POSTER ABSTRACTS
Double Receptor Targeting Multifunctional Iron Oxide Nanoparticles Drug Delivery System for the Treatment and Imaging of Prostate Cancer

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As an alternative to the drawbacks of current advanced prostate cancer chemotherapy, we propose a multifunctional double targeting drug delivery system that utilizes the combination of two cancer-targeting peptides: a modified luteinizing hormone releasing hormone (LHRH), the ligand for luteinizing hormone releasing hormone receptor (LHRH-R), and AE105, the ligand for urokinase type plasminogen activator receptor (uPAR) and loaded with the anticancer drug Paclitaxel (PTX) as the payload. The results obtained from dynamic light scattering (DLS) indicates that conjugation of peptides on IONPs resulted in an increase in the average hydrodynamic size of targeted IONPs (16.34 nm) as compared to non-targeted IONPs (12.51 nm), as well as a decrease of zeta potential from -70.43 mV to -58.06 mV, respectively. Prussian blue staining demonstrated that both, LHRH and AE105 targeted IONPs were internalized efficiently by the human prostate cancer cell line, PC3. In vitro magnetic resonance imaging (MRI) results showed that double-targeted IONPs significantly maintained T2 MRI contrast effect and reduction of T2 values upon internalization by PC3 cells. In vitro MRI imaging confirmed the preferential binding and accumulation of double-targeted IONPs in PC3 cells when compared to normal prostate epithelial cells (RC77N/E). PTX loaded double-targeted IONPs showed an approximately 2-fold reduction in PC3 cell viability when compared to non-targeted IONPs. These were also stable at physiological pH and efficiently released around pH 4. In addition, IONPs system is capable of reducing drug concentration. Our results indicate that we have developed a LHRH-R and uPAR targeted IONPs drug delivery system that potentially provides a MRI tractable delivery of cancer therapeutics such as PTX to PC3 cells. Therefore, our optimized double-targeted IONPs drug delivery system has the potential to significantly improve the health outcomes and quality of life for cancer patients as a novel type of targeted nanomedicine therapy.
Environmental concerns with military use of metallic tungsten (W), which was initially assumed to be an environmentally friendly alternative to lead, arose due to previous investigations that identified fishing weights and munitions containing elemental W can fragment and oxidize into complex monomeric and polymeric tungstate (WO$_4$) species in the environment. The speciation leads to increased solubility and mobility in soils resulting in a greater increase of the potential for toxicity and bioaccumulation into plant and animal tissues. In this study, we expand on our previous research that identified tungsten toxicity, bioaccumulation, and compartmentalization into organisms, and correlate through depth-sensing nanoindentation that the bioaccumulation of W degrades the mechanical properties by over 50% in the gastropod (Otala lactea) shell. Synchrotron-based X-ray fluorescence maps and X-ray diffraction measurements confirmed the bioaccumulation of W and integration into the shell matrix with the observed changes in shell biomechanical properties, mineralogical composition, and crystal orientation.
Silver-Polyvinyl Pyrrolidone (Ag-PVP) Nanoparticles Inhibition of *Chlamydia trachomatis* Inflammatory Mediators in Macrophages is Partly Due to Down-Regulation of Expression of its Major Outer Membrane Protein

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*Chlamydia trachomatis*, the most sexually transmitted diseases globally, affects both men and women and poses a huge economic burden on the population due to its asymptomatic nature. *C. trachomatis* causes symptoms that range from burning during urination, discharge and urethritis to name a few. Also, it can often lead to pelvic inflammatory disease and infertility in women and sterility in men without early intervention. We recently published that Ag-PVP nanoparticles exerted anti-inflammatory actions in mouse macrophages by inhibiting several inflammatory mediators, including receptors, chemokines and cytokines. Here we hypothesized that Ag-PVP anti-inflammatory action in macrophages maybe due to its ability to inhibit *C. trachomatis* bacterial load. Mouse J774 macrophages were exposed to various concentrations of Ag-PVP (3-12 µg/mL) and infected with *C. trachomatis* at a multiplicity of infection (MOI) of 2.5 to 20 for up to 48 hr. We used TaqMan qRT-PCR to quantify the mRNA gene expression of *C. trachomatis* major outer membrane protein (MOMP) as a marker of bacterial load. Our qRT-PCR data showed that Ag-PVP reduced MOMP expression by 70% with no toxicity to cells at all tested concentrations of Ag-PVP, suggesting that nanoparticles potentially reduced *C. trachomatis* bacterial load in macrophages. We further demonstrated by IL-6 cytokine specific ELISA that Ag-PVP inhibited IL-6 in a *C. trachomatis* concentration-dependent manner, correlating with its modulation of MOMP expression. Our data shows that the ability of Ag-PVP to inhibit *C. trachomatis* bacterial load maybe a potential mechanism of its anti-inflammatory actions in macrophages.
Designing Liposomes for Protein Encapsulation

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A liposome is a vesicle, made out of the same material as a cell membrane. Membranes are made of phospholipid bilayer. Phospholipids are molecules that have a hydrophilic head group and a hydrophobic tail group. In the present study, liposomes were prepared for protein encapsulation and delivery. The liposomes were created through multilamellar vesicles (MLV), small unilamellar vesicles (SUV), and dehydration-rehydration vesicles (DRV) method. To prepare liposome, chloroform:methanol (9:1) surfactant solution was used. Synthetic phospholipid-Dipalmitoylphosphatidylcholine (DPPC) (100mg) was dissolved in 1ml of the surfactant solution to prepare the liposome. To stabilize the liposome cholesterol (Chol) was added at the rate of 10 mg/mL in the surfactant solution. The mixture containing DPPC and Chol (16 µmoles each) were placed in a round bottom flask and placed on a rotary evaporator to make a dry lipid film. The film was further flushed with Nitrogen to ensure complete solvent removal. The dried film was rehydrated in PBS (2mL) to get MLV. To prepare SUV liposomes, prepared MLV solution (2ml) was placed in a beaker and sonicated for 5mins to get 100 nm diameter SUV. The SUV suspension was centrifuged at 3,500 g for 10 minutes to remove any debris from the sonicator probe. To encapsulate protein, SUV suspension was placed in a beaker and the Bovine Serum Albumin (BSA) protein (200 ug /2000ul) was added. The mixture was freeze at -20oC for an hr and transferred to freeze-drier overnight. To further prepare DRV, the freeze dried mixture was rehydrated in 100 µl of deionized water. We prepared liposomes with BSA, and blank liposomes with either water or PBS. Work is currently going on to encapsulate drugs in the liposomes for delivery purposes.
Effect of Gold Nanorod Functionalization on the Inhibition of Human Respiratory Syncytial Virus

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Human respiratory syncytial virus (RSV) is a Paramyxovirus causing respiratory tract infections in the infants, children, old adults and immunosuppressed individuals. It is observed that almost every child below the age of 2 years would have had an RSV infection. RSV can lead to pneumonia and bronchiolitis in the pediatric and geriatric populations. There is neither active vaccine against RSV nor any effective drug, except broad spectrum anti-viral drug ribavirin. Recent trends in the RSV research indicate nanomedicine as an alternative option. Functionalization of gold nanorods with drugs or cell penetrating peptides provides longer retention, controlled release, protection from degrading enzymes and enhanced cellular delivery. Here, we have conjugated gold nanorods (GNR) with ribavirin (GNR-R), cell penetrating peptide HIV-TAT (GNR-T) and both together (GNR-RT). The nanoparticles were then characterized for functionalization by dynamic light scattering, zeta potential, Fourier transform- infrared spectroscopy, UV-Visible spectroscopy and transmission electron microscopy. RSV inhibition was assessed by immuno-fluorescence microscopy, real time PCR and plaque assay. Our results show that, RSV was inhibited by GNR. However, functionalization of GNR with ribavirin or/and TAT peptide reduced the RSV inhibition.
Antibiotics are traditionally used to treat bacterial infections; however, many strains of bacteria have evolved and show a propensity to exhibit antibiotic resistance. This overwhelming problem creates a need for a new type of antimicrobial such as Gold (Au) Nanoparticles, which are becoming popular as antibacterials. These nanoparticles have promising effects as antimicrobial nanocomposites, but can be toxic in high levels. To alleviate this problem, the nanoparticles can be combined with antimicrobial peptides to decrease toxicity and increase antibacterial properties. In this study we evaluated the antimicrobial properties of peptide, p557 against Streptococcus pyogenes and E.coli using the Minimum Inhibitory Concentration (MIC). We then evaluated the antimicrobial properties of Gold nanoparticles using the same assay. The MIC of p557 for S. pyogenes was shown to be 1.9µg/mL when only 1mg/mL stock solution of the peptide was used. When 1mg/mL was used against E.coli, p557 showed inhibition at 3.9µg/mL. Evaluation of the Au-Nanoparticle against both S.pyogenes and E.coli revealed that the MIC was much higher and gave a variable range of 250µg/mL-125µg/mL. Our results show that both the peptide and the Au nanoparticle inhibited both gram-positive and gram-negative bacteria. However, the peptide inhibited both bacteria at a lower concentration than the Au nanoparticle. Given the functionality of the peptide and the Au nanoparticle we believe that this shows potential for complete microbial inhibition when conjugated. The interaction of p557 and Au nanoparticles with bacterial cells will be further investigated by Atomic Force Microscopy (AFM), standard plate count, growth-curve assay and real-time PCR.
Electrospinning Poly (ε-Caprolactone) Nanofiber for Bone-Tissue Regeneration

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This research aims to develop polymeric nanofibers that can be used as tissue scaffolds. Nanoscale fiber scaffolds provide an optimal template for cells to seed, migrate and grow. The goal is for the cells to attach to the scaffolds, then replicate, differentiate and organize into normal healthy tissues as the scaffold degrades. In this study, non-woven poly (ε-caprolactone) (PCL) and hydroxyapatite (HA) nanofibers with different wt % compositions were prepared by electrostatic co-spinning technology. It was hypothesized that PCL and PCL/HA scaffolds will mimic the nano-features of the natural extracellular matrix (ECM). To test if these scaffolds mimic the properties of natural ECM, we used TRAMP C2 cell lines derived from transgenic adenocarcinoma of mouse prostate (TRAMP) mice. The scaffolds were analyzed by MTT assay at different time points to verify cell toxicity/proliferation. Characterization for morphology of the electrospun fibers were observed using scanning electron Microscopy (SEM) and SEM micrographs were analyzed using image analysis software. The fibers were characterized for thermal behavior using Differential Scanning Calorimetry (DSC), and for chemical structure using Fourier Transform Infrared Spectroscopy (FTIR). Thus, our objective is to develop biodegradable scaffolds for bone tissue that mimics the size scale and chemistry of the ECM with an interconnected pore structure, and enhanced mechanical properties.
Polyvinyl Pyrrolidone (PVP) Coated Silver Nanoparticles Demonstrates a Capsule Dependent Antimicrobial Effect Against *Streptococcus pneumoniae*

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Both the antimicrobial nature and toxicity of metals are well documented in literature. Advances in nanotechnology have extended the usefulness of metals as antimicrobials while decreasing their toxic effects. Our study examined the effectiveness of metallic nanoparticles on the growth of pathogenic *Streptococcus pneumoniae*. The need for novel antimicrobials which can control pneumococcal growth is becoming more pressing due to increasing numbers of isolates which are resistant to current therapies. Nanospheres of gold (AuNP), titanium dioxide (TiO₂), or polyvinyl pyrrolidone (PVP) coated silver (Ag-PVP) were tested for their ability to inhibit the growth of the pneumococcal model strain D39. Of the formulations tested, Ag-PVP was found to be the most effective and provided the most consistent results. The inhibitory effect of Ag-PVP was seen for serotypes 4, 19F, and 3 in addition to serotype 2. The examination of *S. pneumoniae* strains that completely lack a capsular polysaccharide showed that the lack of the capsule made bacteria more resistant to the action of Ag-PVP. These data demonstrate a serotype independent, capsule dependent bactericidal activity for metallic nanoparticles includes of *S. pneumoniae*.

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Multiscale Modeling of Electrical Properties of Carbon Nanotube-Based Composites

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The relationship between the structure and its property is essential to understand the mechanical characteristics of nano-materials like Carbon Nanotubes (CNT), and based nano-composite systems. In addition to the high tensile strength, carbon nanotubes are also known for their low electrical resistance and their ability to be effective electrical and thermal conductors. Carbon nanotubes are now beginning to show as promising materials for use in integrated electronics, primarily due to their potential to develop flexible nano-electronic systems compared to silicon based electronic systems. In this work, we develop a computational model to understand the thermal and electrical properties of carbon nanotube reinforced composite systems and the computational model would be compared with experimentally published data. One of the major advancement of the developed computational model is the inclusion of the interfacial electrical resistance of carbon nanotubes and study of the effect of the overall electrical conductivity of the nanocomposite using a multi-phase approach. Given the conductivity of the matrix and the nanotube, the model would be able to predict the effective electrical (or thermal) conductivity, for a specific volumetric fraction of the nanotube. The model will also be able to calculate the conductivity of a multi-phased nano-composite for which the CNTs are initially coated with a separate material and then combined into a matrix, using a multi-phase approach.
Iron oxide nanoparticles are widely used for biomedical and industrial purposes and are present in our environment. Interestingly, there are few studies observing the potential impact of nanoparticles on plant and animal species. The goal of this project is to identify the effects of charged *Arabidopsis thaliana*. To achieve this goal, we treated *Arabidopsis* plants with both positively and negatively charged iron oxide nanoparticles dissolved in distilled water. Previous experiments showed that the model plant - Fe$_2$O$_3$ nanoparticles on the growth and development of Fe$_2$O$_3$ nanoparticles are readily absorbed by the root system of *Arabidopsis* and are rapidly dispersed throughout the plant’s tissue including transport into the reproductive structures. In this study, we investigated the effect of iron oxide nanoparticles on plant’s physiology and reproductive abilities. Results describing the effect of iron oxide nanoparticles on seed production, seed germination, pollen viability and root development will be presented.
A Simple Method for the 360-Degree Acquisition of Bioluminescence, Fluorescence, or X-Ray Data using a Mouse Imaging Spinner (MiSpinner)*

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Optical imaging modalities are powerful tools for the in vivo assessment of drug delivery and therapeutic strategies. Current 2-dimensional imaging approaches have inherent limitations that result from the scattering of light as it passes through animal tissues, the interference of that signal by the absorptive properties of the tissue and blood, and the relative orientation of the light source in the animal during longitudinal studies. To account for this, it is commonplace to acquire images from multiple orientations of a single subject, in order to obtain the most accurate representation of a given region of interest (ROI). However, this method leads to subjectivity and inconsistency when manually turning or manipulating the subject in the field of view. We have invented a device that works with existing optical imaging systems that eliminates the subjectivity of the animal positioning through the use of an actuated motor and animal holder mechanism. Our device provides a rapid means of acquiring multiple images in precise intervals around the subject animal in photographic, bioluminescent, fluorescent, and X-ray modalities. Here, we demonstrate the application of this device through imaging a bioluminescent PC3-Fluc xenograph tumor in NCRNu mouse, and graphically illustrate the change in bioluminescent ROI intensity as it relates to the orientation of the mouse around a 360 degrees axis. The ROI intensity data plotted as a function of the degrees of rotation results in a bell-shaped curve, with the peak representing maximal bioluminescent intensity from the tumor source.

*Provisional patent US62/020,056; trademark pending
Exposition of Foreign Peptides on Qβ Coliphage for Au Nanoparticle Binding

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It is known that Au can be used in the treatment of cancer in nano form as a probe to both target and treat cancerous tissues. And although Au itself can be used in the treatment, an anti-cancer biodrug can be coated onto the Au. However, two problems exist. One, nanoparticles tend to aggregate in vivo and are cleared by the immune system. The only way to prevent aggregation is to keep the nanoparticles separated in vivo. The second problem arises with the nature of biodrugs themselves. Biodrugs are made from the same biomolecules that make up the body, as such; they are also subjected to the same enzymes that degrade biomolecules in the body. This leads to indiscriminate distribution, degradation, and a risk of under-medicating. To compensate, a larger dose of the biodrug is given; however, toxicity becomes the risk. Since it is known that certain peptides (nano-tags) bind Au, we hypothesize that displaying these nano-tags on the surface of our bacteriophage Qβ, and allowing them to bind Au will prevent aggregation. This Au can then be coated with an anti-cancer biodrug, and the Au will convey protection to the biodrug. To achieve this, the genes of three gold-binding peptides: Au0 (LKAHLPPSRLPS), Au1 (VSGSSPDS), and Au2 (TGTSVLATPYV) were inserted separately into the genome of Qβ at the end of the A1 gene. The resulting recombinant phages, pQβAu0, pQβAu1 and pQβAu2, were transformed with HB 101 E. coli. The plaque assay provided the titer and phage morphology, and RT-PCR confirmed the tag gene size for each construct. A binding assay allowed different concentrations of Au to bind to the recombinant phage. Confirmation and visualization of the phage-nanoparticle complex was verified via Transmission Electron Microscopy (TEM). The next phase is to focus on coating the Au nanoparticles with chemotherapeutic biodrugs.
Proteomic Studies of Antibacterial Peptides

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Resistance to antibiotics is of grave concern and there is an urgent need for development of new antimicrobial strategies. Antimicrobial peptides (APs) could be a suitable approach as certain antimicrobial peptides have shown antibacterial activity against some of the antibiotic-resistant bacteria. It is also of interest to investigate the mechanism of action. In the present study, we evaluated the antimicrobial effect of two commercially available peptides TP493 and TPOB1013 from Therapeutic Peptides Inc. Minimum inhibitory concentrations (MIC) of both the peptides were investigated against a foodborne pathogen, Salmonella enterica serovar Typhimurium. Post exposures to peptides, the morphological changes were captured by scanning electron microscopy (SEM). The protein profile of outer membrane (OM) and periplasm of the bacteria exposed to both the peptides was also investigated and compared to untreated bacteria. The MICs for TP493 and TPOB1013 were between 3.9 - 7.8 µg/ml, and 1.9-3.9 µg/ml, respectively. SEM analysis revealed the formation of pores in bacteria, damage to the outer membranes, and lysis of the cells. The protein profiles of OM and periplasm of the peptides-treated bacteria showed significant difference compared to untreated bacteria. It was observed that some of the proteins were either significantly expressed or were not observed in peptide treated bacteria compare to untreated bacteria. The results suggest that TP493 and TPOB1013 have antimicrobial potential and could be considered for development of new antimicrobials.

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MicroRNAs (miRs) are small, noncoding RNAs encoded within our genome that regulate gene expression by silencing messenger RNA (mRNA) transcripts. Since being discovered in humans in 2001, much has been learned concerning the many cellular activities that miRs can affect. MiRs have been implicated in almost every cellular activity, including cell fate determination, stress response, metabolism, apoptosis, and carcinogenesis. Importantly, alterations in microRNA activity due to mutation or misexpression have been repeatedly shown to result in tumorigenesis and disease. However, because of their relatively recent discovery, therapeutic tools to suppress miRs are just now being developed. One extremely promising way to inhibit miRs is to use microRNA sponges which consist of ~15 miR “target” sites that can specifically bind and inactivate particular miRs. Unfortunately, microRNA sponge production has proven to be problematic thus far as current production methods involve either costly commercial synthesis or low throughput ligation-based cloning. However, we have recently developed an entirely novel, PCR-based method that allows sponge production in a much more rapid manner. In all, PCR amplification, cloning, and sequence confirmation are readily attainable in less than two weeks and at a significantly lower cost than commercial inhibitor synthesis.
Biofilms created by foodborne pathogens are difficult to eradicate with traditional antibiotics due to challenges that are faced with penetrating biofilms. Therefore, the development of a novel delivery system is urgent. Superparamagnetic iron oxide nanoparticles (SPIONs) are promising candidates in the area of biomedical applications, especially targeted drug delivery. Here, we evaluate the hypothesis that SPIONs combined with antimicrobial peptides can be effective in penetrating biofilms and delivering the peptide to a specific site for treatment. SPIONs can be targeted to the infection sites using an external magnetic field, causing deep penetration of the biofilm. In our present study, we have evaluated a proprietary peptide TP556 from Therapeutic Peptide Inc. as well as carboxylated SPIONs for antimicrobial effects on the planktonic form of the bacteria. The minimum inhibitory concentration (MIC) of TP556 and SPIONs against \textit{Salmonella enterica} serovar Typhimurium (\textit{S. typhimurium}) was assessed. The MIC of TP556 was between 50 and 62.5 \text{µg/mL}. SPIONs did not retard bacteria alone even at concentrations of 250 \text{µg/mL}. We have also begun to evaluate to effects of TP556 conjugated SPIONs against biofilms in the presence of a magnetic field. Magnetically concentrated TP556-SPIONs cause some bacterial killing in the established biofilm.
PLGA Nanoparticles as a Delivery Agent for Cancer Cells

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Historically, it has been difficult to combat cancer in any form because of its ability to elude traditional forms of medicine, such as chemotherapy, radiation, and surgery. In fact, cancer treatments negatively affect the patient and are at times ineffective against preventing cancer entirely. Hopefully, a new form of treatment can be more effective and less hazardous for the patient. In the present study, we wanted to evaluate nanoparticles as drug delivery agents to cancer cells. Anti-cancer drug, Doxorubincin Hydrochloride (DOX) was encapsulated in poly (DL-lactide-glycolide) PLGA nanoparticles to allow low doses of the drug to be released into the body over an extended period of time in order to kill cancer cells. Drug encapsulated PLGA and PLGA nanoparticles were prepared using "emulsion" method. The nanoparticles were characterized using Zeta sizer, TEM, SEM, and FTIR. PLGA-DOX nanoparticles were around 220 nm with a charge of -29 mV. Our results showed 90% drug encapsulation of nanoparticles. FTIR analysis confirmed that DOX was successfully encapsulated in the PLGA nanoparticles. Release of the drug from nanoparticle was evaluated in PBS by continuous shaking and estimating absorbance at 480 nm. Drug was released gradually over the period of time. We observed almost 40% cell death of A549 cells at 250 ug/mL PLGA-DOX. The current results are promising; however, further research is necessary to achieve uniform sized nanoparticles, to increase drug nanoparticles, and to increase drug load so as to have more efficient way to kill cancer cells.
Pegylation of Silver Coated Single Walled Carbon Nanotubes Reduces Toxicity to Human Cells at Their Antibacterial Concentrations

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Silver coated single walled carbon nanotubes (AgCNTs) are well known for their antibacterial activity. However their toxicity to human cells is a serious public health concern. This can be avoided by the process called as functionalization using non-toxic material such as polyethylene glycol (PEG). This may however reduce their antibacterial activity as pegylation may cover the silver coating on carbon nanotubes. Present study was attempted to investigate whether pegylation of AgCNTs reduces their toxicity in vitro, without affecting their antimicrobial activity. For this purpose, AgCNTs were pegylated using phospholipid polyethylene glycol (PL-PEG) and were characterized by zeta potential measurement, Fourier transmission infra-red spectroscopy (FT-IR) and electron microscopy (EM). In vitro cell toxicity assay was carried out using human lung carcinoma (A549), hepatocellular carcinoma (Hep2) and murine macrophages (J774) whereas antibacterial activity was investigated against Salmonella enterica serovar Typhimurium. Shift in the charge (-41.8 to 8) using zeta potential measurements and characteristic FT-IR peaks on pAgCNTs similar to PL-PEG confirmed the pegylation which was further evidenced by electron microscopy which showed increase in size of AgCNTs upon pegylation. More importantly, pAgCNTs were relatively non-toxic to human cells at their antibacterial concentrations (62.5 µg/mL) compared to plain AgCNTs. We are further evaluating the antibacterial activity of pAgCNTs compared to plain AgCNTs at molecular levels.
Investigating the Biological Effects of Iron Oxide Nanoparticle Exposure Using *Drosophila melanogaster*

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The past two decades have brought a myriad of novel medical applications for nanoparticle technology. As the clinical utilities for nanoparticles expand, so too does the need for a comprehensive understanding of their toxicology. To this point, recent reports have confirmed a wide range of deleterious effects associated with the use of gold, silver, and aluminum nanoparticles. These studies, however, have been mostly conducted in complex rodent models or *in vitro* using cultured cells. There remains a need for a practical, whole-organism model to study nanoparticle toxicology *in vivo* and assess the genetic and reproductive effects. Using *Drosophila melanogaster*, our research focuses on evaluating the potential toxic effects of polyacrylic acid (PAA)-coated iron oxide nanoparticles (IONPs) on larval development, reproduction, and the immune response. Interestingly, we found that exposure to low concentrations (0.5-10µg/mL) of PAA-coated IONPs resulted in a higher larval mortality rate than exposure to higher concentrations. Additionally, low-dose exposure caused reproductive defects in adults leading to a reduction in fertility but not fecundity. When investigating the morphology of reproductive tissues, we found abnormalities in the ovarian cells of adults that had been dosed with PAA-coated IONPs as larva. Additionally, we have identified a dose-dependent threshold of IONP exposure required to activate the immune response, which may explain the deleterious effects of only low-dose treatments. Overall, our investigation reveals a tightly-regulated dose-response relationship required for understanding the adverse effects of nanoparticle uses, as well as provides researchers with a robust whole-organism model for assessing nanoparticle toxicology and teratology.
Controlled growth and uniform patterning of graphene/carbon shells encapsulated gold nanoparticles (GNPs) on silicon wafer or on high curvature nanostructures is reported. Gold nanoparticles were uniformly patterned on these substrates via dewetting process. Surface oxidation of these patterned nanoparticles rendered them as sacrificial catalysts for the chemical vapor deposition (CVD) growth of graphene/carbon shells. The shell morphological evolution and thickness as well as surface migration of nanoparticles during the CVD process were studied. It is proposed that graphene/carbon shell growth is controlled by Ostwald’s ripening, surface gold oxide, and reducing CVD growth environment. Furthermore, complex heterostructures based on CNTs coated with GNPs were fabricated. Finally, Discrete Dipole Approximation (DDA) method was utilized to simulate optical properties of GNPs and comparisons were made with gold nanoparticles on various substrates. Tunable optical characteristics of GNPs with resonance peak wavelengths in visible light range were estimated.
The use of natural products have shown tremendous therapeutic prospects as carriers for drug delivery. Natural products, such as genipin, can act as an anticancer drug to treat various forms of cancer. In the present study, the inhibitory effects of genipin were evaluated against human prostate cancer cell line PC3. PC3 cells were seeded in 96-well culture plates and treated with genipin for 72 hours. Cell viability was determined by MTT Assay. 72 hours after incubation, 20 µl of 5 mg/ml MTT solution was added to each well with PC3 cells. The cells were further incubated for 2 hours at 37°C in culture hood. Media was removed and 200 µl of DMSO was added. Absorbance was read at 590 nm. Genipin effect on cellular protein was determined by SRB Assay. After 72 hours of incubation, media was removed and 200 µl of 10% TCA was added to the cells. Protein-bound dye was dissolved in 10 mM Tris base solution. Our studies showed that genipin reduced cell viability by 50% at 87ng in 72hours as shown by MTT assay. SRB assay indicated an IC50 value of 221.7ng in 72hours. Work is currently in progress on the encapsulation of genipin in a liposome for efficient delivery to cells and to increase its efficiency.
Polyvinyl Alcohol (PVA) Influences Polylactic Acid-Polyethylene Glycol (PLA-PEG) Copolymer Morphology and Encapsulation Efficiency Characteristics

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Biodegradable nanoparticles (NPs) have a wide range of possibilities and advantages when compared to other drug delivery systems. Biodegradable polymers typically employed for fabrication of NPs provide controlled release, low toxicity, high encapsulation efficiency, sub-cellular size and bio-distribution in vivo. They are also excellent for vaccines delivery and can be fabricated to evoke immune responses, either by direct stimulation of antigen presenting cells (APCs) or delivering antigens to specific cellular compartments. However, problems associated with NPs formulation include their homogeneity, and rapid protein release (burst effect). Much research has been conducted on the block copolymer polyethylene glycol and polylactic acid (PLA-PEG). Polyvinyl alcohol (PVA) is the most commonly used emulsifier in the formulation of NPs. PVA provides non-aggregating, emulsifying and adhesive properties to NPs and an interconnected network with the polymer at the interface which ultimately can affect their homogeneity, release profile and size. The objective of this study was to determine the concentration-dependent effect of PVA on the size, morphology and release profiles of the modeled protein, bovine serum albumin (BSA) encapsulated within PLA-PEG. NPs were formulated by the Water/Oil/Water double emulsion method using concentrations of PVA ranging from 0.5-3%. Scanning electron microscopy (SEM) analyses revealed that use of 0.5, 1.0 and 2% PVA resulted in smaller NPs (105 - 228 nm). In contrast, 3% PVA resulted in larger NPs (246 - 332 nm). The encapsulation efficiency (EE) of NPs with 0.5, 2 and 3 % PVA was 10-30%, while that of 1% PVA was 40%. Selection of 1% PVA for formulation of NPs with 2X polymer (200 mg polymer with 4 mg BSA) and less BSA (2 mg BSA and 100 mg polymer) resulted in 55% and 64% EE, respectively. These interesting observations will permit the selection of sizes of PLA-PEG NPs formulations for maximal interaction with APCs, but more importantly for vaccine delivery.
Carbon fiber reinforced polymer (CFRP) composites materials have been identified as one of advanced material systems that has been at the forefront of next generation structural materials in aerospace and automotive industries for a number of reasons. Partly due to factors such as high strength-to-weight-ratio and high stiffness and overall cost saving over time. Properties of these materials are further enhanced with the addition of different nanoparticles fillers. With these promising enhancements in properties, there are concerns about their vulnerability to damages caused by constant impact from random foreign objects. In the current research studies, high strain rate tests were conducted on CFRP to understand the mechanical response of CFRP materials subjected to different strain rate compression loading using Split Hopkinson pressure bar setup. Samples used in the study were fabricated using combination of montmorillonite nanoclay (MMT) and carbon nanotube (CNT) hybrid and SC-15 epoxy resin infused into 8 harness satin weave carbon fabric using hand-layup and compression molding. CNT used were carboxylic functionalized multi-walled carbon nanotubes (COOH-MWCNT) and I.30E MMT nanoclay at 0.3 wt. % CNT/SC-15; 2 wt. % MMT/SC-15 and hybrid combination of 2 wt. % MMT and 0.1 wt. % CNT.
Antibiotic resistance is on the rise, leading to what many refer to as the “post-antibiotic era.” Exacerbated by limited new antibiotic types over the past 30 years, there is a need for more rapid, sensitive protocols for high-throughput examination of antibiotic candidates. One major determinant in the characterization of antibiotics is cost-effective analysis of the underlying mechanism by which hit-induced antibiosis occurs; bactericidal agents, which kill the bacterial cell, are far less likely to develop antibiotic resistance than bacteriostatic agents, which merely inhibit cellular growth. Within, we describe a technique that combines classic antibiotic diffusion tests with the use of genetically modified, constitutively active bioluminescent strains of Staphylococcus aureus. We have previously shown that this pathogen-based bioluminescence is a surrogate for cellular and physiological changes, as the cellular level of metabolites directly relates to light production by the engineered luciferase. We demonstrate that this new protocol is able to streamline the differentiation of antibiotic mechanisms, as delayed growth in sub-clinical levels of bacteriostatic agents led to signal recovery of up to 100% untreated cells once antibiosis is reprieved, versus cells that are placed in the same concentration of bactericidal agents with 28% recovery. These differences are mechanism-dependent and due to physiological changes that occur in the nano-scale. Use of this protocol should provide for a more streamlined and cost-effective means of evaluating novel antibiotic candidates, such as coformulations, delivery systems, and peptidomimetics, alleviating barriers which have restricted antibiotic discovery for the past three decades.
The Effects of Positively Charged Iron Oxide Nanoparticles on Survival and Fertility in *Drosophila melanogaster*

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Superparamagnetic nanoparticles have gained interest in medicine for magnetic resonance imaging contrast, cell targeting, controlled drug release, hyperthermia, and tissue repair. Much of this focus has recently shifted toward use of iron oxide nanoparticles (IONP) due to suggestions that iron oxides may be safer for biological applications than comparable nickel and cobalt nanoparticles; however, this safety is also subject to the surface coatings of the particles. While much of the previous work examining this toxicity has used *in vitro* models, this study utilizes *Drosophila melanogaster* as a whole organism model of IONP toxicology. Maghemite IONPs coated with polyethylenimine were fed over 24 hours to 2nd instar *Drosophila* larvae. Fed larvae were then assayed for immune activity, survivorship through feeding, pupation, and eclosion, and adult fertility. Though no effects were found on survivorship at any stage of growth, concentration-dependent deleterious effects on fertility were found in both males and females.
Macrophage Uptake of *Chlamydia trachomatis* Outer Membrane Peptide Encapsulated in PLA-PEG Nanoparticles and Induction of Mucosal Antibodies

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In quest of a vaccine against *Chlamydia trachomatis*, the most reported bacterial sexually transmitted infection, we previously reported that encapsulation of M278, a peptide derived from the major outer protein of *C. trachomatis* within poly (lactic acid)-b-Poly (ethylene glycol) (PLA-PEG) nanoparticles triggered enhanced systemic adaptive immune responses in mice. Because PLA-PEG can facilitate uptake of antigens by antigen presenting cells (APCs) or by increasing the influx of APCs in to the injection site, here in this study, we investigated the potential of encapsulated-M278 to stimulate production of Th1 cytokines by mouse and human APCs. Our results revealed that mouse J774 macrophages and human THP-1 monocytes exposed in vitro to different concentrations of PLA-PEG-PBS (PBS encapsulated PLA-PEG) and PLA-PEG-M278 (encapsulated-M278) induced marked production of IL-6 and IL-12 Th1 cytokines, suggesting the ability of encapsulated-M278 to directly activate APCs. We next immunized four groups of BALB/c mice subcutaneously with PLA-PEG-PBS, PLA-PEG-M278, M278 or PBS and two weeks after the last immunization vaginal wash samples were collected for mucosal antibody analyses. PLA-PEG-M278 immunized mice produced higher IgG and IgG2b M278-specific antibodies as compared to bare M78 immunized mice, suggesting that PLA-PEG potentiated the capacity of M278 to induce mucosal antibody responses in mice. Collectively, encapsulated-M278 holds promise as a vaccine candidate against Chlamydia by triggering both systemic and mucosal antibody immune responses in mice. Studies are ongoing to determine the mechanisms involved in uptake of nanoparticles by APCs and for enhancement of immune responses in mice.
Antimicrobial Effect of Silver Carbon Nanotubes Against Mucoid and Non-Mucoid P. aeruginosa

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Pseudomonas aeruginosa is a major opportunistic Gram-negative bacterium that causes a wide array of human infections particularly in immunocompromised patients. It frequently colonizes mops, waterlines and faucet heads in hospitals, and if not properly disinfected, they could become a reservoir for continuous re-colonization. Due to the high occurrence of P. aeruginosa resistance to commonly used antimicrobials, the identification of novel antimicrobials is needed. One area of rapidly growing interest and study is the use of antimicrobial nanoparticles including nanomaterials coupled with metals. Silver particles coated carbon nanotubes (AgCNTs) are well known for their antimicrobial properties. In the present study we hypothesized that AgCNTs may have bactericidal activity against mucoid and non-mucoid P. aeruginosa. We determined the antimicrobial effect of AgCNT against the viability of both strains of P. aeruginosa, effect on bacterial growth in the presence of AgCNTs, its microbicidal mode of action and effect on the essential genes of P. aeruginosa. Our results demonstrated that antimicrobial activity was significant at minimum inhibitory concentration (MIC) of 62.5 – 31.25 µg/mL for both strains. Scanning and transmission electron microscopy analysis showed disruption of cell membrane integrity and leaking of cytoplasmic content. The outer membrane porin gene, OprD, LasA protease gene, LasA, ClpX protease gene, ClpX and inner membrane protein gene, CreD were significantly down-regulated in the AgCNT-treated mucoid and non-mucoid strain. These results show that AgCNT possess antimicrobial activity against mucoid and non-mucoid strain of P. aeruginosa and down regulate essential genes of both strains of P. aeruginosa. This study indicates that AgCNT can be applicable to antimicrobial coating, disinfecting surfaces and for water treatment and purification due to its insolubility in water.
Inflammation induced by exposure to *Chlamydia trachomatis*, the major etiological agent of bacterial sexually transmitted infections, plays an integral role in its disease pathogenesis. Recently we showed that the anti-inflammatory cytokine, interleukin-10 (IL-10) inhibits pro-inflammatory mediators triggered by *C. trachomatis* and its recombinant major outer membrane protein (rMOMP) in mouse J774 macrophages. The objective of this study is to understand the molecular mechanism(s) by which IL-10 regulates inflammation induced by *C. trachomatis* in macrophages. We focused primarily on the suppressor of cytokine signaling (SOCS) 1 and SOCS3 because they are the potential mediators of the anti-inflammatory effects of IL-10 in macrophages. Herein we employed TaqMan qRT-PCR and demonstrate by concentration-dependent and time-kinetics studies the mRNA gene expression levels of SOCS1 and SOCS3 in J774 macrophages following their exposure to rMOMP in the presence and absence of IL-10. Time-kinetics studies revealed that rMOMP induced marked up-regulation of SOCS3 expression, which was further augmented in the presence of IL-10. Concentration-dependent studies showed that SOCS1 and SOCS3 were induced by as little as 0.1 µg/mL of rMOMP in macrophages. Notably, in the presence of IL-10, SOCS1 was markedly down-regulated, suggesting regulation of SOCS1 and IL-10 by SOCS3. Up-regulation of SOCS3 resulted in a marked down-regulation of SOCS1 expression except at 24 hr post-macrophage exposure, coinciding with reduced SOCS3 expression. Our data shows that SOCS1 and SOCS3 are differentially expressed in mouse macrophages with an ensuing effect on the IL-10-mediated inhibition of pro-inflammatory mediators.
Chemical Ordering in Metal-Based Composite Nanocrystals

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The production of nano-scale materials with predictable and reproducible composition and morphology has been a continuing problem for researchers in nanomaterials. Hyper-branch polyethyleneimine, as a polymer scaffold, was complexed in aqueous solution with Co\textsuperscript{2+} and Pt\textsuperscript{4+} in various ratios to form metal alloy Co\textsubscript{x}Pt\textsubscript{1-x} nanomaterials. Chemical reduction of dendrimer-metal precursor complexes results in the kinetically-favored crystalline, amorphous phase. This research examines whether photo-reduction of the precursor complex results in a thermodynamically-favored chemically-ordered crystalline phase, while also achieving a narrow size distribution. Bulk sample and grain-by-grain measurements are conducted in order to ascertain the effect of chemical versus photo-reduction and molar ratios of precursor compounds on composition and structure. Preliminary results show that the size control previously reported in the literature is achievable through photo- and chemical reduction, and that the polymer prevents aggregation in solution. The binding of the metal to the polymer has been studied via nuclear magnetic resonance spectroscopy, ultraviolet-visible spectroscopy, fluorescence spectroscopy, and cyclic voltammetry in order to understand the process of metal uptake into the polymer, and to produce functional nanomaterials.
Enhanced Targeting and Uptake of Liposome Nanoparticles Via Phospholipase A2 Receptor in Prostate Cancer

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Secretory phospholipase responsive liposomes (SPRL) offer the combined capacity to identify and target cancerous tissue and effectively deliver chemotherapeutic drugs. These lipid-based nanoparticles are degraded selectively by secretory phospholipase A₂ (sPLA₂), an enzyme that is over expressed in many tumors and is associated with cancer metastasis and malignancy. We have shown that a membrane protein for sPLA₂, M-type phospholipase A₂ receptor (PLA2R1), can alter the uptake and drug delivery of SRPL formulations. Flow cytometry and fluorescence microscopy were used to evaluate the uptake of two liposome formulations modified with a fluorescent lipid membrane probe, and the binding/uptake of two fluorescently labelled targeting peptides, expected to interact with the active site of PLA2R1, in a trio of human prostate cancer cell lines, i.e., wild prostate cancer PC-3, a PLA2R shRNA knock down variant (PC-3-PLA2R-KD) and a control - shRNA scrambled knock down (PC-3-PLA2R-SCR) cells. At 72 hr, the PLA2R-KD cell line demonstrated an increase in mean fluorescence versus the regular PC-3 and scrambled shRNA cell line. More importantly, fluorescent signal indicated SPRL liposome uptake was significantly greater (p<0.05) vs. SSL beyond 24hrs. Additionally, our peptide data revealed a consensus sequence peptide with increased fluorescence and binding affinity to the cellular membrane at lower concentration in regular PC3, while the KD cell line demonstrated a marked decrease in fluorescence signal among the peptides. The identification and use of a targeting peptide for PLA2R1 may be used to distinguish indolent vs. malignant disease, aid in detecting metastatic cancers and improve targeted drug delivery.
Surface Redistribution Kinetics of H/Li on Graphene for Advanced Energy Storage

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The motivation for this project is to create advanced materials for energy storage in battery electric and fuel cell electric vehicles, which show great promise as future energy solutions. One of the best candidate materials for enabling this technology is high surface area carbon. In order to leverage the high surface area in batteries and hydrogen storage tanks, investigations on how hydrogen and lithium interact with carbon substrates are required. Thus, in this study, we use first principles calculations to determine the kinetics and thermodynamics of the redistribution of hydrogen and lithium on graphene. We find that hydrogen and lithium move and pattern differently on the surface which we are able to explain in terms of fundamental differences in bonding mechanisms. For future research, we plan to investigate the homogeneity, concentration, and voltage dependency of hydrogen and lithium on graphene.
Development and High Throughput Screening of Targeted Anticancer Nanomedicines

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The past decade has seen an explosion of nanomedicines created to increase the therapeutic index of cytotoxic drugs across different types of cancer, including lung and pancreatic cancers that remain among the leading causes of mortality across the nation. Currently, the clinical prognosis for patients with these forms of cancer is poor with little option of curative treatment. Liposomes have been introduced to the clinical setting with great success and have significantly increased the therapeutic index of existing chemotherapy by encapsulating them within a lipid bilayer, protecting them from degradation and early elimination. Liposomes are then allowed to accumulate by passive transport mechanisms, such as the EPR effect, to enhance the accumulation of drug at the tumor site. Here we show that the use of phage fusion proteins bearing cancer cell-specific peptide fusions inserted into pre-formed, drug-loaded liposomes can increase the activity of nanomedicines in cancer cells. Two landscape phage display libraries were used to identify approximately 85 different families of peptides across >200 different phage clones following selection. A novel insertion method was developed to allow a 10-fold increase in screening throughput of targeted liposomes. This approach allowed us to identify targeted liposomes with greater activity than unmodified preparations. We also show the utility of phage fusion peptides to target various types of nanomedicines by increasing the toxicity of paclitaxel micelles following incorporation of cancer cell-specific peptides into micelles loaded with paclitaxel. Our work shows that phage fusion proteins can be used to significantly increase screening of targeted nanomedicine.
Mechanical and Thermal Characterization of Cellulose Nanofiber Reinforced Polyvinyl Alcohol Composite Film

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The aim of this research work was to prepare poly vinyl alcohol (PVA) thin film with different loading of cellulose nanofibers (CNFs) (1, 3, 5 and 7% loading) and also study the effect of cellulose nanofibers (CNFs) on the mechanical and thermal properties of poly vinyl alcohol (PVA) nano-composite films. With increasing CNFs content, the tensile and thermal properties also were increased up to 5% loading. For 7% loading of CNFs, the properties of composites films were degraded most probably due to the poor dispersion and agglomeration of CNFs. Biodegradability test of the samples showed that with increasing CNFs content increases biodegradability of the thin film.
A Novel Mechanism for the Directional Attachment of Proteins to Inorganic Nanoparticles Under Physiological Conditions

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Biological functionalization of inorganic nanoparticles is of great interest for biomedical applications. One current challenge in nanomedicine is developing multifunctional nanoparticles that will allow for the directional attachment of biological molecules to nanoparticle surfaces without damaging their structure, rendering them nonfunctional for their designed purpose. We have engineered a novel E/K coiled-coil mechanism for conjugation of peptides and proteins to iron oxide nanoparticle surfaces using red and green fluorescent proteins as a model system. This novel conjugation mechanism provides advances over current technologies in two ways. First, proteins can be specifically and directionally attached to the surfaces of nanoparticles, allowing for improved medical functionalization. Second, nanoparticle attachment can be performed under physiological conditions, minimizing structural damage to the conjugated proteins and, thus, enhancing biological functionality. In the present study, we present the expression and purification of several proteins functionalized for nanoparticle attachment and show the specificity of nanoparticle attachment provided by our technology. We also show that our mechanism allows for the potential attachment of multiple different proteins on the same nanoparticle. Future studies will apply this conjugation method to expand the use of inorganic nanoparticles as a platform for biomedical applications.
Chemical Functionalization and Characterization of Crystalline Cellulose Derived from Agricultural Waste Products

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Due to the abundance of agricultural waste products interest has intensified in its use as a biomass source for the extraction of cellulose. However, the extraction of cellulose from different biomasses is a rigorous process and, often, modification of its structure is needed to obtain the desired chemical and physical structural properties. In this research report, we have extracted cellulose from the agricultural waste products wheat straw and peanut shell via acid hydrolysis and, subsequently, subjected its structure to chemical functionalization using the Albright-Goldman and Jones oxidation reactions. Apparently, x-ray diffraction and scanning electron microscopy analyses reveal a structural rearrangement – conversion from CI to CII – for the modified cellulose. Furthermore, thermal analyses indicate a slight improvement in the thermal stability for the modified cellulose when compared to its unmodified counterpart.

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Low velocity impact response of carbon fiber reinforced epoxy nanocomposites after submerging to marine environmental conditioning was investigated. Carbon/Epoxy composites reinforced with 0.3% loading of COOH-MWCNT, 2% of MMT and 0.1% MWCNT/2% MMT binary nanoparticles by weight of epoxy were tested and the results were compared with neat carbon/epoxy composite. At first, dry samples without degradation were tested at 30J and 40J energy levels. The damage area for all modified and control samples were observed using thermographic imaging technique. Modified and control samples were submerged in saline water and tested after 1 month and 6 months of conditioning. From experimental data significant improvement was observed for the binary nanoparticles reinforced composite panels.
Fast and Facile Synthesis of Stable and Biocompatible Silver Nanoparticles Stabilized by Polyethylene Glycol

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The role of green synthesis methods of nanoparticles is very significant in the field of nanotechnology. Herein, we report, the synthesis of stable and biocompatible silver nanoparticles by a fast and facile, one-step process involving polyethylene glycol. Silver nanoparticles show enhanced properties, when supported on a substrate and incorporated into an organic or inorganic matrix. Silver nanoparticles were prepared using silver nitrate (AgNO3) as a precursor in an aqueous solution of polyethylene glycol (PEG) which acted as both a reducing and stabilizing agent. The reducing reactivity of PEG is sensitive to its molecular weight, thus a study has been made on establishing the optimum length of PEG that exhibits maximum reducing abilities. Therefore, different molecular weight PEG, ranging from 200 to 8000 daltons have been tried. Ethylene glycol and PEG 200 were used as a reducing agent and were found to be ineffective in their role in synthesis of silver nanoparticle even at high temperatures (> 150° C). However, under the same conditions, PEG 1000 was able to reduce Ag+ to silver nanoparticles. Further studies demonstrated that the reducing properties of PEG increased with the chain length of the polymer chain of PEG. The size of the nanoparticles depended on the reaction temperature and concentration of the precursor apart from the chain length of PEG. The properties of the synthesized silver nanoparticles were studied at different reaction times. The ultraviolet-visible spectra were in excellent agreement with the obtained nanoparticle studies performed by scanning electron microscopy (SEM), transmission electron microscopy (TEM), atomic force microscopy (AFM) and size distributions. The silver nanoparticles were characterized by using Fourier transform infrared (FT-IR) and zeta potential measurements. The use of biocompatible reagents, such as PEG provides green and economic features to this work.

Keywords: size controlled silver nanoparticles, green synthesis, polyethylene glycol
**Synthesis and Characterization of Peptide Conjugated Silver Nanoparticles for Use as Antibacterials**

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The ongoing trend of antibiotic resistant bacteria makes it necessary to develop novel therapeutic agents. Silver nanoparticles are of great interest for use as antibacterial agents due to their known antimicrobial properties. However, these nanoparticles have proven to be toxic. Another promising alternative to classical drug treatments are antimicrobial peptides. Antimicrobial peptides are a part of the innate immune system and the use of such peptides alone or in conjunction with metal nanoparticles may decrease the toxicity and provide enhanced antibacterial effects. In this study, bioconjugates of silver nanoparticles and TP373, a proprietary peptide from Therapeutic Peptides Inc., have been synthesized and characterized by UV–vis spectroscopy, transmission electron microscopy (TEM) and zeta (ζ) potential. The antibacterial efficacy of the prepared bioconjugates has been tested against *Salmonella enterica* serovar Typhimurium using the microtiter broth dilution method for determination of the minimum inhibitory concentration (MIC). The conjugates of silver nanoparticles and peptide TP373 exhibit antibacterial activity against *S. typhimurium*. Results presented provide insight on future strategies for the development and application of silver nanoparticle-based antibacterials.
Herpes simplex virus type 1 (HSV-1) virions contain a layer of proteins between the capsid and envelope called the tegument. The HSV-1 tegument is made of ~20 different proteins that are delivered to the host cell upon infection and play vital roles in virus replication. The VP22, VP16, and vhs tegument proteins form a complex via VP22-VP16 and vhs-VP16 interactions. Vhs is an RNase that serves to degrade host mRNAs immediately upon infection. VP16 works as a transcription factor at early times in infection, and at late times suppresses vhs’s RNase activity. VP22 promotes viral spread, viral protein synthesis late in infection, and is hypothesized to modulate vhs’s RNase activity. The roles of the various proteins were identified by studying individual deletion mutants. To determine if the VP22-VP16 interaction is necessary for activities previously attributed to the individual proteins, a recombinant virus was made in which this interaction was disrupted (VP22L251A/L252A). Disruption of the VP22-VP16 interaction resulted in decreased plaque size and a change in plaque morphology similar to that observed with the VP22-null virus, suggesting the VP22-VP16 interaction may be as important to viral spread as the VP22 protein itself. Using Scanning Electron Microscopy, we are examining plaque structure in cells infected with the WT, VP22-null, and L251A/L252A recombinant viruses. Confocal microscopy will be performed to examine the cytoskeletal arrangement in cells infected with these viruses. The ultimate objective is to determine the role of the VP22-VP16 interaction in plaque morphology and HSV-1 cell-cell spread.
PLGA Encapsulated Anti-Viral Drugs Used as Potential Inhibitors Against Respiratory Syncytial Virus

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RSV is the most common cause of bronchiolitis and pneumonia in infants in the U.S. and the cause of respiratory infections in elder adults. Currently, RSV has no reliable treatment; thus, patients suffering are unable to combat the virus with any drug. As general methods of treatment, infants can be given oxygen, have mucus suctioned from airways, or intubation with mechanical ventilation. An alternative method for treatment using nanotechnology will be essential for RSV treatment. Ribavirin has shown promise of inhibit influenza virus by acting as a guanine analog. Encapsulation of Ribavirin and other anti-viral drugs with PLGA nanoparticles will inhibit RSV infection. PLGA is both biodegradable and biocompatible, and since both monomers are natural substances it has minimal toxicity. Our results will be further supported by verification assays such as ZetaSizer, SEM, TEM, and MTT assay. Preliminary work shows that this new drug delivery system will change the course of treatment for RSV, by providing a new drug that will be able to be given to infants as well as adults.
Enhanced Optical Absorption by Localized and Non-Localized Plasmon Resonance Modes in Patterned Metal-Insulator-Metal Nanostructures

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We have simulated and fabricated the patterned metal-insulator-metal structure devices for enhancing optical absorption in metasurface in the visible and near-infrared wavelength range. The metal-insulator-metal structure consists of a gold nano-disk array on an aluminum nitride layer deposited on a thick gold film. The thick gold film was pre-deposited on a silicon wafer substrate. Here we find that both localized plasmon resonance and non-localized plasmon resonance can cause the strong light absorption in visible and near infra-red wavelength regime. Absorptions caused by both plasmon resonance modes strongly depend on the size and period of gold nano-disk array.
Characterization of a Suppressor Mutation of the *Listeria monocytogenes* Molecular Chaperone PrsA2

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*Listeria monocytogenes* is a Gram positive rod shaped bacterium that typically lives in nature but has the ability to infect humans. PrfA is a transcriptional activator in *Listeria* that is upregulated during infection. PrfA causes the upregulation of PrsA2, a molecular chaperone that regulates the activity of secreted proteins that contribute to bacterial virulence. As a result, we sought to characterize a PrsA2 suppressor mutant that can compensate for some but not all PrsA2-associated phenotypes when prsA2 is deleted. Complete genome sequencing of the suppressor mutant revealed an E81V mutation in lmo1507, the response regulator of a two component regulatory system for which lmo1508 is the predicted sensor kinase. The lmo1507 E81V/ΔprsA2 mutant was found to have swimming motility and red blood cell hemolysis activities that were equal to or better than those of the wildtype strain suggesting that lmo1507 E81V is a gain of function mutation. However, mouse models of infection comparing the organ load of the lmo1507/ΔprsA2 mutant strain to the wildtype showed decreased bacterial levels of the mutant strain. GUS reporter gene assays were used to determine binding sites within the prsA2 promoter for the response regulator Lmo1507 and PrfA, and we found that Lmo1507 site A as well as the PrfA binding site had a positive effect on transcription, while the Lmo1507 site B had a negative effect. However, when all three sites were mutated, transcription still occurred indicating that additional regulatory sites may exist and that prsA2 is regulated by multiple systems.
Controlled Growth of Silicon-Gold Nanoscale Heterostructures and Their Chemical Sensing Applications

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Silicon nanowire-gold nanoparticle heterostructures have been of recent interest for sensors. Here, we demonstrate the fabrication of such heterostructures in a facile and scalable approach. Fundamental understanding of growth of heterostructures were developed with a special emphasis on interface development. These nanowire heterostructures were characterized using high resolution electron microscopy, X-ray photoelectron spectroscopy, and Raman spectroscopy. Finally, plasmonic sensing using silicon nanowire-gold nanoparticle heterostructures with improved sensitivity and detection limits was demonstrated.
Highly Ordered Assembly of Graphene-Encapsulated Gold Nanoparticle for Surface-Enhanced Raman Scattering Sensor

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The graphene-molecule interactions are of great importance for applications in Raman-based chemical and biological sensing. Herein we demonstrate controlled fabrication of graphene-encapsulated gold nanoparticles (GNPs) for SERS applications. The Au nanoparticle size control in a wet-chemical process allowed for controlled growth of graphene shells around them. The influence of GNP size and density on the SERS sensitivity was demonstrated for model molecule detection. An electro-optical device was also realized using GNPs.
Oxidation of Graphene-Encapsulated Gold Nanoparticles and Their Further Bio-Functionalization

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The combination of graphene and gold nanoparticles is an exciting topic for bio-optical applications. Here, we utilized a novel CVD method to produce graphene shell supported on gold nanoparticles. Further plasma treatment was used for their surface oxidation and bio-functionalization. The oxidation process effectively removed amorphous carbon, created carboxyl groups, and optimized the graphene thickness. The optimized nano-hetero-structure presented unique bio-chemical properties and opportunities. The bio-chemical functionalization approaches used allowed for integrating plasmonic nanoparticles, DNA, and other nanostructures to the surface of graphene. Both double-strand λ-DNA and single-strand NH2-DNA were attached to the graphene shell and demonstrates the ability of such hybrid nano-architectures for bio-applications. This combination will be remarkably importance in the future DNA detection/recognition and bio-device applications.
Patterned Architectures of Graphene-Encapsulated Gold Nanoparticles Tagged With Carbon Nanotubes

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Integrating highly conductive noble metal nanoparticles and carbon nanostructures such as graphene, carbon nanotubes (CNTs) are of great interest for advanced bio-electronic systems. Here we report the fabrication of a single-walled CNTs based composite network filled with uniformly dispersed graphene encapsulated gold nanoparticles (GNPs). This involved the chemical vapor deposition method and functional biochemistry to achieve the hybrid architectures. Morphology and structure of the architecture was observed using high resolution microscopy and spectroscopy. The influence of GNP incorporation in the CNT network and the introduction of biotin-streptavidin was demonstrated in detail and the properties were validated using mathematical modeling methods. This study provides interesting view for understanding the fundamental biochemistry of the CNT-GNP combination.
Molecular Simulation of Bismuth Telluride Exfoliation in an Ionic Liquid Solvent

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Nanosheets of bismuth telluride (Bi\textsubscript{2}Te\textsubscript{3}) are of great research interest because of their potential applications in diverse material applications, such as thermoelectrics, heterogeneous catalysis, and superconductors. One proposed method of their fabrication is by ionic liquid (IL) assisted exfoliation. Ionic liquids display unique and tunable solvation properties, and they are considered to be green alternatives to conventional solvents. In this work, molecular simulations are used to probe the mechanism of exfoliation of nanosheets of Bi\textsubscript{2}Te\textsubscript{3} in the ionic liquid [BMIM]Cl. We study the thermodynamics, kinetics, and structure of the exfoliation process over a wide temperature range. We observe spontaneous exfoliation without artificial forces, allowing a kinetics-based estimate of the apparent activation energy of exfoliation. We also estimate the surface free energy of Bi\textsubscript{2}Te\textsubscript{3}, and the results are comparable to experiment. The structure of the IL solvation layers is found to be strongly ordered, with density oscillations near the interface alternating in charge. This is consistent with the observed stability of experimental dispersions of Bi\textsubscript{2}Te\textsubscript{3}, as well as previous simulation results. We find that surface free energy is independent of the size of the Bi\textsubscript{2}Te\textsubscript{3} model used, which implies that the size of the system studied is adequate to describe experimental scale systems and to predict effective exfoliation conditions.
Isothermal Release of Dibucaine from Polymer Micelles

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Our multidisciplinary team is building a targeted, thermally triggered drug delivery system for cancer chemotherapy. The delivery system consists of polymer micelles made from either poly(ethylene glycol-b-caprolactone) diblock polymers or poly(ethylene glycol-b-caprolactone-b-lactic acid) triblock polymers. The poly(ethylene glycol) block was hydrophilic and formed a corona around the core of the micelles. The polycaprolactone block or polycaprolactone-polylactic acid) blocks were hydrophobic and formed the core of the micelles. The polycaprolactone block was semi-crystalline with a melting endotherm in the range of 40 to 50 °C. Dibucaine, a local anesthetic, was used as an inexpensive surrogate for more expensive cancer drugs. Dibucaine was loaded into the core of the polymer micelles. The loaded micelles were soaked either at 27, 37, 57 or 67 °C and periodically sampled to determine the percent release. This gave curves of percent release as a function of time for each temperature. The curves were fitted to Crank's model from release of a small molecule from a sphere, giving values of D/r², where D was the diffusion coefficient and r was the radius of the micelle core. For each case D/r² increased when the temperature was above the melting point of the micelle core. The diffusion coefficient was higher when the core melted. The melting of the core was the trigger for thermal release of dibucaine.
Mammary epithelial cells within the body reside in a chemically and mechanically complex 3D environment known as the extracellular matrix (ECM). Though the ECM has been shown to play an important role in both the development and maintenance of breast architecture, the role of external forces that deform the matrix surrounding the epithelial cells is still unclear. In this study, we applied a compressive strain that generated a transient force to a 3D malignant breast epithelial culture and found that single malignant cells could be “phenotypically reverted” to develop into growth-arrested, polarized structures. To further characterize the inputs that lead to this type of mechanically induced phenotypic reversion, the effectiveness of mechanically induced phenotypic reversion, and the pathway through which mechanically induced phenotypic reversion occurs, we needed a high-throughput method capable of imaging multiple developing 3D cell cultures in real-time. To address this need, we developed an inexpensive, tablet-based, automated microscope to collect time-lapse images of the growth and behavior of 3D breast epithelial models.
Influence of Different Peroxide Initiators on the Cure Behavior of Bio-Based and Recycled Unsaturated Polyester Resins

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Effects of four different peroxide initiators on the cure behavior and thermal properties of unsaturated bio-based Envirez™ 70301 and recycled polyester resins Envirez™ 50380 provided by Ashland Incorporated were studied. Peroxide initiators used in the study were Methyl Ethyl Ketone Peroxide (MEKP), Tert-butylperoxy benzoate (TBPB), Luperox® CU80 and Luperox® IS-300 measured at one part per hundred for initiation of polymerization process during curing. Most reactions of polyester resins involving initiators may be uncontrollable, and lead to thermal runaway of the reactions; hence the objective of this study was to investigate initiator with most controllable reaction and their effects on cure behaviors and development of composite material properties. Differential scanning calorimetry (DSC) was utilized in dynamic and isothermal modes and results of the scans analyzed using Flynn-Wall-Ozawa, Kissinger and Kamal models of kinetic analysis. Kinetic parameters such as activation energy, pre-exponential factor, reaction rate constants and orders were determined and used in selecting the most suitable initiator for each resin with a controlled reaction. Activation energy determined from Flynn-Wall-Ozawa model for Envirez™ 70301 and Envirez™ 50380 were 84, 106, 81 and 97 kJ/mol; and 71, 102, 84, and 104 kJ/mol for MEKP, TBPB, Luperox® CU80, and Luperox® IS-300 respectively. The results also showed MEKP has a much broader and more relaxed exothermic peak, while TBPB showed the highest and narrow exothermic peak compared to the other initiators. These results indicate Luperox® CU80 as most viable initiator to achieve fast reaction rate constant for fast line speed used in pultrusion applications.
Poster # G-111

Moisture Absorption, Thermal and Mechanical Studies of Jute Fiber and Jute Fiber-Reinforced PHBV Bio Composites With/Without Chemical Treatments

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The main aim of this study is to understand the moisture absorption on the thermal and mechanical properties of jute fiber reinforced PHBV bio composites. Moisture absorption, mechanical and thermal properties of jute fiber-reinforced PHBV bio composites was investigated. Aging plays a crucial role in natural fibers when they are exposed to the environment. Natural fibers will degrade due to the absorption of water molecules. Chemical treatments on the fiber can be done in order to increase the fiber moisture resistance properties and also to improve the fiber matrix adhesion. Three types of chemical treatments were done. Jute fibers were treated with 1, 3, 5 and 7% solution of NaOH, another batch was treated with 2% in addition to the fibers previously treated with 5 % of NaOH. The third batch of fibers were treated with only Silane in 1, 2, and 3% solutions. Moisture absorption studies for a period of 3 months for chemical treated and untreated fibers were performed. Natural fiber reinforced bio composites were fabricated using chemically treated and untreated fibers and Poly (3-hydroxybutyrate-co-3-hydroxyvalerate) PHBV as the matrix. X-ray diffraction, thermo gravimetric and dynamic mechanical analysis were performed. Moisture absorption results showed that fibers treated with NaOH were more sensitive to moisture since alkaline treatment modify the fiber surface and may create voids where water can penetrate. XRD results showed that NaOH treatment changes the crystalline structure of the jute fiber, 1, 3 and 5% of NaOH showed an increment in crystallinity. However, 7% of NaOH showed a decrease. Thermo gravimetric analysis also revealed an increment in the decomposition temperature for 1, 3, and 5% of NaOH, and a decrease for 7% of NaOH.
One challenge associated with the development and optimization of lipid-based nanomedicines is the ability to extract them from biological milieu and distinguish them and their metabolites from endogenous phospholipids. We developed an acidified Bligh-Dyer (BD) extraction method in combination with LC-MS/MS and applied this approach to intracellular uptake of secretory phospholipase A2 (sPLA2) responsive liposomes (SPRL), into human prostate cancer cells (PC-3). Acidification of samples prior to and/or after BD extraction significantly improved the recovery of anionic lipids DSPA (79.4% to 94.0%), DSPS (78.6% to 89.5%) and DSPG (83.8% to 91.6%) without any negative impact on the extraction of zwitterionic lipids DPPC, DSPC and DSPE. Further, the acidified procedure allowed for accurate, simultaneous quantification of lipid components in a complex liposome formulation where the lipid concentrations differed by 10-fold. To quantify uptake and track degradation of formulations, deuterated lipid (d70-DSPC) was included in SPRL liposome preparations in different amounts (10%, 50% and 80% lipid mole %). Formulations, cell culture media and PC-3 cells were extracted and lipids and metabolites were quantified by LC-MS/MS. We demonstrated a correlation between the uptake of d70-DSPC and d35-steric acid in cells and the increased amount of d70-DSPC in SPRL formulations. These data suggest that d70-DSPC and d35-steric acid are good probes for quantifying the uptake of SPRL. This study suggests that pre- and post-acidification overcomes some drawbacks of conventional BD extraction for anionic phospholipids, and BD extraction combined with LC-MS/MS is a useful approach for tracking the disposition, uptake and degradation of lipid-based nanoparticles.
Poster # G-303

Surface Area and Toluene Adsorption Capacity for Fabricated Single-Walled Carbon Nanotube (SWNT) Buckypaper

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To use single-walled carbon nanotubes (SWNTs) in volatile organic compound (VOC) passive samplers, SWNT buckypaper were fabricated in three different ways and their adsorption efficiencies were examined. 200 mL of the SWNT solution (arc discharge SWNTs suspended in 1% sodium cholate and sodium dodecyl sulfate) was diluted in 400 mL of acetone, vacuum-filtered through a polytetrafluoroethylene membrane filter, and buckypaper was obtained by delaminating the layer of SWNTs from the filter (not cleaned). A cleaning process was added to the above fabrication process. After SWNT solution was vacuum-filtered, SWNTs on the filter were cleaned with 250 mL of deionized water and 50 mL of acetone (acetone-cleaned). As another cleaning process, methanol was used to dilute and clean SWNTs (methanol-cleaned). The fabricated buckypapers were investigated for surface area and toluene adsorption isotherm. As a result, the cleaning process increased BET surface area; 43, 217, and 348 m²/g Brunauer, Emmett and Teller (BET) surface area for not cleaned, acetone-, and methanol-cleaned buckypapers, respectively. The adsorption capacity increased with increasing surface area of buckypapers; 52, 58, and 69 mg (toluene)/g (buckypaper) for not cleaned, acetone-, and methanol-cleaned buckypapers, respectively. Methanol-cleaned buckypapers were the most adsorptive, hinting for further investigation in desorption efficiency for the application to VOC passive samplers.
Self-Assembly of Protein Cages with Polymer and Nanoparticles

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Protein cage based multicomponent, hierarchical nano-architectures hold enormous potential in the fields of energy, catalysis, and bio-applications owing to their tunable material properties. In particular, the bacteriophage P22 offers vast possibilities for bottom-up self-assembly because it is easily produced, can be genetically modified, and contains surface features or portal protein complex for potential interaction with other synthetic components. Additionally, the structure of P22 has been well-studied and is considered a hallmark example of viral self-assembly. Multiple ligands are compiled within a single P22 unit to provide versatile targeting capacity. Here, the self-assembly of P22 with inorganic nanoparticles and dendrimers is demonstrated for the first time. The assembly of P22 with other components in aqueous phase was systematically investigated using freshly-synthesized cationic inorganic nanoparticles (iron oxide and Au) and polyamidoamine dendrimers (PAMAM) as model systems. To build binary three-dimensional self-assembly structures, the negatively charged P22 surfaces were targeted with water-soluble cationic nanoparticles via controlled electrostatic attraction. The size and surface charge of the nanoparticles were found to play key roles in the self-assembly architectures. In addition, the PAMAM dendrimer facilitated ordered assembly of P22 procapsids, likely via interaction of terminal amine groups of the dendrimer with P22 surfaces. The mass ratio of dendrimer to P22 procapsids and the electrolyte concentration in the aqueous medium were found to affect the size of self-assembly structures. These bio-inspired, P22-based ordered nano-architectures will be particularly useful to develop novel and environment-friendly materials of tunable properties for different applications.
The Susceptibility of *Streptococcus pneumoniae* to Clindamycin Encapsulated PLGA Nanoparticles

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*Streptococcus pneumoniae* is a major respiratory pathogen which remains a major cause of morbidity and mortality worldwide in spite of available vaccines and antibiotics. The development of a novel antimicrobial drug is needed in order to conquer existing mutating *S. pneumoniae* isolates. Our goal was to investigate the usefulness of clindamycin loaded PLGA (poly lactic-co-glycolic acid) nanoparticles in inhibiting the growth of planktonic *S. pneumoniae*. PLGA nanoparticles were prepared by emulsification-diffusion method. The synthesized smooth and spherical PLGA and clindamycin encapsulated PLGA (PLGA-Clin) nanoparticles measured approximately 150-200nm in diameter. The inhibitory potential for PLGA and PLGA-Clin were examined in pneumococcal isolates with varying sensitivity to clindamycin. The encapsulate (PLGA-Clin) showed reduced viability when compared to PLGA in pneumococcal strains that are sensitive or resistant to clindamycin. Therefore, the novel encapsulate antibiotic shows promise in combating antibiotic resistant strains of *S. pneumoniae*.

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Development and Characterization of a Gold-Lipidic Nanocomposite Chemotherapeutic Delivery System

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Traditional chemotherapeutic drugs such as doxorubicin are cytotoxic agents that are effective at killing cancer cells but are toxic to non-target healthy cells. For many, their selectivity is based upon their ability to inhibit the growth of rapidly-dividing cells, leading to undesirable effects in naturally rapidly-dividing cells such as those found in the gastrointestinal tract or bone marrow. Liposomal drug carriers are an effective strategy for improving efficacy and reducing toxicity, but their clinical use has been limited due to non-optimal drug release, leading to poor exposure and ineffective treatment. We hypothesized that nanocomposite systems consisting of functionalized gold nanoparticles encapsulated within liposomes may be used to improve the efficacy of traditional chemotherapy and permit non-invasive imaging. Here we present the synthesis of 2 nm glutathione-capped gold clusters, which are stable in aqueous media, readily conjugated using simple chemical techniques, and retain characteristic fluorescence and absorbance properties of gold nanoparticles. We then demonstrate the formulation of the liposomal nanocomposites comprised of gold clusters encapsulated with a standard “stealth” liposome. These nanocomposites exhibit minimal cytotoxicity, are readily taken up by PC-3 human prostate cancer cells in vitro, and demonstrate tumor-imaging capabilities in vivo in a human xenograft mouse tumor model. These studies support our hypothesis that composite gold-lipidic nanoparticles can be prepared and used to improve cancer detection and treatment. On-going research with these nanocomposite systems includes determining the effect of the gold nanoparticles on doxorubicin loading and release and functionalization of the gold nanoparticles with paclitaxel for dual-drug delivery capabilities.
Current research objectives are to find optimal uses for natural fibers and to address known challenges, such as a high degree of moisture absorption and poor thermal stability. In this research study, chemical treatment were used on a commercially obtained woven flax fiber. Alkali chemical treatment was carried out at various times and concentrations. Thermogravimetric analysis (TGA) display samples treated for 1, 2 and 4 hours showed an increase of 20°C or 6% in the peak decomposition temperature compared to the neat. There was an 18.17% reduction in the amount of residue compared the neat samples at 18.17%. These results indicate that the treatment causes the amount of moisture to reduce and removal of the lignin from the fiber structure which leaves less char. Scanning Electron Microscope (SEM) was used to study specific treatment time and concentration where the fibers began to dissolve the outer surface of the cell walls. From the SEM results, each treatment increases the roughness of the fiber surface which will lead to better interfacial adhesion between the fiber and the matrix. Thermal properties showed a ~ 10°C improvement in the peak decomposition and at 50% weight loss. DMA displays a 27% and 38% increase in the storage modulus and loss modulus respectively. Flexure showed enhancement at the 4 hours treatment time. From this study, the most improvement in the properties, at a treatment time of 4 hours with KOH concentration of 3% is the best.
Selected Material Binding Peptides Displayed on Qβ Coliphage Surface

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It is known that nanoparticles are of great interest when it comes to biological applications, specifically as an aid in biodrug delivery. So the combination of nanoparticles and biodrugs come to mid; but there are a couple of problems that arise. First is with the nanoparticles themselves. Nanoparticles tend to aggregate in vivo, when this occurs the immune system will clear these aggregated particles. Second is with the biodrugs. Biodrugs are made from the same biomolecules that make up the body, as such; they are also subjected to the same enzymes that degrade biomolecules in the body. To compensate, a larger dose of the biodrugs are given which can lead to toxicity issues. Since it is known that certain peptides bind to nanoparticles, we hypothesize that displaying these nano-tags on the surface of our bacteriophage Qβ, and allowing them to bind to nanoparticles that will prevent aggregation. These nanoparticles can be coated with biodrugs. To achieve this, the genes of material binding peptides: Co (HSVRWLLPGAHP), Ag (AYSSGAPPMPPF), and Au (TGTSVLIATPYV) were inserted separately into the genome of Qβ at the end of the A1 gene. The resulting recombinant phages, pQβCo, pQβAg and pQβAu, were transformed with HB 101 E. coli. The plaque assay provided the titer and phage morphology, and RT-PCR confirmed the tag gene size for each construct. Confirmation and visualization of the phage-nanoparticle complex can be verified via Transmission Electron Microscopy (TEM). The next phase is to focus on coating the material binding nanoparticles with biodrugs.
Polymeric Thermo-Sensitive Systems for Cancer Hyperthermia Therapy

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To avoid patient discomfort and prevent serious side-effects associated with cancer therapy, nanoparticle-loaded temperature-sensitive polymeric gels and micelles were devised to deliver localized chemotherapy and hyperthermia in response to external stimuli. Polymeric systems were conceptualized to include hyperthermia therapy through the use of magnetic nanoparticles combined with localized chemotherapy triggered by magnetic heating. This system should efficiently generate heat inside human body, release the desired quantity of drug triggered by temperature rise, be completely non-toxic in vivo, and possess the ability to target cancer tumors. Here we investigate the design and performance of thermo-sensitive hydrogels and block copolymer micelles with iron oxide nanoparticles. We also experimentally evaluate the heating efficiency, effect of viscosity on temperature rise, drug release efficiency, and toxicity of these drug delivery systems.
Antibody Conjugated Iron Oxide Nanoparticles for Highly Efficient Neuroblastoma Targeting

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The potential for simultaneous imaging and drug therapy point to iron oxide nanoparticles as an extremely effective material for biological applications. In order to achieve the full potential of iron oxide nanoparticles, specific targeting is key. Here, highly efficient neuroblastoma cell targeting was achieved by modifying the nanoparticle surface with the anti-GD2 antibody. The nanoparticles were first functionalized with dopamine; the amine group attached to the nanoparticle surfaces and the quinone structure available for further surface modification. Activation of the surface through basic conditions allowed for conjugation of the antibody via catechol reactions. Fourier transform infrared spectroscopy (FTIR) and dynamic light scattering (DLS) were utilized to verify successful surface modification and stability of the nanoparticles. Targeting efficiency of the antibody-conjugated nanoparticles to GD2-positive neuroblastoma cells were verified through fluorescence microscopy, Prussian blue staining, and transmission electron microscopy. The conjugated nanoparticles quickly attached to the GD2-positive cells within 4 hours, but did not attach to cells without the antibody. These detailed studies implied the anti-GD2 antibody active surface retained functionality after conjugation and was solely responsible for cellular uptake. Perhaps, more importantly, this conjugation method may be used for a variety of targeting moieties and further surface modification can allow for successful drug delivery to a targeted area.

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Light and Temperature Responsive Hydrogels Embedded With Nanoscale Heterostructures

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Development of multifunctional hydrogels for controlled release is critical for designing programmable delivery devices. We report a surfactant-free approach to fabricate carbon nanotubes (CNTs) decorated with one or more kinds of noble metal nanoparticles. These heterostructures were embedded in a temperature-responsive poly N-isopropylacrylamide (NIPAAm) hydrogel. These nanocomposites hydrogels could swell and shrink under light illumination due to optical to thermal energy conversion and generating temperature gradients between ~3.2 \times 10^{-3} and 3.8 \times 10^{-3} °C/s. Controlled delivery of model molecules in optical cycles followed by a burst release under a temperature cycle was demonstrated. Such nanocomposite hydrogels represents a truly multifunctional controlled release system activated by multiple triggers and compatible with physiological conditions. The use of low-energy light illumination as a trigger mechanism makes this a safe delivery approach.
Biomechanics of Blood Flow Through Cerebral Artery Under Elevated Intracranial Pressure Due to Traumatic Brain Injury

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Elevated intracranial pressure (ICP) is a major contributor to morbidity and mortality especially in severe head injury or traumatic brain injuries. It has been found that significant intracranial damage occurs for elevated ICP > 20 mm Hg in almost 72% of the patients. To examine the effect of the intracranial pressure (ICP) waveforms on the wall shear stress distribution in cerebral artery, fully coupled fluid structural interaction (FSI) simulations are carried out. Three varying ICP waveforms and three constant ICP profiles are analyzed with the arterial wall considered as elastic material and with inlet velocity and outlet pressure conditions. The results of the analysis demonstrate that the arterial wall experiences significant deformation depending on the ICP waveforms, but no significant effect has been found for the arterial wall shear stress (WSS) except a small change at the peak systole with different ICP Profiles. In addition, since the blood pressure is peak at peak systole of the cardiac cycle, the results demonstrate that the strains on the cerebral arterial wall are also near maximum. Similarly, the strains are minimum at the low diastole. Results describing the importance of wall shear stress and intracranial pressure on blood flow through arteries will also be presented.
**The Role of Suppressor of Cytokine Signaling (SOCS) 1 Protein in *Chlamydia trachomatis*-Induced Inflammation in Mouse Macrophages**

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*Chlamydia trachomatis* (CT) is the most frequently reported bacterial sexually transmitted infection, inflicting asymptomatic genital tract infections which contribute to propagation between unaware sexual partners. It is also the leading cause of infectious blinding trachoma caused by chronic conjunctival inflammation. An obligate intracellular pathogen, CT has the properties of manipulating inflammatory immune responses by regulating the expression of various immunological molecules. Suppressor of cytokine signaling (SOCS) proteins are negative feedback inhibitors for cytokines where their inhibitory effects are derived from interaction between cytokine receptors and/or Janus kinases (JAKs), thereby prohibiting recruitment of signal transducers and activators of transcription (STATs) to the signaling complex. This study investigated the role that SOCS proteins may play in regulating inflammation as induced by CT in innate immune cells. Mouse J774 macrophages were stimulated with the recombinant major outer membrane protein (rMOMP) of CT. RNA was extracted at time points up to 90 minutes to quantify SOCS1 expression levels. TaqMan qRT-PCR was utilized to determine that macrophages incubated with MOMP augmented SOCS1 expression levels (by up to a 50-fold increase) in a kinetic fashion, suggesting that SOCS1 may potentially act as direct regulators of inflammatory cytokine signaling pathways. The primary objective of this study was to determine the mechanism(s) by which CT regulates cytokine signaling to avoid the innate immune response and the underlying pathways in which this method is accomplished.

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A Bio-Gel Enriched Fibro-Porous Small Diameter Vascular Nano-Scaffolds

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There is a huge demand for small-diameter vascular grafts, as the majority of vascular disease cases involve small-caliber blood vessels. Recently, electrospinning has gained attention as a valuable technique for the fabrication of scaffolds for blood vessel engineering, as electrospinning produces nanofibers that closely approximate the structure of native extracellular matrix (ECM). Electrospun scaffolds for tissue engineering applications must have the bioactivity necessary for cell adhesion, as well as high mechanical properties matching those of native blood vessels. Accordingly, electrospun scaffolds were fabricated in 3D tubular structure from a blend of the synthetic polymers, viscoelastic and durable polycaprolactone (PCL) and relatively fast degrading shape-memory poliglecaprone (PGC), and coated with a physiological biogel matrix, containing protein-cocktail of collagens, laminin, and proteoglycans. The biohybrid fibro-porous graft exhibited mechanical properties comparable to those of native blood vessels, and the HuBiogel™ coating imparts the necessary bioactivity for the growth of vascular cells. The scaffolds were crosslinked using two crosslinking agents, the traditional crosslinker EDC and the natural crosslinker genipin, to improve the stability of the coating in aqueous environments. The effect on mechanical, structural, and morphological properties was evaluated for application in vascular tissue engineering. Additionally, the effect of crosslinking on coating stability was investigated to assure the presence of protein matrix on scaffold for effective cell-matrix interactions.

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Surface Plasmon Resonance Spectrometer Biochemical Sensor With Patterned Gold Nanodisk Gratings

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We investigate and have demonstrated coherent surface plasmon resonance spectrometer biochemical sensor with an e-beam patterned gold nanodisk array grating. The patterned gold nanodisk array grating is a two dimensional gold nanodisk array with a small nanodisk array period and a large grating period. Due to the coherent surface plasma radiation from the patterned gold nanodisks, surface plasmon resonance spectrum can be measured in the first order diffraction with a CCD. Larger resonance shift was measured in first order diffraction than in zeroth order transmission after a layer of Bovine serum albumin (BSA) protein was applied. A new surface plasmon resonance spectrometer sensor with a patterned gold nanodisk grating has been demonstrated for bio-chemical sensor application.
In order to examine the effect of a bio sourced filler material on a high green content polymer formulation, eggshell nanopowder (ENPs) was prepared using mechanical attrition and ultrasound techniques. This was characterized with XRD and TEM. Bio based epoxy/ENPs composites were then fabricated and characterized using AFM, thermal, thermomechanical and mechanical testings equipment. The results showed significant improvements of 7-22 % in the storage moduli as well as 3-17 % reduction in coefficient of thermal expansion (CTE). Also, major delays in 5 % decomposition temperatures and increases in char yields were realized. The flexure strength, modulus and toughness significantly increased by 6-31 %, 11-37 % and 10-36 % respectively due to the addition of ENPs. Microstructure analysis of fractured surfaces showed deflected crack paths which contributed to improve the toughness.
Functionalized Gold Nanoparticles Inhibit Respiratory Syncytial Virus and Down Regulate RIG-1-Like Receptor Signaling Genes

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Gold nanoparticles (GNPs) have been effectively used for biomedical applications including antibacterial and antiviral therapy. We here show the applications of gold nanoparticles in the inhibition of respiratory syncytial virus (RSV). RSV is one of the most significant causes of infantile respiratory infections, yet there is no licensed vaccine. We used GNPs and anti-RSV F fusion inhibitor peptide(s) (RF-482 and RF-491) functionalized GNPs (fGNPs) against RSV. The GNPs and fGNPs did not bear any cytotoxic effects on HEp-2 cells. RSV inhibition was found to be 90% with GNPs, the 88% with peptide RF-482 and 89% with RF-482-GNP respectively. RF-491 did not inhibit RSV significantly; however, RF-491-gold nano-conjugate did inhibit RSV. These results were confirmed by qPCR and immunofluorescence and Western blotting. Immune response was studied in HEp-2 cells for MCP-1, IP-10, RANTES, IL-8 and IL-6. We also, performed antiviral immune response PCR array and found that RSV up regulates the RIG-1-like receptor signaling pathway. The genes ATG5, AZI2, CASP10, CASP8, CHUK, DDX3X, IKBKB, MAPK14, IL18 and FOS were up regulated by RSV; however, these genes were down regulated upon treatment with peptides, GNPs or fGNPs. Other pathways significantly altered include NOD-like receptor signaling and TLR receptor signaling. The study is currently underway to determine the further effects of these receptors and their consequences on the host cells.
The presented work focuses on the effects of fluid shear stress on circulating tumor cells (CTCs). CTCs are cells that enter blood circulation during the process of cancer metastasis. Detection of CTCs proves to be challenging due to the low number of CTCs in circulation. Lately, CTCs have been identified as either identical to or as a subset of cancer stem cells (CSCs). CSCs are a subpopulation of tumor cells that are self-renewing and have the ability to form new tumor cells. Due to these characteristics, CSCs are proposed to be the basis of relapse and metastasis in patients. Therefore, if CTCs are indeed specialized CSCs, there should be an overlap or co-expression of CTC- and CSC-markers. Recent studies exploring CTCs and CSC have not extensively studied in fluid shear stress environment which more properly addresses the role of CSC in metastasis. This work uses controlled microfluidic shear stress to determine whether CTCs share or co-express CSC markers. We hypothesize that the application of microfluidic shear stress can preferentially select and enrich CTCs/CSCs in-vitro. A programmable syringe pump attached to non-adherent polymeric tubing will be used in which CSC-enriched populations will be subject to precisely controlled fluid shear stress based on fundamental fluid dynamics principles. Physiological shear stresses, which arise from predominantly laminar flow with low Reynolds number, will be used. If our hypothesis is validated, there is potential to expand our detection strategies to include CSCs and thereby improve the detection of rare CTCs.
Theoretical Investigation and Mesoscopic Modelling of Thermal Conductivity of Carbon Nanotube Materials

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The effective thermal conductivity of materials composed of carbon nanotubes (CNTs) is investigated analytically and in mesoscopic simulations. The mesoscopic simulations of CNT materials are performed with a model that represents individual nanotubes as chains of stretchable cylindrical segments and describes van der Waals interaction between nanotubes by the mesoscopic tubular potentials. The model of the heat transfer accounts for the contact heat transfer between nanotubes, the finite thermal conductivity of individual CNTs, and the thermal resistance of bending buckling kinks. The mesoscopic model of heat transfer is parameterized based on results of atomistic simulations of heat transfer performed for several representative systems composed of (10,10) CNTs. The results of mesoscopic simulations reveal a strong effect of the finite thermal conductivity of individual nanotubes on the conductivity of the CNT materials. The physical origin of this effect is explained in a theoretical analysis of systems composed of straight randomly dispersed CNTs. An analytical equation for quantitative description of the effect of finite thermal conductivity of individual CNT on the effective conductivity of CNT materials is obtained. Contrary to the common assumption of the dominant effect of the contact conductance, the contribution of the finite conductivity of individual nanotubes is found to control the value of conductivity of CNT films and vertically aligned arrays at material densities and nanotube lengths typical of real CNT materials.
Resole phenol formaldehyde resins have been used in various applications due to their outstanding physical and chemical properties of flame retardancy, solvent resistance, and thermal stability. However, major disadvantages are associated with the synthesis of resole phenol formaldehyde resins. One disadvantage includes the toxic effects of the phenol and formaldehyde chemical precursors on the human body. Many studies are using renewable resources, lignin, as partial replacement with the phenolic synthesis starting precursors to produce less hazardous materials. Lignin is a three-dimensional, highly cross-linked macromolecule composed of three types of substituted phenols which include: coniferyl, sinapyl, and p-coumaryl alcohols by enzymatic polymerization yielding a vast number of functional groups and linkage. As a natural and renewable raw material, obtainable at an affordable cost, and great chemical and physical properties, lignin's substitution potential extends to any products currently sourced from petrochemical substances. In order to produce less hazardous materials, the goal of the current research is geared towards the synthesis of novel resole phenolic type systems based on the best thermally stable lignin extracted from different biomass resources. Hence, lignin was extracted from wheat straw, pine straw, alfalfa, and flax fiber by formic/acetic acid treatment followed by peroxyformic/acetic acid treatment. Resulting lignin samples were characterized by Fourier transform infrared spectroscopy (FTIR), Thermogravimetric analysis (TGA) and Differential scanning calorimetry (DSC) analyses to compare thermal properties and chemical composition. In addition, void-free, homogenous, solid novel resole phenolic type resin systems have been synthesized using various ratios of the extracted lignin for the phenol precursor.
Development of a Molecularly Imprinted Polyacrylamide Polymer for Applications in Biosensing

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Molecular imprinting of polymers is a maturing technology which has been shown to be an effective approach which synthetically replicates natural biological recognition processes. Molecularly imprinted polymers (MIPs) are essentially synthetic receptors, capable of binding target molecules with high specificity. Typical recognition systems for proteins or biomarkers rely upon highly specific immunohistochemistry techniques. However, these antibody based assays have problems with stability and standardization, and might not be available for a particular protein or biomarker of interest. In addition, the most frequently used methods of MIP synthesis are not suitable for biosensing applications involving proteins, because they use solvents, such as dimethylsulfoxide, chloroform or tetrohydrofuran, which disrupt the three dimensional structures of naturally aqueous proteins. We propose that patterning arrays of pico-liter MIP sensing elements, followed by in situ polymerization, would be desirable over bulk polymerization by offering a higher surface area to volume ratio of the MIP, thereby increasing the number of available binding sites, potentially leading to the development of an MIP based, “lab-on-a-chip” biosensing tool. We investigated parameters influential in the generation of arrays of highly ordered, aqueous, Polyacrylamide P(Aam) MIPs synthesized via scanning probe ‘dip-pen’ nanolithography (DPN) techniques. We investigated the incorporation of polyethylene glycol and polvinylalcohol linear polymers into the crosslinked P(Aam) MIP, the resultant effects on surface wetting properties, and mechanical stability of the polymer. Using a fluorescent model template, we demonstrate proof-of-concept imprinting of the polymer dots, illustrating the potential of a P(Aam)/polymer blend MIP biosensing array.
Synthesis of Molecular Electronic Components for Self-Assembly Onto Metal Electrodes

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Molecular electronics is the synthesis and study of single-molecule electronic devices. Such devices have the potential to be smaller and more efficient than their silicon-based analogs. Our present goal is to design and synthesize a carbon-based molecular diode. Current work is centered on molecules bearing an electron-rich dimethoxybenzene donor ring and an electron-poor quinone acceptor ring separated by a single bond. We have successfully synthesized a template molecule, dibromohemibiquinone – which can then be converted to aminohemibiquinone – that will allow for the substitution of functional groups at its attachment sites. One purpose of such groups is bonding to metal electrode surfaces. Through deprotonation and acylation at the amino site of aminohemibiquinone, it may be possible for attachment groups to be added to the hemibiquinone framework. Some particularly useful groups for bonding to metal surfaces are nitriles and thiols. A nitrile moiety has been incorporated via cyanobenzoyl chloride. In order to append a thiol group, we have prepared 4,4’-dithiobenzoic acid. Activation of the acid group then allows for acylation of the aminohemibiquinone molecule. Once these substitutions are completed, surface studies will be conducted in order to determine the geometry of a monolayer of self-assembled molecules on a gold surface. Ideal surface geometry would be near perpendicular, as the purpose of the diode is to allow unidirectional electron flow between two surfaces via attachment to each. In addition, molecules similar to the hemibiquinones have been synthesized for electrochemical and spectral comparison.
Using LIBS for Nanomaterials Analyzation and Quantification

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Laser induced breakdown spectroscopy (LIBS) has been used since the late 1980s as an analytical breakdown technique. LIBS evaluates the relative abundance of each constituent element, or to monitor the presence of impurities. LIBS may be used to detect the major and minor elements of a particular material. The technique can be used to analyze solids, liquids, aerosols, and other materials. In the present study, LIBS was used to detect, analyze, and quantify silver nanoparticles. A pulsed Neodymium Yttrium Aluminum Garnet (Nd:YAG) laser operating at 532 nm was used to perform the experiments. The laser has a pulse length of approximately 8 ns. The silver nanoparticles were prepared and deposited onto pure silicon and aluminum substrates. In this experiment we used five different concentrations of Ag nanoparticles which included 1.0, 0.50, 0.25, 0.10, and 0.050 µg/mL. The wavelengths 328.07 nm, 338.29 nm, 520.91 nm were used for the analysis of the Ag nanoparticles. The typical precisions using Andor Shamrock 303i ranged from 5% to as high as 39% Relative Standard Deviation (RSD). The precision using a non-intensified CCD Avantes Spectrometer was within the same range using silicon as a substrate. The precision ranged from 19% to as high as 55% RSD using pure aluminum as the substrate. The calibration curves for Ag nanoparticles gave linear results with $r$-squared values ranging from 0.91 to 0.99 from both spectrometers. An ongoing study is also in preparation to determine if LIBS could be used for the analysis of nanoparticles inside of human cells.

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Highly Stratified Stimuli-Responsive Multilayer Hydrogels for Sensing

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Polymer coatings with stimuli-triggered significant thickness change are of considerable interest for development of chemical and biological sensors. We report on (poly-N-vinylcaprolactam) (PVCL)-containing nanothin multilayer hydrogels with highly reversible volume transitions in response to temperature variations. The hydrogels were produced by glutaraldehyde-assisted cross-linking of hydrogen-bonded multilayers of PVCL-co-NH2 and poly(methacrylic acid). A layer of glutathione–stabilized gold nanoparticles was introduced within the PVCL hydrogel to initiate an optical response in the presence of anions. We found the signal intensity of (PVCL)81-Au hydrogels and the plasmon band position to be largely controlled by ion type and concentration when the temperature reversibly changed from 20° to 50°C. The band consistently shifted to lower wavelengths with an increase in chloride concentration. In contrast, a red shift was observed with increasing iodide concentration. The (PVCL)81-Au hybrid hydrogels afforded a clear and fast optical monitoring of hydrogel temperature-triggered response at varied ion concentrations. We also found that the pH-triggered swelling of ultrathin poly(methacrylic acid) multilayer hydrogels can be controlled by controlling their internal structure. The architecture of poly(methacrylic acid) hydrogels was tailored from well-stratified to highly intermixed by regulating deposition conditions for layer-by-layer templates used in the hydrogel fabrication. PMAA multilayer hydrogels capable of swelling up to 18 times the original dry thickness at pH=7.5 were obtained from well-stratified 'spin-assisted' templates; while hydrogels swelling only one third of this were formed from highly intermixed “dipped” templates. We believe that regulating architecture at the nanoscale is crucial for developing hydrogel-based materials for sensing.
Bacteriophages have emerged as useful biotemplates for material synthesis due to their unique recognition ability for inorganic components. Bacteriophages, which are assembled from protein subunits into precise 3D nanoscale structures and amenable to express foreign protein insets through genetic engineering, can be employed for the controlled growth of desired inorganic nanostructures. We report the use of the bacteriophage P22 virus-like particles (VLP) as a platform for the biotemplated synthesis of photocatalytic CdS constrained inside VLP, along with selective growth of plasmonic gold nanoparticles on the shell of VLP. The confined synthesis of CdS inside VLP is realized by fusing CdS specific binding peptides into the scaffolding proteins of P22, which are positioned in the inner cavity of P22. Gold nanoparticles are then selectively synthesized on the shell of VLP. As compared to CdS inside P22 alone, the VLP constructed Au/CdS plasmonic photocatalytic nanostructures exhibit greatly enhanced photoactivity for the photodegradation of methylene blue using solar simulated radiation.
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