TUESDAY, OCTOBER 26TH, 2010 **Polymer Science Research Center Auditorium**

SESSION: DESIGN AND SYNTHESIS **CHAIR: MAREK URBAN**

8:00-8:35 Stimuli-Responsive Block Copolymer Bioconjugates; ***Brent Sumerlin****, Southern Methodist University, USA*

8:35-9:10 Controlled Synthesis of Functional Smart Materials; ***Dirk Kuckling****, University of Paderborn, Germany*

9:10-9:45 From Reactive Polymers to Stimuli-Responsive Polymers, Materials and Surfaces; ***Patrick Theato****, University of Mainz, Germany*

9:45-10:20 Stimuli-Responsive Nanomaterials through Integration of Funtional Organic Dyes into Nanostructured Environments; ***Christoph Weder****, University of Fribourg, Switzerland*

10:20-10:35 BREAK

SESSION: BIOMIMETICS **CHAIR: SERGEI NAZARENKO**

10:35-11:10 Self-Oscillating Polymers and Gels as Novel Biomimetic Materials; ***Ryo Yoshida****, The University of Tokyo, Japan*

11:10-11:45 Designing Synthetic Cilia Using Self-Oscillating Polymer Gels; ***Pratyush Dayal****, University of Pittsburgh, USA*

11:45-12:20 Molecular Wear in Active Nanosystems; ***Henry Hess****, Columbia University, USA*

12:20-1:45 LUNCH

SESSION: FROM VESICLES TO STIMULI-RESPONSIVE FILMS **CHAIR: ROB STOREY**

1:45-2:20 Responsive Micelles, Vesicles and Organogels From Polypeptide-Containing Block Copolymers; ***Daniel Savin****, The University of Southern Mississippi, USA*

2:20-2:55 Smart Layer-by-Layer Assemblies Based on Selectively Modified Polysaccharides for Biomedical Applications; ***Rachel Auzely-Velty****, Centre de Recherches sur les Macromolecules, France*

2:55-3:30 Stimuli-Responsive Hydrogel Films and Particulates; ***Sergiy Minko****, Clarkson University, USA*

3:30-3:45 BREAK

3:45-4:20 Hydrophilic Grafted Layer with Tunable Strength and the Range of Hydrophobic Interactions; ***Igor Luzinov****, Clemson University, USA*

4:20-4:55 Photogenerated Responsive Polymer Thin Films**; *Mingdi Yan****, Portland State University, USA*

5:00-8:00 POSTER SESSION – Polymer Science Research Center Foyer

WEDNESDAY, OCTOBER 27TH, 2010 Polymer Science Research Center Auditorium

SESSION: STIMULI-RESPONSIVE BIOMATERIALS CHAIR: CHARLES MCCORMICK

8:00-8:35 New Generation of Macromolecular Therapeutics Inspired by Coiled-Coil Recognition in Smart Biomaterials; ***Jindrich Kopecek****, University of Utah, USA*

8:35-9:10 Poly (n-Isopropyl Acrylamide) as a Bioadhesive; ***Buddy Ratner****, University of Washington, USA*

9:10-9:45 Smart Polymers and Biomacromolecular Legos: From Sensing Applications to Functional Protein Scaffolds; ***Stefan Zauscher****, Duke University, USA*

9:45-10:20 Characterization and Understanding of Enzyme Modified Polymer Thin Films; ***James Rawlins****,The University of Southern Mississippi, USA*

10:20-10:35 BREAK

SESSION: STIMULI-RESPONSIVE POLYMERS IN CANCER THERAPY CHAIR: DEREK PATTON

10:35-11:10 Construction of Targeted siRNA-Polymer Polyplexes and Their Delivery to Cancer Cells with Subsequent Specific Gene Down-Regulation; ***Faqing Huang****, The University of Southern Mississippi, USA*

11:10-11:45 Brain Tumor Growth Inhibition by Intravenous Poly(β-L-malic) Acid Nanobio-conjugates with pH-Dependent Drug Release; ***Julia Y. Ljubimova****, Cedars-Sinai Medical Center, USA*

11:45-12:20 A Novel Enzyme-Responsive Colon-Targeted Drug Delivery System for the Treatment of Local Colonic Pathologies; ***Valence M. K. Ndesendo****, University of Witwatersrand, South Africa*

12:20-1:30 LUNCH

SESSION: MULTI-COMPONENT STIMULI-RESPONSIVE MATERIALS CHAIR: SARAH MORGAN

1:30-2:05 Stimuli Responsive Block Copolymers and Materials From Ionic Liquid Reactive Surfactants; ***John Texter****, Eastern Michigan University, USA*

2:05-2:40 Responsive Conjugated Polymer/Carbon Nanotube Composites; ***Lei Zhai****, University of Central Florida, USA*

2:40-3:15 Molecular Design for Functional Thermo-Responsive Polymers and Their Biomedical Applications; ***Takao Aoyagi****, National Institute for Materials Science, Japan*

3:15-3:30 BREAK

3:30-4:05 pH Sensitive Microcapsule Whose Membrane Undergoing Volume Phase Transition; ***Takayuki Narita****, Saga University, Japan*

4:05-4:40 Photoresponsive Liquid Crystal Polymer Networks: Glassy Adaptive Materials; ***Timothy White****, Wright Patterson Air Force Laboratory, USA*

4:40 Concluding Remarks: **MAREK URBAN**

SYMPOSIUM ABSTRACTS

PLENARY LECTURES: Tuesday, October 26, 2010

Tue. 8:00-8:35 STIMULI-RESPONSIVE BLOCK COPOLYMER BIOCONJUGATES

Brent Sumerlin, Southern Methodist University, USA

Simplified routes to well-defined “smart” polymer-protein conjugates with tunable bioactivity will be discussed. Protein modification with a reversible addition-fragmentation chain transfer (RAFT) agent and subsequent room temperature polymerization in aqueous media led to conjugates of responsive polymers with model proteins. Representing the first example of polymer-protein conjugation by the grafting-from approach via RAFT, high molecular weight and reductively stable conjugates were accessible without extensive purification or adverse effects on protein structure. Alternatively, postpolymerization conjugation of the responsive polymers labeled with maleimides, thiols, or activated esters also allowed polymer-protein conjugates to be prepared in a straightforward manner. The responsive behavior of the immobilized polymer facilitated conjugate isolation and allowed environmental modulation of bioactivity.

Tue. 8:35-9:10 CONTROLLED SYNTHESIS OF FUNCTIONAL SMART MATERIALS

Dirk Kuckling - University of Paderborn, Germany

The volume phase transition in stimuli sensitive hydrogels is important for many applications, e. g. as (micro-) actuator and sensors materials, or in controlled cell attachment-detachment and controlled drug delivery. Most investigations focus on temperature or pH sensitive polymers, however, a variety of other parameters (e. g. ionic strength, UV light, magnetic fields etc.) has been studied. The majority of these applications require the use of hydrogels as thin layers at surfaces and interfaces. Therefore, the behavior of bulk hydrogel may not be necessarily extended to these types of geometries. Responsive polymers networks are interesting materials for a variety of different applications due to the fact that they can perform a large volume transition. However, the swelling transition is a diffusion limited process. Thus, the decrease of the feature size (e. g. in thin layers) is an appropriate way to create structures with reasonable response time. The possibility to pattern responsive polymer networks makes them useful for application in micro-system technology as well as in biomedicine. The transition behavior of these films showed similar trends to those of the corresponding linear polymers whereas confinement effects have been found for thin hydrogel layers. The ability to optimize the integration of these polymers is critical for the fabrication and development of platforms that harness the unique abilities of responsive polymer networks. Further decrease of the gel size led to the development of colloidal hydrogels with diameters down to 50 nm. Even complex structures like core-shell-morphologies can be prepared.

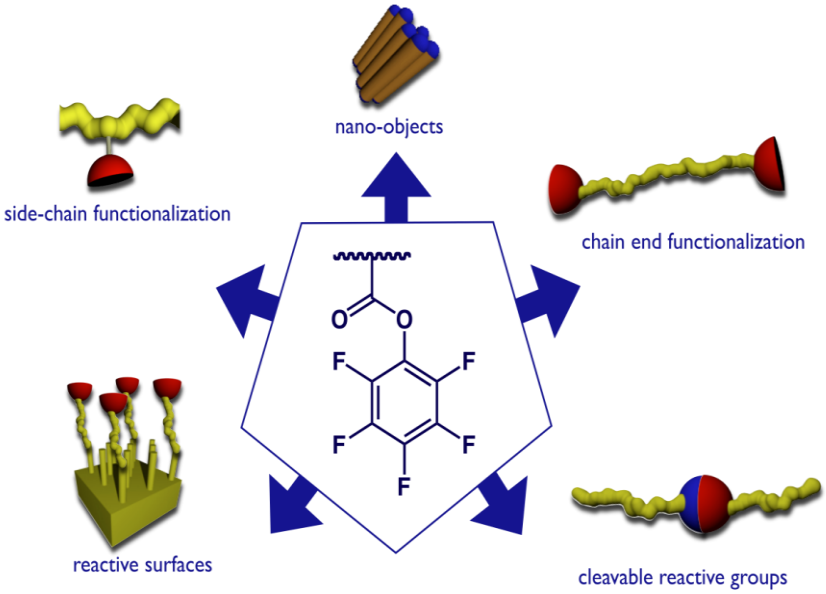
Tue. 9:10-9:45 FROM REACTIVE POLYMERS TO STIMULI-RESPONSIVE POLYMERS, MATERIALS AND SURFACES

Patrick Theato, University of Mainz, Germany

Within recent years the defined synthesis of functional polymers and in particular stimuli-responsive polymers has gained a dramatic momentum due to the development of various controlled polymerization techniques. Additionally, the establishment of efficient functionalization reactions, which Sharpless summarized under the term “click chemistry”, provides the possibility to prepare various functional polymers by utilization of efficient post-polymerization modifications.

Over the last years, our group has established a profound expertise in the post-polymerization modification utilizing activated esters. In combination with controlled radical polymerization techniques, this has led to the well-defined synthesis of functional polymers with a precise architectural control. As such, we could successfully apply this chemistry to the synthesis of

polymers, block copolymers, bio-conjugates, surfaces and nano-objects, all exhibiting a stimuli-responsive behavior. In selected examples, this presentation will discuss the synthetic possibilities towards very well defined stimuli-responsive polymers utilizing our activated ester chemistry. Further, the applications of such smart materials and smart surfaces will be presented.



Tue. 9:45-10:20 **STIMULI-RESPONSIVE NANOMATERIALS THROUGH INTEGRATION OF FUNCTIONAL ORGANIC DYES INTO NANOSTRUCTURED ENVIRONMENTS**

Christoph Weder, University of Fribourg, Switzerland

Fueled by academic curiosity and the demand for inexpensive and versatile integrated high-speed optic devices, nanostructured optical materials have become the subject of intense research activities. Especially the possibility to create periodically structured nanomaterials and devices, which display photonic band gaps, i.e., frequency regimes over which radiation cannot propagate irrespective of direction, has been widely used. These so-called photonic crystals promise to be useful in many (integrated and miniaturized) optical elements including waveguides and interconnects, switches, interferometers, filters, laser structures and many others. A hitherto little exploited, yet exceedingly attractive approach is the integration of functional (responsive) dyes into such nanostructures. This talk will summarize our recent collaborative and interdisciplinary efforts to integrate specifically designed fluorescent, aggregachromic, and nonlinear-optical organic dyes into porous silicon and multilayer polymer nanostructures. Several optically-responsive nanomaterials and devices enabled by this approach will be discussed, including distributed Bragg reflector (DBR) and distributed feedback (DFB) lasers, optical data storage elements, and tunable waveguides. It will be shown that minute control over the dye's integration (special distribution, morphology) into the nanostructures is important for many applications.

Tue. 10:35-11:10 **SELF-OSCILLATING POLYMERS AND GELS AS NOVEL BIOMIMETIC MATERIALS** ***Ryo Yoshida, The University of Tokyo, Japan***

So far stimuli-responsive polymer gels and their application to smart materials have been widely studied. On the other hand, as a novel biomimetic polymer gel, we have been studying polymer gel with an autonomous self-oscillating function, since firstly reported in 1996. We succeeded in developing a novel self-oscillating polymer and gels by utilizing the oscillating reaction, called the Belousov-Zhabotinsky (BZ) reaction, which is recognized as a chemical model for understanding several autonomous phenomena in biological systems. The self-oscillating polymer is composed of poly(N-isopropylacrylamide) network in which the catalyst for the BZ reaction is covalently immobilized. Under the coexistence of the reactants, the polymer undergoes spontaneous cyclic soluble-insoluble changes or swelling-deswelling changes (in the case of gel) without any on-off switching of external stimuli. Several kinds of functional material systems utilizing the self-oscillating polymer and gel such as biomimetic actuators, mass transport surface, etc. are expected. In this talk, these recent progress on the self-oscillating polymer and gels and the design of functional material systems are summarized.

Tue. 11:10-11:45 **DESIGNING SYNTHETIC CILIA USING SELF-OSCILLATING POLYMER GELS** ***Pratyush Dayal, University of Pittsburgh, USA***

Using theory and simulations, we model the dynamic behavior of synthetic cilia made from soft, active materials. In designing this system, we harness the properties of polymer gels that undergo the self-oscillating Belousov-Zhabotinsky (BZ) reaction. Driven by the periodic reduction and oxidation of a ruthenium catalyst that is grafted onto the polymer backbone, these BZ gels undergo rhythmic swelling and de-swelling by chemomechanical transduction. When these BZ gels are tethered to a substrate, they form cilia that can pulsate autonomously in response to the BZ reaction. To simulate the behavior of the BZ cilia, we developed a nonlinear 3D model that captures the effect of the diffusion of BZ reagents into the surrounding fluid. Using this approach, we determine the factors that govern the bending and beating of individual cilium. Our findings provide guidelines for designing ciliated surfaces that can exhibit biomimetic functionality.

Tue. 11:45-12:20 **MOLECULAR WEAR IN ACTIVE NANOSYSTEMS** ***Henry Hess, Columbia University, USA***

Mechanically active nanosystems, such as kinesin-powered molecular shuttles, experience accelerated degradation when activated. An understanding of these wear mechanisms is critical for the design of synthetic systems with sufficient lifetime and for an understanding of biological systems from an engineering perspective. After an introduction to kinesin-powered molecular shuttles, the talk will describe our observations of wear in these nanodevices, and discuss these results in the context of molecular theories of force-dependent unbinding.

Tue. 1:45-2:20 **RESPONSIVE MICELLES, VESICLES AND ORGANOGELS FROM POLYPEPTIDE CONTAINING BLOCK COPOLYMERS**

Daniel Savin, The University of Southern Mississippi, USA

In these studies, amphiphilic AB diblock and ABA triblock copolymers containing poly(lysine) (PK) and poly(glutamic acid) (PE) were synthesized and their solution assembly studied using dynamic light scattering, circular dichroism spectroscopy and transmission electron microscopy. Rod-coil block copolymers containing polypeptides are able to self-assemble into responsive micelles and vesicles, as well as organogels and liquid crystals. The hydrophobic block used was poly(propylene oxide), which exhibits a tunable critical point below which the block copolymer is in the 'double hydrophilic' limit. In these multiply-responsive materials, we exploit secondary structure changes that occur within the peptide chain to observe changes in solution morphology as a function of solution conditions. This talk will present some recent results on the pH responsiveness of peptide-based ABA triblock copolymers and A_2B 3-arm star copolymers in aqueous media as well as ionic liquids. The effect of morphology changes due to secondary structure transitions will be discussed in the context of the interfacial curvature changes with pH and temperature. These dynamic materials have potential applications as viscosity modifiers, liquid crystals and gels.

Tue. 2:20-2:55 **SMART LAYER-BY-LAYER ASSEMBLIES BASED ON SELECTIVELY MODIFIED POLYSACCHARIDES FOR BIOMEDICAL APPLICATIONS**

Rachel Auzely-Velty, Centre de Recherches sur les Macromolecules, France

In recent years, among the various naturally occurring polymers, chitosan (CHI) and hyaluronic acid (HA) have attracted a special attention in the field of biomaterials due to their excellent biocompatibility, biodegradability, and their unique biological properties. Several studies demonstrated promising applications for these polysaccharides as materials for drug delivery, tissue engineering, and implantable biomaterials. In the design of smart biomaterials, polyelectrolyte multilayer films (PEM) that are made by the layer-by-layer (LbL) technique can act as a multifunctional platform. This technique allows depositing thin films on various kinds of supporting materials with a high degree over the control of physico-chemical and biological parameters. In particular, planar thin films made of linear (bio)polymers have been appeared as ideal substrates for specific and non-specific adhesion of cells. However, the methods proposed to detach the multilayer films from the substrate rely on harsh conditions which are not suitable for uses in biology and medicine. In this presentation, we will develop our recent studies aimed at designing novel sacrificial platforms based on the reversible host-guest complexation between olysaccharides, allowing for the detachment of multilayer films. Moreover, taking advantage of the specific properties of CHI and HA, we developed new layer-by-layer capsules with unique biological properties. As will be also discussed in this presentation, these multi-compartment systems could be useful for the treatment of various diseases.

Tue. 2:55-3:30 **STIMULI-RESPONSIVE HYDROGEL FILMS AND PARTICULATES**

Sergiy Minko, Clarkson University, USA

These engineered materials can mimic high selectivity of interactions and ability to adapt to the changing environment observed in living systems. They could recognize specific signals and respond in an intelligent way, that is vitally important for biomedical and technical applications, cloth and constructions. It is obvious that this kind of intelligent materials could be approached through a hierarchical organization of engineered functional building blocks. Owing to their unique ability to undergo large, reversible volumetric changes in response to small amounts of external chemical and physical stimuli, responsive hydrogels are promising building blocks of complex stimuli-responsive systems. The responsive hydrogels powered with the energy of chemical reactions are attractive components in miniaturized (bio)sensors, autonomous drug delivery systems, microfluidic valves and flow switches, "smart" cell-culture supports, for regulation of the rate of electrochemical reactions, and many other advanced applications.

Tue. 3:45-4:20 **HYDROPHILIC GRAFTED LAYER WITH TUNABLE STRENGTH AND THE RANGE OF HYDROPHOBIC INTERACTIONS**

Igor Luzinov, Clemson University, USA

The ability to vary, adjust, and control hydrophobic interactions is crucial in manipulating interactions between biological objects and the surface of synthetic materials in aqueous environment. To this end we have synthesized a grafted polymer layer (multi-component mixed polymer brush) that is capable of reversibly exposing nanometer-sized hydrophobic fragments at its hydrophilic surface and of tuning, turning on, and turning off the hydrophobic interactions. The brush was comprised of a hydrophilic non-ionic homopolymer (poly(ethylene glycol), PEG) and an amphiphilic block copolymer (polyacrylic acid-b-polystyrene, PAA-b-PS). The PEG part of the mixed brush formed a hydrophilic reference surface. The hydrophobic PS block forms nanometer-sized hydrophobic clusters. The grafted PAA-block of the copolymer is an inherently responsive polyelectrolyte macromolecule. It serves as a delivery vehicle to bring the hydrophobic PS-part to the surface upon external stimuli. The reversible switching occurs in response to changes in the environment and alters the strength and range of attractive interactions between the layer and hydrophobic or amphiphilic probes in water. The grafted layer retains its overall hydrophilicity, while local hydrophobic forces enable the grafted layer to sense and attract the hydrophobic domains of protein molecules dissolved in the aqueous environment. Using Atomic Force Microscopy force measurements we have observed a long-range attractive and contact-adhesive interaction between the material and a hydrophobic probe, which are controlled by environmental conditions. Switching of the layer exterior is also confirmed via protein adsorption measurements.

Tue. 4:20-4:55 **PHOTOGENERATED RESPONSIVE POLYMER THIN FILMS**

Mingdi Yan, Portland State University, USA

A thin layer of organic or polymer film on solid substrates is an effective way to tailor the chemical and physical properties of the surface, and to introduce functions to materials. We are interested in developing photochemically-initiated surface functionalization techniques that allow for fast reaction and control over spatial surface features. One method involves irradiating polymer thin films by UV light followed by solvent extraction. The process is simple, and the resulting films are robust, stable, and can be used as etch resists and dielectric thin films in device fabrication. In this talk, we discuss our recent studies on UV-crosslinked polymer thins films as reversibly responsive coatings that controlled surface wettability and swelling toward external stimuli of solvents and pH. Self-assembled polymer nanostructures were generated by irradiating polymer thin films followed by solvent exposure. Periodic patterns were obtained on various substrates, and the shapes and sizes of which were controlled by the molecular weight, film thickness, and the irradiation time. The photochemistry will be discussed and mechanism of the nanostructure formation will be elucidated. In addition, pH-responsive polymer thin films were fabricated. These films showed unique surface properties as a function of pH.

PLENARY LECTURES: Wednesday, October 27, 2010

Wed. 8:00-8:35 NEW GENERATION OF MACROMOLECULAR THERAPEUTICS INSPIRED BY COILED-COIL RECOGNITION IN SMART BIOMATERIALS

Jindřich Kopeček, University of Utah, USA

Molecular biorecognition forms the basis for the design of smart systems, including targeted therapeutics and self-assembled biomaterials. We have designed self-assembling hybrid hydrogels composed of a synthetic *N*-(2-hydroxypropyl)methacrylamide (HPMA) copolymer backbone and coiled-coil peptide motifs. A pair of oppositely charged pentaheptad peptides (CCE and CCK) formed antiparallel coiled-coil heterodimers and served as physical crosslinkers of HPMA graft copolymers, CCE-P and CCK-P (P is the HPMA copolymer backbone). These graft copolymers self-assembled into hybrid hydrogels with a high degree of biorecognition. We hypothesized that this unique biorecognition of CCK and CCE peptide motifs could be applied to a living system and mediate a biological process. This would provide a bridge between the designs of biomaterials and macromolecular therapeutics. To verify the hypothesis we chose induction of apoptosis in CD20 positive cells. CD20 is a biomarker for B cell non-Hodgkin's lymphoma (NHL); it is a non-internalizing antigen and its crosslinking results in apoptosis. We designed a system composed of CCE and CCK peptides, Fab' fragment of the 1F5 anti-CD20 antibody, and HPMA copolymer. The exposure of CD20+ Raji B cells to Fab'-CCE resulted in the decoration of the cell surface with multiple copies of the CCE peptide. Further exposure of the decorated cells to HPMA copolymer grafted with multiple copies of CCK resulted in the formation of CCE-CCK coiled-coil heterodimers on the cell surface. This biorecognition process induced crosslinking of CD20 receptors and triggered apoptosis of Raji B cells in vitro and was effective in a disseminated NHL model in vivo.

Wed. 8:35-9:10 POLY(N-ISOPROPYL ACRYLAMIDE) AS A BIOADHESIVE

Buddy Ratner, University of Washington, USA

Poly(n-isopropyl acrylamide)(PNIPAM) has been widely studied as a thermoresponsive polymer. At 37°C, in aqueous medium, it is a relatively hard, hydrophobic polymer. At 25°C it is a soft, swollen hydrogel. We have observed that if PNIPAM at room temperature is contacted with wet, biological tissue, it adheres. Upon cooling, it deadheres. In this talk, this phenomenon will be examined with both an RF-plasma-deposited PNIPAM thin films and with a PNIPAM gel. The plasma deposited films will be discussed as a "cell adhesive-cell detachment" surface and as a surface to reversibly adhere medical devices to wet tissue. A biodegradable PNIPAM injectable gel has been developed and its application for drug delivery will be presented.

Wed. 9:10-9:45 SMART POLYMERS AND BIOMACROMOLECULAR LEGOS: FROM SENSING APPLICATIONS TO FUNCTIONAL PROTEIN SCAFFOLDS

Stefan Zauscher, Duke University, USA

Self-assembly of molecular and macromolecular systems widely exists in Nature where it is used as a powerful and versatile approach to create large ordered structures. Here we present a synthetic DNA-protein route to construct bio-functional macromolecules from DNA-protein building blocks we term biomolecular "Legos". We show how we synthesize these building blocks by conjugating an oligo-peptide or a protein with two non-complementary DNA strands, one at each terminus, to provide programmable and specific hybridization between the "Lego" building blocks. We demonstrate the patterned assembly of these biomolecular legos on surfaces in a vertical layer-by-layer fashion, and we discuss concepts of how this assembly strategy can be used for the collocation of enzymes on protein scaffolds, mimicking Natures enzymatic nanomachines.

Wed. 9:45-10:20 **CHARACTERIZATION AND UNDERSTANDING OF ENZYME MODIFIED POLYMER THIN FILMS**

James Rawlins, The University of Southern Mississippi, USA

Conventional thin films are designed to hide, protect, and decorate substrates. Our labs have incorporated bioactive materials, i.e., enzymes, into polymeric thin films for self-synthesis functions. We identified, harvested/mimicked, and stabilized the unpurified enzymes in several synthetic polymer matrices. The functional films have been characterized via ATR-FTIR for enzyme-polymer activity, polymer-pesticide sorption rates, and pesticide hydrolysis versus time and conditions of application to thin film surfaces. The results confirm that pesticide decontamination is possible, kinetically practical and that polymer-pesticide compatibility is a key variable for optimal reaction kinetics. Furthermore, our method development using ATR-FTIR is a straightforward and powerful approach for realistic kinetic rates and understanding functional film activity, stability, and longevity.

Wed. 10:35-11:10 **CONSTRUCTION OF TARGETED SIRNA-POLYMER POLYPLEXES AND THEIR DELIVERY TO CANCER CELLS WITH SUBSEQUENT SPECIFIC GENE DOWN-REGULATION**

Faqing Huang, The University of Southern Mississippi, USA

Posttranscriptional gene silencing by RNA interference (RNAi) has proven to be a powerful pathway in regulating cellular functions in various living organisms including the human. Practically any given gene can be down-regulated specifically by small interfering RNA (siRNA), The exceptional gene sequence specificity and high gene knockdown efficiency of siRNA have led to expectations that the next generation of RNA-based therapeutics may be developed to achieve high potencies and low side toxicities. However, RNA is susceptible to hydrolysis by cellular RNA nucleases, and it does not penetrate cell membranes easily due to its relatively high molecular weight and polyanionic nature. Although a number of transfection agents based on cationic liposomes (lipofectamine, DharmaFECT, etc), dendrimers, and polymers have been formulated for effective *in vitro* siRNA delivery, development of therapeutically acceptable and efficient siRNA delivery strategies still poses great challenges.

Taking the advantage of recent advances in RNA chemistry, aqueous RAFT (Reversible Addition-Fragmentation chain Transfer) polymerization, and targeted therapy, we have established an interdisciplinary collaboration among an RNA chemist, a polymer chemist, and a cell biologist to develop targeted siRNA delivery systems. Using HPMA (HydroxyPropyl MethAcrylate) as the main components of a carrier system to provide hydrophilicity and siRNA protection, additional components, such as DMAPMA (DiMethylAminoPropyl MethacrylAmide) for RNA complexation and folate as the cancer cell targeting device, are conjugated with the carrier system. Our results indicate that our polymer-based siRNA delivery system can i) bind siRNA to form polyplexes, ii) protect siRNA from nuclease digestion, iii) deliver siRNA specifically to cancer cells that express folate receptors, and iv) suppress both mRNA and protein of a pre-determined target gene. We are currently optimizing the siRNA delivery system to improve both RNA delivery and RNAi efficiency.

Wed. 11:10-11:45 **BRAIN TUMOR GROWTH INHIBITION BY INTRAVENOUS POLY(β-L-MALIC) ACID NANOBIOCONJUGATE WITH PH-DEPENDENT DRUG RELEASE**

Julia Y. Ljubimova, Cedars-Sinai Medical Center, USA

Effective treatment of brain neurological disorders such as Alzheimer's disease, multiple sclerosis or tumors should be possible with drug delivery through blood brain barrier (BBB) or blood tumor barrier (BTB) and targeting specific type of brain cells with drug release into the cancer cell cytoplasm. A polymeric nanobioconjugate drug based on biodegradable, non-toxic and non-immunogenic polymalic acid as a universal delivery nanoplatform was used for design and synthesis of nanomedicine drug for intravenous treatment of brain tumors. The polymeric drug

passes through BTB and tumor cell membrane using tandem monoclonal antibodies targeting BTB and tumor cells. The next step for polymeric drug action was inhibition of tumor angiogenesis by specifically blocking the synthesis of a tumor neovascular trimer protein laminin-411 by attached antisense oligonucleotides (AONs). The AONs were released into the target cell cytoplasm via pH-activated trileucine, a novel endosomal escape moiety. Drug delivery to brain tumor and release mechanism were studied for this nanobiopolymer. Introduction of trileucine endosome escape unit compared to pH-independent leucine ester resulted in significantly increased AON delivery to tumor cells, inhibition of laminin-411 synthesis *in vitro* and *in vivo*, specific accumulation in brain tumors, and suppression of intracranial glioma growth. The availability of systemically active polymeric drug delivery system that passes through BTB, targets tumor cells and inhibits glioma growth gives hope for a new successful strategy of glioma treatment. This newly designed delivery system with drug release into the brain-specific cell type could be useful for treatment of various brain pathologies.

Wed. 11:45-12:20 A NOVEL ENZYME-RESPONSIVE COLON-TARGETED DRUG DELIVERY SYSTEM FOR THE TREATMENT OF LOCAL COLONIC PATHOLOGIES

Valence M. K. Ndesendo, University of Witwatersrand, South Africa

Purpose: To formulate an enzyme-responsive drug delivery system that targets the model drug mesalamine directly to the colonic mucosa. **Methods:** Tablets were prepared by dispersing crosslinked chitosan-mesalamine granules within a matrix of polysaccharides (pectin, xanthan gum, and carboxymethylcellulose). $BaCl_2$ was used to crosslink pectin *in situ*. Tablets were coated with a solution of pectin/ ethylcellulose to a 9-10% weight increase. The enzyme-responsiveness was determined based on the drug release in simulated human gastric, intestinal, and colonic fluids (SHGF:pH 1.2; SHIF:pH 6.8; SHCF:pH 5.9) at 2, 4 and 18 hours respectively, with and without commercially available colonic enzymes. The influence of colonic enzymes on the formulation (SHCF absorption ability and erosion) was determined gravimetrically. FTIR was performed to assess the influence of colonic enzymes on the vibrational/structural properties of the formulation while energy refinement force field simulations (ERFFS) were performed to corroborate the experimental findings. **Results:** For the first 6 hours in SHGF and SHIF no drug was released. However, after 12 hours in SHCF with colonic enzymes 80.3% of drug was released compared to 30.4% in SHCF without enzymes. The extent of uptake of SHCF-containing enzymes was 101.68% compared to 54.57% without colonic enzymes. Colonic enzymes also resulted in greater erosion of the formulations (45.14% vs. 27.74% after 18 hours in SHCF). FTIR spectra and ERFFS revealed structural variations in the polymeric backbone chains of the tablet and coating indicating cleavage of the polymer backbones by the colonic enzymes. **Conclusion:** A novel enzyme-responsive drug delivery system was successfully developed for colon-targeted drug delivery.

Wed. 1:30-2:05 STIMULI RESPONSIVE BLOCK COPOLYMERS AND MATERIALS FROM IONIC LIQUID REACTIVE SURFACTANTS

John Texter, Eastern Michigan University, USA

Reactive imidazolium-based surfactants that also are ionic liquids have been used to create a new class of hydrogel/solvogel copolymers and latexes by microemulsion polymerization, polymeric ionic liquids by solution polymerization that are ionic liquids after polymerization, distimuli responsive diblock copolymers and triblock terpolymers with tunable LCST transitions, and stimuli responsive triblock copolymers with dramatic dispersion stabilization and destabiization switches. The hydrogel/solvogel materials can be reversibly driven into open cell porous materials by anion exchange and by solvent shifting. Transparent latex films can be porated by stimuli responsive ion exchange. Both of these pore-forming processes are driven by spinodal decompositions. The stimuli responsive homopolymer can be used to precipitate new classes of hydrogel particles by selective hydrophobic anion exchange. Distimuli responsive diblocks are used to demonstrate core/shell particle inversion, and related terpolymer triblocks also illustrate controlled thermoreversible precipitation to produce ultrastable core/shell nanoparticles. New symmetrical triblocks in dispersion stabilization can be used for controlled and switchable flocculation and for immunizing colloids against indifferent salt induced coagulation.

Wed. 2:05-2:40 **RESPONSIVE CONJUGATED POLYMER/CARBON NANOTUBE COMPOSITES**

Lei Zhai, University of Central Florida, USA

Carbon nanotubes (CNTs) have attracted enormous attention due to their remarkable mechanical, thermal, and electrical properties. The CNTs applications include nanoelectronics, sensors, energy storage devices, photovoltaics, nanocomposite materials and many others. One of the key challenges to fully realize the extensive applications of carbon nanotube materials is the dispersion and functionalization of carbon nanotubes. We have developed a simple and versatile approach to disperse CNTs within various solvents and polymer matrices using conjugated block copolymers with tunable functionalities. With a simple sonication, the conjugated polymer blocks, such as polythiophenes, can form strong π-π interactions with carbon nanotube walls, while the non-conjugated polymer blocks will provide the de-bundled CNTs with good solubility and stability in a wide range of organic solvents and host polymer matrices. The non-conjugated polymer blocks can also introduce a variety of functionalities to CNTs, generating responsive conjugated polymer/carbon nanotube composites. For example, Ultra-light flexible multi-walled carbon nanotube (MWCNT) aerogel was fabricated from a wet gel of well-dispersed pristine MWCNTs by poly (3-(trimethoxysilyl) propyl methacrylate) (PTMSPMA). The MWCNT aerogel is hierarchically porous with a surface area of 580 m^2/g, a density of 0.4 mg/cm^3 and electrical conductivity of 3.2×10^{-2} $S\cdot cm^{-1}$ (0.67 $S\cdot cm^{-1}$ after high-current pulse treatment). The MWCNT aerogel demonstrates excellent compression recovery property. The unique anisotropic honeycomb structure combining with the hierarchical porosity with large surface area, compression recovery property, and high electrical conductivity makes the MWCNT aerogel promising for applications as chemoresistance vapour sensors and ultra-sensitive pressure sensors. Other potential applications of the MWCNT aerogel may include sensors, catalyst supports, and novel electrodes.

Wed. 2:40-3:15 **MOLECULAR DESIGN FOR FUNCTIONAL THERMO-RESPONSIVE POLYMERS AND THEIR BIOMEDICAL APPLICATION**

Takao Aoyagi, National Institute for Materials Science, Japan

To obtain poly(N-isopropylacrylamide)-based functional materials, in this study, we newly designed functional monomers. The monomers are simple derivatives of N-isopropylacrylamide, which have specific functional groups on the isopropyl group. The simple reaction of acryloyl chloride and functional compounds such as amino-acid, amino-alcohol derived to the corresponding monomers. The resulting copolymers contain comonomer random sequences based on very similar copolymerization reactivity, as well as show both the good chemical reactivity and nice stimuli-response.

Using the copolymers, we investigated both fundamentals and biomedical application. In many cases, phase transition and phase separation are confused, therefore, we make it clear using hydoxylated poly(N-isopropylacrylamide) that was obtained the copolymerization of N-isopropylacrylamide and 2-hydroxyisopropylacrylamide. The phase transition and separation was much influenced by the content of hydroxyl groups. In some case, the observing turbidity is based on the coacervate droplet formation. The coacervate is very stable and used for stimuli-responsive microgel.

The combination of inductive heating by alternating magnetic field (AMF) and such stimuli-responsive polymers gives some unique biomedical application. We could prepare the magnetic nanoparticles chemically covered with such polymer. The surface-modified magnetic nanoparticles showed the sensitive response to AMF. The similar concept was applied to development of AMF-responsive chromatography. Taking the scale-up of biomolecule separation into consideration, this separation system would have some advantages because of no use of water-miscible organic solvent that is required for a conventional reverse-phase chromatography. Moreover, the mobile phase heating is unnecessary that is required for temperature-responsive chromatography. Other application will be presented.

Wed. 3:30-4:05 **pH Sensitive Microcapsule Whose Membrane Undergoing Volume Phase Transition**

Takayuki Narita, Saga University, Japan

Volume phase transition of hydrogel often uses as one of stimuli-response, which is induced by environment changing such as temperature, ion concentration, pressure, and pH. Since the kinetics of volume phase transition dominated by the characteristic size of hydrogel, it is not easy to adjust the response speed if a fixed size of gel is required. Microcapsulation is a useful way to control the dynamics of volume phase transition because its membrane thickness govern the dynamics, which may allow them to fit the response speed even the particle have same sizes.

In this presentation, we demonstrate that Poly(L-lysine-alt-terephthalic acid)(PPL)microcapsule have pH sensitive membrane and undergo volume phase transition. Results of our studies showed that microcapsulations allow reducing the required time to reach the equilibrium volume drastically compared with the same sized hydrogel particles and also demonstrate that the transition dynamics are different to that of the particles whose inside is filled with hydrogel. The volume phase transition dynamics could be analyzed by considering the two parameters, each related to the ratio of the elastic force of the gel polymer network to the frictional force and the ionization of the membrane.

Our studies also showed that pH sensitive microcapsules can use as a substrate sensitive material with quick response. Encapsulation of glucose oxidize(GOX) into the PPL-microcapsule was successfully response to glucose solution. Drug release properties from the PPL-microcapsules encapsuling GOX and ammonium salt were also estimated from the absorbance of dispersed ammonium salt in glucose solution. The drug release curve as the time course of released an ammonium salt obviously varied immediately after the volume transition of PPL microcapsule is induced, and therefore appearing as two different exponential functions. We will also introduce a unique volume oscillation phenomenon of PPL microcapsule in buffer solution which was recently discovered.

Wed. 4:05-4:40 **Photoresponsive Liquid Crystal Polymer Networks: Glassy Adaptive Materials**

Timothy White, Wright Patterson Air Force Laboratory, USA

Light-generated responses can have the advantages of remote, spatial, and temporal control. In polymeric materials, photon generated responses have been sought after to tranduce light energy into mechanical work. In the last decade, a number of results have shown that the small photogenerated responses observed in conventional polymeric materials can be amplified by embedding photoresponsive moieties such as azobenzene into a liquid crystalline elastomeric or glassy network (liquid crystal network, LCN). Recently, we have a variety of synthesized glassy azobenzene-LCN (azo-LCN) and demonstrated a number of responses; including polarization controlled forward/reverse bending, and large frequency oscillations. In this presentation, we report on the unique combination of shape memory in these photoresponsive materials that extends their potential utility as adaptive materials. In this early demonstration, a temporary shape is fixed into the azo-LCN material by thermal means. The sample retains its photoresponsive shape memory, and accordingly can be reconfigured with light. The shape memory response can be released thermally or photothermally – allowing for an all-optical response if desirable. Additionally, engineered responses through combination fabrication of hybrid systems of a variety of materials will be also be discussed.

Symposium Poster Session

Tuesday, Oct. 26, 5 – 8 pm Polymer Science Research Center Foyer

110. The Effects of Nanoparticle Incorporation in Thiol-ene Networks

Olivia McNair and Adam Richardson

Highly uniform, high energy-damping networks result from the rapid UV-curing of thiol-ene based networks. As increased cross-linking negatively affects mechanical properties, rigidity decreases the usefulness of these materials. In certain cases nanoparticle incorporation has been shown to improve physical properties and toughness of composite films. Alkyne-functionalized silica nanoparticles (AFSNs) were synthesized and covalently bound into a thiol-ene matrix composed of 3T and TTT. The kinetics of the crosslinking reaction was monitored using real-time FTIR. Thermal and mechanical properties of the nanoparticle-filled composite films were measured and compared to the native matrix. DMA showed relatively similar tan δ max values, centered around 47°C for all films. According to DSC, the Tg of the composite films decreased by approximately 12°C regardless of the type of nanoparticle used. Aggregation in films noticeably decreased with particle functionalization as observed by TEM, and tensile testing showed that AFSN-filled composites demonstrated a higher strain before break.

111. Microwave Assisted Synthesis and Evaluation of pH Responsive Sago Starch Grafted Acrylamide as Biomaterial for Drug Delivery

Akhilesh V Singh, Lila K Nath, and Manisha Guha

In the present investigation an attempt was made to graft acrylamide on the sago starch bacjbone under microwave irradiation. The grafted polymer was characterized by FT-IR and DSC. The rheological and swelling study of the grafted polymer was done to evaluate pH dependant stimuli. The grafted product showed high gelling property than native sago starch. FT-IR and DSC data revealed addition of amide groups and change in transition temperature. Swelling study indicates pH dependent swelling and release of model drug lamiivudine from this novel biomaterial.

112. Tailoring the Binding/Release of siRNA via Hydrophilic-b-Cationic Copolymers Synthesized via RAFT Polymerization

Andrew Holley, Adam York, Deedee Smith, and Charles McCormick

With the ability to knockdown virtually any gene of interest, the use of siRNA as a therapeutic has the potential to produce groundbreaking results in the treatment of diseases. Current research efforts are focused on the development of siRNA carriers that will not only minimize degradation of siRNA during transport but also increase transfection efficiency into cells. Commonly, commercially-available cationic polymers have been utilized to form IPECs; however, these polymers have ill-defined structures and often inherent toxicity. Recent advancements in controlled polymerization strategies have allowed for the construction of narrowly dispersed (co)polymers of predetermined molecular weight and architecture. Specifically, advancements in aqueous reversible addition-fragmentation chain transfer (aqueous RAFT) polymerization have allowed the direct, controlled polymerization of amine-containing monomers. In the proposed research, RAFT was used to polymerize hydrophilic, biocompatible N-(2-hydroxypropyl)methacrylamide (HPMA) that is chain extended with a cationic monomer N,N'-(dimethylaminopropyl)methacrylamide (DMAPMA). The charge density is mitigated by varying the hydrophilic nature of the cationic block through the incorporation of varying molar percentages of HPMA in the feed. These (HPMA-

statistical-APMA)-block-(HPMA-statistical-DMAPMA) copolymers, where the first hydrophilic block contains HPMA and APMA (HPMA/APMA) in a 91/09 molar ratio, and the second block contains HPMA and DMAPMA (HPMA/DMAPMA) in varying molar ratios, specifically 75/25, 50/50, 25/75, and 100/0, were complexed with tRNA, and their binding efficiency was monitored utilizing gel electrophoresis. Size and charge density of the polymer/RNA complexes were determined utilizing DLS and zeta potential, respectively. Also, the release efficiency is compared to the binding strength involving gene knockdown experiments of siRNA/copolymer complexes.

113. Stimuli-responsive polypeptide-based triblock copolymers: Unique morphology transitions with pH

Jake G. Ray, Ashley J Johnson, and Daniel A. Savin

Stimuli-responsive copolymers demonstrate diverse aggregation behavior in aqueous solution and in ionic liquid mixtures. In general, the molecular architecture and the balance of hydrophilic and hydrophobic volumes influences morphology. This study involves ABA and BAB responsive peptide-based triblock copolymers which display unique pH-induced morphology transitions compared with analogous AB diblock copolymers. Model systems for this study are poly(L-lysine)-b-poly(propylene oxide)-b-poly(L-lysine) (KPK) and the inverse, PKP, triblock copolymers with high lysine weight fractions. PK diblocks in this composition range yield spherical micelles over the entire pH range, whereas current studies with KPK systems exhibit morphological transitions with varying pH. Light scattering and TEM were used to determine aggregate size and morphology as a function of pH, and circular dichroism (CD) spectroscopy was used to observe the helix-to-coil transition within the K blocks. This study shows how changes in the secondary structure of the peptide blocks influences aggregation behavior, and in certain systems leads to morphological transitions.

114. Environmentally Friendly Bio-molecule Chromatography Employing Grafted Smart Polymers as Induction Heating Induced 'on-off' Switchable Trap

Hisashi Yagi, Mitsuhiro Ebara, Kazuya Yamamoto, and Takao Aoyagi

Recently, to develop bio- and environmental- friendly separation system, much attention has been focused on 'smart' polymer-based technologies. Among them, the most extensively studied smart polymer poly(N-isopropylacrylamide) (PNIPAAm) exhibits lower critical solution temperature (LCST). Grafting of PNIPAAm onto solid surfaces can make them 'on-off' switchable surfaces where the surface hydrophobicity can be controlled with temperature. We have developed a novel separation system composed of PNIPAAm modified magnetic particles as stationary phase for separation of bioactive molecules in a self-heating, temperature-responsive chromatography. Ferrimagnetic materials are known to generate a heat when subjected to an alternating magnetic field (AMF) as a consequence of a magnetic hysteresis loss. Since magnetic particles generate a heat when subjected to AMF, hydrophilic/hydrophobic phase separation of the grafted polymer on the particles was successfully controlled by on-off switching of AMF. In this study, we investigated the to assess effect of grafted polymer composition and architectures of temperature-responsive copolymer, poly(NIPAAm-co-2-carboxyisopropylacrylamide) (P(NIPAAm-co-CIPAAm)) for the effective separation of bioactive molecules. Different composition of grafted polymers on the magnetite-silica composites were successfully prepared by varying the architectures of CIPAAm while keeping their grafted polymer densities constant. AMF application on the column, grafted polymer composition strongly influences analyte-polymer hydrophobic interactions due to differences in the dynamic motion of the grafted polymer chains. By optimizing the grafted polymer composition and graft density, this system will offer a more accurate, prompt, and simple 'on-off' control of the elution profiles for bioactive molecules.

115. Synthesis of Biodegradable HPMA Copolymer Conjugates via Combination of RAFT Polymerization and Thiol-ene Coupling Reaction

Huaizhong Pan, Jiyuan Yang, Pavla Kopečková, and Jindřich Kopeček

N-(2-Hydroxypropyl)methacrylamide (HPMA) copolymers have been one of the most frequently studied water-soluble biocompatible carriers. However, the molecular weight of copolymers used in clinical trials was suboptimal due to need to keep the whole molecular weight distribution below the renal threshold (approximately 45 kDa for non-biodegradable random coil polyHPMA). We have shown that by combination of RAFT polymerization and thiol-ene click reaction long-circulating backbone degradable drug carriers can be prepared. We designed a new bifunctional RAFT chain transfer agent, N^{α},$N^{\varepsilon'}$-bis(4-cyano-4-(phenylcarbonothioylthio)pentanoyl glycylphenyl-alanylleucyl-glycyl) lysine (Peptide2CTA), which contains a peptide sequence (GFLG) degradable by lysosomal enzymes. Kinetics studies indicated that HPMA polymerizations were well controlled over molecular weight and polydispersity by peptide2CTA. Telechelic water-soluble HPMA homopolymer (Mw 30.3 kDa, PDI 1.08) and HPMA copolymer-doxorubicin (DOX) conjugate (Mw 27.8 kDa, PDI 1.19) have been synthesized by RAFT polymerization mediated by Peptide2CTA using AIBN as the free-radical initiator at 50 or 60 °C. Post-polymerization aminolysis followed by chain extension with bis-[1,13-(3-maleimidopropionyl)amido]-4,7,10-trioxatridecane (Bis-MAL-dPEG3) by thiol-ene reaction at room temperature resulted in linear high molecular weight multiblock HPMA copolymer conjugates. Exposure of the high molecular weight (>200 kDa) fractions of these conjugates to cathepsin B or papain resulted in rapid degradation of the polymer backbone into segments with molecular weight close to the starting material, along with concomitant release of DOX. The new multiblock HPMA copolymers hold potential as new carriers of anticancer drugs.

116. Multiblock of HPMA Copolymers: Synthesis, Characterization and Degradation

Jiyuan Yang, Kui Luo, Huaizhong Pan, Pavla Kopečková, and Jindřich Kopeček

To endow biodegradability to non-degradable poly(N-(2-hydroxypropyl)methacrylamide) (polyHPMA), two functional RAFT chain transfer agents (CTAs) were designed to produce homo- and heterotelechlic copolymers via RAFT polymerization. Multiblock copolymers were then generated by connecting synthetic polymer chains via enzymatically cleavable oligopeptide bridges through CuI catalyzed azide-alkyne cycloaddition reaction. A dialkyne-functionalized trithiocarbonate was synthesized to produce clickable telechelic HPMA-based copolymers in one-step. A polyHPMA, with 10,000 (g/mol) of molecular weight and narrow polydispersity, was obtained in DI H_2O in 3 h using V-501 as initiator at 70^{o}C. The livingness of the polyHPMA was confirmed by kinetics studies and the use of the isolated polymer as macroCTA. The end-group reactivity was demonstrated by chain extension through coupling reaction with diazido-modified tetrapeptide linker. Heterotelechelic polyHPMAs were synthesized using an alkyne-modified dithiobenzoate as CTA. Post-polymerization modification with diazido-functionalized V-501 resulted in the formation of HPMA copolymers containing terminal alkyne and azide groups. The important feature of the new RAFT agent is the insertion of an enzyme cleavable peptide linker (GFLG) in its structure, which makes it a versatile tool for the synthesis of polymers with biodegradable backbones. Chain extension of such polyHPMA (via click reaction) resulted in high molecular weight biodegradable multiblock copolymers. This approach avoids the difficulty of 1:1 stoichiometry for polymeric step-growth click reactions. Upon exposure to papain, multiblock copolymers from either approach degraded into the initial blocks. This study provides a facile approach to regulate the molecular weight as well as the biodegradablility of water-soluble polymeric drug carriers.

117. Structopendent Transformation of RAFT Block Copolymers via Sequential Urethane and Thiol-Ene Click Reactions: A Facile Route to Well-Defined Functional Systems

Joel D. Flores, Nicolas J. Treat, and Charles L McCormick

We describe a robust strategy utilizing reversible addition-fragmentation chain transfer (RAFT) polymerization and sequential transformations involving urethane formation and the thiol-ene click chemistry to effectively synthesize well-defined functional block copolymers. A well-defined block copolymer scaffold, poly((N,N-dimethylacrylamide)-b-(N-(2-hydroxyethyl)-acrylamide) (PDMA-b-PHEA) was first prepared. The hydroxyl groups of the HEA block were then reacted with either 2-(acryloyloxy)ethylisocyanate (AOI) or allylisocyanate resulting in acrylate- and allyl-functionalized copolymers, respectively. The efficiencies of both Michael and free radical-mediated thiol-ene addition reactions were investigated using selected small molecule thiols having functionality including alkyl, aryl, hydroxyl, amine, carboxylic acid, amino acid or saccharide moeities. In order to demonstrate the utility of this method, copolymers targeted for self-assembly, complex formation *via* electrostatic interaction with tRNA and specific binding to lectins have been synthesized. The steps of RAFT polymerization, isocyanate-hydroxyl coupling and thiol-ene click addition are accomplished under mild conditions, thus offering routes to functional copolymers potentially suitable for various biological applications.

118. The Effects of Nanoparticle Incorporation in Thiol-ene Networks

Adam Richardson and Olivia McNair

Highly uniform, high energy-damping networks result from the rapid UV-curing of thiol-ene based networks. As increased cross-linking negatively affects mechanical properties, rigidity decreases the usefulness of these materials. In certain cases nanoparticle incorporation has been shown to improve physical properties and toughness of composite films. Alkyne-functionalized silica nanoparticles (AFSNs) were synthesized and covalently bound into a thiol-ene matrix composed of 3T and TTT. The kinetics of the crosslinking reaction was monitored using real-time FTIR. Thermal and mechanical properties of the nanoparticle-filled composite films were measured and compared to the native matrix. DMA showed relatively similar tan δ max values, centered around 47 °C for all films. According to DSC, the Tg of the composite films decreased by approximately 12 °C regardless of the type of nanoparticle used. Aggregation in films noticeably decreased with particle functionalization as observed by TEM, and tensile testing showed that AFSN-filled composites demonstrated a higher strain before break.

119. An Electro-Rheological Fluid as an In situ Forming Implant for Controlled Stimuli-Responsive Liberation of Diclofenac Sod

Valence M. K. Ndesendo, Viness Pillay, Yahya E. Choonara, Refilwe B. Mosane, Pradeep Kumar, and Lisa C. du Toit

Purpose: To develop an in situ forming elecroactive co-polymer (EAP) implant gel from polyethylene glycol (PEG) and sodium polystyrene sulfonate (NaPSS) for electro-liberation of diclofenac sodium. **Methods:** The electro-activeness of PEG and NaPSS were determined using a galvanostat followed by synthesis of a drug-loaded PEG/NaPSS-EAP gel employing diethyl acetamidomalonate as a crosslinker. Various physicochemical and physicomechanical characterization tests were performed on the gel including thermal analysis, morphological evaluation and FTIR spectroscopy. The ability of the gel to release the drug following electrical stimulation was evaluated while Molecular Mechanics Simulations were performed to elucidate the experimental findings. **Results:** A stable and reproducible electro-active PEG/NaPSS-EAP gel exhibiting good cycling stability was produced with desirable rigidity (BHN=35.4N±0.33 N/mm^2; resilience=10.91±0.11%), thermal properties (Tg = 70ºC; Tc = 200ºC), homogeneous morphology and a pH-stable equilibrium swelling ratio (0.139). The structural transitions in the crosslinked polymer matrix displayed band broadening and intensification as compared to the constituent polymers. The in vitro drug release analysis revealed "ON–OFF" pursatile drug release kinetics upon applying electric stimulation intermittently, indicating that the drug release from the gel was electrically controlled. The quantity of the drug released increased gradually (37-94%) in a pursatile manner from t30min-t180min. Global energy minimisations visualized the effect of external electric field on the erosion/subsequent drug release of/from the polymeric matrix. **Conclusion:** The galvanometric and Molecular Mechanistic studies revealed that the developed PEG/NaPSS-EAP gel is capable of releasing diclofenac sodium in a controlled manner following electric stimulation and therefore, it may be suitable for application as a subcutaneous drug delivery implant.

120. An Injectable In Situ Forming Implant for the Treatment of Solid Tumors Utilizing a Central Composite Design

Ameena Wadee, Viness Pillay, Yahya E. Choonara, Lisa C. du Toit, Clement Penny, and Valence M.K. Ndesendo

Purpose: To develop an injectable, in situ forming implant (ISFI) for the treatment of solid tumors using poly(methylvinyl ether) (PMVE) which is a thermo-responsive polymer that converts from a solution to a gel upon exposure to temperature. **Methods:** A two-factor face-centered central composite design (FCCCD) was employed to develop an optimal ISFI formulation which was easily injectable, able to gel around body temperature and capable of delivering a chemotherapeutic agent over prolonged periods of time. To the PMVE solutions (15-30%w/v), $CaCl_2$ (0.08-0.5M) was added followed by the model drug, (folic acid; 5mg/mL) to formulate 14 ISFI formulations in accordance to FCCCD. The response of ISFI to temperature was determined by exposing samples to fixed strain and oscillation (18Pa, 10Hz) while increasing the temperature, using a Rheometer System. Drug release analysis was performed while a Textural Analyzer was utilized to determine the injectability of the ISFI formulations by comparing the maximum force required to depress the plunger of a formulation-filled syringe against a water-filled syringe. **Results:** ISFI formulations showed gelation temperatures of below 36±0.11^{o}C with the formulation containing the highest concentration of $CaCl_2$ (0.5M) displaying the lowest gelation temperature (32.1±0.6^{o}C). Prolonged release of folic acid (<45% released over 30 days) was achieved from all of the ISFI formulations with formulations containing higher quantities of salt showing lower initial burst release profiles. Low polymer concentrations (15%w/v) resulted into easily injectable formulations. **Conclusion:** An optimal implant formulation that may provide sustained release of entrapped chemotherapeutics for the treatment of solid tumors was successfully developed.

121. Electro-Conductive Hydrogel for Controlled Stimuli-Responsive Liberation of Indomethacin

Tong-Sheng Tsai, Viness Pillay, Yahya E. Choonara, Lisa C. du Toit, Girish Modi, Dinesh Naidoo, Pradeep Kumar, and Valence M.K. Ndesendo

Purpose: To design electro-conductive hydrogel (ECH) based on poly(vinyl alcohol) (PVA) crosslinked with diethyl acetamidomalonate (DAA) as the hydrogel component and polyaniline (PANi) as the inherently conductive component to confer electro-liberation of indomethacin at various potential differences. **Methods:** A Box-Behnken experimental design was used employing 1.2V as the baseline potential difference for the fabrication of optimized formulation. The hydrogels were characterized for surface morphology, effect of crosslinking on the rate of erosion and voltage optimization based on the drug release profile. Cyclic Voltammetry (CV) was employed for electro-activity and conductivity analysis. In order to investigate the electro-liberation of indomethacin, potential energy functions based on atomic-level statistical mechanics' simulations were performed with periodic boundary conditions under the influence of external electric field. **Results:** The devices demonstrated high electrical conductivity (~130 Sm^{-1}) with "ON–OFF" drug release kinetics via electrical switching obtained by an "ON–OFF" application of an electric potential ranging from 0.3-5.0V for 60 seconds at hourly intervals. The cumulative drug release obtained ranged between 4.7-25.2% after 4 release cycles respectively. Drug entrapment efficiency ranged between 65-70%. CV indicated oxidation peaks at 0.6V and 1.4V and reduction peaks at 1.5V and -1V ensuing ionic interactions at various interfaces between the PANi, hydrogel matrix, electrode and the electrolyte which were also corroborated by various interaction energies (bond stretching, angle bending and van der Waals forces) computed for the polymer matrix. **Conclusion:** The DAA crosslinked PANi-PVA ECH may be potentially useful as a local electro-actuable controlled drug release delivery system while sustaining a mild operating environment.

122. A Pepsin-Responsive Polymeric Drug Delivery System for the Targeted Delivery of Loperamide HCl to the Small Intestine

Priya Bawa, Viness Pillay, Yahya E. Choonara, Lisa C. du Toit, Valence M. K. Ndesendo,** and Pradeep Kumar*

Purpose: To formulate a novel drug delivery system comprised of an inner placebo tablet surrounded by an outer polymeric shell that targets loperamide HCl to the small intestine by being negatively-responsive to pepsin. **Methods:** Polymeric shells fabricated by dip-coating placebo lactose tablets into drug-loaded gelatine solutions were crosslinked in a glutaraldehyde-lactose mixture for 6 hours. In vitro drug release studies were conducted in simulated human gastric fluid (SHGF) (pH 1.2) with and without pepsin for 2 hours and simulated human intestinal fluid (SHIF) (pH 6.8) for 4 hours. The influence of pepsin on SHGF uptake ability and erosion of the gelatine shells was determined gravimetrically. FTIR spectroscopy and Molecular Mechanics (MM) simulations were performed to visualize the influence of pepsin on the polymeric backbone of the cross- linked shells. **Results:** Only 18.2% drug was released in SHGF with pepsin compared to 100% release in SHGF without pepsin in 90 minutes. Complete drug release was achieved within 4 hours in SHIF indicating the intestinal targeting ability and pepsin-responsiveness of the shell. Formulations unexposed to pepsin experienced a greater degree of swelling. A reduced intensity of the peak at ~3280 cm^{-1} in the shells is attributable to the loss of –COOH in SHGF while the peaks at 3282 and 1627cm^{-1} from shells exposed to pepsin, showed a relatively greater intensity suggesting that both the –COOH and $–NH_2$ groups remained intact as corroborated by MM geometrical preferences. **Conclusion:** A novel pepsin-responsive polymeric shell for the targeted delivery of loperamide HCl to the small intestine was successfully developed.

123. A pH-responsive Mucoadhesive Membrane for Prolonged Oral Drug Delivery

Rubina P. Shaikh, Viness Pillay, Yahya E. Choonara, Lisa C. du Toit, Valence M.K. Ndesendo, and Pradeep Kumar

Purpose: Chitosan (0.5-3%w/v), poly(vinyl alcohol) (PVA) (1-5%w/v), and poly (vinylpyrrolidone) (PVP) (2-10%w/v) were investigated for the development of a gastric-responsive mucoadhesive membrane for prolonged oral drug delivery. **Methods:** A 2-Factor Central Composite Design comprising of 13 formulations was used to determine the optimal formulation. Differing concentrations of the polymeric solutions were film-cast and dried at ambient conditions to fabricate mucoadhesive membranes. For comparative purposes, simulated mucosal membranes were exposed to simulated human gastric fluid (pH 1.2±0.5) or simulated human intestinal fluid (pH 6.8±0.5) for 12 hours, and tested for mucoadhesion at 2 hours interval using a textural analyzer. Surface morphology, which affects mucoadhesive properties, was assessed using SEM analysis. Molecular Mechanics Computations were employed to elucidate the intermolecular interactions, responsible for mucoadhesion, between the polymers and the fabricated membranes. **Results:** Muco-adhesion, determined by measuring the force required to detach the membrane from a simulated gastric membrane, was found to be higher when exposed to a pH of 1.2±0.5 (0.8674±0.004N) as compared to membranes exposed to pH 6.8±0.5 (0.38145±0.0734N). Membranes maintained their mucoadhesive properties over 12 hours, with a 20-60% decrease in overall mucoadhesion between 8-12 hours.Membranes were irregular in surface morphology, thus promoting mucoadhesion through stronger mechanical interactions. The spatial disposition and energetic profile of the sterically constrained and geometrically optimized multi-polymeric complex corroborated the experimental results in terms of the mucoadhesive strength of the fabricated membrane. **Conclusion:** The pH-responsive nature of the mucoadhesive membrane may potentially be employed to produce prolonged site-specific drug release in the gastric region for multiple or single drug formulations

124. RAFT-Synthesized, Thermally-Responsive Triblock Copolymer for in Situ Formation of Gold Nanoparticle-Decorated, Shell Crosslinked Micelles

Xiaonan Kou, Adam Smith, Xuewei Xu, and Charles McCormick

Stimuli-responsive block copolymers with pendant functional groups have potential applications in preparing cross-linked micelles and polymer complexes with biological moieties. Among functional groups, activated esters have distinct advantages due to facile conjugation with drugs, proteins, or other ligands. In this work, a narrowly dispersed triblock copolymer poly(N,N'-dimethylacrylamide)-b-poly(N,N'-dimethylacrylamid-s-N-acryloxysuccinimide)-b-poly(N-isopropylacrylamide) (PDMA101-b-P(DMA66-s-NAS22)-b-PNIPAM130) was synthesized via RAFT polymerization. This triblock copolymer contains a permanently hydrophilic block PDMA for polymer stabilization in aqueous solution, a P(DMA-s-NAS) middle block for cross-linking and polymer functionalization, and a thermally responsive third block PNIPAM for self-assembly. The triblock copolymer assembles into uniform micellar structures when temperature is raised above 44^{o}C at 1.0 mg/mL copolymer concentration. The micelles have an average hydrodynamic diameter of 50 nm as measured by dynamic light scattering (DLS). The P(DMA66-s-NAS22) middle block was reacted with cysteamine resulting in free thiol-containing copolymer. This functional copolymer was then utilized in the formation of gold nanoparticle (AuNP)-decorated shell cross-linked micelles. The AuNPs were produced by an in situ reduction of $NaAuCl_4$ using $NaBH_4$. The final stabilized nanostructure had an average diameter of 60 nm as characterized by DLS and transmission electron microscopy (TEM).

125. Real-Time Imaging of Folate-Conjugated Copolymer/siRNA Complexes Trafficking to Cancer Cells

Yilin Zhang, Adam W. York, Charles L. McCormick,Yan-lin Guo, and Faqing Huang

siRNA-based therapeutic approaches rely on the efficient siRNA delivery to the cytoplasm, and the convenient evaluative systems to monitor and assess the multistep process, which enables to accelerate the development of novel siRNA delivery strategies. Herein, we combine several facile real-time imaging tools to evaluate siRNA uptake and intracellular trafficking taking advantages of Confocal-based fluorescence microscopy and software-assisted quantification. In particular, the Pearson's correlation coefficient (PCC) is utilized to dissect siRNA endosomal escape, a key rate-limiting step in delivery processes, showing great convenience and applicable potential. As an example, our previously reported, well-defined, multivalent folate-block copolymer conjugate, (HPMA315-stat-APMA13)-b-DMAPMA23) (FAPol13) is applied to demonstrate cell-specific siRNA delivery to FR-bearing cells, KB, HeLa, and SKOV3. In addition, non-toxicity of FAPol13 and desirable gene downregulation upon FAPol13/siRNA polyplexes treatment have been demonstrated. Taken together, our findings suggest the potential utility of FAPol13 as a siRNA carrier for targeted cancer therapy, and importantly a wide application of these evaluation approaches for optimizing siRNA delivery.

126. Stimuli-responsive Self-assembly System That Can Form and Stabilize Nanoparticles at the Desired Size by Simple Mixing and Heating/Cooling of the Selected Block Copolymers

Youhei Kotsuchibashi, Mitsuhiro Ebara, Kazuya Yamamoto, and Takao Aoyagi

We propose here a unique protocol to produce stimuli-responsive self-assemblies using two block copolymers, poly(N-isopropylacrylamide (PNIPAAm))-b-P(NIPAAm-co-N-(hydroxymethyl) acrylamide (HMAAm)) and PNIPAAm-b-P(NIPAAm-co-sodium 2-acrylamido-2-methylpropane sulfonic acid (AMPS)). These block copolymers were synthesized by atom transfer radical polymerization (ATRP) method. PNIPAAm was selected as the common block to trigger macromolecular assembly in aqueous environment above the lower critical solution temperature (LCST).Stable core-shell assembly was produced only by mixing two block copolymers above the LCST of PNIPAAm when the common blocks became hydrophobic. Upon heating above the second LCST, P(NIPAAm-co-HMAAm) became dehydrated and the size growth of assemblies was observed. The P(NIPAAm-co-AMPS), however, still formed a hydrated shell that prevents further aggregation and precipitation due to the electrostatic stabilization through the anionic groups of AMPS. In other word, nanoassemblies, grown at the second LCST, are stabilized at the desired size by P(NIPAAm-co-AMPS). The second LSCT and the resulting diameter were controlled by varying the HMAAm content. Nanoassemblies can also be reversibly disentangled at temperature below the LCSTs, with recovery of soluble block copolymer chains. Thus, the proposed protocol enables to prepare stimuli-responsive nanoassemblies and customize their size by a simple mixing and heating/cooling of the selected block copolymers. Using temperature as a single on-off parameter to induce self-assembly in water circumvents the need of using organic solvents. The system reported here may be potentially useful for a range of applications, including drug and gene delivery, biosensing, or separation of biological molecules.

127. Structural and Morphological Features of Concentric Iron Oxide/Carbon Nanotubes Obtained from Phospholipids

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Biologically active 1,2-bis(10,12-tricosadiynoyl)-sn-glycero-3-phosphocholine ($DC_{8,9}PC$) nanotube-forming phospholipids (PLs) have been utilized as templates to prepare ferromagnetic nanotubes (FMNTs) that exhibit responsiveness to magnetic and electric fields. Combining X-ray diffraction (XRD), selected area electron diffraction (SAD), high-resolution transmission electron microscopy (HRTEM), Raman, and Mössbauer spectroscopy measurements, FMNTs morphological features and chemical composition were determined. These studies showed that FMNTs consist of iron oxide/carbon/iron oxide concentric nanotubes with the amorphous carbon phase sandwiched between two iron oxide layers. The iron oxide phase consists of nanocrystalline magnetite (Fe_3O_4) which coexist as tetrahedral Fe^{3+} and octahedral $Fe^{2.5+}$ sites containing minute quantities of hematite (α-Fe_2O_3) phase. The carbon phase consists of amorphous carbon forming an amorphous carbon nanotube (ACNT). Magnetic measurements showed that saturation magnetization (M_s) of FMNTs is 79 emu/g, but upon removal of the iron oxide outer and inner layers, ACNTs become paramagnetic. The electrical resistivity (ρ) of single FMNT is 3.3×10^{-2} Ω·m, which decreases to 5.06×10^{-4} Ω·m for ACNT. These magneto-electric properties can be easily tailored, depending upon desired applications and needs.