Sample Responses to Select Questions on the NSF Graduate Research Fellowship Application—Student #1

Question Summary: Describe any personal, professional, or educational experiences or situations that have contributed to your desire to pursue advanced study in science, mathematics, or engineering.

Simply put, learning for the sake of understanding the world better is what drives my intellectual pursuits. This desire to know pervades my daily life—too much so according to some. However, by this point in my life, I have come to realize and accept that many people find my outlook on learning and life somewhat odd. Still, learning is my passion, and through this "odd" view of the world I have come to recognize an important pattern in the educational process. By fervently studying one subject area you begin to appreciate its enormity. Once reaching this appreciation, you become capable of selecting an appealing subset of that area to further study. Yet this subset expands beyond any hope of total understanding, forcing you to choose an even more specific area and thus continuing the cycle. Paramount to understanding how this cycle relates to my educational goals is to realize that my passion for learning increases (exponentially so) as I choose more and more specific fields to study. But perhaps I have gotten ahead of myself and should start from the beginning: high school.

In high school I took all of the advanced science and math courses available. With this expansive background, I realized that I enjoyed science and wanted to study it further but appreciated the need to find a specific focus. Hence, when I stumbled upon materials science, I recognized it as an amalgamation of the scientific areas I most enjoyed studying. Without my broad scientific background, though, I would not have been able to make this decision as definitively. This appreciation for having a well-rounded knowledge of a field has remained with me during my undergraduate studies. For example, although I have already chosen to focus on electronic/photonic materials, I have opted to take additional courses, which explore polymers, glasses, and refractories. These classes benefit me in two ways. First, they expand my knowledge base. Second, by exposing me to such topics as conducting polymers and glass-ceramic electronic packages, these classes diversify my appreciation for electronic/photonic materials. Moreover, in contrast to my general fondness for high school science classes, studying materials science generates a fervor for learning in me that I never thought possible.

As my passion for materials science grows, I realize that it is time once more to refine and focus my learning objectives. To some extent, this change will be a difficult one because I honestly love the entire field of materials science. However, through my various work experiences, I have come to realize that there exists yet another level of learning in which you act as both student and teacher. At this level you can become so engrossed in learning that you feel a sense of ownership for the work. Such learning has shown me education's ultimate satisfaction. Such learning is called research.

Unfortunately, my previous exposures to research have only provided me partial fulfillment. With just a single summer to complete a research project, the feeling of ownership only begins to coalesce near the end of the appointment. In fact, I often feel a void within myself when I am forced to leave the project incomplete. To that end, I have been known to work extra hours, even weekends, just to satisfy my own needs of completeness in my research. This is why I have chosen to pursue graduate school. In graduate school I will be able to continue my passion for learning in a research-oriented environment. Hence, it will become possible to expand that feeling of ownership for a project beyond any of my previous experiences. Simultaneously, I will be creating my own learning—learning that I genuinely hope will benefit the rest of society.

Question Summary: Describe your experiences in the following or describe how you would address the following in your professional career: integrating research and education, advancing diversity in science, enhancing scientific and technical understanding, and otherwise benefiting society.

As an undergraduate I have been very involved with student organizations in both my college and department. I have been a member of the Mythic University Student Council and the student branch of the American Ceramics Society (ACerS). Furthermore, I have held various positions in these organizations ranging from vice president to social chair. Thus, I consider myself quite active in the professional, educational, and social proceedings that affect me most, and I plan to continue my involvement after graduation. More relevant, though, is my motivation for becoming involved in these specific groups.

Six years ago, when I witnessed a demonstration of shape-memory alloys at an engineering convention, I became enticed to enter the field of materials science. Since that time, I have wanted to educate others about the field in the hopes of also captivating their interests. Discussing materials science with others is one of my favorite hobbies, and I have been pursuing this mission since that fateful day six years ago. Even from conversations with friends during my meagerly informed high school days, I was able to influence one peer to pursue a degree in materials science and another to pick up a minor in polymers. (I guess pure excitement alone can be sufficiently persuasive at times.) However, in college I wanted to extend this personal campaign even further, and therefore chose to join groups that allowed me the opportunity to communicate with prospective students and undecided undergraduates.

During my undergraduate career, I have been involved with every recruiting opportunity made available to me. At these events, my goal has never been to simply coax these students to come to Mythic University, but instead to inform them of what a fantastic career choice materials science and engineering can be. In the early spring, I am awake several hours before dawn to prepare decorations and displays for the Mythic University's annual open house, which is organized by the Student Council. Although this deprives me of several hours of sleep (on a Saturday even!), I still manage to exude excitement when I explain to prospective students all the wonderful "stuff" that materials scientists get to explore. Similarly, as a part of ACerS, I participated in a materials science departmental tour for high schoolers visiting Mythic University for the annual

Junior Science and Humanities Symposium. This activity involved leading discussions on materials-related exhibits set up throughout the department. A third activity that I continually participate in is the Mythic University's annual phone-a-thon. This involves calling all prospective students accepted to the college for the upcoming year. I found this experience so rewarding that last year I took over as chair of the event. Additionally, I have also participated in various other engineering open houses and outreach programs, acting as a representative of the materials science department.

Recently I met up with a student who thanked me for persistently leading her and her parents to the materials science exhibits at the spring open house. That experience made her select materials science as her field of study. Like many others, she had never heard of materials science until that day but was immediately drawn to all of the opportunities it offered. This unexplainable magnetism that materials science can induce drives me to further educate others and compels me to extend my outreach efforts.

In the future, I would like to develop a short interactive lecture that could be presented in high school chemistry or physics classrooms and would relate concepts these students already know to the field of materials science. This would expose the students to the field, show them its similarities and applications to subjects they are already familiar with, and hopefully inspire a few to pursue a degree in materials science. It is my hope that student branches of materials-related professional organizations (like ACerS) could act as the distributors for such classes. Whether such a project would then lead to even more involved endeavors like websites or textbooks is unclear, but no matter where my career takes me, I will continue informing others about the wonders of materials science.

Question Summary: In a clear, concise, and original statement, describe research topics you may pursue while on fellowship tenure, and include how you became interested in these topics. Your statement should reflect your own thinking and work, demonstrate your understanding of research principles necessary to pursue these interests, and explain the relationship to your previous research, if any. Present your plan with a clear hypothesis or questions to be asked by the research. If you have not yet formulated a plan of research, your statement should include a description of one question that interests you and an analysis of how you think the question may best be answered.

As early as grade school, I was intrigued by the fact that energy can transform between multiple forms. This notion that heat, light, motion, and electricity are all forms of the same abstract quantity known as energy continues to fascinate me even today. Therefore, it should be of little surprise that as a materials scientist, I am most intrigued by the properties of materials that convert energy from one form to another. These materials are valuable because certain forms of energy are often more useful than others. Hence, numerous practical devices rely on these principles, including thermocouples, solar cells, and light-emitting diodes. However, of greatest interest to me are ferroelectric/piezoelectric materials that are capable of transforming electrical energy into mechanical motion.

One of the most innovative uses of piezoelectrics in recent years is as a component of microelectromechanical systems (MEMS). Piezoelectric materials truly represent a means for coupling electronics with mechanical motion and so seem destined for integration into MEMS technology. The material of most interest for these applications is the solid solution, ferroelectric lead zirconate titanate (PZT).

At room temperature, PZT is equilibrated as a tetragonal or rhombohedral perovksite phase depending on the composition. The piezoelectric response of this phase can be divided into two components: the intrinsic and extrinsic contributions. The intrinsic contribution is simply the result of the B-site cation shifted along the c-axis with respect to the oxygen sub-lattice. Although slightly more complex, the extrinsic contribution is typically attributed to domain wall movement between adjacent domains with non-180o orientations. Each of these factors contribute about 50% to the piezoelectric response of bulk PZT.

However, PZT thin films show a significant decline in piezoelectric response. In the literature, this unfortunate outcome is often attributed to mechanical constraints placed on the film, which hinder the extrinsic contribution. To appreciate the mechanisms for this constraint, consider the Si-PZT system. Silicon has a considerably lower thermal expansion coefficient than PZT. Hence, upon cooling a crystallized PZT film, tensile stresses will arise in the PZT layer. Because crystallization is performed well above the Curie temperature, PZT will be in the non-ferroelectric cubic phase. However, as the film is cooled below the Curie temperature, the tensile stresses present will energetically favor tetragonal phases with the c-axis parallel to the plane of the film. Therefore, very few non-180° domain walls will develop, and the extrinsic contribution will be vastly diminished. Thus, silicon-based MEMS must work around this limitation when incorporating PZT into the device.

However, during my recent senior thesis work, I have become fascinated with the possibilities of ceramic microsystems. Similar to how MEMS evolved from silicon processing technology, ceramic microsystems are spawning from multilayer ceramic technology, which was originally developed for electronic packaging and multilayer capacitors. Today, this technology is becoming a viable way for constructing three-dimensional systems on the micro-scale for applications such as microfluidics and micro-combustion. These ceramic microsystems offer many advantages over silicon MEMS such as parallel processing, ease in packaging, and lower equipment costs. More relevant, though, is the closer match in thermal expansions between these ceramic substrates and PZT in comparison to the match between silicon and PZT. Thus, I propose a project that would focus on determining the piezoelectric capabilities of thin film PZT on multilayer ceramic substrates.

The first step in such a process would be to fabricate these PZT films on electroded ceramic substrates. I am intimately familiar with this topic since it is the crux of my current undergraduate thesis. Therefore, I confidently anticipate that these films will be fabricated using sol-gel techniques. Once this process is reasonably optimized, uniform test samples will need to be prepared. A set of control samples with silicon substrates should also be prepared. Next, electrical tests will need to be performed to determine the extent of intrinsic and extrinsic contributions to the piezoelectric effect and dielectric constant. Typically, this information is extracted from one of two methods. The first involves making measurements as a function of increasing frequency. At high frequencies, the extrinsic contribution is eliminated and the pure intrinsic contribution can be determined. However, this technique is only applicable for dielectric measurements. To determine the contributions to the piezoelectric response, measurements must be made as a function of temperature. At temperatures near absolute zero, the thermally activated extrinsic component is effectively nullified and again the intrinsic component can be determined. However, both of these techniques have their shortcomings, and I will need to take these issues into consideration while developing these experiments.

Furthermore, piezoelectric measurements on thin films are complicated at best. The same mechanical constraints imposed by the substrate that limit the extrinsic response are also responsible for limiting the indirect piezoelectric response. Often a more appropriate approach is to derive the piezoelectric coefficient from the direct response. This measurement involves applying stress to the film and monitoring the charge build-up. The ferroelectric group at Mythic University has been a world leader in developing techniques to make such measurements, and this fact has contributed to my serious consideration of continuing at this institution for my advanced degree.

In summary, the basic hypothesis for this work is that PZT thin films with thermal expansion matched ceramic substrates will have a higher extrinsic contribution to piezoelectric and dielectric properties than films on substrates with lesser thermal expansion matches, such as silicon. If this hypothesis is found to be valid, then PZT films on ceramic substrates should show stronger piezoelectric responses, assuming all other film properties (such as structure, thickness, and composition) are equal. Consequently, such films would be extremely useful in advancing ceramic MEMS technology. Apparatuses such as pumps for microfluidics and valves for microcombustion chambers could all be possible consequences of such technology. In addition, this research would lead to a better scientific understanding of the intrinsic and extrinsic contributions to ferroelectric properties.

As a final note, let me briefly comment on my selection for possible graduate school institutions. Clearly, Mythic University is a leader in ferroelectric materials science, and a transition into its graduate program would be nearly seamless for me. Thus, I could promptly begin my research and have the opportunity to work with faculty at the top of their field. On the other hand, I realize the professional advantages of changing environments, and as a result, I am also seriously considering other institutions. My two major criteria for evaluating institutions are my own interests in the research opportunities available and the facilities that these institutions offer.

Question Summary: Describe any scientific research activities in which you have participated, such as experience in undergraduate research programs, or research experience gained through summer or part-time employment or in work-study programs, or other research activities, either academic or job-related. Explain the purpose of the research and your specific role in the research, including the extent to which you worked independently and/or as part of a team, and what you learned from your research. In your statement, distinguish between undergraduate and graduate research experience. If you have no direct research experience, describe any activities that you believe have prepared you to undertake research.

During my short scientific career, I have conscientiously strived to gain as much research experience as possible. In fact, I began my first research project in materials science while still in high school. During the summer of 20xx, I worked at a local failure analysis company, MATCO Incorporated. For my project, I performed some basic studies on the oxidation of titanium and examined how different processing parameters affected the resulting color change. With the close of the summer, I submitted a report based on my findings and outside research. Admittedly, the project was rather mundane, and in fact, at the time I failed to grasp all of the underlying science involved. Yet, my work at MATCO gave me valuable experience in a laboratory environment, as well as exposed me to the daily routine of a materials science engineer. Most importantly, though, this experience solidified my desire to study materials science and seeded the notion to follow a research-oriented career path.

During my undergraduate career, I quickly developed an exact yet flexible plan on how I intended to spend my summers. My goal was to acquire three internships, one for each summer, and have these internships cover the three major working environments in which I could possibly find myself once I graduated: industry, academia, and government. I can happily say that I have accomplished this goal.

I spent my first summer in a research experience for undergraduates (REU) program at Mythic University. In this program I worked in a biomaterials laboratory learning how to manipulate the surface wettability of glass substrates. My objective was to create radially symmetric gradients of wettability. To accomplish this task I diffused hydrocarbon molecules with silane functional groups through a gel that was in contact with the glass surface. These molecules would then "silanate" the surface creating a region of lower wettability. Since the silane was diffused from a central location, the amount of "silanation" decreased radially from this point, hence forming a wettability gradient. To analyze my gradients, I used a Wilhelmy balance. I also developed a fairly basic, although useful, mathematical model (based on wetting forces) that helped to explain the data I collected from the Wilhelmy balance. Perhaps my most ingenious accomplishment, though, was analyzing the silanated glass substrates with optical microscopy while cooling them on a piece of ice. Cooling the glass samples forced water to condense on the surface. These condensed water droplets would bead in different shapes and sizes depending on the surface characteristics, hence allowing me to "see" my wettability gradients. This tool, which I discovered on my own, proved invaluable in providing me with both qualitative and semi-quantitative data. Overall, this research experience was outstanding because although the initial idea was my mentor's, I was left to independently carry out the research. By the end of the summer, I had a much better grasp on the scientific process and the importance of creating a research plan and modifying it when necessary.

I spent my second summer working at Carpenter Technologies, a specialty steel manufacturer. This was my introduction to working in industry. Although the work I did at Carpenter did not necessarily follow a purist's view of the scientific process, it did allow me to hone my skills in sample preparation, optical microscopy, and hardness testing. However, more importantly, this internship exposed me to working in a team environment and interfacing with multiple people to solve problems. In fact, at one point I traveled with my mentor to a hot rolling conversion facility outside the company to discuss problems occurring with Carpenter billets that they had been hot rolling. Also on that trip, we visited with a slitting facility to discuss possible methods of reducing the amount of scrap. These experiences and many others became invaluable lessons in how to communicate ideas and network with technical and non-technical personnel in order to achieve a desired goal. Hence, the communication tools that I gained from my work at Carpenter will better allow me to interface with professors, technicians, and other graduate students once I enter graduate school. Additionally, I have learned that working in a group can often be the wisest path for solving a problem.

However, my internship this previous summer at Oak Ridge National Laboratory (ORNL) proved to be the most rewarding and enjoyable of the three. This extremely positive experience was certainly the result of being able to synthesize my past experiences and use these lessons to perform research that was both efficient and valuable. Essentially, my project entailed coating metallic and ceramic components using pack cementation and then evaluating the effects microwave heating had on the process. My laboratory duties included preparing the samples and powder pack, operating the furnaces, mounting and polishing samples, and performing the necessary characterization. The important characterization tools I used were optical microscopy, scanning electron microscopy, energy-dispersive x-ray analysis, x-ray diffraction, and hardness testing. Furthermore, I performed nearly all of the data analysis on my own and reported my conclusions in both a poster and a technical paper. During the three months I spent at ORNL, I was the sole researcher on this project and was allowed to direct my own course of research.

Of course, initially I did receive training on the equipment, but even during these sessions I was treated as an intellectual equal who already understood the underlying scientific concepts of each technique. In fact, this was the treatment I received during my entire stay at ORNL. Because of this, I gained more confidence in my "textbook education" and in my ability to apply this knowledge. For the first time, I felt like a capable and valuable researcher. Still, I did acquire many knew skills that will benefit my future research endeavors. The two most vital skills were maintaining a lab notebook and analyzing collected data. My ability to keep a complete and well-organized lab notebook improved over the summer and was aided by suggestions from my mentors. Now, I feel much more comfortable with maintaining a scientific record of my work.

Currently, I am performing research at Mythic University's Materials Research Laboratory as part of my senior thesis project. In this project, I collaborate with one of the faculty members and present my results in a thesis that will be archived in the library. My specific project involves depositing lead zirconate titanate films with liquid source misted chemical deposition on ceramic substrates similar to those used in electronic packaging. In the process, I will also be learning how to operate sputtering equipment and how to measure dielectric and piezoelectric properties of thin films. This work will certainly serve to further my research experience as well as teach me how to organize a literature review and prepare a thesis. I look forward to the challenges that this project presents as well as the opportunities for further maturation as a practicing scientist.

Sample Responses to Select Questions on the NSF Graduate Research Fellowship Application—Student #2

Question Summary: Describe any personal, professional, or educational experiences or situations that have contributed to your desire to pursue advanced study in science, mathematics, or engineering.

Although math and science have been my favorite subjects since elementary school, with math games such as “Around the World” and “24” piquing my interest, it was not until high school that I decided upon engineering as my future career. In tenth grade, I began to study C++ and computer programming and learned to love the feeling of accomplishment that came with the solution of a difficult problem. In eleventh and twelfth grades, I participated in the American Computer Science League competitions with a team of two other students. Both years, our team earned a trip to the National All-Star competition where we placed in the top ten, and I was awarded for my individual performance. Success in this contest and in other traditionally male-dominated classes such as calculus, chemistry, and physics led me to believe that I could succeed in the field of engineering.

Another long-standing desire of mine has been to help others. From a young age, I have volunteered with different organizations in a range of capacities. In particular, since elementary school, I have enjoyed tutoring fellow students; helping a peer to understand a difficult concept is an extremely rewarding experience. Because of this, I searched for a way to integrate mentoring, math, and science into a career. I explored becoming a doctor or a teacher, but I found neither satisfactorily combined my academic and personal interests.

An event in my junior year of high school solved this enigma. That year, I toured the Bioengineering Department at the Mythic Medical Center. While there, I realized what I wanted to do with my life: become a bioengineering professor at a major research university, concentrating in the area of tissue engineering. This career path appears to be the perfect combination: I can apply my research to improve health care, while at the same time, mentoring and instructing future scientists and engineers.

Since then, I have pursued my career choice by becoming actively involved in biomedical research, beginning in my sophomore year. I find research challenging, and I enjoy the sense of accomplishment when a difficult problem is solved, yielding new knowledge that contributes to the betterment of society. Finally, I greatly enjoy working in the academic atmosphere that embraces the sharing of this new knowledge.

My academic success in college and my involvement with science-related extracurricular activities have encouraged me to persist in my goal of earning a Ph.D. in bioengineering. I am in the top 0.5% of my class and, in the last year, have been awarded the Barry M. Goldwater and the Astronaut Scholarship Foundation Scholarships. I have also helped to found an undergraduate chapter of the Biomedical Engineering Society (BMES) at Mythic University and have served as webmaster for the club. Through this club, I have had the opportunity to participate in outreach to high school students. Finally, I have confirmed my desire to become a professor by serving as a mentor to incoming freshmen in the Mythic University Honors College.

All of these factors have led me to believe that a career in academic research will best match my passions.

Question Summary: Describe your experiences in the following or describe how you would address the following in your professional career: integrating research and education, advancing diversity in science, enhancing scientific and technical understanding, and otherwise benefiting society.

"A hundred years from now it will not matter what my bank account was, the sort of house I lived in, or the kind of car I drove. But the world may be different because I was important in the life of a [child]."

—Forest Witcraft, Boy Scouts of America

My belief in the veracity of the statement by Witcraft is one of the reasons I have decided to become a research professor. I believe that this career will allow me to share my fervor for science and discovery with future generations, especially young women. From a young age, and continuing throughout my college career, I have tried to embody this principle and to volunteer in other capacities in order to improve the community around me.

One of the ways in which I have been able to share my field of bioengineering with others has been through the Biomedical Engineering Society (BMES). Last year, I worked with Prof. John Teacher and a few of my peers to co-found an undergraduate chapter of BMES at Mythic University. The purpose of this club, according to the BMES, is to "promote the increase of biomedical engineering knowledge and its utilization." Our chapter seeks to fulfill this mission by bringing together undergraduate and graduate students and supporting activities such as mentoring, career information sessions, and outside speakers. As part of our outreach, I had the opportunity to return to my high school over spring break to speak to science classes about biomedical engineering and to share some of my experiences of college life. I have also assisted the BMES at the annual Engineering Open House, which is an event geared to helping high school seniors learn more about the different engineering disciplines, hopefully encouraging them to consider engineering as a career. In addition, I have served as the captain of a BMES-sponsored intramural women's soccer team. Team sports depend upon each player cooperating and putting forth 100% effort toward a common goal, which directly translates to the demands of a research environment. This team not only encouraged bioengineers to interact outside of classes, but it also gave me the opportunity to promote communication between science and non-science majors, since I actively invited non-bioengineers to join the team.

Since beginning my honors thesis research as a sophomore, I have had many opportunities to share the knowledge I have gained by presenting my results in various settings. These have included a publication ("Procoagulant Stimulus Processing by the Intrinsic Pathway of Blood Plasma Coagulation," in *Biomaterials*) and several poster presentations among members of my field. I also participated in a poster presentation that included entries from all undergraduate majors. This presentation gave me the chance to explain my work to people from non-science backgrounds, challenging me to present technical details in a way that is meaningful to a wide variety of viewers.

I have also positively impacted the lives of incoming freshmen by serving as a mentor for the Mythic University Honors College students. I have helped these freshmen to make a smooth transition from high school to college by offering advice on ways to succeed in and out of the classroom and also by lending an ear to whatever troubles they may be experiencing. One of my former mentees recently informed me that I inspired her to succeed in her engineering studies despite it being a traditionally male-dominated field. She also gained interest in working towards the Goldwater Scholarship as a result of my award last year.

Finally, I seek to serve the rest of the surrounding community through my participation in Habitat for Humanity. Our chapter helps to raise money to build houses for people who would not ordinarily be able to afford them by performing odd jobs for people in the community, asking for donations from local people and businesses, and by holding an annual "House Walk," in which each walker is sponsored by family, friends, and members of Mythic University community.

Throughout my career, I hope to continue my commitment to public service by serving as a mentor to young women, volunteering for summer science enrichment programs, and performing other acts of community service such as participating in the Adopt-a-Highway program. In this way, I can share with others the blessings that have been given to me throughout my life.

Question Summary: In a clear, concise, and original statement, describe research topics you may pursue while on fellowship tenure, and include how you became interested in these topics. Your statement should reflect your own thinking and work, demonstrate your understanding of research principles necessary to pursue these interests, and explain the relationship to your previous research, if any. Present your plan with a clear hypothesis or questions to be asked by the research. If you have not yet formulated a plan of research, your statement should include a description of one question that interests you and an analysis of how you think the question may best be answered.

<u>Introduction and Relevance</u>: Musculoskeletal pain was the most cited reason for visiting a physician in the year 2000 (1). Current orthopedic repairs utilize artificial materials such as ceramics, metals, and polymers, which cannot replicate the function of natural tissue and do not fully integrate with the body. Tissue engineering seeks to cultivate tissues that are physiologically similar to native tissue to solve these problems. Impeding the realization of these complex structures is the failure to successfully integrate cells, scaffolds, and signaling. My goal is to create a scaffold that will facilitate incorporation

of implanted cells, growth factors, and extracellular matrix proteins in order to rebuild and repair cartilage tissue in joints.

Molecular self-assembly, or building from the "bottom-up," is increasingly being recognized as the next step in the development of novel biomaterials. In particular, researchers have begun investigating the utility of self-assembling polymers and peptides in the field of tissue engineering. In the development of tissue-engineered scaffolds, peptides have several advantages over polymers, including versatility in composition, chemical properties, and morphology. For example, polymer scaffolds typically only include one or two different biological ligands on their surfaces because it is difficult to control the concentration and arrangement of these ligands. Peptides offer the ability to easily synthesize different sequences with different properties that can then be combined to form self-assembled scaffolds. Peptides can also be designed to form gel structures under physiologic conditions.

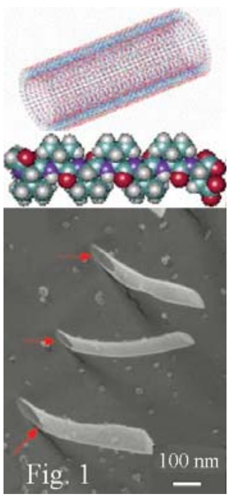

Fig. 1

Ground-breaking studies by Zhang et al. (2) demonstrated that chondrocyte proliferation can be supported by self-assembling peptides made of alternating hydrophobic and hydrophilic residues that do not elicit an immune response. However, these peptides have been shown to only assemble into the beta-sheet type nanofibril, the kind typically seen in the amyloid fibrils of Alzheimer's disease. This group has also recently developed surfactant peptides that self-assemble to form nanotube structures as seen in Fig. 1. (3). These surfactant peptides have the advantage of forming well-defined hydrogel structures while remaining relatively easy to modify, which may lead to the ability to incorporate cell-binding sequences and other biomolecular sites on their surfaces. Stupp et al. (4) have recently reported on the construction of scaffolds made of self-assembling amphiphile peptides that contain a sequence promoting neurite growth. These scaffolds were seeded with neural progenitor cells and successfully induced neuron differentiation *in vitro*. Stupp et al. have also shown that the scaffold can self-assemble when a peptide solution is injected into tissue.

<u>Background and Research Objective</u>: I have focused my undergraduate degree of Bioengineering on biomaterials by choosing a concentration in materials science and by performing my honors thesis research in a biomaterials laboratory. I intend to build upon this foundation by pursuing my Ph.D. in Biomedical Engineering under the guidance of Dr. Phillip Messersmith at Northwestern University. Northwestern University is a leader in the nanotechnology field and recently expanded its facilities with the addition of the Robert H. Lurie Medical Research Building. This building is the new home of the Institute for BioNanotechnology in Medicine (IBNAM), which performs research in fields such as self-assembly, tissue engineering, genomics, and smart drug delivery. Dr. Messersmith's research is based upon utilizing biological strategies to develop new biomaterials and tissue engineering approaches for the repair, replacement, or augmentation of human tissue. His group has investigated the use of the natural tissue enzyme, transglutaminase (TG), in combination with stimuli-responsive lipid vesicles

containing calcium (Ca) to induce the rapid *in situ* formation and cross-linking of peptide, protein, and polymeric hydrogels (5,6).

My research will build on this background, with the goal of developing a self-assembling scaffold made of surfactant peptides, which employs Ca-dependent TG cross-linking. This peptide will include the cell-adhesion sequence RGD, intended to attach chondrocytes to the scaffold. Cross-linking will be triggered *in situ* by the release of Ca from lipid vesicles upon exposure to light, as demonstrated by Messersmith (5). Growth factors—transforming growth factor beta (TGFb) and basic fibroblast growth factor (bFGF)—will also be included in the vesicles in order to encourage cell growth and differentiation. While each of these components has been investigated individually, the proposed combination of them is novel and will advance the goal of producing injectable scaffolds for the repair and regeneration of tissue. In order to prepare for this research, I will take courses at Northwestern University in biochemistry, biophysics, nanotechnology, tissue engineering, and self-assembled materials.

<u>Research Design</u>: The surfactant peptides described by Zhang et al. (3) include hydrophilic head groups and hydrophobic tails of the form n'-AAAAAAD-c'. My molecule will use this backbone, but sites for TG (Q, K) and cell binding (RGD) will be added. As a starting point, I propose the amino acid sequence: n'-AAAAQARGDK-c'. A peptide solution will be formed by mixing the cell-binding peptide with peptides that do not contain the cell-binding sequence of the structure: n'-AAAAAAQAAK-c'. Self-assembly will be confirmed by analyzing the peptides with transmission electron microscopy (TEM), circular dichroism, and other methods. If these molecules do not self-assemble quickly enough for clinical applications (within three minutes), the Q may be disrupting the hydrophobicity of the tail, in which case the A sequence of the tail will be changed to the more hydrophobic V or L. Additionally, the position of the TG sites could be varied: more Q and/or K sites may be added, or the current sites may be moved.

I have included TG sites in my peptide because this family of enzymes is found in fluids and extracellular matrix (ECM) throughout the body, and components of cartilage ECM cross-link with TG, enabling the scaffolds to integrate with native tissue. Sperinde and Griffith (7) have shown that poly(ethylene glycol) can be cross-linked with a lysine-containing polypeptide by the use of TG, thereby improving mechanical properties. This combination can form a hydrogel network that can be injected into the body.

Since TG is dependent upon Ca, the eventual goal will be to deliver Ca to the body by the use of vesicles that release their contents upon exposure to a light source of a certain wavelength and intensity. But first, I will test the ability of my peptides to cross-link by adding different concentrations of CaCl2 and animal-derived TG to a solution of peptides *in vitro*. Once cross-linking has been optimized, I will then advance to testing my system with Ca-containing vesicles *in vitro*. Finally, the possibility of adding the growth factors TGFb and bFGF to phototriggerable vesicles will be explored. These growth factors are important for stimulating chondrocyte activity and also for decreasing cartilage degradation.

Next, I will test the cell-binding capabilities of the RGD sequence by incubating assembled scaffolds with chondrocytes harvested from calves at the cell density of 15 x 106 cells/mL. After 3, 6, and 9 weeks, sections of scaffold will undergo histological examination in order to determine the amounts and kinds of collagen being produced by the embedded chondrocytes. Based on the results of these tests, the ratio of peptides with and without the cell-binding sequence in the peptide solution will be varied.

Finally, the *in vivo* properties of the scaffold and vesicles will be tested by injecting a solution into an animal model and triggering gelation with a light source. The scaffold's mechanical, immunological, and histological properties will be analyzed.

<u>Long-term Goals</u>: In the future, the incorporation of peptides with a variety of cell-signaling sequences will be investigated with the ultimate goal of injecting the scaffold into human subjects to repair damaged cartilage. This will potentially have a great impact on the treatment of osteoarthritis, a debilitating joint condition that affects millions of Americans each year. My career goal is to become a Professor of Bioengineering at a major research university concentrating in the area of tissue engineering and regenerative medicine. I look forward to sharing my research with the next generation of scientists and engineers in the classroom and in the surrounding community.

References:

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Question Summary: Describe any scientific research activities in which you have participated, such as experience in undergraduate research programs, or research experience gained through summer or part-time employment or in work-study programs, or other research activities, either academic or job-related. Explain the purpose of the research and your specific role in the research, including the extent to which you worked independently and/or as part of a team, and what you learned from your research. In your statement, distinguish between undergraduate and graduate research experience. If you have no direct research experience, describe any activities that you believe have prepared you to undertake research.

Biomedical devices, ranging from catheters to ventricular assist devices, are used by the millions annually. Many novel coatings and materials have been developed for these applications, yet the ideal materials for these varied uses remain to be discovered (1). In particular, for blood-contacting applications, the body's reaction to biomaterials continues to be plagued by two major problems: bleeding and thrombosis (2,3). Thrombosis is usually the result of adverse interactions between the artificial material and the body. Bleeding becomes a problem when attempting to prevent thrombosis by administering excessive anti-coagulants. Therefore, without a better understanding of the process by which the body responds to foreign materials, promising technologies such as self-assembled nanomaterials cannot reach their full potential as hemocompatible materials (4,5). I have been performing research towards my honors thesis since my sophomore year, under the guidance of Prof. John Teacher at Mythic University. This research has focused on understanding how the body reacts to the introduction of foreign materials. In particular, I have concentrated on blood-surface interactions and the engineering of novel hemocompatible surfaces.

Blood coagulation occurs through a cascade of enzymatic reactions involving many plasma proteins, lipids, and ions resulting in the production of a fibrin clot. This cascade can be divided into the intrinsic, extrinsic, and common pathways. The intrinsic and extrinsic pathways are initiated by distinct events and converge into the common pathway. The intrinsic pathway is activated when blood interacts with an artificial surface, while a tissue injury activates the extrinsic pathway (6). The intrinsic to common pathway can be conceptualized as occurring through linked sets of enzyme reactions, termed compartments. In this work, the intrinsic cascade has been modeled in terms of three such compartments: activation, transfer, and coagulation.

My research on blood-surface interactions seeks to quantify dose-response relationships, connecting surface properties of a biomaterial with the tendency to activate the intrinsic pathway of the blood coagulation cascade. In the various experimental assays used in my work, the "dose" results from applying a surface to human plasma or from adding an activating enzyme to human plasma. The "response" is the formation of a plasma clot as measured by coagulation time. Two primary questions raised by these experiments ask: How does dose propagate through the cascade to yield a response? What is the relationship between intensity of the dose and response?

Another aspect of my research, mathematical modeling, seeks to answer these questions. The model uses the compartmentalized cascade to treat the intrinsic pathway as a "black box" leading to the output of thrombin in the common pathway. This model allows me to apply derived equations to the experimental data to obtain rate parameters that will give quantitative information about the entire coagulation process. This information is expected to lead to a better understanding of how changing material properties affects hemocompatibility.

The effect of adding an amount of surface area to plasma is one example of a dose-response relationship explored in my research. I performed experiments in human plasma with beads made of two different materials: glass and silanized octadecyltrichlorosilane (OTS). Glass is a high-energy, hydrophilic surface, while OTS is a low-energy, hydrophobic surface. These experiments have shown that glass activates the coagulation cascade significantly more than OTS based on coagulation times. Mathematical modeling quantified this observation, showing that the activating potential of the surface scales exponentially with surface energy. Another interesting result is that both materials begin to saturate at the same amount of surface area. This observation has led to the hypothesis that thrombin is produced as a bolus in proportion to the amount of surface area added, instead of being slowly produced the entire time until coagulation. This work is currently in press in *Biomaterials*, a leading peer-reviewed journal in the field (7).

During the past two summers, I began work on engineering surfaces that have regions of one chemical functionality on the nanometer scale within a continuous matrix of a second functionality. The goal of this research is to test the hypothesis that nanoscopic organization of chemistry can influence the activation of blood coagulation. In order to create these nano-surfaces, I chose to use the method of forming self-assembled monolayers of organosilanes on glass substrates. Self-assembled monolayers (SAMs) are ordered assemblies that form spontaneously by the adsorption of a surfactant with a specific affinity of its headgroup to a substrate (8).

In this work, I have used two organosilanes: 3-aminopropyltriethoxysilane (APTES) and n-butyltrichlorosilane (BTS). A monolayer of APTES has an intermediate surface energy, while a monolayer of BTS has a low surface energy similar to that of OTS. APTES and BTS molecules have nearly the same chain length. Therefore, the combination of these two silanes on the same substrate results in a smooth surface. First, I created partial monolayers, or "islands," of APTES on a clean glass surface. Next, I back-filled the surface with BTS. I then examined the surfaces using atomic force microscopy (AFM) in contact mode. Because the surfaces were smooth, with an average roughness of only 0.15 nm, I relied on friction images to determine the make-up of these surfaces. Through this analysis, I determined that the islands of APTES had an average diameter of 500 nm and appeared in a regular arrangement across the substrate (Fig. 1). The next step was to create glass beads with APTES islands and back-fill with BTS in order to perform surface area titrations as described earlier. This allowed me to compare these new surfaces with previously characterized surfaces. The result of a

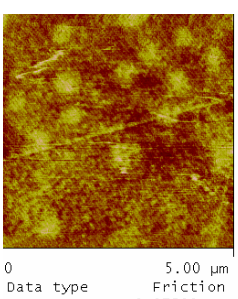

Fig. 1

surface area titration of the APTES/BTS beads showed that these beads activate the coagulation cascade less than beads made of purely APTES or purely BTS. To better understand these potentially positive results and to finalize them for publication, I am completing surface characterization by techniques such as atomic force microscopy, contact angle tensiometry, and x-ray photoelectron spectrometry.

Solving the problem of how dose is propagated through the plasma coagulation cascade will contribute to the understanding of how a surface activates the blood coagulation process. Ultimately, this understanding will aid in the design of a hemocompatible material that results in the lowest activation of the cascade. This improved interaction with the body will enable patients to take less anti-coagulant medicine, producing better results following the use of biomedical devices.

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