of Tokyo, Tokyo, Japan.

Chaperonin proteins GroEL and T.th cmp assist folding of newly formed or denatured proteins by the action of ATP. These chaperonins have a nanoscopic cylindrical cavity, where denatured proteins are captured. The included proteins, after folding, are released by the action of ATP as the result of an induced conformational change of the cavity [Roseman, A.M.; Chen, S.; White, H.; Braig, K.; Saibil, H.R. Cell 1996, 87, 241]. We succeeded in the formation of the first ATP responsive nanomachine, based on the unique biological mechanism involving chaperonin proteins into the chemistry of semiconductor nanoparticles [Ishii, D.; Kimbara, K.; Ishida Y.; Ishii, N.; Ozochi, M.; Yohda, M.; Aida, T. Nature 2003, 426, 238]. CdS nanoparticles (2-4 nm) were prepared according to a method reported by Marakoshi and coworkers. For the complexation with chaperonins, a DMF solution of CdS nanoparticles was added to a Tris/HC1 buffer solution of GroEL and T.th cmpl. Complexes of T.th cmpl and GroEL with CdS nanoparticles were isolated by size-exclusion chromatography (SEC). For T.th cmpl an analytical SEC trace of this solution with an UV/fluorescence dual detector showed single, sharp elution peaks, which were superimposable with one another at nearly the same elution volume as intact T.th cmpl. Since intact T.th cmpl is hardly fluorescent, the above results strongly indicate that CdS nanoparticles are colocalized with T.th cmpl to form an inclusion complex [T.th cmpl/CdS nanoparticle]. A TEM picture of [T.th cmpl/CdS nanoparticle] showed that the central part of the cavity of T.th cmpl is considerably dark, due to the presence of CdS nanoparticles within the protein cavity. [T.th cmpl/CdS nanoparticle] is thermally stable and maintains its characteristic photoluminescence activity up to 80 C, which is a range for which GroEL/C contact printing, is only up to 60 C. When a Tris/HC1 buffer solution of ATP containing magnesium chloride was added to a buffer solution of [T.th cmpl/CdS nanoparticle] containing KC1, the mixture turned slightly cloudy within few seconds, which is consistent with centrifugation was no longer fluorescent. The release of CdS nanoparticles from [T.th cmpl/CdS nanoparticle] by the action of ATP was clearly demonstrated by analytical SEC with an UV/fluorescence dual detector. After the addition of ATP, the UV response of the SEC trace of [T.th cmpl/CdS nanoparticle] showed a sharp elution peak assignable to T.th cmpl and an additional broad peak in the lower molecular weight region due to ATP and its hydrolyzed products, which was corresponding to the response of ATP for these two peaks. The fraction corresponding to T.th cmpl, isolated
Structural Investigation of Bi-Directed Hierarchical Assembly of Multifunctional Materials from Proteins and Dilablock Copolymers. Linda Katherine Molnar1,2, Dongseok Shin3, Rebekah Breitenkamp3, Todd Emrick2 and Thomas P. Russell2.

1. NAS Ance Center for Nanotechnology, NASA Ames Research Center, Moffett Field, California; 2. Ecolab Corporation, Sunnyvale, California; 3. Polymer Science and Engineering, University of Massachusetts, Amherst, Massachusetts.

Our goal is to combine polymers and proteins to form a hierarchically structured multifunctional material that has both the highly ordered structure of the polymer and the order and biological function of the protein. By chemically linking or embedding self-assembling biological elements in stipling block copolymers, the self-organization of the biomolecules can affect the evolution of the block copolymers, and similarly, the structural evolution of the copolymers can affect self-assembly of the proteins. The materials utilized were an asymmetric diblock copolymer of poly styrene (PS) and polyvinylpyrolidone (PVP) denoted P(S-b-EO) and horse sperm ferritin (HSF). Solvent casting has been shown to be a viable and rapid route by which arrays of nanoscopic PEO domains oriented normal to the surface can be produced in a glassy PS matrix in films with thickness several times the period of the copolymer. HSF in modified (genetic or chemical) or unmodified forms has shown varying effects on the self-assembly and microphase separation of the P(S-b-EO) block copolymer. Our goals are to design a system to aid in probing studies of the phase outcomes for the fabrication of hybrid inorganic-organic materials. Ferritins are iron storage protein cages belonging to Class II dicon-ribonucleotides proteins composed of 24 subunits arranged in octahedral symmetry, which are capable of forming 12-nm diameter cage with a 7.5-8.0 nm diameter cavity. About 4000 iron atoms can be stored in the central core of ferritins as iron (III) hydroxide, mainly ferric hydroxide (FeO(OH)). Most ferritins are very stable particles, and can withstand 65 °C in aqueous suspensions. Temperature can affect the stability and activity of proteins. Many studies have demonstrated that ferritins can be used as nanoreactors for the formation of inorganic nanocrystals. Combined with their ability to self-assemble into well-defined 2-D structures on a solid surface or at an interface as well as the possibility of detecting direct electron transfer from ferritin to gold electrodes, makes them attractive biomolecules for both structural studies and applications. The production of these new multifunctional materials with the order of polymers and the specificity of proteins are expected to form the functional component of devices where both organization and specific biological function are required, e.g., sensors, adaptable materials, biocompatible devices.

Magnetite-PLGA Microparticles As Potential Oral Delivery Vehicles of Therapeutic Proteins. Jiannan Chen1, Dennis Ho2, Chris Yim2, Omid C. Farokhzad2, and Arnaldo Varela-Ramirez1.

1. Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts; 2. Department of Anesthesiology, Brigham and Women’s Hospital, Harvard Medical School, Cambridge, Massachusetts.

Oral delivery of peptides and protein therapeutics has been extensively studied in the past several decades. This route of administration is preferred because it increases patient compliance and comfort over parenteral route, which accounts for the administration of more than ninety percent of FDA approved protein drugs. Clinically effective oral delivery systems for protein therapeutics have not been established. Proteins administered orally result in extremely poor absorption into circulatory system due to the degradation of the proteins in harsh acidic and enzymatic conditions in stomach and low permeation of proteins across the intestinal membranes. Polymeric nano- and micro-particles are found to effectively protect encapsulated protein from acidic or enzymatic degradation in gastrointestinal tract, but majority of the particular protein delivery vehicles pass through small intestines without being absorbed. Retention of these oral delivery vehicles in the small intestine for an extended period of time may result in an increase of the degradation rates of the encapsulated particulate systems. Polymeric nanoparticles have been used in in-vivo imaging and targeted drug delivery, and can successfully localize imaging ligands or drugs in disease sites. In this study, we investigated magnetic-responsive particulate carriers for oral protein delivery. Magnetite (Fe3O4) nanoparticles co-encapsulated with insulin into poly(lactide-co-glycolide) (PLGA) microparticles (1-10 mm size, visualized by SEM) through the double-emulsion method. After the magnetite-insulin-PLGA microparticles were orally administered to mice, a magnetic field was created externally to the mouse abdomen around the mouse intestine area to retain or slow down the transit of these magnetite-insulin-PLGA microparticles. A single administration of 50 units of these microparticles to fasted mice resulted in a gradual decrease of whole blood glucose concentration from 130 mg/dl at t = 0 to 50 mg/dl at t = 12 hours in the presence of external magnetic field. As a comparison, the whole blood glucose concentration in mice administered in the same way in the absence of an external magnet reached the lowest level of 70 mg/dl at t = 8 hours and recovered to above 80 mg/dl after t = 10 hours. Other data that show effective oral insulin delivery using this magnetic-responsive particulate system will also be presented.
reflected light. There are a few experimental reports on the phase detection. In most of the studies, the phase detection is based on the heterodyne detection because it provides real-time measurement that is important for biological affinity kinetic measurements. The rotating analyzer method is another way for phase detection. Although it does not provide the rapid detection, the advantages of the rotating analyzer method are easily understood with the help of the heterodyne technique, are (1) the optical geometry is simple (2) it can be applied to spectroscopic measurements (3) it is applicable not only to sensor applications such as affinity biosensors but also highly sensitive spectroscopy. However, there are only a few reports that adopted the rotating analyzer method for phase detection and little is known about the details in the analysis. In this paper we demonstrate the highly sensitive sensing of molecular adsorption on metal surfaces using the rotating analyzer method under the condition. We found that the method yields the RI resolution of the ambient medium 10-7, which is almost compatible with that of the heterodyne method and is two orders of magnitude better than that of the conventional SPR method based on the angular detection. Real-time measurement using this method is also demonstrated.


Chemically functionalized apertures with large aspect ratios constitute a platform of choice for bio-organism sensing. We fabricated apertures on pre-patterned silicon platforms with aspect ratios up to 300:1 driven by ion beam etching. We employed both dry/wet oxidation. Localized DNA functionalization of the nanopores was then achieved by self-assembled monolayer chemistry combined with a silicon nitride mask. Ionic flow measurements recorded through single nanopores revealed selectivity for the DNA-functionalized devices will be investigated by measuring the duration and amplitude of the ion current blockades generated by single DNA-functionalized beads electrophoretically driven through the apertures. Future applications include the selective detection of bacteria and viruses. This work was performed under the auspices of the U.S. Department of Energy at Lawrence Livermore National Laboratory under contract No. W-7405-ENG-48. UCRL-ABS-207152.


Box jellyfish are simple animals with an unusually impressive set of eyes. Each individual has four sensory clubs carrying two different imaging eyes and two different pairs of non-imaging eyes. This makes for a total number of 24 eyes of four different types. The information from the eyes is processed in one nervous centre in each sensory club, and the animal does not possess any other central processing units. The consequence is that the behaviour of the jellyfish is controlled by four parallel brains. Our unusual design is sufficient for a relatively complex visual behaviour. The animals display courtship behaviour and are very skilled at using visual cues to position themselves very close to the shore where food is abundant. The visual behaviours indicate that the animals can detect and adequately respond to a number of different visual cues. Electrophysiological measurements suggest the possibility of colour vision, and optical investigations have shown that the imaging eyes deliver information which is unlike that of all other eyes in the animal kingdom. In other eyes, the photoreceptors (raw pixels) generally display very narrow Gaussian receptive fields, which is the basis for high-resolution visual tasks. In box jellyfish, the receptive fields of individual photoreceptor cells are very wide and thus are capable of reflecting the complex visual field of the nervous system.

9:00 AM *K6.4 Controlling the Flow of Color: Photonic Systems in Lepidoptera. Peter Veklerov; School of Physics, University of Exeter, Exeter, Devon, United Kingdom.

Studies of structural color in terrestrial systems, such as those associated with brightly coloured insects and birds, have seen significant advances in the past few years. Conformational changes of synthetic polymers and 3D periodicity potentially manipulates the flow of light in all directions. In certain butterflies the common 3D structure, referred to as inverse-opal, comprises hollow voids surrounded by a honeycomb of crystals. The physical structure of this inverse-opal hexagonal crystal, while varying somewhat between examined species, appears consistently as a mixture of tetrahedral and cubic structures. Recently, band gap calculations indicate that a perfect tetrahedral configuration offers the highest reflectivity over the broadest angle range for a given refractive index contrast between component media. Given constraints associated with cuticular morphology and the ecological and intraspecific selection pressures thought to exist, it appears that the physical design of this photonic structure has converged towards one of the most optically efficient configurations. Numerous studies, of them very recent, have sought to discover and characterise the phase-matching range of material tuning, for example, through the use of natural series. Many of them have revealed system designs that have evolved and existed naturally for millennia and that were, until their discovery in nature, thought to have been the recent product of technological innovation. Particularly, this talk will describe recent advances made in the characterisation of Lepidopteran photonic systems, believed to be among the most diverse in the natural world.


We are interested in learning from natural optical systems, whose hierarchically nested and hybrid character offers outstanding optical properties and enable multi-faceted roles. It was found that in light-sensitive brittlestars, uniform microlens arrays with integrated pores are formed, which allow high-magnification of pigment-filled chromatophore cells through the pores. Such biolens exhibit tunable transmission, refraction, wavefront aberration, numerical aperture, refraction, aperture, wavelength selectivity, minimization of the "cross-talk" between the lenses, and improved angular selectivity. By using only the unique lens structure and functionality, we have created porous hexagonal microlens arrays that are analogous to the biological systems. Using the porous network as a microfluidic system, we induce the pigment movement in the brittlestar and are able to actuate the movement of the lens. The results indicate the possibility of actuating different liquids (e.g. with selective refractive index and/or including dyes that absorb light) in and out of pores, to achieve a wide range of tunability of the lens optical properties.

9:45 AM K6.6 Conjugated Polyelectrolytes: Conformation Sensitive Optical Probes for the Recording of Biological Processes. Peter Nilsson 1, Anna Herland 1, Johan Olsson 1, Johan Rydberg 2, Lars Balter 2, Peter Konradsson 2, Per Hammarstrom 2 and Olle Inganas 1; 1IFM, Biomedical and Organic Electronics, Linkoping, Sweden; 2IM, Organic Chemistry, Linkoping, Sweden; 3IFM, Chemistry, Linkoping, Sweden.

Conjugated polyelectrolytes with ionic side chains have been used for the detection of single nucleotide polymorphism (SNP) in DNA [1], conformational alterations of synthetic peptides [2, 3], conformational alterations of Calmodulin and binding of Ca2+-activated Calmodulin (CaM) to Calcinemia (a part of the intra-cellular signal pathway) [4], and amyloid fibril formation of amyloidogenic proteins. Inspired by the conformational flexibility of polymers, also found in conjugated polyelectrolytes, allows direct connection between the geometry of the conjugated polyelectrolyte backbone, an alteration of the absorption and emission properties from the polyelectrolyte to be observed. The detection method is based on non-covalent assembly of the conjugated polyelectrolyte and the receptor of interest. Upon
exposure to the analyte of interest or a conformational change of the receptor, a conformational alteration of the polymer backbone and a change in the optical properties of the sensor occurs, and these alterations can be detected by absorption or fluorescence from the polymer. The introduction of the receptor molecules will induce aggregation of the polymer chains and planarization of the polymer backbone, detected as a decrease of the intensity and a red shift of the fluorescence. Upon addition of the desired analyte the intensity of the emitted light is increased and blue shifted. This phenomenon is due to a separation of the polymer chains and twisting of the polymer backbone, induced by the receptor-receptor interaction. Conjugated polyelectrolyte can be used as novel conformation sensitive optical probes for the detection of several biomolecular processes. The biomolecular interaction or the conformational alteration of the biomolecule acts as an alteration of the geometry and the electronic structure of the bound polyelectrolye chains and has so far been detected by absorption and emission, but electrical detection of these transitions will most likely be possible. We foresee that the present mechanism may be used for detection of a variety of biomolecular processes, and that the simplicity and the diversity of this methodology make it suitable for making inexpensive and DNA-chips for rapid detection of biomolecular recognition.

The development of small particles of microporous Si as components of an autonomous system that can sense, perform rudimentary signal processing, communicate, and move about will be described. Each particle contains in its nanostructure the necessary components to allow self-assembly, spectroscopic identification, chemical sensing, and motion. The particles are generated by electrochemically etching discrete porous one-dimensional dielectric stack (rugate) mirrors into silicon. The complex multilayered structure produces a distinctive reflectivity spectrum that serves as a robust code, allowing positive identification and discrimination of many different types of particles. The intensity and wavelength of reflected light is determined in part by the refractive index of the porous nanostructure, which is modified by adsorption of vapors or by specific chemical reactions within the chemically modified porous Si matrix. Sensing is accomplished when liquid or vapor infuses into the porous mirrors, inducing predictable shifts in the optical spectra. Chemically asymmetric particles are also described, which can spontaneously align at an organic liquid/water interface. Finally, the synthesis of photonic crystals with superparamagnetic nanoparticles of Fe3O4 incorporated into the porous nanostructure will be described. The addition of magnetic properties allows the materials to chaperone microliter-scale liquid droplets by application of an external magnetic field.

Biointerface of Magnetic Nanoparticles and Incorporation into a Magnetic Tunnel Junction Based Biosensor. Stephanie Grancharov1, 2, Hao Zeng1, Shouheng Sun1, Stephen O’Brien2, Chris Murray1, John Kirtley1 and Glenn Helf1; 1Nanostructure Materials and Devices, IBM, Yorktown Heights, New York; 2Applied Physics and Applied Math, Columbia University, New York, New York.

Methods of synthesizing monodisperse, strongly magnetic ferrite nanoparticles (NPs) have been well documented, however, encapsulation of particles within a layer of biologically active molecules and their subsequent stabilization in a physiological medium has not yet been reported. Such particles could be used to bind and transport proteins. Following introduction into a living organism, these particles could provide a means of monitoring and influencing cellular processes. Perhaps most importantly, these bio-functionalized magnetic NPs would provide a crucial component in the sub-cellular delivery of therapeutic drugs and nucleic acids. We report the successful bio-functionalization of 12 nm manganese ferrite (MnFe2O4) NPs. We demonstrate the site-specific binding of biotin and DNA functionalization NPs onto protein and complex biological structures, respectively. Imaging these substrates with scanning confocal microscopy, we show that these particles retain their magnetic properties. Finally, we demonstrate a novel method of detecting the hybridization of these magnetic NPs within microarrays at room temperature using a bioassay comprised of a protein patterned magnetic lens functioned to detect in orthogonal magnetic fields.

11:15 AM K6.9
Electropermeabilization of Mammalian Cells Visualized with Fluorescent Semiconductor Nanocrystals (Quantum Dots). Yinghua Sun1, 2, P. Thomas Vernier2, Jingjing Wang3, Andras Kuthi3, Laura Marra3, 4 and Martin A. Gundersen1, 2, 1Department of Macromolecular Science, University of Southern California, Los Angeles, California; 2Department of Electrical Engineering/Electrophysics, University of Southern California, Los Angeles, California; 3MOSIS, Information Sciences Institute, University of Southern California, Los Angeles, California; 4Cellular-Scale Medical Center, University of Southern California, Los Angeles, California; 5Department of Biomedical Engineering, University of Southern California, Los Angeles, California.

As a bright and stable inorganic fluorescence probe quantum dots have great advantages for the long-term cell observation and in vivo tracking. Electroporation or electropermeabilization has been effectively studied recently as an effective technology for gene transfection and drug delivery. Pulsed electric fields can induce reversible membrane breakdown and result in dynamic pores in the cell membrane. This makes the cell permeable to specific molecules in short time but these pores can spontaneously reseal without lethal consequences for the cell. It is found the transfer of small molecules with electroporation is very rapid and efficiency but the big challenge is the transfer of macromolecules, such as plasmids. According to the experiment and simulation result, we did not enter cells freely by diffusion like small molecules or ions. An electropermeabilization model has been proposed and discussed by Zirnstein and Taisei that electric field can trap large particles on the cell membrane and then cells take them inside by some uncertain kinetics in a relatively long time. In this work the behavior and processes of electroporation were tracked in 48 hours with quantum dots focused on their special properties. First it is the fluorescent nanometer-scale particles with the similar size as DNA molecules. Secondly quantum dots can keep photostability and chemical stability inside cells for over days or even weeks without strong decay in fluorescence and obvious effect on the cell viability. In addition, their high brightness is very helpful to track the motion of small amount of particles in a dynamic live system. The long-term observations revealed that quantum particles were trapped on the cell membrane after pulsing and the trapping efficiency of nanoparticles depends on cell types and particle sizes. Most quantum dots taken by cells aggregated in lysosomes in the cytoplasm without entering nuclei. And the motion of quantum dots inside cells and the behavior of myeloma and ovarian cells were tracked in 48 hours after electroporation.

11:30 AM K6.10
Biocompatible Gd@C60 (Carbon Nanoshell) as Advance Contrast Agents for Magnetic Resonance Imaging. Balaji Sethuraman1, 2, 3, Keith Hartman1, 2, Kyle Kissell1, 2, 3, Lesa Walker1, 2, 3, Lon J. Wilson1, 2, 3, Irene Rusilova4, Robert D. Bokshar5, Sabrina Luss6, Eva Toth7, Alain Borel8, Gabriel Gonzalez9, Lothar Helml0, and Andre E. Merbach1, 2, 3, 1Chemistry Dept, Rice University, Houston, Texas; 2Center for Nanoscale Science and Technology, Rice University, Houston, Texas; 3Center for Biological and Environmental Nanotechnology, Rice University, Houston, Texas; 4Texas Center for Superconductivity, University of Houston, Houston, Texas; 5TITA Research Inc., Westlake Village, California; 6Chimie Moleculaire et Biologique, Ecole Polytechnique Federal de Lausanne, Lausanne, Vaud, Switzerland; 7Departament de Quimica Inorganica, Universitat de Barcelona, Barcelona, Barcelona, Spain.

Paramagnetic gadolinium-containing carbon nanostructures are currently being pursued as a new paradigm in magnetic resonance imaging (MRI) contrast agent (CA) design. These compounds offer fundamental advantages over commercially-available Gd-based chelated compounds, the most important being the complete lack of metal-ion dissociation under physiological conditions. Additionally, these systems exhibit unusually large proton relaxivities (efficacies) and infer the potential for intra-cellular and extracellular targeting recent work with derivatized Gd@C60-based nanomaterials, Gd@C60(COOH)2)10 and Gd@C60(OH)2, have shown them to exhibit exceptionally large proton relaxivities approaching 1000 mM-1s-1, approximately twenty times that currently used MRI contrast agents. Water proton relaxivities have been measured in aqueous solution at variable temperature (278-335 K) and, for the first time, as a function of magnetic field (5T-14 T), revealing high brightness is very helpful to track the motion of small amount of particles in a dynamic live system. The long-term observations revealed that nanometer particles were trapped on the cell membrane after pulsing and the trapping efficiency of nanoparticles depends on cell types and particle sizes. Most quantum dots taken by cells aggregated in lysosomes in the cytoplasm without entering nuclei. And the motion of quantum dots inside cells and the behavior of myeloma and ovarian cells were tracked in 48 hours after electroporation.

Biofunctionalization of Magnetic Nanoparticles and Incorporation into a Magnetic Tunnel Junction Based Biosensor. Stephanie Grancharov1, 2, Hao Zeng1, Shouheng Sun1, Stephen O’Brien2, Chris Murray1, John Kirtley1 and Glenn Helf1; 1Nanostructure Materials and Devices, IBM, Yorktown Heights, New York; 2Applied Physics and Applied Math, Columbia University, New York, New York.

Methods of synthesizing monodisperse, strongly magnetic ferrite nanoparticles (NPs) have been well documented, however, encapsulation of particles within a layer of biologically active molecules and their subsequent stabilization in a physiological medium has not yet been reported. Such particles could be used to bind and transport proteins. Following introduction into a living organism, these particles could provide a means of monitoring and influencing cellular processes. Perhaps most importantly, these bio-functionalized magnetic NPs would provide a crucial component in the sub-cellular delivery of therapeutic drugs and nucleic acids. We report the successful bio-functionalization of 12 nm manganese ferrite (MnFe2O4) NPs. We demonstrate the site-specific binding of biotin and DNA functionalization NPs onto protein and complex biological structures, respectively. Imaging these substrates with scanning confocal microscopy, we show that these particles retain their magnetic properties. Finally, we demonstrate a novel method of detecting the hybridization of these magnetic NPs within microarrays at room temperature using a bioassay comprised of a protein patterned magnetic lens functioned to detect in orthogonal magnetic fields.

Bio-functionalized monodisperse magnetic nanoparticles (NPs) with small size would enable the ultra-sensitive magnetic detection of both proteins and nucleic acids. When introduced into a living organism, they could also provide a means of monitoring and influencing cellular processes. Methods of synthesizing monodisperse and magnetically stable ferrite NPs with size smaller than 20 nm have been developed. However, encapsulation of these particles within an overlayer of biologically active materials and their subsequent stabilization in a physiological medium has been a challenge. In this letter, we report the bio-functionalization and detection of 12 nm manganese ferrite NPs. We have achieved the site-specific binding of biotin functionalized DNA functionalized NPs onto complementary DNA patterned silicon oxide substrates and DNA functionalized NPs onto complementary DNA patterned silicon oxide substrates. Scanning SQUID microscopy images of these substrate bound NPs show that they retain their magnetic properties and thus can be detected by a magnetic tunnel junction (MTJ) field sensor. Finally, we demonstrate a novel method of detecting either protein binding or DNA hybridization at room temperature using the NPs and a MTJ biosensor situated in orthogonal magnetic fields.

SESSION K7: Bio-inspired Devices
Thursday Afternoon, March 31, 2005
Room 3002 (Moscone West)

1:30 PM *K7.1

Energy-consuming transport systems play a key role in a wide array of biological processes such as chromosomal segregation, organelle positioning, and cell motility. More reorganized, non-equilibrium processes in nanomaterial architectures may enable the development of new devices and materials in which the assembly, disassembly, and organization may be programmed or self-regulated. Our work has specifically focused on a biological active transport system consisting of kinesin biomolecular motors and microtubule filaments as means for organizing and transporting nanocomposite materials at synthetic interfaces. For this work, surface-tethered kinesin motor proteins are used in the gliding motility geometry to propel functionalized microtubule "shuttles" across a surface. A number of critical technical issues have been addressed and include: (1) engineering robust biological components, (2) developing interfacial chemistry for attachment of synthetic nanoparticles, and (3) characterizing factors affecting nanoparticle transport. The prerequisite and enabling technologies necessary to utilize kinesin and microtubules to develop integrated nanomaterials and devices will be discussed. In addition, several key demonstrations will be presented to illustrate the application of this transport system in hybrid systems.

Novel nanomaterials for bioassay applications represent a rapidly progressing field of nanotechnology and nanobiotechnology. Here, we review the advancements in developing 1) electron microscopic sensors based on single-walled carbon nanotube (SWNT) field effect transistors (FET) and 2) a generic approach for patterning bio-molecules on SiO2 or quartz surface using SWNT thin film as the anchor. The SWNT is a quasi-one dimensional wire with only surface atoms. The electronic properties of a SWNT are extremely sensitive to its surrounding chemical and electrostatic environment, thus allows direct electrical detection of biological events on tube surface [1]. In addition, SWNT-FET sensors (nm to ~m in size) can be integrated into massive arrays in lab-on-chip fashions for analyzing and detecting [2,3] large numbers of bio-molecules with high throughput. Carbon nanotube synthesis by catalyzed Chemical Vapor Deposition (CVD) combined with microfabrication is our basic approach to fabricate microarrayed nanotube devices for sensing applications. Real-time monitoring of 15mer and 30mer DNA hybridization at ~nM concentration in phosphate buffered saline (PBS) has been demonstrated. Single molecule detection is anticipated with short channel (~10nm) SWNT-FET with a single semiconductor tube across the source and drain electrodes. SWNT-FETs passivated with hydroxylthiol molecules exhibit excellent sensitivity to pH and are proven to be stable in a wide pH range. pH-sensitive SWNT-FETs will serve as a platform for building Enzyme-Modified FETs (EnFET) where hydrogen ions are produced or consumed by the enzymatic reaction. Recent progress has been made in synthesis and purification of high density SWNT thin films on both SiO2 and Si surfaces, which are easily patterned by photolithography techniques. Bio-molecules such as protein and nucleic acid oligomers can then be linked to the patterned SWNT thin film and the immobilization chemistry can be investigated by optical fluorescence measurements. Polymer chains irreversibly adsorb onto nanotubes to form a monolayer via van der Waals and hydrophobic interactions in aqueous solutions [4]. Synthesis of SWNT-Bio-complexes directly on surfaces provides an alternative to current immobilization chemistries in DNA micro-array and proteomics. Confocal images of fluorescence labeled DNA oligos and biotin immobilized on patterned nanotube arrays will be presented. References: 1. R. Chen, H. Choi, S. Chang, H. Yenilmez, X. Tang, Q. Wang, Y. Chang, and H. Dai, JACS 126, p. 1563. 2. R. Chen, S. Bangsaruntip, K. A. Drouvalakis, N. Wang Shi, M. Shim, Y. Li, W. Kim, F. J. Utz, and H. Dai, PNAS 100 (2003), 14984. 3. G. Gracheva, B. Popey, E. Obrzutova, Y. Shtogum, Chem. Phys. Lett. 372, p. 432. 4. M. O'Connell, P. Boul, T. L. Lloyd Carroll, Daniel B. Ericson, C. Hufnagle, Y. Wang, E. Haroz, C. Kuper, J. Tour, K. Ausman, R. Smalley, Chem. Phys. Lett., 342, p. 205.
Controlling the behavior of viable, multipotent stem cells is a major challenge in regenerative medicine. By tuning specific properties of a biomaterial, we have made significant progress towards precise in vitro control of stem cell behavior. Such scaffolds have been extensively studied and one of the most promising systems has been the use of polymer matrices. In this context, we have developed new approaches to control the behavior of stem cells by modulating the mechanical properties of the scaffold. These scaffolds are made of poly(lactide-co-glycolide) and collagen, which were chosen for their biocompatibility and ability to support cell proliferation and differentiation.

In proliferating culture conditions, the RGD-containing peptides supported the attachment and proliferation of osteoblast cells seeded on the scaffolds. The highest proliferation (increase from 6000 cells/cm² to 28,000 cells/cm² after 5 days) was observed for scaffolds with high G* (130 Pa) and low G* (10 Pa) and RGD concentration. Implantation of degradable hydrogels (G* = 130 Pa, RGD) completely degraded in 24 hours in vivo, but not completely in the absence of RGD. These results suggest that synthetic polymeric surfaces containing only RGD-modified hydrogel surfaces, consisting of a biocompatible, non-fouling interpenetrating polymer network (IPN) of poly(acrylamide-co-ethylene glycol/acyric acid) [P(AAm-co-EG/AAc)]. The bioactive component of the hydrogel was a 15 amino acid oligopeptide containing the Arg-Gly-Asp (RGD) sequence, which is present in many active domains in extracellular matrix proteins found within extracellular matrix (e.g. laminin in the brain) and binds to integrin receptors. Both proliferation and differentiation of neural stem cells were supported and influenced by the biomatrix.

In proliferating culture conditions, the RGD-containing peptides stimulated cells to proliferate and fostered adoption of cell monolayer morphology consistent with increased proliferation. Proliferation on RGD-negative control surfaces was severely reduced, and different cell morphologies were observed. Cell spreading in the order of 92% attained compressive modulus of 8.16 MPa and supported differentiation at high cell densities for 1-2 weeks. However, scaffold structure. These encouraging results support the potential engineering applications. This work was supported by the grant NIH-NHLB (HL64387-03) and University of Washington Engineered Biomaterials Research Center (NSF-EEC 0529161).

Scaffolds for bone repair have in the past generally consisted of bone grafts, which are inherently limited in supply and variable in quality. More consistent supply and quality may be achieved with synthetic biomimetic scaffolds. Additionally, as matrix viscoelastic properties have been shown to be important for bone formation, the synthesis of hydrogels with tunable viscoelastic properties has become essential. Scaffolds for tissue engineering composed of semi-interpenetrating polymer networks (siIPNs) of poly(N-isopropylacrylamide-co-ITA)-based collagenase-labile peptide (QPPGLAK-NH₂) were synthesized by redox free radical addition polymerization in the presence of polyacrylic acid-graft-RGD. With the QPPGLAK-NH₂ crosslinker providing biodegradability, and the RGD peptide providing cell-binding domains, the siIPNs contained bioactive hydrogels with tunable viscoelastic properties. The hydrogels were designed to systematically study the effect of hydrogel complex shear modulus (G*) and cell-adhesiveness on bone cell proliferation and differentiation. These hydrogels with various G* and RGD concentrations were synthesized. G* of the hydrogel was determined by rheology at 22°C and 37°C. The temperature-responsive properties of the hydrogels were manifested as significant increases in G* with temperature. For a particular siPN, G* increased from 60 Pa at 22°C to 170 Pa at 37°C. Hydrogel degradation was measured over several days in various scaffold environments. siIPNs completely degraded in 24 hours in 2% gelatin collagenase; however, the hydrogels were not susceptible to nonspecific degradation by other proteases and thus were stable in the absence of collagenase. Invitro measurements of osteoblast proliferation on siIPNs with various G* and RGD concentrations were performed with the WST-1 metabolic assay. Both adhesion and proliferation of bone cells were dependent upon G* and RGD concentration; hydrogels with high G* (170 Pa) and high RGD concentration (100 μM) correlated with the greatest proliferation (increase from 6000 cells/cm² to 28,000 cells/cm² after 5 days), whereas those with low G* (10 Pa) and without RGD did not support proliferation. Implantation of degradable hydrogels (G* = 130 Pa, 80 μM RGD) for 4 weeks in the femoral narrow spaces of rats stimulated new bone formation. Analysis of the rat femurs by μCT indicated a significant amount of mineralized bone where degradable hydrogels had been implanted, while femurs implanted with control hydrogels with non-degradable crosslinks produced significantly less new bone. These results have demonstrated the potential of a synthetic biomimetic hydrogel to serve as a scaffold for bone tissue formation and the importance of complex modulus on tissue engineering scaffold design. This work was supported by a Whitaker Foundation Graduate Fellowship to EHP and an NIH NIAMS Grant.

Chitosan-alginate Hybrid Scaffolds for Bone Tissue Engineering, Zhengshen Li1, 2, Miqin Zhang1, Kip D. Hauch1, Denin Xiao9 and Hassna Ramay1; 1Material Sciences and Engineering, University of Washington, Seattle, Washington; 2Department of Orthopedics, Shenzhen People’s Hospital, Shenzhen, China.

Here we report on the development of a biodegradable porous scaffold made from naturally derived chitosan and alginate polymers with significantly improved mechanical and biological properties as compared to its chitosan counterpart, and it is structurally stable due to the strong ionic bonding between the amine groups of chitosan and the carboxyl groups of alginate. The chitosan-alginate scaffold with porosity of ~92% attained compressive modulus of 8.10 MPa and yield strength of 0.46 MPa, respectively, which are about three times of the values for the pure chitosan scaffold. The cell-material interaction study indicated that osteoblast cells seeded on the chitosan-alginate scaffold cultured in osteogenic medium appeared to attach and proliferate well and promoted the deposition of minerals in a very short time. Unlike chitosan scaffolds which can only be fabricated from acidic solutions, the chitosan-alginate scaffold developed in this study can be polymerized in neutral, basic or neutral solution. This unique attribute provides a favorable environment for incorporating proteins with less risk of denaturation for sustained release in vivo. The in vivo study showed that the chitosan-alginate scaffolds promoted rapid remodeling and deposited connective tissue and calcified matrix within the entire scaffold structure. These encouraging results support the potential applications of the chitosan-alginate scaffolds as an improved alternative to natural bone scaffolds for tissue engineering applications. This work was supported by the grant NIH-NHLBI (HL4387-03) and University of Washington Engineered Biomaterials Research Center (NSF-EEC 0529161).

Biodegradable and Thermoresponsive Poly(N-isopropylacrylamide) Hydrogels for Bone Tissue Engineering, Eugene H. Chung1, Dale R. Summer3 and Kevin E. Healy1, 2; 1Department of Bioengineering, University of California at Berkeley, Berkeley, California; 2Department of Materials Science and Engineering, University of California at Berkeley, Berkeley, California; 3Department of Anatomy and Cell Biology, Rush Medical College, Chicago, Illinois.

Scaffolds for bone repair have in the past generally consisted of bone grafts, which are inherently limited in supply and variable in quality. More consistent supply and quality may be achieved with synthetic biomimetic scaffolds. Additionally, as matrix viscoelastic properties have been shown to be important for bone formation, the synthesis of hydrogels with tunable viscoelastic properties has become essential. Scaffolds for tissue engineering composed of semi-interpenetrating polymer networks (siIPNs) of poly(N-isopropylacrylamide-co-ita)–based collagenase-labile peptide (QPPGLAK-NH₂) were synthesized by redox free radical addition polymerization in the presence of poly(acrylic acid-graft-RGD). With the QPPGLAK-NH₂ crosslinker providing biodegradability, and the RGD peptide providing cell-binding domains, the siIPNs contained bioactive hydrogels with tunable viscoelastic properties. The hydrogels were designed to systematically study the effect of hydrogel complex shear modulus (G*) and cell-adhesiveness on bone cell proliferation and differentiation. These hydrogels with various G* and RGD concentrations were synthesized. G* of the hydrogel was determined by rheology at 22°C and 37°C. The temperature-responsive properties of the hydrogels were manifested as significant increases in G* with temperature. For a particular siPN, G* increased from 60 Pa at 22°C to 170 Pa at 37°C. Hydrogel degradation was measured over several days in various scaffold environments. siIPNs completely degraded in 24 hours in 2% gelatin collagenase; however, the hydrogels were not susceptible to nonspecific degradation by other proteases and thus were stable in the absence of collagenase. Invitro measurements of osteoblast proliferation on siIPNs with various G* and RGD concentrations were performed with the WST-1 metabolic assay. Both adhesion and proliferation of bone cells were dependent upon G* and RGD concentration; hydrogels with high G* (170 Pa) and high RGD concentration (100 μM) correlated with the greatest proliferation (increase from 6000 cells/cm² to 28,000 cells/cm² after 5 days), whereas those with low G* (10 Pa) and without RGD did not support proliferation. Implantation of degradable hydrogels (G* = 130 Pa, 80 μM RGD) for 4 weeks in the femoral narrow spaces of rats stimulated new bone formation. Analysis of the rat femurs by μCT indicated a significant amount of mineralized bone where degradable hydrogels had been implanted, while femurs implanted with control hydrogels with non-degradable crosslinks produced significantly less new bone. These results have demonstrated the potential of a synthetic biomimetic hydrogel to serve as a scaffold for bone tissue formation and the importance of complex modulus on tissue engineering scaffold design. This work was supported by a Whitaker Foundation Graduate Fellowship to EHP and an NIH NIAMS Grant.

Blending Polymer of Polysulfone/ Polycaprolactone for Improvement of the Hemocompatibility and for Drug Controlled Release. Xun-Yu Liu1, Chia-Hui Tsai2, Dean-Mo Liu3 and San-Yuan Chen4; 1Material Science and Engineering, National Chiao Tung University, Hsinchu, Taiwan; 2ApaMatrix Technologies Inc., Moffatt Road, Richmond, British Columbia, Canada.

Controlled release of drugs of polysulfone (PSF), polycaprolactone (PCL) and a combination of both components are theoretically important for enhanced medication efficacy after administration with a lowest dosage, where some clinically-observed side effects for certain of toxic drugs can be minimized. Property modification as a result of surface blending may not only manipulate the drug released, but also influence the biocompatibility and the hemocompatibility of the resulting blended polymers, the latter has been recognized as an important factor for a number of blood-contacting implant devices. In this study, the permeation of ibuprofen through polysulfone (PSF), polycaprolactone (PCL) blend membranes was investigated. Controlled release could be completely manipulated by altering the composition of polysulfone and polycaprolactone in the membranes. The biocompatibility [TH] of the blend membrane was measured using the cellularity spreading in the order of 10-5 to 10-7cm²/hr. The surface morphology of the blend polymers appeared to be smooth and flat before diffusion test. The PSF/PCL blend polymer had a widely permeating fenestral narrow spaces of rats stimulated new bone formation. Analysis of the rat femurs by μCT indicated a significant amount of mineralized bone where degradable hydrogels had been implanted, while femurs implanted with control hydrogels with non-degradable crosslinks produced significantly less new bone. These results have demonstrated the potential of a synthetic biomimetic hydrogel to serve as a scaffold for bone tissue formation and the importance of complex modulus on tissue engineering scaffold design. This work was supported by a Whitaker Foundation Graduate Fellowship to EHP and an NIH NIAMS Grant.
Molecular imprinting of synthetic polymers is a cost-effective and versatile method to synthesize robust man-made receptors. Here, we describe the first attempt to imprint polymers with mammalian cells. Polyurethane thin films were surface imprinted with whole erythrocytes and erythrocyte ghosts using a rational imprint-lithography technique. AB0 blood group determination was achieved with piezoelectric devices coated with the bioimprinted polyurethanes. The imprinted polymers show a high selectivity for the adsorption of intact red blood cells rather than for mechanically ruptured cells. Red blood cells are selectively adhered on films imprinted with the same templating erythrocytes. The selectivity pattern of AB0 was reproducible and the antigen composition of the erythrocyte membrane. Furthermore, blood group typing was performed in whole blood samples. The implications of these results for biotechnological applications will be discussed.

The sweat glands are coiled, tubelike structures located in the dermis and subcutaneous layer of the skin. Each tube extends to the skin surface of the nanoparticle systems using various techniques (such as sol-gel formation in targeted areas of weak osteoporotic bone). The formation in areas not desirable. This is because these agents are often delivered in non-specific ways (such as through the mouth, directly into the blood stream, etc.). Second, if delivered locally to the tissue around the area of low bone density, they rapidly diffuse to adjacent tissues which limit their potential to promote prolonged bone formation in targeted areas of weak osteoporotic bone. It is because of these limitations that even the best strategies to sufficiently increase bone mass (although, to date, still unproven) route for at least one year to see any change; a time period not acceptable especially for the elderly. For these reasons, in this study we used nanotechnology (or the design of materials with 10-9 m dimensions) to develop novel drug delivery systems that will specifically attach to osteoporotic (not healthy) bone and distribute pharmaceutical agents locally to quickly increase bone mass. Specifically, inorganic and organic biodegradable nanomaterials (including polymers like poly-lactic-co-glycolic acid and ceramics like hydroxyapatite) were functionalized with bioactive chemicals such as bone morphogenetic protein-2 (BMP-2) that bond to bone of low mass. Such bioactive groups were placed on the outer surface of the nanoparticle systems using various techniques (such as amine-based silane chemistry). After bonding specifically to osteoporotic bone and not healthy bone, nanoparticle systems are designed to deliver bioactive compounds to locally increase bone mass. Lastly, the outer coating of the embedded nanoparticle systems were created to have different biodegradation rates for the release of bone-building agents over various time spans; this will allow for not only quick bone formation but also long-term sustained bone regeneration. In this manner, this study took a new approach to fight osteoporosis through the design of intelligent, nanoparticle systems that can attach to areas of low bone mass and then release bioactive agents to subsequently increase bone mass; such efforts represent a new direction to reverse osteoporosis.

Fluorescent dye-labeled periplasmic binding proteins constitute a rapidly advancing area of biosensor development. Such proteins can be functionalized with different kinds of binding motifs for specific recognition of target analytes. This is particularly true for low molecular weight targets, such as oligonucleotides. The U.S. Bureau of Census has clearly demonstrated that we are an aging demographic. For example, the percentage of the population greater than 65 years of age is expected to increase from 12.4 to 23% between the years 2000 and 2050. Not surprisingly, a similar upward trend is projected for the debilitating osteoporosis. Specifically, osteoporosis cases will rise from 10.1 million in 2002 to 13.9 million in 2020. More importantly, worldwide, approximately 1.5 million bone fractures per year are attributed to osteoporosis. None of the current methods used to treat osteoporosis have experienced overwhelming success. For example, several major barriers exist for the use of any pharmaceutical agents to stimulate new bone formation. First, the agents can cause specific bone formation in areas not desirable. This is because these agents are often delivered in non-specific ways (such as through the mouth, directly into the blood stream, etc.). Second, if delivered locally to the tissue around the area of low bone density, they rapidly diffuse to adjacent tissues which limit their potential to promote prolonged bone formation in targeted areas of weak osteoporotic bone. It is because of these limitations that even the best strategies to sufficiently increase bone mass (although, to date, still unproven) route for at least one year to see any change; a time period not acceptable especially for the elderly. For these reasons, in this study we used nanotechnology (or the design of materials with 10-9 m dimensions) to develop novel drug delivery systems that will specifically attach to osteoporotic (not healthy) bone and distribute pharmaceutical agents locally to quickly increase bone mass. Specifically, inorganic and organic biodegradable nanomaterials (including polymers like poly-lactic-co-glycolic acid and ceramics like hydroxyapatite) were functionalized with bioactive chemicals such as bone morphogenetic protein-2 (BMP-2) that bond to bone of low mass. Such bioactive groups were placed on the outer surface of the nanoparticle systems using various techniques (such as amine-based silane chemistry). After bonding specifically to osteoporotic bone and not healthy bone, nanoparticle systems are designed to deliver bioactive compounds to locally increase bone mass. Lastly, the outer coating of the embedded nanoparticle systems were created to have different biodegradation rates for the release of bone-building agents over various time spans; this will allow for not only quick bone formation but also long-term sustained bone regeneration. In this manner, this study took a new approach to fight osteoporosis through the design of intelligent, nanoparticle systems that can attach to areas of low bone mass and then release bioactive agents to subsequently increase bone mass; such efforts represent a new direction to reverse osteoporosis.

Fluorescent dye-labeled periplasmic binding proteins constitute a rapidly advancing area of biosensor development. Such proteins can be functionalized with different kinds of binding motifs for specific recognition of target analytes. This is particularly true for low molecular weight targets, such as oligonucleotides.
be modified to bind to their ligand (the analyte) and provide a direct fluorescence signal proportional to ligand concentration. Conformational changes are often referred to as "reagentless" as they do not use competitive binding partners or other additional reagents. A change in fluorescence of the fluorescent label occurs due to protein conformational change upon binding of the protein to its corresponding ligand. Binding proteins must be immobilized within a biosensor matrix in a manner that allows analyte-induced conformational change of the binding molecules. Here, we describe methods of chemically immobilizing dye (IANBD) labeled maltose binding protein (MBP) immobilized within a polyethylene glycol (PEG) hydrogel. The results showed that upon adding free maltose solution, the fluorescence intensity of immobilized MBP increased ~2 fold over that of ligand-free MBP, a fluorescence change close to that of MBP in solution. Determination of the immobilized protein's equilibrium dissociation constant was performed by titrating immobilized MBP with different maltose concentrations; the dissociation constant (Kd) obtained was ~2.8 mM maltose. We also demonstrated that the hydrogel matrix for MBP immobilization showed close correlation of these findings suggest that immobilized engineered binding proteins in PEG hydrogels could enable development of implantable, continuous-reading biosensor.

K9.5
Bioinspired Sensors. Nikolas Chalikias1 and Emmanuel Giannelis2.
1Chemical and Biomolecular Engineering, Cornell University, Ithaca, New York; 2Materials Science and Engineering, Cornell University, Ithaca, New York.

Nanohybrid artificial membranes made by intercalation of amphiphilic molecules into the galleries of a layered host exhibit characteristics similar to biological membranes and they can be used as sensors. Specifically the nanohybrid membranes can be used as sensors for different analytes including saccharin. Different responses have been observed even for saccharin based on features for example, saccharin and its sodium salt suggesting that the nanohybrid might be useful in developing an electronic nose. The dynamic range of the saccharin sensor is 20 - 500uM. In this paper we will present our results on sensor fabrication and testing and discuss possible sensing mechanisms.

K9.6
Physically Tunable Amphiphilic Diblock Copolyelectrolyte Vesicles. Eric Peter Holowka1, Lisa Pakstis2, Darrin Pochan2 and Timothy J. Deming2.
1Materials Engineering, University of California Santa Barbara, Goleta, California; 2Materials Engineering, University of Delaware, Wilmington, Delaware.

Recently, the transition metal mediated living polymerization of block copolypeptides from α-amino-N-carboxyanhydrides (NCA) has allowed the synthesis of copolypeptides having a high degree of chain length control as well as the ability to incorporate a wide range of amino acids and amino acid analogues. An attractive benefit of this system is the ability to tailor polymer structure with amino acids that form known secondary structures, which can then be used to drive self-assembly of complex supramolecular structures. Spontaneous formation of copolyptide unilamellar vesicles, which are stable upon formation, has been observed specifically showing morphologies in a glucose-modified lysine-block-leucine copolyptide. In this system, vesicle size was modified through changes made to the block segment lengths within the copolyptide amphiphile. This is in contrast to liposomes, which can be physically processed to yield vesicles of different sizes. The cost of physical processability in liposomes is illustrated in the lack of stability of these vesicles over useful timescales. A valuable alternative would be a polymeric system capable of being physically processed into stable vesicles of different sizes. We report a lysine-block-leucine amphiphilic diblock copolyptide vesicle forming system where vesicle size can be modified by physical methods. These vesicles have been found to be stable and do not lyse for 3 weeks after formation. These assemblies are also stable in the presence of sucrose, which can be encapsulated within the vesicle shells.

K9.7
National Institute for Materials Science, Tsukuba, Japan.

Hydroxyapatite/collagen (HAp/Col) nanocomposites have been studied as bone filling materials that will substitute for autogeneous bone implants. We have developed a novel HAp/Col nanocomposite with similar nanostructure to natural bone tissues through a self-organization mechanism. The consolidated HAp/Col nanocomposite showed excellent bio-compatibility and bio-integrative activity for the bone tissues. The control of pore structure in the composite will improve cell migration and mechanical strengths, and regenerate neo-vascularizations. In this study, porous HAp/Col nanocomposite with one-directional connective micropores was prepared by unidirectional solidification and subsequent freeze-drying processes. We elucidate the effects of pore structure and porosity on mechanical properties. The HAp/Col nanocomposite (HAp:Col weight ratio = 60:40) were synthesized by a co-precipitation method using Ca(OH)2, H3PO4, and Col as starting substances. The temperature and pH were kept at 40°C and 8-9, where Col fibril formation and HAp crystallization are active. The as-synthesized HAp/Col nanocomposite fibers was washed with H2O and freeze-dried. The freeze-dried composite was thoroughly stirred with 200 mM Na-phosphate buffer of pH 6.8 at a concentration of 1.25 g/L. The protein-Ligand complexes was filled into a plastic cylindrical container with a brass bottom. Only the bottom face was immersed in liquid N2 as a refrigerant and the ice crystals grew in the vertical direction from the bottom face. The frozen paste was freeze-dried, cut into 100 μm cubes, and dehydrothermally treated in vacuo at 140°C for 12 h to crosslink among the Col molecules. The pore structure was observed by a scanning electron microscopy (SEM). The mechanical properties were investigated by a compressing test using a texture analyzer. Uniaxial pore structures were formed by the unidirectional solidification and freeze-drying. It was observed that unidirectional open pores (about 20 μm in diameter) were formed along the ice growth direction over the entire sample, except for the interfacial region (1 mm in thickness) between the paste and the brass bottom, where only random nanoparticles were observed. The diameter of the unidirectional pore was increased with increasing the freezing temperature. The HAp/Col nanocomposite with one-directional connective mechanical strengths and viscoelastic properties; the compressive strength parallel to the pore-axis was twice higher than that perpendicular to it, and the stress relaxation against pressure parallel to the pore-axis was much faster than that perpendicular to the axis. These results clearly indicate that the pore structure is of great importance for controlling the mechanical properties.

K9.8

Conjugated polyelectrolytes (CPs), conjugated polymers with ionic functionalities, can be utilized to study many kinds of biomolecular events, thus enabling different biosensor devices. CPs offer possibilities for very sensitive measurements, and may become ubiquitous for genomics and proteomics in the future, as the optical or electronic processes in these materials can be used to track biomolecular events. One such CP that has demonstrated many useful interactions together with biomolecules is the polythiophene POWT and related polythiophene derivatives. Examples of biomolecular events that can be studied using this class of CPs are: analyte/receptor interaction [1], DNA hybridization [2], conformational changes in proteins [2]. The development of biospecific devices capable of selectively types of biomolecular interactions is highly topical, for parallel and high throughput detection. One condition to be able to use CPs detection of molecules is biological samples, or competent, compatible with an aqueous environment. We have shown that POWT is active and capable of changing its conformation on a solid support using SPR [3] and QCM-D [Asberg, manuscript in preparation]. Therefore, POWT has good characteristics to follow biomolecular events in a biochip format. In this work we have focused on how to make biospecific devices capable to distinguish between correctly folded and misfolded proteins. Detection of misfolded proteins or peptides is of special interest with the rising problem of prion diseases, and large scale production of protein pharmaceuticals. The present method is based on the modification of a surface using soft lithographic methods, microcontact printing (μCP) with PDMS stamps. Patterned PDMS stamps are used to create a hydrophilic pattern (nano-hydrophilic substrate) [4]. Surface modification using μCP on selected areas is a process that minimizes the waste material. Sensitive molecules, such as biomolecules, should preferably be applied to the channel in their optimal solution. Depending on the type of analyte the solution on the patterned substrate, the solute/surface interactions adsorbed molecules appear in a negative or positive pattern on the hydrophobic/hydrophilic pattern. This may depend on the degree and pattern of hydrophobic/hydrophilic exposure, the charge density distribution on the biomolecule or conformation of the biomolecule. Using these detector materials anchored onto solid surfaces, we have been able to distinguish between native and fibrillar insulin as well as α-synuclein peptide in random coil α-helix form [4].

K9.9
Electrodeposition of Biotin-doped Polypyrrole on Microfabricated Electrodes. Paul M. George1, David A. LaVan2, Ching-Yuan Chen2 and Robert Langer2; 1Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, Massachusetts; 2Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts; 3Department of Mechanical Engineering, Yale University, New Haven, Connecticut.

Polymer (PPy) is a conducting polymer with growing applications in the biomedical field. Various dopants have been incorporated into PPy to improve properties ranging from conductivity to biocompatibility. Recently groups have modified the pyrrole monomer by the addition of a biotin molecule to create immunoassay applications. Small molecules and a protein tightly bound by the protein, streptavidin. The biotin/streptavidin complex has been utilized to create sensors and anchor biotinylated molecules to various surfaces. The ability to incorporate biotin as a dopant during the electrodeposition step would eliminate the need for the complicated process of chemically altering the pyrrole monomer. We have used biotin in combination with sodium dodecylbenzenesulfonate (NaDSB) as dopants for the electrodeposition of PPy. NaDSB has the desired conductivity and structural properties, while the biotin creates the interactive polymer surface. Because the biotin-doped PPy is formed in one electrodeposition process, the production complexity and times are greatly reduced from currently available methods. Drug delivery applications, the biotin is not part of the polymer backbone. The incorporation and functionality of the biotin in the PPy has been demonstrated through the addition of a fluorescein-conjugated streptavidin after PPy electrodeposition. Fluorescent intensity was measured to determine the biotin/streptavidin binding levels. The stability of the biotin in the polymer is important for future biomedical applications. This stability of the biotin moiety in the matrix was shown by fluorescent intensity measurements over a three week period. The ability to incorporate biotin into PPy through the electrodeposition process provides a unique platform for future sensor and drug delivery applications.

K9.10
Development of Bioactive Polymers for use in Cardiac Tissue Engineering. Samuel Thomas Wall1, Kris Saha2, David V. Schaffer1 and Kevin E. Healy3; 1Bioengineering, UC Berkeley, Berkeley, California; 2Chemical Engineering, UC Berkeley, Berkeley, California; 3Material Science and Engineering, UC Berkeley, Berkeley, California.

Tissue engineering to replace diseased or damaged tissue is a potentially effective potential for treating medical conditions that currently have poor prognosis. This investigation focuses on the development of synthetic constructs for such treatment of ischemic cardiac injury as a result of myocardial infarction. To address this issue, we focus on matrix-assisted myocardium regeneration (MAMR), or the use of engineered materials to foster the restoration of functional tissue in damaged myocardium. Our lab has created, artificial extracellular matrices (ECMs) that are environmentally responsive and orthogonally tunable with respect to mechanical properties (e.g. G*), biological ligands, tissue adhesion, and protease degradation. We have characterized the physical properties of semi-interpenetrating polymer networks (sIPNs) consisting of linear polyacrylic acid (pAAc) chains within a thermo-responsive N-isopropylacrylamide-co-acrylic acid network [p(NIPAam-co-AAc)]. To impart bioactivity into the hydrogels, the pAAc linear chains have been functionalized with peptides containing the cellular binding domain RGD and a potent angiogenic growth factor. These modified p(NIPAam-co-AAc) serve as useful tools for studying cell-matrix interactions within three dimensional structures and have the potential to be used as injectable scaffolds for MAMR cardiac engineering applications. The work presented here focuses on the development of the angiogenic aspect of this modular system. The active G* terminal region of the growth factor sonic hedgehog (Shh) was recombiantly produced with specific amino acid modifications to allow for maximal potency and direct conjugation to desired materials. Shh was targeted as it is a potent upstream regulator of numerous cellular growth and differentiation cascades and has been shown to promote the growth of robust vasculature when used in animal models. In this study, Shh was covalently linked to linear pAAc through the addition of maleimide functionality to the pAAc chain with EDAC, NHS, and EDC, which can then react with an added cysteine-sulphhydril on the protein surface. Reaction conjugation efficiency is ~ 80% as evaluated by gel electrophoresis. The engineered protein and the conjugated protein were tested using a cellular transmigration assay, as an in vivo angiogenesis assay, and a rat hindlimb ischemia model. Both the lead and a control group were treated with an injection of saline phosphate (AP) expression in a dose-dependent manner in the 1 to 500 nM range; however, the conjugates did not show expected activity, and subsequent tests demonstrate linear pAAc inhibits the Shh induced differentiation in a dose dependent manner. Additional work is required to determine the nature of the differentiation inhibition by pAAc and if this in vitro reading has any in vivo significance.

K9.11
Disposable Microchip-Based Electrochemical Detector using Prussian Blue-Modified Indium Tin Oxide Electrode. In-Ho Kim1, In-Je Yi1, Chi-Jung Kang2 and Yong-Sang Kim1; 1Electrical Engineering, Myongji University, Yongin, Kyunggido, South Korea; 2Physics, Myongji University, Yongin, Kyunggido, South Korea.

The amperometric detection of dopamine and catechol on a Prussian blue (PB) thin film, which is electrodeposited on indium tin oxide (ITO) glass substrate, was studied in this work. The PB thin film, or ferric hexacyanoferrate, can improve the electrocatalytic rate of the analyte. The capillary electrophoretic and a three-electrode system were used in our experiment. The system was realized with polydimethylsiloxane (PDMS)-glass chip and indium tin oxide (ITO) electrode. The injection and separation channels (80 μm wide X 40 μm deep) were produced by molding a PDMS against a microfabricated master with relatively simple and inexpensive methods. ITO electrode was fabricated by patterning the ITO film deposited on a fusion glass. A PB thin film was galvanostatically deposited onto an ITO electrode in a plating solution consisting of 20 mM FeCl3, 20 mM K3[Fe(CN)6], 0.2 M KCl, and 0.1 M HCl. A capillary electrophoresis and a three-electrode electrochemical detector were fabricated on the same chip. For comparing the performance of the PB-modified ITO electrodes with the bare electrodes, bare ITO electrode microchip was fabricated with the same dimension. The running buffer was prepared by 10 mM 2-(N-morpholino)ethanesulfonic acid (MES) titrated to pH 6.5 using 0.1 N NaOH. The testing analytes are consisted of 1 mM dopamine and 1 mM dopamine. Separation of dopamine and catechol was performed using an electric field strength of 60 V/cm after applying an injection electric field of 60 V/cm. The electrochemical detection circuit could mostly decouple the interference of a separation electric field. Electrophoretic measurement of dopamine and catechol mixture is successful in the ITO electrode microchip. Results are indicated consistent and rapid separation and detection of two compounds, with a total time of around 80 see applying a separation electric field of 60 V/cm. The measured current peaks of dopamine and catechol are proportional to their concentrations. For comparing the performance of the PB-modified ITO electrodes with the bare ITO electrodes, electropherograms was measured for CE-ECD device with PB-modified electrodes under the same conditions. The performances including sensitivity and resolution of CE-ECD microchip with PB-modified ITO electrode are improved compared with bare ITO electrode. When we are using an ITO glass modified by an electrodeposited PB thin film can efficiently catalyze the oxidation of dopamine and catechol. In addition, we believe that the PB-modified ITO electrode can be a viable candidate for the fabrication of a portable, disposable, and digital biosensor.

K9.12
Transferred to K11.1

K9.13
Single Walled Carbon Nanotube as an Efficient Platform for Biosensor: Electrical Biosensing and Fluorescence-Microarray based Protein Chip Application. Hee Cheul Choi and Hye Byung Byun; Department of Chemistry, Pohang University of Science and Technology, Pohang, South Korea.

Recent observations of spontaneous adsorption of protein molecules as well as covalent coupling of specific protein molecules on the sidewalls of SWNT have inspired development of various types of biosensors. Carbon nanotube-field effect transistor (CNT-FET) composed of single walled carbon nanotube (SWNT) are successfully demonstrated as a highly selective electrical biosensor. Further systematic studies for the elucidation of the mechanism of the conductance changes have been performed by fabricating CNT-FET devices having metal contact such as Pt/Au, with self-assembled monolayers of nPEGS-SH. Metal-nanotube contact area of the CNT-FET is evicted to be highly responsible for the generation of the electrical signals while direct charge injection from biomolecules into self-assembled monolayer is negligible. Parallel to the electrical sensing approach, fluorescence-microarray based technique which is one of the most conventional methods for protein chip application is also attempted using high yield SWNT film as an efficient protein immobilization surface. Contrast to the typical flat surfaces used for protein chip, high yield SWNT forms a pseudo-3D network structure on which immobilizing protein molecules occupy minimum contact area. This increases the stability of the original protein structures after immobilization and eventually improves selectivity and sensitivity of the chip. In this presentation, successful demonstration of SWNT film
as a platform for the protein chip will be introduced. Typical values based on fluorescence intensity counts for specific and non-binding
sites are 60,000 and 100, respectively.

and Tieling Foa.1,2 1Materials Science and Engineering, University of Florida, Gainesville, Florida; 2Pathology, Immunology and Laboratory

Tissue engineering has become a great interest in materials science research in the last decade. Porous foams have a vital role by creating a scaffold structure for tissue regeneration. Structural integrity is a key attribute during the course of tissue formation. Scaffolds supply the necessary foundation for cell attachment, proliferation, and vascular differentiation, providing diffusional transport. Three important factors for cell scaffolding success are the addition of growth factors and/or other protein coatings. Our lab has chosen a synthetic biodegradable polymer that can create an interconnected foam structure. We have fabricated porous polycaprolactone (PCL) 3-D scaffolds and later seeded them with mouse embryonic stem cells (ES cells). In vitro degradation studies were conducted at 37°C while submerged in a phosphate buffered solution. The scaffolds were analyzed for mass loss, morphology, and molecular weight. Our PCL scaffolds lost less than 4% of their mass during the 9 week degradation study. It was also found that this tough and elastic material remains in its originally designed morphology much longer than other porous synthetic polymers (e.g., polylactic acid, polyglycolic acid). ES cells were seeded onto the scaffold after various protein coatings were applied. We explored various coating techniques to modify cellular results using these scaffolds. When PCL foams were coated with a mixture of protein substances and fully characterized, adhesion and differentiation within the scaffolds. We feel these robust and durable scaffolds will be useful in future tissue engineering research.

K9.15 Viscoelastic Properties of Ultrathin Films of Hyaluronic Acid As Measured using a Quartz Crystal Microbalance with Dissipation. James Eric McEvoy,1 Kevin E. Healy,1 Department of Bioengineering, UC Berkeley, Berkeley, California.

Hyaluronic acid (HA) has been proposed as an implant coating due to its nonantigenic and nonfouling nature. Its performance may relate to its viscoelastic properties, which have been shown to modulate cell response in other systems.1 To elucidate these properties, the shear modulus, shear viscosity and thickness of HA thin films on quartz substrates were determined using a surface-sensitive technique termed quartz crystal microbalance with dissipation monitoring (QCM-D). The technique is an expanded variant of the linearized Sauerebre approach for rigid thin films, which allows for incorporation of lossy effects that are frequency dependent. Standard-coated, single-cycled quartz (QCM) were grafted with HA (1.3MDa, Genzyme) using a standard carbodiimide chemistry protocol.2 The surface chemistry was characterized with XPS and contact angle goniometry, where the values were comparable to literature.2 The QCM-D details were analyzed under N2 gas in a Qsense D300 to characterize the dried HA film thickness using the Sauerbrey approach. Modeling software by Qsense was used to delineate the viscoelastic properties of HA when swelled in PBS (Gibco) by using a Kelvin-Voigt (KV) approach. Humidity and buffer swelling experiments were performed to highlight the propensity of HA to adsorb large amounts of water. Ex situ measurements showed a dried HA layer thickness of 4 nm (according to Sauerebre) and a PSS-swelled thickness of 29 nm (according to KV modeling), giving a swelling ratio over 7. The maximum shear modulus in buffer was 41 kPa, while the shear viscosity in buffer ranged from 0.3 to 2.5 Cp. Fibrinogen (Fgn) adsorption and hyaluronic mouse subcutaneous activity was tested with QCM-D, while short-term osteoblast cell adhesion was measured in order to compare to the known nonfouling nature of HA. Fgn adsorption was performed at 10% serum concentration in PBS, while HAse activity experiments were performed in 1% PBS. Fgn adsorption to HA was inhibited by 80% compared to control, similar to radiolabeled experiments.3 MC3T3-E1 cells were seeded at 105 cells/well (12 well TC plate) onto quartz crystals grafted with identical chemistry protocol and frequency monitored with 1% FBS. After 2 hours, control and HA-treated surfaces were rinsed and cell numbers were counted. The HA chemistry resisted cell adhesion, even though measurable serum protein adhesion to HA-grafted surfaces was observed. HAse appeared to have no effect on collagen II short-term osteoblast cell adhesion, but QCM-D, XPS and contact angle studies demonstrated detectable HAse activity towards the grafted HA film, contrary to previous reports.2 References: 1. Wang H-B, Dembo M, et al. (2000) Am J Physiol 279: C1345 - C1349. 2. Stile RA, Barber TA, et al. (2002) J Biomed Mater Res 61: 391-398. 3. Defife KM, Hagen KM, et al. (1999) J Biomater Sci Polymer Edn 10: 1063 -1074. 4. Lowry KM, Beavers EM. (1994) J Biomed Mater Res 28: 861 - 864. Acknowledgments: Funded by NSF Grant number: AR43187

K9.16 A Rapid Antigen Detection Assay Using Whole Antibodies. Robert Saavedra,1 Kristyan Master2, Christopher Bowman1,3 and Kristi Anseth1,2,3 1Chemical and Biological Engineering, University of Colorado-Boulder, Boulder, Colorado; 2Howard Hughes Medical Institute, Chevy Chase, Maryland; 3University of Colorado-Boulder, BioMolecular Sciences Center, Biomaterials Research Center, Denver, Colorado.

Antibody surface immobilization techniques have had a significant impact on protein-bioconjugates for specific diagnostic applications. To date, most antigen detection assays (e.g., standard enzyme-linked immunosorbent assays) rely on monolayer formation or physisorption methods to immobilize antibodies to surfaces. However, that approach exhibits drawbacks associated with antibody coating, and the application of a novel photopolymerization method, which allows patterning and fabrication of polymer microfluidic assays based on antibody-antigen detection. These immunoassays have demonstrated an antibody-antigen selectivity and stability, the retention of antibody-antigen selectivity in a variety of biological relevant analyte environments, and the application of a novel photopolymerization method, which allows patterning and fabrication of polymer microfluidics assays based on antibody-antigen detection. These immunoassays have demonstrated a variety of antigens with varying molecular weight, biological stability and functionality. Also, current work is being investigated to facilitate the detection of microbial antigens.

K9.17 Mossbauer and Raman Spectroscopy of the Iron (III) -Porphyrin Biomaterial for Potential Application as a Spin Based Electronic Device. Aloubak Schedidhi Boye1,4, Sosse Nlou1, Bassirou Lo1, Oumar Sako1,3,4, Papa Doua Doua Tall4, N. Pearson1, O. Munro5, R. M. Erasmus5, Vittoria Pischiedda6, Giovanni Hohosy6,7 and Wole W. Soboyejo5,4; 1Groupe de Physique des Solides et Science des Materiaux, Universite Cheikh Anta Diop de Dakar, Dakar, Senegal; 2School of Chemical and Physical Sciences, University of Natal, Pietermaritzburg, Natal, South Africa; 3School of Physics, University of the Witwatersrand, Johannesburg, Gauteng, South Africa; 4International Material Institute, Princeton University, Princeton, New Jersey.

Resonant Raman and 57Fe Mossbauer Spectroscopy (MS) under hydrostatic pressure in a diamond-anvil cell are used to investigate the spin-structure response of the 3d manifold of Fe in the ferric haem-porphyrin [Fe(TPP)(NCS)] complexes. Extreme pressure conditions using different Mossbauer system have enabled the magnetic investigations of samples in a volume of picolitre in the sample cavity of a Diamond Anvil Cell. The study of the pressure response of such organo-metallic systems is fundamentally important because iron porphyrins are found in biology as haem proteins whose activity is sensitive to the structural configuration which in turn be influenced by the iron spin-state configuration. The results of 57Fe Mossbauer Spectroscopy (MS) under hydrostatic pressure show a pressure-induced spin-switching from the high-moment (nominal atomic spin S = 5/2) to the lowest moment (nominally S = 1/2) electronic state in [Fe(TPP)(NCS)] compound. Such a spin-switching is shown to occur at moderate pressure conditions of 5-10 GPa at room temperature. Resonant Raman spectra of both spin states were obtained and associated with different structural configurations of the molecule. Resonant Raman Spectroscopy is used to get additional informations on the vibrational modes. The change of the magnetic moment of such paramagnetic compound from ca. 5.6 BM at low

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pressure to ca. 1.8 BM at high pressure is discussed in view of potential applications in molecular electronics.

K9.18
Immobilization of Proteins on the Surface of Silanized Hydroxyapatite. Akira Morozumi, Toshiyuki Honma, Syunj Yuuki, Yuri Kimmagi and Junzo Tanaka; Biomaterials Center, National Institute for Materials Science, Tsukuba.

Hydroxyapatite (HAp) is widely used as bioceramics for bone and dental tissue reconstruction due to its biocompatibility [2] with hard tissues and high osteoconductivity. HAp has an interesting property as an adsorbent for biopolymers such as protein. The absorption ability of HAp is useful for the preparation of HAp/protein complexes. However, the proteins were easily removed from the HAp surface in vitro and in vivo studies, which depend on the ionic strengths and pH values in aqueous systems. To overcome these problems, it is necessary to bond protein onto HAp surface firmly by using an adhesion coupling agent. Silane coupling agent is one of bonding materials with the ability to bond inorganic materials such as glass, mineral fillers, metals and metallic oxides to organic resins. Furthermore, previous studies showed that the silane coupling agent is useful material for coating on the HAp surface. This study focused on the coupling agent as a binding material between HAp and four different proteins such as acidic proteins of fibrinogen, fibronectin and vitronectin, and basic proteins of collagen. These proteins are important factors for the cell attachment onto the materials surfaces in cell culture. We immobilized these proteins onto the surface of HAp sintered body with 20 mm in diameter and 2 mm in thickness by introducing covalent bonding of 3-aminopropyltriethoxysilane (APS). The existence of APS on the HAp surface was confirmed by zeta-potential measurements. The proteins immobilized on the pure HAp and APS/HAp were observed by atomic force microscopy (AFM, SPM 9500) analyses and zeta-potential measurements. The stability of protein/APS/HAp and protein/HAp composites was evaluated after soaking in PBS and NaCl solutions with various concentrations. AFM analyses and zeta-potential measurements revealed that proteins were firmly bonded on the APS/HAp surface in the solutions. However, the Col/HAp composite is unstable in the high NaCl concentrations. The fibrogen, fibronectin and vitronectin are unstable and removed from the pure HAp surface in the PBS solution, however, the APS/HAp was firmly bonded on the proteins in the PBS solution. We concluded that proteins immobilized on the APS/HAp are more stable than those immobilized on the normal HAp in high ionic strength solutions (PBS and NaCl).

K9.19
Transferred to K10.1

K9.20
Hydroxyapatite Coatings Deposited by KrF-Laser Ablation and its Adhesion to Metallic and Ceramic Implants. Won-Jun Lee1, Sang-Wook Lee1, Ihyeon Kim1, Dae-Joon Kim1 and Jung-Sang Hahn2; 1Department of Materials Science and Bioengineering Research Center, Sogang University, Seoul, South Korea; 2Department of Prosthodontics and Dental Research Center, College of Dentistry, Seoul National University, Seoul, South Korea.

Hydroxyapatite (HAp), Ca10[PO4]6(OH)2, is currently used as a biomaterial for many applications in both dentistry and orthopedics, because it is the main chemical component of bone. Nevertheless, due to the poor mechanical properties of bulk HA, it cannot be used as an implant device materials for load-bearing applications. The solution is to apply HA as a coating on Ti or Ti-based alloy implants. In this way, the mechanical properties of the implants are supported by the metallic structure, while the osteointegration is promoted by the bioactive surface of HA. Plasma-spray (PS) was the first method used for coating implants with HA, and the PS coatings exhibited better bone healing than uncoated implants; however, there were some issues affecting the long-term stability of the implants. The main problems of PS coatings are related with the presence of other calcium phosphate phases, the porosity and the poor coating-substrate adhesion. In this study, the HA coatings with a high degree of crystallinity (crystalline HA films) were obtained using a KrF excimer laser (at 248 nm) by a metal atomic force microscope (AFM) tip. Here, we report on experiments in which we measure currents higher than 220 nA at 2 V, indicating charge transport through 26 base-pairs long DNA molecules of complex sequence. Moreover, we observe a non-zero gap and a peak structure in the current-voltage curves that is reproduced for many molecules and by two different measurement methods. We present a comprehensive set of control experiments that support our findings. These include simultaneous time-resolved maps, measurements on non-complementary strands, current-distance upon stretching the molecules, 3D-mode measurements performed on the insulating surrounding layer and checking the effect of humidity. 1. Cui, X. D.; Primak, A.; Zarate, X.; Tomfohr, J.; Sankey, O. F.; Moore, A. L.; Moore, A. T.; Gust, D.; Harris, G.; Lindsay, S. M. "Reproducible Measurement of Single-Molecule Conductivity" Science 2001; 294, 551. 2. Claude Nogues, Sidney R. Cohen, Shirley S. Daube, and Ron Naaman. "Electrical properties of short DNA oligomers characterized by conducting atomic force microscopy", PCCP, 2004, 18, 3. Heyz Cohen, Claude Nogues Ron Naaman and Danny Porath "Direct Measurement of Electrical Transport Through Single DNA molecules", submitted.
To combat the deleterious effects of radiation and other stresses on long-term human space exploration, it is critical to better understand cardiovascular and skeletal adaptations. The combination of molecular, cellular, and mechanico-electro performance of muscle cells will provide us with complete dynamic data to develop adequate countermeasures to combat these adverse effects. Unlike the conventional measurements techniques, we have developed a novel method capable of characterizing the mechanical properties of muscle at both tissue and single-cell levels using a self-assembly system. This system has shown the capability of spatially and selectively directing growth and differentiation of myocytes into single muscle bundles in situ, attachment of these functional bundles to MEMS structures, and the controlled release of the resultant hybrid devices without any manual assistance. The mechanical properties of the neonatal ventricular myocytes 1-3-day-old Sprague-Dawley rats (NVMYs), such as substrate-induced stress and Young’s modulus, have been measured using this force transducer and were found to be 2-2.5 kPa and 40 kPa respectively. Here we expand this system to dynamically monitor the cellular activities in response to the external applied stresses. It has been noted that intracellular calcium concentrations of cardiac myocytes fluctuate between 10-5M - 10-7M upon contraction and relaxation respectively. Using an intracellular fluorescent calcium indicator we can correlate fluorescent density with cellular function. By monitoring the fluorescent signal, we can visualize calcium fluxes and in turn determine what state a particular cell is in. In addition to detecting cellular activity, the effect of UV radiation and mechanic stresses on the cells are also under investigation. Further study of genetically engineered cells will enable us to in situ monitor the molecular and genetic information and simultaneously investigate the self-assembly process with the assistance of the system. The self-assembly system established is not only suitable for studying dynamic mechanics of muscle cells, including the correlation of intracellular activities with external factors, but also applied to the studies of other cells.

SESSION K10: Biomaterials: Theory and Experiment
Chair: Elaine DiMasi
Friday Morning, April 1, 2005
Room 207 (Moscow West)

8:30 AM K10.1 Simulations and Design of a New Green Fluorescence Protein Mutant. Murat Cetinbayra1, Aline Zeytun1b, Andrew Bradbury2 and Melik C. Demirelc1.

A set of new green fluorescence protein (GFP) mutants are experimentally created by modifying four loop regions of GFP. The excitation/emission spectra of these mutants were determined and base-pairing interactions in DNA experiments and DFT calculations. We show that, after a gentle deposition of the binary mixture G-C (purine-pyrimidine pair of complementary bases) and A-C (purine-pyrimidine pair of non-complementary bases) by STM, the Na base guanine (G), deposited under ultra-clean conditions onto the inert Au(111) substrate, self-assembles into a hydrogen-bonded network of G-quartets with the same structure as that found in quadruplex telomeric DNA. Comparison with our Density Functional Theory (DFT) calculations shows that the strong preference of G molecules to form quartets arises from a cooperative effect that strengthens the hydrogen bonding in the G-quartet network relative to those in isolated G dimers.

8:45 AM K10.2 Nano-Photonics in Biological Systems. Alexander A. Balandin and Vladimir A. Fonoberov; Nano-Device Laboratory, Department of Electrical Engineering, University of California, Riverside, California.

Viruses have recently attracted attention as biological templates for assembly of nanostructures and nanoelectronic circuits [1]. They can be coated with metals, silica or semiconductor materials and form end-to-end or end-to-nanorod assemblies. Such viruses as tobacco mosaic virus (TMV) and M13 bacteriophage have appropriate cylindrical shape and particularly suitable dimensions: M13 is 860 nm long and 8.5 nm in diameter, while TMV is 300 nm long, 18 nm in diameter and with a 4 nm in diameter axial channel. The knowledge of the phicon, i.e., vibrational, modes of these viruses is important for material and structural characterization of the virus-based nano-templates, for in-situ monitoring of the nanostructure self-assembly, and for understanding properties of the biological-inorganic interfaces. In this paper we review our recent theoretical and experimental results on phonon spectra of TMV and M13 bacteriophage immersed in air and water. The low-frequency phonon dispersion has been rigorously calculated using the complex-frequency approach. The radial breathing modes of TMV and M13 viruses in air are found to be 1.85 cm-1 and 6.42 cm-1, respectively [2]. The quality factor Re(w)/Im(w) for radial vibrations of TMV in water is about 3.6 for the radial breathing mode and about 10 for the second radial mode. Strain-induced modifications since new residue insertions to this region cause drastic unfolding of the beta-bar structure of GFP, confirming our hypothesis for the change in fluorescence intensity of the protein. We have also performed simulations regarding other loop regions and compared with the corresponding experimental data.

9:00 AM K10.3 Guanine Quartet Networks Stabilized by Cooperative Hydrogen Bonds. Roberto Otero Martin, Maya Schoeck, Luis M. Molina, Erik Laegaards, Ivan Stensgaard, Bjork Hammer and Flemming Bensenbacher; Department of Physics and Astronomy, University of Aarhus, Aarhus, Denmark.

Hydrogen bonding between DNA or RNA bases is one of the main interactions determining the structure of these single-stranded polymers. The high thermodynamic stability, structural and functional properties of DNA and RNA are tightly controlled by the hydrogen bonding of nucleobases. The ratio of G-C to A-T pairs is critical to better understand the hydrogen bonding in DNA and RNA and its effect on the functionality, conformational stability, and folding of the biopolymer. We have used ab initio quantum chemistry (DFT) calculations and electronic absorption and emission at each wavelength to calculate the hydrogen bonding between DNA and RNA bases. We propose that DNA and RNA bases form a hydrogen bonding network of G-C quartets, which is the basis for the complementarity in DNA and RNA. This mechanism is responsible for the high thermodynamic stability of DNA and RNA. In the DNA quartet, the G-C pairs explain the enhanced thermal stability of the combined G-C mixture. This result shows that the hydrogen bonding interaction alone can steer the processes necessary for molecular recognition to take place in 2D networks, thereby opening new avenues to design molecular self-assemblies with desired geometries.

9:30 AM K10.5 A Solution to the Streptavidin-Biotin Paradox? Frederic Pincet and Julien Husson; Laboratoire de Physique Statistique, Ecole

Studied by STM. Maya Schoeck, Eva Rauls, Roberto Otero Martin, Wei Xu, Erik Laegaards, Ivan Stensgaard, Bjork Hammer and Flemming Bensenbacher; Department of Physics and Astronomy, University of Aarhus, Aarhus, Denmark.

Molecular recognition events between complementary nucleic acid bases are fundamental for many biological processes, like DNA replication. Those processes have been found on applications in the field of Nanotechnology, and strands of complementary DNA sequences have been used to direct the self-assembly of nanostructures. In principle, the complementarity in hydrogen-donors and acceptors groups in single DNA bases might as well be controlled by molecular recognition processes, that could be used to control 2D molecular assemblies as well. However, the existence of "wobble" or "deviant" base pairs, and a possible disturbing effect of the substrate on the hydrogen bonds made this possibility more difficult to explore. In this contribution we compare the 2D molecular networks formed on Au(111) upon deposition of the binary mixtures G-C (purine-pyrimidine pair of complementary bases) and A-C (purine-pyrimidine pair of non-complementary bases) by STM experiments and DFT calculations. We show that, after a gentle annealing to 80 C the non-complementary bases separate into inlands of pure A and a network of pure C, whereas the complementary bases G and C form a network that cannot be separated by annealing up to the desorption temperature for C. High-resolution STM images allow us to identify structures that contain G-C bonds, possibly with the same shape as the Watson-Crick pairs in DNA molecules. The stronger bond between G and C molecules with respect to G-G or G-C pairs explains the enhanced thermal stability of the combined G-C mixture. This result shows that the hydrogen bonding interaction alone can steer the processes necessary for molecular recognition to take place in 2D networks, thereby opening new avenues to design molecular self-assemblies with desired geometries.
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Interfaces.

Blacksburg, Virginia.

of Physics and Astronomy, The

AM K10.6

software and the constant improvement of computer performance have

solvent, could provide an inadequate description of adsorption,

that interfacial adsorption models based on the molecular mechanics

this complex. In this presentation, all these results will be conciliated

structure and orientation of molecules at the interface. Presented

stretching [2] and flow chamber [3] experiments lead to very different

Quantum Chemistry Approach to Modeling of Molecular

polypeptides at crystal interfaces.

Empirical methods of quantum mechanics to address the role of the solvent for

membrane-bound molecules. New interface-specific techniques based

influence of membrane fluidity on the incorporation and structure of

results will include determination of the gel-fluid phase transition

nucleus to the surface topography and elasticity map. In the human tooth, we observed a vector electromechanical response of a single collagen molecule bundle that allows the local molecule orientation to be reconstructed. This allows us to repeat Galvani's experiment on the nanoscale, 230 years later and with a million times higher resolution. The future opportunities of electromechanical SPM for characterization of complex biological systems are discussed. Research performed as a Eugene P. Wigner Fellow (SVK) at ORNL, managed by UT-Battelle, LLC under DOE contract DCE-AC05-00OR22725. AG acknowledges financial support of the National Science Foundation (Grant No. DMR02-35632).

11:00 AM K11.3

Aspartate Chain Length Controls Calcite Step Morphology by Differential Step Recognition. Selin Elhai1, Edward Salters2, Andrzej Wierzbicki2, Patricia Dove3, Nizhou Han3 and James De Yoreo3. 1Chemistry, University of South Alabama, Mobile, Alabama; 2Chemistry and Material Sciences, Lawrence Livermore National Labs, Livermore, California.

Most controlled crystallization is believed to be achieved under the direction of macromolecular protein-based templates with specific affinities for assembling and assembling the desired growth units. This reliance upon cellular proteins with specific sequences and structures suggests that the chemistry and stereochemistry of the amino acids forming the proteins are essential in conferring targeted activity in controlled biosynthesis. Calcium carbonate is a key biogenic mineral and model system to study the molecular mechanisms by which amino acids and polypeptides interact with individual steps. Investigations of molecularly resolved crystal-peptide interactions can reveal how biomolecules achieve regulated growth during biomineralization. Our previous studies have focused on the role of specific single and dipeptide species known to contain a significant fraction of the proteins involved in biomineralization processes, in particular, acidic amino acids and aspartate. In this study, we extend our investigation to the role of aspartate chain length because they represent an integral part of the active site of these biomineralization sequences. In particular, the effect of polypeptides (Asp, n=1,2,4,5,6) on the kinetics and thermodynamics of calcite growth were investigated and compared with models of calcite-Asp interactions. Using in situ Atomic Force Microscopy and precisely characterized solutions, our experimental measurements of growth kinetics and observations of the calcite hillock morphology at the nanoscale show that step directions with acute and obtuse geometries are affected differently for all aspartate derivatives. Short chain aspartates (n<=2) roughen acute steps more strongly than obtuse steps. This situation is exactly reversed for longer chain aspartates (n>3). Further, the Asp concentration required to roughen the steps decreases with increasing length of the Asp peptide. Circular Dichroism measurements were performed to confirm the aspartate conformations assumed in the modeling. We examine the molecular origins of these experimental findings using molecular modeling. Not unexpectedly, due to cooperative binding, the concentration required to affect step edge morphology is predicted to decrease exponentially with increasing aspartate chain length. This trend correlates with the measured inhibition or activation of the catalytic role of aspartate can be explained by relating chain length to calcite step binding and dehydration energy. Our findings suggest that there is a qualitative change in the nature of aspartate-calcite step interactions with increasing aspartate chain length. This change is accompanied by an exponential increase in the degree of aspartate binding. This chain length dependent differential binding to opposing calcite steps may be an additional mechanism by which biomineralizing proteins can achieve regulation of calcite growth.
Session K12: Biomimetic Minerals and High Resolution Probes
Friday Afternoon, April 1, 2005
Room 207 (Moscone West)

11:15 AM K11.4
Probing the Effect of Different Polypeptide Biomimetic Recognition on the Growth of Calcite. J. Woollam Kim1, Molly R. Darragh2, Christine A. Orme2 and John Spencer Evans3; 1Laboratory for Chemical Physics & Center for Biomolecular Materials Spectroscopy, New York University, New York, New York; 2Department of Chemistry and Materials Science, Lawrence Livermore National Laboratory, Livermore, California; 3Department of Chemistry, University at Buffalo, SUNY, Buffalo, New York.

Recent studies have established that the nacre layer of mollusks possess a number of proteins that assist in the formation and stabilization of the aragonite polymorph during shell development. However, very little is known regarding the mechanism of protein manipulation of calcium carbonate biomimetic formation. In particular, the interaction between proteins and the recognition of mineral surface features is not clearly understood. Previously, we identified 30 AA N-terminal mineral binding domains that originate from three different nacre-specific proteins (AP7, AP24, n16). These domains, termed MBD1, MBD2, and MBD3, induce morphological changes in calcium carbonate in vitro and are similar in amino acid composition, but differ significantly from each other with regard to their primary sequences. Using a flow cell-equipped AFM instrument, we investigated the sites of adsorption of each mineral-binding domain onto calcite dislocation hillocks. We find that AP7-N and AP24-N both preferentially interact with the acute step edges of dislocation hillocks, leading to bunching of these step edges. Moreover, AP24-N and AP25-N both induce the formation of deposits on terrace surfaces. Comparatively, AP24-N exhibited higher mineral modulation activity over AP27-N with regard to step edge inhibition and deposit formation. In contrast, n16-N exhibits an interaction preference for terrace surfaces, which leads to pilling effects that block the advance of acute and obtuse hillock steps and the emergence of new non-parallel steps. Random scrambling of the n16-N and AP7-N sequences resulted in substantially reduced mineral modification activity, indicating that primary sequence of both polypeptides is crucial for recognition of surface features.

11:30 AM K11.5
In-Situ Characterization of Surface Evolution on Titanium in Hydrogen Peroxide Containing Solutions. Julie J. Muyeck1,2, Jeremy J. Gray1, Timothy V. Ratto1, Christine A. Orme1, Joanna McKittrick2 and John Frangos1; 1Lawrence Livermore National Laboratory, Livermore, California; 2University of California, San Diego, La Jolla, California; 3La Jolla Bioscience Institute, La Jolla, California.

Titanium implants have been used for decades with success in various applications. The characteristic of titanium that allows acceptance in the body is not well defined. It is hypothesized that the interaction of titanium implants with inorganic components of bodily fluid is key to the acceptance of titanium in the body. The component of bodily fluid that is important for controlling mineralization is the inorganic phosphates. Citrate was chosen to isolate the effect of carboxylic acid groups on the growth morphology and it has been shown that citrate inhibits brushite growth in bulk experiments. Osteopontin is an important protein involved with bone formation and is known to affect the growth of both hydroxyapatite and brushite. We present data from an in-situ AFM study that shows the kinetics of step motion and alters the step directions. Citrate on the other hand, has little effect on the step kinematics but changes the step-edge free energy leaving the step directions unchanged. Changes to the step-edge free energy affect the overall growth rate of the crystal by changing the density of steps on the surface. It is interesting to note that it may be much more efficient for organisms to control growth rate by adding small quantities of surfactant than to change the local solution supersaturation and that this may represent a new pathway for controlling mineralization. This work was performed under the auspices of the US Department of Energy under contract W-7405-Eng-48.

1:30 PM *K12.2
Nonocrystalline Calcium Phosphates and Plaster of Paris from Deep-Sea Medusae - What can be Learned from Biomimatisation? Matthias Epple, Inorganic Chemistry, Univ Duisburg-Essen, Essen, Germany.

Biomimatisation is the utilisation of inorganic materials by living organisms. Bone, teeth, and mollusk shells are prominent examples. By investigating and mimicking these biological processes and the structure of biomimetics, new and better biomaterials for clinical use can be prepared. This is demonstrated first on nonocrystalline calcium phosphates that have chemical and crystallographic properties close to bone mineral. In combination with biodegradable polymers, individual implants for the regeneration of skull defects can be prepared. However, nature's ability to crystallise biominerals is still not achieved by materials scientists. This is shown on the example of deep-sea medusae that use calcium carbonate hydrate (Plaster of Paris) for orientation. It is impossible to crystallise this hydroscopic material in the chemical laboratory.

2:00 PM K12.3
Synchrotron X-ray Studies on the Effect of Mg Ions on Oriented Growth of Calcite on Alkanethiol Functionalized Self-Assembled Monolayer. Seo-Young Kwak1, Elaine DiMasi1, Yong-Jin Han1 and Joanna Aizenberg2; 1National Synchrotron Light Source, Brookhaven National Laboratory, Upton, New York; 2Bell Laboratories, Lucent Technologies, Murray Hill, New Jersey.

The effects of Mg2+ ions upon the nucleation of oriented calcite crystals in the presence of self-assembled monolayers (SAMs) of α-oxidized alkanethiols (HS(CH2)nxX; X = CO2- and SO3-, n= 10 and 15) supported on gold films were studied with Synchrotron X-ray diffraction. Mg2+ ions were added to the crystallizing solution in various molar ratios of Mg2+/Ca2+ (m) ranging from 0 to 4.0. Mg2+ ions are of particular interest since they are found in biological environments in high concentrations and are believed to play a critical role in CaCO3 formation. This study revealed new details about the underlying substrate texture; preferred orientations of calcite crystals nucleated from different monolayers were different and affected the crystalline planes depending on the functional groups. For low Mg2+ content, SO3- functionalized films nucleated primarily the (106) calcite face, C15 films nucleated the (012) face, and C16 films showed a greater number of surface-normal (104) peaks. However, Mg2+/Ca2+ ratio of 2 and greater defeated this preferred orientation and created a powder pattern. In-plane diffraction from the coarse calcite powders indicated a shift to higher two-theta and a corresponding peak broadening with increasing Mg2+/Ca2+ ratio. According to the refinement of lattice
parameters, Mg\(^{2+}\) incorporation shrinks the calcite lattice by a few percent (2Δa ≈ 1.3% and Δc ≈ 2.0%). We discuss these SASM-nucleated details in the context of geological and biogenic magnesian calcites.

2:15 PM K12.2

Modification of Macromolecules Extracted from Natural Bioceramics: Maria Soledad Fernandez\(^1\), Andronico Neira-Carrillo\(^2\), Patricia Hernandez-Arias\(^3\), Marcos Farinas\(^4\) and Jose Luis Arias\(^5\); \(^1\)Veterinary Sciences, Universidad de Chile and CIMIT, Santiago, Chile; \(^2\)History and Embryology, Universidade Federal Rio de Janeiro, Rio de Janeiro, Brazil.

Biominalization leads to the formation of inorganic crystals with unique, ordered, refined shapes that are regulated by specific macromolecules. Bioceramics are composite materials, composed of an intimately associated organic matrix and inorganic crystals. The surface characteristics of bioceramics, but also contributes to the nucleation, growth, shape and final organization of the inorganic phase. In order to know how the organic phase regulates the formation of hard tissues, we evaluated the effect of soluble matrices extracted from different bioceramics on crystal morphology. We obtained obtained after decalcification of the bioceramics were biochemically characterized by electrophoresis and dotblot using monoclonal antibodies against some proteoglycans, and the effect on crystal morphology using in vitro crystallization assays was analyzed by SEM. Crystal morphology modifications are closely related with the structure and charging of the organic macromolecules involved.

2:30 PM K12.4

Lipidated Peptides as Templates for CaCO\(_3\) Mineralization: Kros Alexander\(^1\), Silvia Cavalli\(^2\), Daniela C. Popescu\(^2\), Elnily E. Tellers\(^1\), Mark Overhand\(^1\) and Nico A. J. M. Sommerdijk\(^2\); \(^1\)Institute for Collaborative Biotechnologies, University of California, Santa Barbara, Santa Barbara, California; \(^2\)Department of Chemistry, Leiden University, Leiden, Netherlands.

The formation of crystals in nature is a very sophisticated process. In order to gain a deeper understanding of this fascinating organic-biomineralization, we focused on biomimetic mimics that are templates as well-defined Lamguur monolayers can be employed as molecular blueprints for the oriented nucleation of inorganic materials. In our study a series of amphiphilic peptides were designed incorporating a peptide head group of variable length: two, three and four repeated units of alternating hydrophilic and hydrophobic amino acid residues. This alternation plays a primary role in the generation of beta-sheet secondary structure at the air/water interface. Furthermore a phospholipid tail was introduced to stabilize the monolayer. This approach should provide a network of carboxylic acid groups positioned at specific distances in order to direct CaCO\(_3\) calcite crystal growth. In the work described here self-organizing beta-sheet monolayers acted as template in the crystallization of CaCO\(_3\), resulting in habit-modified calcite crystals with two main kinds of morphologies.

2:45 PM K12.5

Investigating Protein-Mineral Interactions in a Marine Invertebrate System: Germaine Py\(^1\), Suresh Vallyverdú\(^2\), Brigitte Vogena\(^3\), Siping Roger Qiu\(^4\), James J. De Yoreo\(^5\) and Daniel E. Morse\(^6\); \(^1\)Biomolecular Science and Engineering Graduate Program, University of California, Santa Barbara, Santa Barbara, California; \(^2\)Institute for Collaborative Biotechnologies, University of California, Santa Barbara, Santa Barbara, California; \(^3\)Department of Chemistry, National University of Singapore, Singapore, Singapore; \(^4\)Department of Earth and Planetary Sciences, Washington University, St. Louis, Missouri; \(^5\)Department of Chemistry and Materials Science, Lawrence Livermore National Laboratory, Livermore, California.

The predominance of acidic proteins and polysaccharides detected in biomineralized CaCO\(_3\) structures suggests that mineralization is controlled through interactions between charged macromolecules and mineral ions and surfaces. In this study, the most acidic proteins were selectively isolated from abalone shell mucus. These proteins are two variants of 8.7 and 7.8 kDa designated AP8 (for aragonite proteins of approximately 8 kDa) and AP8, respectively. The AP8 protein compositions dominated by Asx (~55 mol%) and Gly (~40 mol%) residues, indicating that their structures have high Ca\(^{2+}\) binding capacity and backbone flexibility. In vitro mineralization of CaCO\(_3\) in the presence of the purified AP8 proteins results in elongated calcite crystals asymmetrically rounded at the acute edges of the rhombohedral faces. In contrast, crystals grown with narcotic proteins depleted of AP8 retain the morphology of unmodified calcite rhombohedra, demonstrating that the AP8 proteins are more effective crystal-modulators than other proteins from the same biomineralized material. AFM analyses reveal that stereochmical recognition by the AP8 proteins occurs at the step edges of crystal hillocks to modify both the kinetics and morphology of crystal growth. By combining molecular with conventional macroscopic crystal analyses, we provide direct evidence to support the hypothesis that protein-mineral interactions at the step edges of crystal surfaces can be responsible for the corresponding morphologies of macroscopic crystals. These observations thus help resolve the competing theories of face- versus step-specific interaction between proteins and crystal surfaces proposed for related biomineralization systems. We propose a complex interaction that take place between newly forming biogenic minerals and the macromolecules that control their crystallization.

SESSION K13: Biomimetic Bone and Implant Materials

Chair: Elaine DiMasi

Friday Afternoon, April 1, 2005
Room 2007 (Moscone West)

3:30 PM K13.1

Well Dispersed Nanophase Titania in Poly-lactic-co-glycolic Acid (PLGA) Scaffolds for Bone Tissue Engineering Applications: Himnah Liu\(^1\), Elliott B. Slimovich\(^2\) and Thomas J. Webster\(^1\); \(^1\)Materials Engineering, Purdue University, West Lafayette, Indiana; \(^2\)Biomedical Engineering, Purdue University, West Lafayette, Indiana.

Bone substitutes are often required to replace damaged tissue due to injuries, diseases and genetic malformations. Traditional bone substitutes, such as autografts, allografts, xenografts and metal implants, are far from ideal and each have their own specific problems and limitations. Bone tissue engineering offers a promising opportunity for bone regeneration in a natural way. However, currently the scientific challenge is the design of biocompatible and bioactive scaffolds which can improve the properties of the bioceramic, but also contributes to the nucleation, growth, shape and final organization of the inorganic phase. In this procedure the present study demonstrates that PLGA composites offers an exciting approach to combine the advantages of a degradable polymer with nanosize ceramic grains to optimize physical and biological properties for bone regeneration. Importantly, nanophase titania mimics the size scale of constituent components of bone since bone itself is a nanoscooped composite material. Several randomized well-dispersed titania nanophase in PLAGA was enhanced by increasing the sonication time and that greater osteoblast adhesion correlated with improved nanophase titania dispersion in PLAGA. Moreover, for the first time, results correlated better osteoblast long-term functions, such as alkaline phosphatase activity and calcium-containing mineral deposition, with improved nanophase titania dispersion in PLAGA. Furthermore, the present study demonstrated that PLGA composites with well-dispersed nanophase titania can improve osteoblast functions necessary for improved bone tissue engineering applications.

3:45 PM K13.2

Dentin Matrix Protein 1 (DMP1) Actively Participates in Initiating and Modifying Calcium Phosphate Morphology during Crystal Growth: Swinkumar Gajjarannan, Karthikeyan Natarajan, Sankalp Jain, Andrew Ramachandran, John George; Oral Biology, University of Illinois at Chicago, Chicago, Illinois.

Mineralization of bones and teeth occur by the nucleation of hydroxyapatite crystals in an extracellular matrix consisting of predominantly type I collagen and a variety of noncollagenous proteins. Among the noncollagenous proteins, dentin matrix protein1(DMP1) is an acidic protein found in the mineralized matrix of bones and teeth has been postulated to play an important role in interacting with calcium ions and mineral surfaces. To investigate on the mineral initiating role of DMP1 we have devised a methodology to study its properties in a semi solid medium mimicking the extracellular environment in mineralized tissues. In this procedure the crystals were grown by controlled chemical reaction between calcium and phosphate ions at physiological pH and temperature with and without recombinant DMP1 (+DMP1). After 45 days of growth the calcium phosphate deposits were detected using electron microscopy (SEM). Results demonstrate the presence of spherical and platy crystals in the absence of r-DMP1, whereas only spherical crystals were seen in the presence of DMP1. These crystals were
Our strategy involves starting with a monolithic, glass during Eo. Further, the calcium and phosphorous content were confirmed by EDX analysis and the Ca/P ratio of the crystals grown in the presence of r-DMPI was found to be between 1.64-1.67. Thus, DMP1 can control the calcium phosphate crystal morphology during crystal nucleation and growth. This research was supported by NIH grant 16553.

4:00 PM K13.3
Probing In Vitro Interactions of Immortalized Human Bone Marrow Stromal Cells with Novel Bioactive Glass Coatings.
Jie Song¹ ², Eduardo Sain², Vincent Eng³, Carolyn R. Bertozzi¹ ² ³ and Antoni P. Tomsia¹ ²; ¹Materials Sciences Division, Lawrence Berkeley National Lab, Berkeley, California; ²Molecular Foundry, Lawrence Berkeley National Lab, Berkeley, California; ³Departments of Chemistry and Molecular and Cell Biology, University of California, Berkeley, California.

Metals have been widely used for fracture fixation, joint replacement and dental applications. To improve the ability of bioinert metallic implants to bond to osseous and dental tissues, bioactive surface coatings such as hydroxyapatite (HA) are often applied via plasma spray. Although these bioactive ceramics have been shown to facilitate the implant-tissue integration and lead to faster healing, in vivo studies have demonstrated that the unreliable metal-ceramic adhesion contributes to the long-term failure of these implants. A novel glass family in the Si-Na-K-Mg-Ca-P-O system has been developed to prepare graded glass-HA coatings on metallic implants using a simple enamelning technique. The coatings consist of a high silica layer in contact with the alloy and a surface layer that is a mixture of a low silica glass and HA particles. The coatings form apatite in simulated body fluid while maintaining excellent adhesion with the alloy. To probe the physiological relevance of these novel coatings for potential implant applications, the proliferation and expression of osteoblastic marker proteins of normal human osteoblastic cells on these glasses should be examined. Normal human osteoblasts (NHOst) and bone marrow stromal cells (BMC) have limited proliferative life span in culture and gradually lose their osteogenic potential in culture, making the use of these cell lines for screening biocompatible implant coatings inconvenient. Immortalized human bone marrow stromal cells (hTERT-BMCs), established via ectopic expression of human telomerase in normal human BMCs, have extended life span in culture and do not exhibit growth deregulation. They were seeded onto a number of novel glasses, alloy substrates with graded coatings, and Ti6Al4V and tissue culture polystyrene controls for in vitro cell culture studies. These cells were cultured in the presence of 1,25-dihydroxyvitamin D3, which is known to induce differentiation of BMCs into osteoblasts lineage. Cell lysates were collected at various time points, and cell proliferation was examined using a dsDNA quantification assay. The expression of osteogenic marker proteins including osteocalcin and osteopontin, as well as important extracellular matrix proteins such as collagen I and cytoskeletal protein -tubulin, was examined by Western blotting and microtiter plate immunoassays. The expression of alkaline phosphatase activity and the extent of mineralization in culture were also quantified.

4:15 PM K13.4
Hydroxyapatite Thin Films Produced by Radio Frequency Magnetron Sputtering from Two Facing Targets.
Donald E. Ellis¹ ², Z. Hong¹, L. Luan¹, Alexandre Rossi¹, Alexandre Mello³, J. G. Eon³, John Ketterson¹ and Joice Terra³; ¹Physics and Astronomy, Northwestern University, Evanston, Illinois; ²Chemistry, Northwestern University, Evanston, Illinois; ³Centro Brasileiro de Pesquisas Fisicas, Rio de Janeiro, RJ, Brazil; ⁴Instituto de Quimica, Fed. University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

We have produced hydroxyapatite (HA) thin films on fused silica using R.F. magnetron sputtering from two facing targets in a right angle geometry. This design greatly reduces negative-ion resputtering effects caused by oxygen ions, and thus preserves the stoichiometry of the targets. We studied both as-sputtered and annealed films (800°C in Ar) Water vapor was introduced during either the deposition or annealing process. Films were characterized by XRD, stylus profilometry, XRF, XPS, FTIR and Raman spectroscopy. Our XPS measurements showed that the as-sputtered films retain the same Ca/P ratio as that of the targets over a wide range of Ar pressures. Our XRD results show that the films are highly-textured along the HA(x00) direction. A comparison was also made for growth on several different substrates (SiO2, Si(100), Si(110), Si(111) and Ti. Structural and bonding characteristics of the films are discussed in the light of atomistic simulations and Density Functional electronic structure calculations.

4:30 PM K13.5
Template-free Routes to Hierarchically Porous Inorganic Monoliths. Eric Toberer and Ram Seshadri; Materials, University of California, Santa Barbara, Santa Barbara, California.

Mammalian lungs possess a fractal pore morphology that combines large active surface areas with high flow-through. In a similar manner, we have developed novel template-free routes that permit the formation of hierarchically porous structures in functional inorganic materials. Our strategy involves starting with a monolithic, single-phase material, which we convert to a two-phase composite, and then successively leach out components of the material such that a hierarchically porous material is left behind. Porous monoliths of various transition metal oxides have been prepared that possess a continuous porosity on the order of one micron, and a finer scale of porosity on the order of tens of nanometers.