I have always been interested in doing research that would directly help the medical field. I want to work on a project that is relevant and needed in the present time. In February 2015, 189 people were exposed to bacteria that have become resistant to our medicine at the University of California – Los Angeles, with two patients dying as a result. As bacteria become more resistant to our best antibiotics, the need for alternative medicines has led to the development of antimicrobial polymers. The most common antimicrobial polymers tend to have positively charged groups to allow for the adsorption to the negatively charged membranes of the bacteria. Antimicrobial polymers also have the ability to carry cargo to increase their toxicity to bacteria. The biggest challenge is that polymers suffer from dilution effects and breakdown in the presence of a large amount of water. One way to circumvent this problem is to develop antimicrobial nanoparticles. To develop these nanoparticles, surfactant monomers will be made to essentially decorate the surface of the particle with positive charges. These positive charges will function as stabilizers to the nanoparticles while also providing antimicrobial properties. The main objective is synthesizing surfactant monomers and incorporating them into nanoparticles. This project is part of ongoing research in my advisor’s group. My goal upon graduating is to attend graduate school and do research in the field of medicine. This project is perfect in equipping me with the necessary tools to do the research I have always wanted. This research would be instrumental in developing my problem solving abilities, while also giving me practical laboratory experience. I am excited about doing research this summer in a field of science that is becoming increasingly relevant to issues present in our society.
Introduction/Rationale (approximately 500 words): What is your project and why is it significant?

What is your scholarly question (e.g., hypothesis)? Provide a discipline-specific context and rationale for the project. Cite appropriate research and/or creative literature using in-text citations.

Currently, bacteria are becoming increasingly resistant to most antibiotics. The lack of available treatments for patients has led to the development of alternative antimicrobial agents such as polymer based treatments. The most common antimicrobial polymers tend to have positively charged groups to allow for the adsorption to the negatively charged membranes of the bacteria. Additionally, antimicrobial polymers contain a hydrophobic portion of the polymer, which interacts with the lipophilic membrane of the bacteria. These polymers behave essentially the same as surfactants, and like surfactants, these polymers suffer problems of dilution in large amounts of solvent. One way to circumvent this problem is to covalently link these surfactant polymers together. A potentially feasible route is through surfactant monomers or “surfmers”. Surfmers possess the properties of regular surfactants (e.g. hydrophilic head and hydrophobic tail), but also contain polymerizable functionality which can be incorporated in the backbone of a polymer based nanoparticle.

Surfmers possess the properties of regular surfactants (refer to Figure 1a), and can be employed in emulsion based polymerizations as an easy route to functional nanoparticles. Owing to the structure of the surfmer, the molecule is covalently incorporated into the nanoparticle with charged quaternary ammonium groups on the surface, and should not suffer from dilution effects. The process that I will use to synthesize these polymer nanoparticles is called miniemulsion. A miniemulsion is a kinetically-trapped, thermodynamically unstable emulsion produced by high-energy homogenization, and usually yields quasi-stable and narrowly distributed droplets with a size ranging from 50 to 500 nm. These droplets can be converted to polymer using a variety of polymerization processes, including photopolymerization. The Patton Group recently published a paper on photopolymerization in miniemulsions as a route to nanoparticles. However, it is not currently known how the size of the charged nanoparticle will influence the antimicrobial activity. A key question remains: Will smaller nanoparticles show increased potency toward killing bacteria?

The objective of this proposal is to design and synthesize polymeric nanoparticles with covalently linked quaternary ammonium functional groups using to “surfmers” in miniemulsion polymerizations to confer antimicrobial properties. This proposal is predicated on the hypothesis that the charged surface of the nanoparticle will provide antimicrobial activity, and that the size of the nanoparticle will significantly influence the killing efficacy. I predict that smaller nanoparticles will be better due to a higher surface area for interaction with microbes. This nanoparticle platform could open the door for future alternative treatments for antibiotic resistant bacteria.

![Figure 1. Synthetic route to develop “surfmers” and charged nanoparticles.](image-url)
Process (approximately 300 words): What will you do to complete your project?
How will you answer your scholarly question? Describe the creative process, research design, and/or methods you will employ. Include a description of materials and equipment necessary to complete the project.

To evaluate the antimicrobial properties of the polymer nanoparticles prepared from surfactant monomers (surfmers), the first step is small molecule organic synthesis. The general structures of the surfmers of interest are shown below in Figure 1a. To synthesize the surfmer library, two organic reactions (Figure 1b) will be performed – including a quaternization of 1 to give 2, and etherification of 2 to give the allyl-functionalized surfmer 3. Previous literature has shown that the length of the hydrophobic tail on the surfactant (or surfmer in my case) directly influences the antimicrobial efficacy. Specifically, a chain length of twelve or fourteen carbons consistently showed the highest antimicrobial efficacy against a variety of microbes. Based upon this literature, a C12 chain length will be synthesized as my initial target for antimicrobial testing, and other chain lengths (C10, C16, C18) will be explored following initial assessment of the first target. With this specific surfmer in hand, I will carry out miniemulsion photopolymerizations to incorporate the surfmer into polymer nanoparticles. For nanoparticle synthesis, monomer, surfmer, photoinitiator, and solvent will be emulsified in water using ultrasonication, which will then be subjected to ultraviolet light to induce polymerization. Within the miniemulsion process, ultrasonication energy and time will dictate the final particle size – parameters that we can control and optimize. With these process parameters, I will synthesize particles that range from 40 nm to 500 nm. Nanoparticles will be characterized by dynamic light scattering and transmission electron microscopy. A critical evaluation of the resulting quaternary ammonium functionalized nanoparticles against a variety of bacteria will be performed, including methicillin resistant bacteria. The nanoparticles will be evaluated for antimicrobial activity via minimum inhibitory concentration and zone of inhibition experiments. These experiments will allow me to test my hypothesis that antimicrobial activity will increase as nanoparticle size decreases. My role in this project will be to synthesize the surfmers and prepare the nanoparticles under the supervision of my graduate student.

Expected Outcomes (approximately 150 words): What will you produce? How will you disseminate your results to others in your field?
Describe the anticipated outcomes, products and/or results of your project and how they will contribute to the scholarly community.

The work will demonstrate a straightforward synthetic route to utilize surfmers for the development of charged polymer nanoparticles as antimicrobial agents. The anticipated outcomes of this research proposal include the following: 1) Developing a surfactant monomer which will have antimicrobial properties; 2) Once incorporated into a nanoparticle via miniemulsion, the surfmer will confer antimicrobial properties; 3) Nanoparticles of different sizes will be controlled by the ultrasonication time and energy, which will in turn, affect the antimicrobial properties. Nanoparticles that show high performance will be evaluated against mammalian cells in order to see if there is any cytotoxicity to non-bacterial cells. The results of this project will be submitted for peer-reviewed publication and further disseminated to the scientific community through presentations at local and regional meetings including the Mississippi Academy of Sciences, Waterborne Symposium, and regional American Chemical Society meetings.

Timeline (approximately 150 words): How will you schedule your time?
Provide a detailed plan for the time you plan to spend on specific phases of your project during the semester.

I currently work 10-19 hours per week in the Patton research lab and will continue this work schedule if this proposal is successfully funded.

Weeks 1-4: Synthesis of a surfmer and subsequent purification and analysis. Surfmers are difficult to synthesize because of their solubility in both organic and aqueous solutions. Additionally, because this approach has not been demonstrated before, there is minimal literature to guide the specific synthesis in the project. Additional time may be required to purify the surfmers via column chromatography.

Weeks 5-10: Incorporation of a surfmer into nanoparticles via miniemulsion polymerization. The optimum nanoparticle size will be determined by varying ultrasonication parameters (sonication time/energy) as well as formulation parameters such as the concentration of different ingredients.

Weeks 11-16: Testing the efficacy of different sizes of antimicrobial nanoparticles. Microbial testing will be performed through standard zone of inhibition experiments to visually compare antimicrobial effects. This timeline is a best estimate.
**Budget:** *How will these funds be spent?*
Standard allocation is $1000 for student stipend to be deposited in the faculty mentor’s developmental account. List each item to be purchased individually; do not aggregate them. See guidelines for items approved for purchase.

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Please indicate any other sources of support you will receive for this project (e.g., Honors College or McNair Program funding, funds from other grants (including those awarded to mentor)).

My mentor, Dr. Patton, will also support this project with funding from NSF EPSCoR Grant: Smart MATerial Design, Analysis and Processing (SMATDAP) Consortium.
Bibliography
Include complete reference list of works cited and consulted in the style most appropriate to the discipline.