Chemical Engineering
Spring, Summer and Fall 2019
Undergraduate Research Project Descriptions

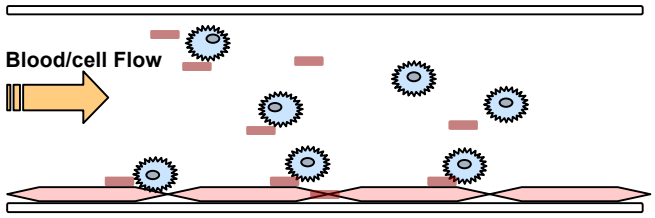
The following pages describe undergraduate research projects available in the chemical engineering department for the Spring, Summer and Fall 2019 terms.
See https://che.engin.umich.edu/research/ for more information on obtaining research positions.

Professor Eniola Adefeso

Our overall research interest is in understanding dynamics of blood flow adhesion. Characterization of blood flow dynamics can help increase understanding of important biological processes like the cellular immune and inflammatory responses, and lead to the development of technologies such as cell separation and targeted drug delivery.

Leukocyte Adhesion Studies in Parallel Plate Flow Chambers – Evaluation of Platelet-Enhanced Neutrophil Adhesion

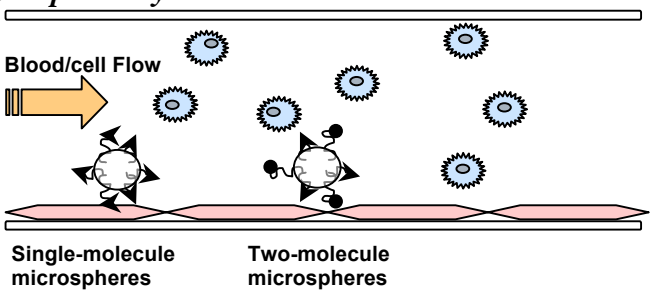
Dynamic interactions between leukocytes in the blood stream and the endothelial cells lining the blood vessels in response to inflammation are a hallmark of immune physiology. These interactions are mediated by cell adhesion molecules expressed on leukocyte and endothelial cell surfaces and are governed by blood flow dynamics and tissue-produced chemical stimuli. A recently published work suggests a role for platelets in leukocyte adhesion from flow and migration into tissues. We seek to elucidate the mechanism by which blood platelets enhance leukocyte (neutrophils) adhesion to the endothelium. This project will involve *in vitro* flow adhesion assays with human platelets, neutrophils and endothelial cells. Student(s) will also learn cell culture and fluorescence imaging techniques.



Schematic of leukocyte – endothelium interaction in a parallel-plate flow chamber

Characterization of the Flow Adhesion Dynamics of Vascular Targeted Drug Carriers Evaluation of Drug Carrier Blood Compatibility

Vascular-targeted drug carriers are often designed to locally deliver therapeutics that can eliminate (or control) disease phenotype in targeted tissue. For this reason, it becomes important that these carriers themselves do not elicit immune responses that can exacerbate the status quo. While blood concentration of targeted particles is not likely to elicit leukocyte reaction, a significant concentration bound to the endothelium at the target site could potentially affect local leukocyte-EC interaction by physical contact or molecular interaction. Student will use *in vitro* flow adhesion assays to evaluate increased leukocyte-endothelium interaction that is due to the presence of targeted drug carriers. Particularly, human leukocytes (neutrophils and monocytes) in whole blood (obtained by venipuncture from healthy donors) or isolated will be perfused in a flow chamber over activated endothelial monolayers with endothelium-targeted drug carriers already bound to their surface.



Schematic of flow chamber leukocyte mimetic-blood compatibility experiments

Professor H. Scott Fogler

Research of my group can be seen at
http://cheresearch.engin.umich.edu/fogler/

Safety Module Development. We are now in the process of developing initiative to have a safety module for every core chemical engineering lecture course. The modules will consist of (1) viewing a Chemical Safety Board (CSB) video related to the course, (2) filling out a safety algorithm on the video and (3) making a calculation related to the video and the course. This project will not only satisfy our ABET safety requirement, but more importantly it will expose all our undergraduates to the importance of safety across the curriculum. A Web site is currently being developed (*http://umich.edu/~safeche/*) for posting the materials as they are being developed. I am looking for students interested in developing materials for this initiative.

Professor Erdogan Gulari

Improving the Industrial Capabilities of Hydrogen-oxidizing Bacteria
Hydrogen-oxidizing bacteria have the ability to convert gaseous substrate in the form of hydrogen, oxygen, and carbon dioxide into desirable products such as fuels, polymers, and biomass. To date, yields from these bacteria have been too low for any process utilizing them to be economically viable. This work seeks to improve the industrial capabilities and relevance of hydrogen-oxidizing bacteria through the application of pressurized environments and cellular engineering. The specific investigations that will be conducted are: to examine the effects of varying pressure and gas composition on growth characteristics such as rate, density, and yield; utilize directed evolution and genome shuffling to create strains with desirable phenotypes; correlate phenotype to genotype; and determine the composition of the bacterial biomass. The interested student will have the opportunity to learn skills relevant to the fields of biotechnology and genomics.

Professor Jinsang Kim

Purely organic phosphors for display and sensors
Phosphorescent materials are enhancing and broadening the usefulness of organic compounds in a wide variety of applications including OLED, photovoltaics, and sensors. OLEDs and solid-state lighting (SSL) research in both academic and commercial settings are driven by the promise of highly efficient devices manufactured via economic and versatile processes. Of the emissive materials employed in OLEDs and SSL, phosphorescent compounds produce much higher efficiency devices than those based on fluorescent emitters by utilizing spin-parallel electrons and emitting photons from the decay of triplets. Organo-metallic compounds are thus often doped into organic hosts to impart a phosphorescent pathway into otherwise triplet-forbidding carbon-based materials. However, phosphorescence from metal free, purely organic, compounds is almost always either strictly forbidden or only extremely weakly allowed, leaving pure organics undesirable for useful applications. We developed a novel material system, metal-free purely organic phosphors recently and demonstrated. Directed intermolecular heavy atom effects are uniquely implemented in aromatic carbonyl molecules to promote spin-orbit coupling and suppress vibrational dissipation. Color tuning by rational molecular design, highly sensitive optical sensors, and PhOLED are the research topics for development.

Self-signal Amplifying Molecular Biosensors
We have been devising molecular sensors having a dual-signaling capability: visible color change and fluorescence emission. The capability to generate a visible color change upon recognition of a target analytes will allow equipment-free detection. Fluorescence emission signaling upon detection is designed to provide a high sensitivity by means of signal amplification via the fluorescence resonance energy transfer (FRET). The sensory molecules are composed of a receptor, a diacetylene moiety, and a fluorophore. The molecules are devised to self-assembled to form a liposome followed by topochemical polymerization of the diacetylene moiety. The receptor will undergo a shape change upon recognition of a target analyte. This shape change will turn on the mechanochroism of the polydiacetylene unit of the liposome and produce a color change and develop fluorescence emission. Once the fluorescence emission is turned on the fluorescence energy of the fluorophore will amplify the turned-on signal through FRET. This research project has various interesting aspects: molecular design, self-assembly, sensor physics, and device fabrication.

Professor Nicholas Kotov

Nanomaterials for Energy Applications (Batteries from aramid nanofibers, Semiconductor nanoparticle assemblies for cathodes/anodes;

Chiral Nanomaterials (Chiral catalysis, origin of homochirality on Earth)

Hedgehog Particles

Please see details at www.umkotov.org

Professor Mark J. Kushner

http://uigelz.eecs.umich.edu
Our research group computationally investigates how plasmas (partially ionized gases) activate chemistry for materials processing, energy and healthcare applications. A typical undergraduate research project might include, for example, aiding in the development and use of computer models to investigate how plasma activated liquids beneficially interact with tissue, or how reactive fluxes to surfaces can uniquely craft nano-scale electronics.

Atmospheric Pressure Plasmas for Catalysis
Atmospheric pressure plasmas are able to activate gases by creating radicals and ions at low gas and materials temperatures. An active area of research is plasma-catalysis, using this ability to efficiently produce radicals to speed the rate of processing of catalysts and improve their selectivity. These processes are being investigated to produce "solar fuels" – using solar generated electricity to produce plasmas, which convert CO_2 into high value fuels and hydrocarbon feedstocks. The research project will involve a computational investigation of reactor configurations and strategies to address chemical conversion in plasma catalysis.

Professor Joerg Lahann

Biomedical Coating Project
The main objective of this project is to synthesize UV-induced surface-grafted polymer layers using CVD polymer film as the initial anchoring film, creating copper chelating surfaces, which could generate NO. The long-term goal of this project would be to fabricate biomaterials that would be used as ***cardiovascular stent coatings***. The surface-grafted layers will be characterized using different surface characterization techniques such as infrared spectroscopy (FTIR), contact angle measurements. The student will be working closely with graduate students in the lab. This will enable the student to gain valuable insight and experience in chemical synthesis as well as a variety of surface characterization techniques. The candidate should have an interest in surface science and biomaterials, be highly motivated, and enjoy both independent and collaborative research.

Nanoparticles for Drug Delivery
This interdisciplinary research project consists of two main parts: 1) production of biphasic nanoparticles by electrified jetting and their characterizations, and 2) investigation on interactions between the biphasic nanoparticles and cells.
We will utilize electrified jetting process to produce organic or inorganic biphasic nanoparticles. In this process, we apply high electrical potential on a jetting liquid to generate a cone and jet. At certain experimental conditions, this liquid jet is accelerated and eventually breaks down to form solid particles with diameter in nanometer scale. Using a special setup, we will produce biphasic nanoparticles, which have two different characteristics inside of one particle in dipolar fashion. We will utilize several materials for this process and characterize the resulting nanoparticles with electron microscopes (SEM and TEM) and confocal microscope. The produced nanoparticles will be used for the study on the interactions between the biphasic nanoparticles and several different cells. The possible applications of this study are targeted drug delivery, cell imaging, and the development of biosensors. The project will provide insights in advanced polymer technology, biomedical research, and possibly cellular biology.

Smart Surfaces Project
An undergraduate research position is open in the Lahann Lab to support studies in the area of biomaterials surface science, specifically the design and development of engineered "smart" surfaces with dynamically switchable properties for biosensor and tissue engineering applications. Switchable surfaces with the capacity for controlled and reversible transitions between states such as hydrophobic/hydrophilic or bio-active/bio-inactive have the potential to revolutionize surface science and its related technologies, such as coatings or biomedical implants and biological diagnostics and research tools. The position will involve computer simulation of "smart" surfaces, as well as the preparation of ultra-thin monolayer films on solid supports, characterization of the resulting surfaces, and assessment of surface-environment interfacial interactions. Strong analytical and writing skills are required. Experience with running controlled experiments and familiarity with molecular simulation software and spectroscopic analytical techniques is preferred. The candidate should have an interest in surface science and biomaterials, be highly motivated, and enjoy both independent and collaborative research.

Bioswitchable Surfaces and their Applications in Tissue Engineering
The purpose of this project is to develop advanced biomaterials with surfaces that allow for reversible switching between physiologically active and non-active states. We have demonstrated in preliminary studies the design of "smart surfaces" that can dynamically adapt their properties in response to stimuli without altering their chemical identity. We believe these surfaces offer a fundamentally new paradigm for engineering of interfacial properties as they undergo reversible conformational transitions at a molecular level. We

further reported studies to establish their feasibility for switching between a hydrophilic and a hydrophobic state in response to an electrical potential. In this design, the hydrophobic state defines a physiologically active state the supports protein adsorption and cell adhesion and the hydrophilic state establishes a physiologically passive state. We intend to evaluate these switchable surfaces as model systems for dynamically altering surfaces and to evaluate their applicability to tissue engineering. In addition, the analogue design of a surface that allows switching between a molecular state that exhibits cell receptor binding and a state that does not support binding will be pursued. The fact that controlled conformational reorientations of single-layered molecules induced observable changes in wettability raises hope that these findings may, with further study, have implications in dynamic regulation of macroscopic properties, such as wettability, adhesion, friction, or biocompatibility. The specific goal of this proposal is to evaluate molecular designs for potential switch candidates using molecular modeling to identify suitable candidate molecules. The molecular switches will respond to an external stimuli, such as an electrical potential, by transforming from a physiologically active to a non-active state.

Bioinert Polymer Coatings

The purpose of this project is to develop a generically applicable technique that allows creating protein-resistant polymers surface on virtually any solid substrate. Although the broad implications of protein-resistant surfaces to bio- and nano-technology has fueled intensive research in this field, this approach towards protein-resistant surfaces is unique in that it takes advantage of a novel polymer technology based on CVD polymerization. The CVD technology comprises deposition of nanometer thin functionalized poly-*p*-xylylenes films from substituted precursors. The functionalized polymer films can be deposited as convergent films and provide a flexible solution to surface engineering challenges as they decouple surface design from bulk properties. The high chemical reactivity of their functional groups supported rapid conversion with binding partners, even without further chemical activation. So-called *reactive coatings* were used for surface patterning via microcontact printing. In principle, these polymers seem to be well suited as platform for stable confinement of non-fouling molecules. An approach based on CVD technology will be pursued to prepare protein-resistant surface coatings.

The working hypothesis is that by preparing thin polymer interfaces and using the functional groups to bind non-fouling molecules, we will be able to develop stable non-fouling surface modifications and will render materials protein-resistant.
A great emphasis will lay on quantitative analysis of surface reactions using a combination of (1) X-ray photoelectron spectroscopy, (2) surface titration after binding of reporter groups, and (3) imaging ellipsometry.

Nanoparticles Made by Electrified Jetting

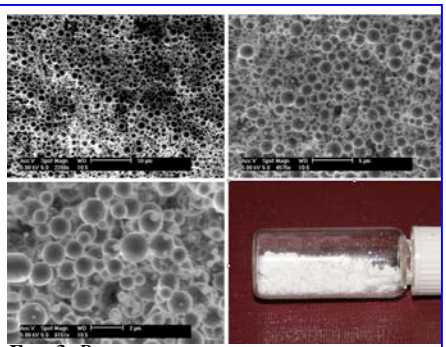


FIG. 3. PIGMENTS COLLECTED IN A VIAL AND MAGNIFIED VIEWS ON THE NANOPARTICLES.

Nanoparticles have recently attracted intense attention due to unique properties that make them distinctly different from bulk solid-state materials. For instance, nanoparticles were found to have unique magnetic, electronic, optical, chemical, and even biological characteristics. Our approach differs fundamentally from the currently employed methods in that it takes advantage of electrified polymer jets to create an anisotropic materials distribution in nano-objects. Electrified jetting is a process to generate liquid jets by use of electrostatic forces. It is well known that high electrical potentials (typically several thousand volts) applied between the jetting liquids that are fed through a capillary and a collecting substrate will induce jetting of a charged liquid. Building on the existing bulk of knowledge with respect to electrified jetting, we developed an approach towards biphasic nano-objects that was named

"electrified co-jetting" (Roh, Martin, Lahann, *Nature Materials* ***2005***). The goal of this project is to evaluate concepts for scale up in order to fabricate nanoparticles in the gram range.

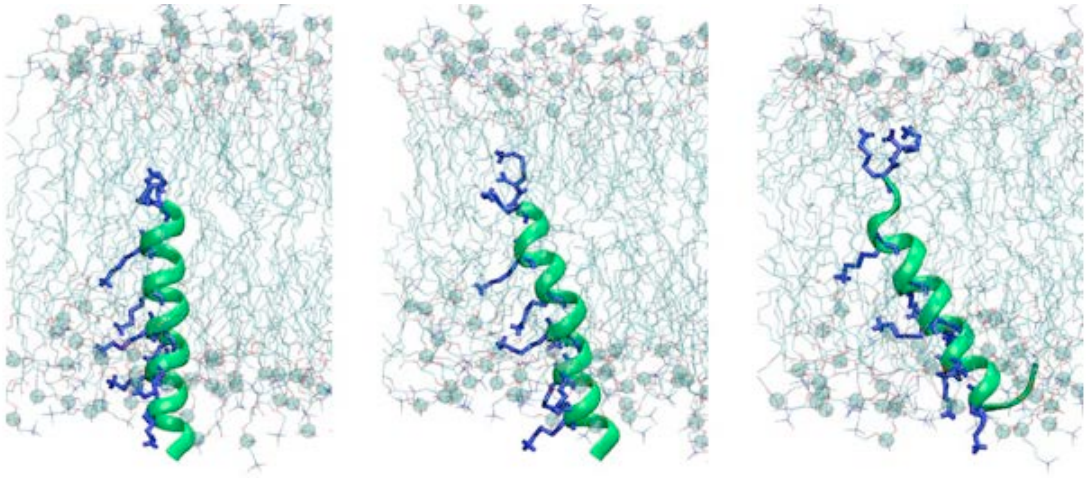
Professor Ronald Larson

Polymer Fluid Mechanics

Polymers are shaped into final products through fluid flow. The aim of this project is to develop practical models of a polymer chain that can be used in fluid flow predictions. The project involves computer predictions of polymer chain deformations in flows and how this affects fluid flow properties. Previous undergraduate students on this project have been co-authors of a paper published in the scientific literature. No prior programming experience is required but familiarity with any programming language would be very useful. The student would have an opportunity to learn about computer simulations and data analysis and would learn how polymer molecules in flow can be modeled.

Molecular Dynamics Simulations

Using molecular dynamics simulations, we seek to understand how molecules interact and determine function in both biological systems, such as cell membranes, and in commercial products, such as shampoos and drug formulations. In this project, the student will be trained to carry out molecular dynamics simulations of either a lipid membrane, or a chemical formulation, and discover how these molecules determine important behavior. In the figure below, an antimicrobial peptide penetrates a cell membrane, eventually killing the cell. Such peptides are used to fight bacterial infections



(a) Start (b) After 1 ns (c) After 20ns

in the human body. Other examples of simulations in our group include determining how lung surfactants enable breathing, how shampoos can be better formulated to obtain customer satisfaction, and how polymers can be used in drug capsules to deliver the drugs to the bloodstream.

Professor Xiaoxia (Nina) Lin

Elucidating Bacterial Interactions in the Vaginal Microbiome Using Microfluidic Droplet Co-cultivation Technology

There is increasing evidence which suggests the bacteria in the human vagina, referred to collectively as the vaginal microbiome (VMB), plays fundamental roles in women's health and susceptibility to diseases. For instance, bacterial vaginosis (BV), the most common vaginal infection in women of reproductive age in the United States, is characterized by disturbances in the VMB and can cause an increased susceptibility for contracting sexually transmitted infections, such as HIV. However, the question of how these diverse microorganisms interact with one another and with their host remains largely unanswered. To characterize interactions between bacterial species in the VMB, we use microfluidic droplet co-cultivation technology to grow bacteria and fluorescence in situ hybridization (FISH) to analyze interactions. Inhibited growth in co-culture and increased growth in mono-culture indicate a negative interaction. Investigating microbial interactions in the VMB will have important implications for diagnosing, treating and improving women's health worldwide. In this study, students will use microfluidic technology and an rRNA based fluorescent-staining technique (FISH) for microbiological analysis.

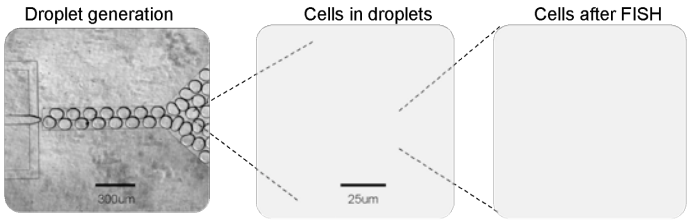
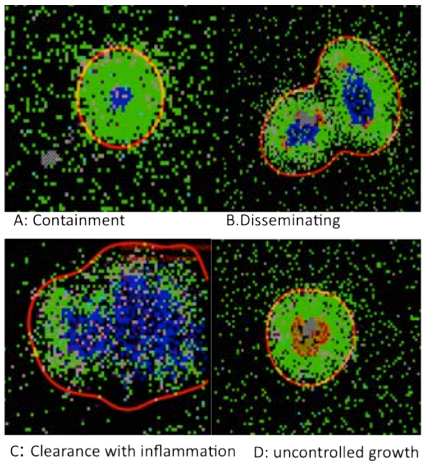


Figure 1: Fluorescence in situ hybridization (FISH) on cells from micro-droplets

System-Level Modeling and Engineering of Microorganisms for Bio-Fuel Production

Bio-fuels, derived from renewable biomass, offers a promising alternative to conventional fossil fuels which will potentially benefit US significantly by promoting agricultural growth, energy security and environmental sustainability. To achieve cost-effective large-scale production of bio-fuels such as ethanol derived from plant cell walls, it requires multidisciplinary research efforts to overcome many biological, technological and economical challenges. Our lab is interested in developing computational and experimental approaches for better understanding and engineering of micro-organisms that play important roles in bio-fuel production, for example, in the fermentation of cellulosic sugars into ethanol. More specifically, one new strategy we are exploring is to utilize microbial communities for accomplishing complex bioconversion processes. Interested undergraduate students are encouraged to participate actively in our research and will learn experimental techniques in applied microbiology and/or computational methods such as metabolic network modeling.

Professor Jennifer Linderman (Spring/Summer only)



Systems Biology of Tuberculosis

An estimated one-third of the human population is infected with the bacteria *Mycobacterium tuberculosis* (Mtb). Granulomas are self-organizing collections of immune cells that form in the lungs after inhalation of Mtb. They both contain the infection and provide a niche for bacterial survival. Persons with latent tuberculosis can survive for decades with granulomas (and thus the bacteria) in their lungs. Understanding granuloma formation and maintenance thus provides a key to identifying as

well as manipulating factors that lead to different outcomes following infection. We are developing computational models to understand the factors that influence granuloma formation. Students will study current tuberculosis treatments (antibiotics) and possible new strategies for treatment using simulations.

Professor Sunitha Nagrath

Microfluidic Systems for Cancer Cell Trafficking - Motility, Migration, Microenvironment and Metastasis

Until recently most studies of metastasis only measured the end point of the process — macroscopic metastases. Although these studies have provided much useful information, the details of the metastatic process remain somewhat mysterious owing to difficulties in studying cell behavior in the intermediate stages. Metastasis is a multi-stage process involving cancer cell motility, intravasation, transit in the blood or lymph, extravasation and growth at a new site. Additionally, only a subset of tumor cells can overcome these diverse challenges, and therefore metastasis is generally an inefficient process. The small number of cells involved at various stages of the process combined with the inaccessibility of the relevant anatomical sites has hindered our ability to study metastasis. The research project is to develop microfluidic model systems for the study of cancer cells spreading from their site of origin and arriving at secondary sites including, cell trafficking, migration of cells, and micro environment that lead to metastasis. Also, the rare cell subtypes that are the seeds for metastasis will be identified. This requires a detailed analysis of CTC subtypes, with the eventual goal of isolating metastatic precursors, whose full characterization may yield profound insight into the process of blood-borne metastasis.

Investigation of Circulating Cells in Peripheral Blood of Cancer Patients

Metastasis is a complex, multi-step process by which primary tumor cells invade adjacent tissue, enter the systemic circulation (intravasate), translocate through the vasculature, arrest in distant capillaries, extravasate into the surrounding tissue parenchyma, and finally proliferate from microscopic growths (micrometastases) into macroscopic secondary tumors. To develop a deeper understanding and a framework for metastasis, it is essential to do an in depth investigation of CTCs from cancer patients, and identify the subpopulations and their correlation with clinical parameters. Isolation and characterization of various circulating non-hematopoietic cells in blood will provide detailed information regarding various metastasizing cells, their characteristics and the interplay between different cell types as tumor cells leave the primary tumor and arrive at secondary sites. This project involves the identification of molecular pathways that contribute to tumor cell motility and invasion is essential for understanding how motility is initiated in tumor cells and how the tumor microenvironment contributes to cell migration. In this research we will study the circulating tumor cells for cell motility. We plan to obtain the range of level of expression of cofilin in circulating cells. We also would like to define the level of aneuploidy in individual cells. These analyses will provide important insight into the heterogeneity of CTC populations, and the degree to which this heterogeneity represents the metastasis potential of these cells.

Spatiotemporal Modeling of Cancer Systems

The specificity of cellular responses to receptor stimulation is encoded by the spatial and temporal dynamics of downstream signaling networks. Temporal dynamics are coupled to spatial gradients of signaling activities, which guide pivotal intracellular processes and tightly regulate signal propagation across a cell. Computational models can provide insights into the complex relationships between the stimuli and the cellular responses, and reveal the mechanisms that are responsible for signal amplification, noise reduction and generation of discontinuous bistable dynamics or oscillations. Activation of cell-surface receptors and their downstream targets leads to the spatial relocation of multiple proteins within the cell. During evolution, cells have developed not only means to control

the temporal dynamics of signaling networks, but also mechanisms for precise spatial sensing of the relative localization of signaling proteins. The regulation of signaling within the cellular space is pivotal for several physiological processes, such as cell division, motility and migration. This project's aim is to develop quantitative models for several RTK pathways including EGFR and ErbB, which generate novel, experimentally testable hypotheses, and will have an increasingly important role in post-genomic cancer biology. The developed modeling framework will integrate data on the distinct spatio-temporal dynamics of signaling from different cellular compartments and provide insights into the connection between external stimuli and the signaling outcome in terms of gene-expression responses. Challenges of the combinatorial complexity of signaling networks and experimental uncertainty in parameter values will be addressed by modular approaches Understanding the mechanisms that underlie the functions of signaling networks in metastasis may lead to breakthrough in the identification of the critical controlling factors which will be targets for pharmacological interventions in the treatment of cancer.

Professor Johannes Schwank

Novel Photocatalysts
This project is a collaboration between the Schwank group, the Laine group in MSE, and the Zgid group in Chemistry. This project involves the synthesis and performance evaluation of a novel class of photocatalysts based on mixed-metal oxides and oxynitride interfaces. Photocatalysts have many potential applications including water splitting, oxidation of VOCs, and self-cleaning and anti-fogging surfaces. The classic TiO_2 photocatalyst has serious limitations for use as a visible light catalyst due to its relatively negligible activity outside the ultraviolet range. By adding dopants, it is possible to alter the band structure and thereby improve light absorption in the visible range. The work proposed here aims to examine interfacial effects in metal oxide and mixed-metal oxide nanoparticle photocatalysts through controlled synthesis methods, detailed surface characterization, and complimentary modeling work. The Laine group will synthesize the novel photocatalysts, the Schwank group in ChE will conduct their photocatalytic activity studies in novel photocatalytic plate reactors, and the Zgid group in Chemistry would undertake modeling studies to explore the effects of doping and materials compositions on band gaps.

Professor Michael Solomon

Synthesis and Assembly of Nanocolloids
Nanocolloids are constituents of materials that are applied in many areas such as inks, coatings, optical materials, sensors and drug delivery. These particles are smaller than about one micron. In this project you will learn methods to synthesize, assemble and characterize such particles. The synthesis procedures you will master include methods to produce monodisperse particles. You will learn how to characterize what you make by electron and confocal microscopy. You will assemble particles by means of sedimentation, spin coating or applied electric fields. You will gain experience characterizing the rheological and electrokinetic properties of the particles you synthesize. At the conclusion of the project you will be well prepared to work or perform research in the many areas and industries that work with colloidal particles.

Physical Characterization of Bacterial Biofilms
To survive in the many environments they inhabit, bacteria may grow in communities in which individual organisms are embedded in a polysaccharide matrix. Biofilms are examples of such communities. Biofilms adhere to a variety of surfaces, including substrates relevant to human health, such as catheters. Confocal microscopy is a tool widely used in microbiological research because it can resolve multiple fluorescence

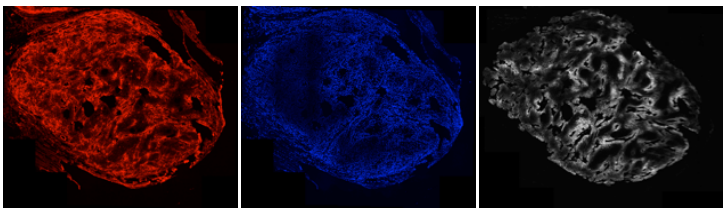
emissions in three dimensions. Our aim here is for students to apply microscopy methods to characterize the microstructure of bacterial biofilms and aggregates. Students participating in the project will receive training in microscopy, computer image processing, and bacterial communities. This unique combination of research in soft matter/complex fluids and microbiology will provide students with a strong foundation from which to pursue subsequent research experiences and graduate training.

Professor Peter Tessier

Bioinformatics and computational methods for improving antibody discovery
The success of therapeutic antibodies depends not only on their specific bioactivities but also on their highly variable and difficult-to-predict physicochemical properties (solubility, specificity, and biodistribution). The goals of this project are to develop predictive computational and bioinformatics methods for designing, optimizing and identifying drug-like monoclonal antibodies for therapeutic and diagnostic applications. Interested candidates should have experience in programming and MATLAB, and an interest in biotechnology.

Professor Greg Thurber

The human body can be treated as a large Chemical Engineering transport problem, where oxygen, nutrients, and drugs distribute based on a multitude of factors including passive transport (e.g. diffusion) and active mechanisms (e.g. drug transporters or 'pumps'). Two areas in particular remain poorly understood: transient distribution of small molecule imaging agents and therapeutic distribution of novel biologics. Our lab is interested in integrating drug and physiological factors into simulations for designing more effective imaging agents and therapeutics. Transport across multiple length and time scales must be included in detailed simulations to predict the impact of drug delivery mechanisms and therapeutic design, from the whole body and organ level down to the tissue, cellular, and subcellular distribution of the drugs.

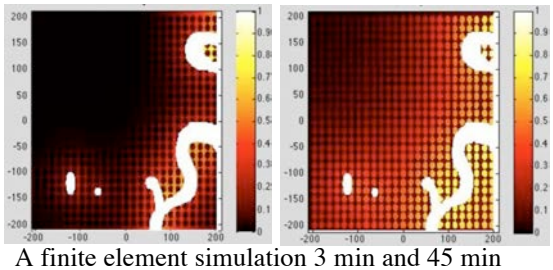


Distribution of three imaging agents within a ~5 mm tumor. The molecular weight, charge, lipophilicity, and target affinity all impact the pattern of uptake within the tumor (above) and surrounding healthy tissue (not shown) affecting the TBR. Images taken by Sumit Bhatnagar.

Novel Breast Cancer Imaging Agents for Early Diagnosis
Our lab is developing novel imaging agents for the early diagnosis of cancer. A critical parameter in designing new agents is the target to background ratio (TBR). A high TBR agent can detect a very small cancer lesion against a large background of normal tissue, allowing a surgeon to intervene early, before the cancer has metastasized (spread) to the rest of the body. The TBR is a complex function of passive diffusion through tissue and active binding to the target of interest. In this project, the student will measure the specific binding affinity of novel imaging agents against a series of cancer cells grown in the lab and measure passive transport rates across cell barriers (e.g. endothelial cells lining blood vessels). From these rates, the optimal properties will be selected and combined with drug distribution simulations to predict the smallest lesion the imaging agent can detect. These probes can also be used during surgery to ensure complete removal of the tumor. Such intraoperative imaging agents are currently undergoing clinical trials in several countries.

Predictive Finite Element Mesh (FEM) Simulations of Cancer Drug and Imaging Agent Distribution

The transient distribution of drugs and imaging agents is a complex function of transport rates throughout the body. These processes are highly non-linear, and computer simulations are required to solve the partial differential transport equations. Our lab has previously developed models of transient drug and imaging agent distribution, including Krogh cylinder models and finite element mesh simulations. The student will use these simulations to predict the distribution of drugs and imaging agents that are currently in clinical trials to treat lung and breast cancer. The simulations will also be used in designing experiments in our lab and comparing the predictions with fluorescence microscopy data. Students will learn basic programming techniques for imaging agent distribution using Matlab and/or Comsol.



A finite element simulation 3 min and 45 min after i.v. injection. The agent targets the cell nucleus with positive contrast at later times. Blood vessels in white; region is 400x400 um.

Professor Angela Violi

Research in the Violi group focuses on nanoscale systems for various applications. We use state-of-the-art computational techniques to discover the fundamental principles that govern the behavior of nanoparticles, in order to control and engineer their characteristics. Projects available are:

Project Title: ***Nanoparticle formation in flames and engines***
Research Areas: ***Nanotechnology, Combustion, Chemistry***

Understanding the chemistry behind nanoparticle formation during combustion has large implications from public health (emission control) to industrial production (volume synthesis of ceramic and metallic nanoparticles) and aerospace (materials for radiation shielding or with enhanced mechanical properties). Our lab is in the position of developing a deeper understanding of the complex chemistry behind these phenomena through the development of a stochastic NanoParticle Simulator computational code. This unique code provides atomistic insights on the characteristics of carbonaceous nanoparticles formed during combustion and is currently being expanded to study inorganic materials.

Project Title: **Design of tunable graphene quantum dots.**
Research Areas: **Materials, Nanotechnology, Quantum Dots, Molecular Dynamics**

Graphene quantum dots (GQDs) are relatively new materials with an exciting array of tunable properties. GQDs display properties and behaviors typical of nanomaterials, while retaining the functionalization flexibility typical of single molecules. We are investigating through molecular dynamics simulations how this flexibility affects GQDs properties, from their chirality and aggregation propensity to their optical and electrical properties. The understanding of the correlation between GQDs' structures and characteristics is a critical step in the design of tailored nanomaterials for a wide variety of applications.

Project Title: **Tailored nanomaterials for medical applications.**
Research Areas: **Nanotechnology, Bioengineering, Mechanobiology, Molecular Dynamics**

One of the most noteworthy applications of nanomaterials is in the medical field, from imaging to drug uptake and cancer treatment. Our lab employs different computational techniques to aid the design of these materials by understanding their interactions with different biological systems, like cellular membranes (to understand their uptake), and proteins (to understand their toxicity and effects on signaling).

More information can be found at:
http://www.umich.edu/~violilab/

Professor Henry Wang

Rapid Development of Sterile Polyvalent Immunoglobulin (Ig) Products to Combat Ebola Outbreak

Traditional design, development and biomanufacturing of drugs or biologics often cannot be used to combat sudden outbreak of infectious diseases like Ebola. The most immediate option is to isolate antibody-rich plasma from people who have recovered from the infectious disease, purify it and develop it into a "hyper-immune" product that could subsequently be transfused into patients. It has recently become possible to replace some key elements of a bioprocessing system such as centrifugation and microfiltration with disposable elements that can potentially reduce the cost of manufacturing significantly and most important of all, shorten the time to bring life saving medicines to the patients. This is particularly suitable for personalized medications tailored for specific patient needs. We would like to design a disposable affinity isolation system to isolate and enrich the polyvalent immunoglobulins (Igs) from recovered but healthy patients and immediately use these to treat patients within a local hospital environment. Such a disposable system must be demonstrated to be safe and effective and is compatible with the current methods of blood donation.

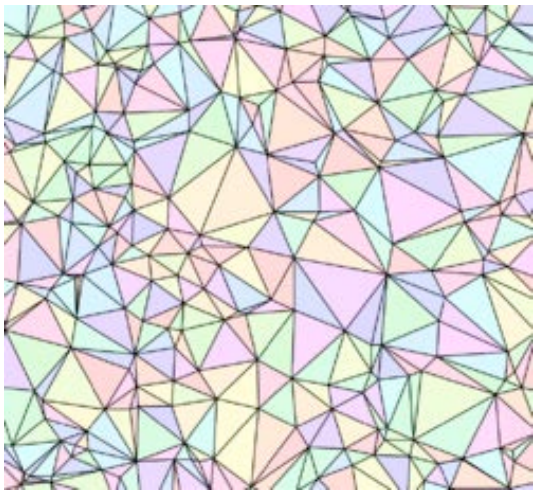
Bio-Refinery Platform Design, Development, and Integration

Biomass is the world's fourth largest energy source worldwide, following coal, oil and natural gas. Theoretically, biomass has the capacity to provide 100 percent of the world's energy requirement; however, current production approaches and use of biomass for energy are not sustainable. We propose the development of a Bio-Oil platform CO_2 utilizing oil producing plants and microalgae to supplement the existing oil refining infrastructure through synthetic biology, hydrothermal processing, microalgae cultivation and anaerobic digestion. Several engineering bottlenecks such as bioprocess robustness of using mono-cultures, wet biomass harvesting and microseparation of trace impurities have been identified and need to be addressed. By combining cellular photosynthesis and anaerobic bioprocessing, we intend to develop an integrated process engineering solution to overcome these bottlenecks.

Digital Manufacturing in Pharmaceutical Innovation

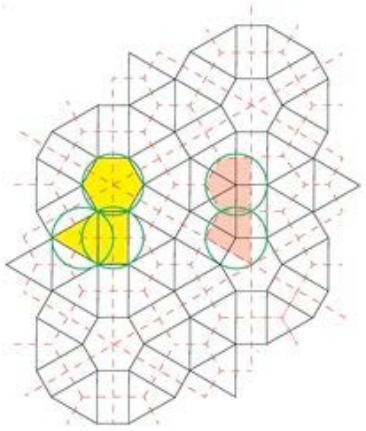
Most non-communicable diseases like diabetes and cardiovascular diseases are polygenic in nature while many infectious diseases like HIV and TB require more than one active agent to combat the disease without developing drug resistance. Thus, polypharmacy concept of using three or more active pharmaceutical ingredients (APIs) has been advocated in various disease management these days. One technical hurdle of this trend has been to develop a cost effective manufacturing platform to generate a polypill that can be mass-produced and can also be customized according to a specific patient need. We would like to explore the feasibility of using 3-D printing technologies developed for other manufacturing sectors as a means for pharmaceutical manufacturing of a polypill. The initial phase of this research is to study the feasibility of using such advanced technology to generate a polypill containing 5 APIs: Metformin, Glyburide, Lipitor, Lisinopril, and Aspirin help to prevent the onset of diabetes in patients diagnosed in the "pre-diabetes" stage.

Professor Robert Ziff



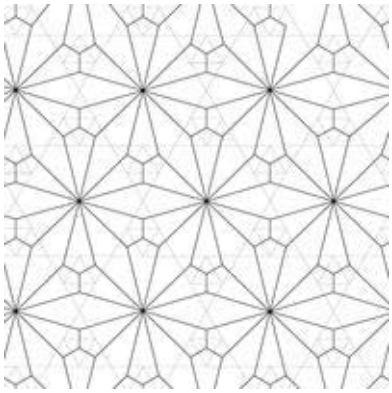
The Study of Networks and Percolation

Many problems in science and engineering involve random networks and porous media. When the connection is sufficiently high, long-range flow is allowed and the system is known to "percolate." Related problems include electrical conductivity of random conductor/insulator mixtures, dissolution of pills that are made of soluble/insoluble aggregates, and the spread of disease though a population of susceptible and unsusceptible individuals.



These various problems can be modeled by a simple and elegant probabilistic geometrical model in which a regular lattice is made random by making some of the edges or "bonds" open or shut.

The project is to study various forms of these networks through computer simulation and mathematical analysis, to determine connectivity and transport processes, especially near the critical threshold. If you are interested in programming, the project can entail running jobs on a computer (based upon current programs, modified accordingly), and analyzing the results.



Other aspects of this project include literature searches, assistance in manuscript preparation (especially figures), and additions to web and Wikipedia pages on this subject. Several previous undergraduate student projects have resulted in publications in journals.

Drug delivery modeling

The process of drug delivery via ingested pills is modeled using concepts from chemical engineering, including reaction engineering, fluids, and thermodynamics. Analytic differential equation modeling as well as numeric solutions are used to find the behavior as the pill breaks up, dissolves, and moves through the different parts of the digestive track (stomach, duodenum, ileum, cecum). Percolation theory can be used to study the breakup of composite pills, and computer simulation can also be applied to this problem. The goal is related to a project to evaluate the efficacy of generic drugs compared with original drugs that have been tested on humans, without having to repeat the human testing trials.