I. Intellectual Merit: Bacteria interact with their environment in many ways, but a primary mechanism is through the use of long protein filaments that extend from the surface of the bacterial cell (Fig. 1, upper left). These very strong filaments can grow to be micrometers in length, which is longer than the cell's diameter. Bacterial filaments function as "grappling hooks", allowing bacteria to attach to and move along surfaces, to link together with other bacterial cells, and to attach to cell surfaces in a host organism. My group's work on bacterial filaments is currently funded by the National Science Foundation (NSF) through a Research at Undergraduate Institutions (RUI) grant (Awarded June 2018, $266,149). Recent filaments we have worked on are from *E. coli* bacteria, which they use to attach to the lining of the digestive and urinary tract and cause potentially fatal disease. Our recent work has included experimental collaborators from Umea University in Sweden and Boston University School of Medicine. Together, we try to understand how much force bacterial filaments can resist before they break or detach from the host organism they have infected. Importantly, bacterial filament structures are very similar as they are made up of many copies of a protein called pilin (Fig. 1, upper middle panel, filament with a single pilin highlighted blue). Pilins are proteins made of amino acids, and there can be thousands of them in a bacterial filament. Therefore, they are like the "Lego building blocks" that assemble together to create these dynamic structures. Upon surface attachment bacterial filaments come under extremely high tension forces (some are known to withstand forces 1000 times the bodyweight of the bacteria!). This is because they have to keep holding onto host cells even in the presence of high velocity flow of fluids such as urine and blood. Their ability to do this allows them to create persistent bacterial infections, and therefore these bacterial filaments are considered potential drug targets. This MUSE award will help me to train additional students on this NSF project (for which the funding is almost entirely used), and to continue to expand and strengthen our ties with our experimental collaborators. I have trained more than 30 undergraduates in my lab who have contributed to numerous poster presentations and publications, and I have been able to successfully train students to utilize the TCNJ supercomputer ELSA for simulations during the summer MUSE period previously.

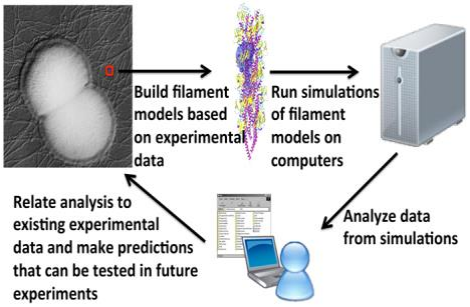

Figure 1. Depicts our research workflow, which involves model-building based on experimental data, computer simulations and data analysis, and making predictions based on that analysis for new experiments.

Our group has made great strides in modeling these systems already through previous SOSA, MUSE, and support during sabbatical via the Gitenstein-Hart Award. This summer, I plan to continue pushing our work on bacterial filaments forward by using our developed computational methods to build models of bacterial filaments and simulate their motion (Fig. 1, upper central and right panels). I will train my two students this summer, [redacted] and [redacted], to engage in this research. Most available experimental (non-computational) methods only provide a few static snapshots of what a protein looks like at a particular instant in time, much like a photograph. Our simulations allow us to create many computational "snapshots" of the filaments and string them together to make a movie of how the system changes over time. Computer simulation is the only current method available to generate a "movie" of filament behavior at the molecular level. The computational research proposed here will provide deep insights into the underlying chemistry and physics that give rise to the biomechanical properties of bacterial filaments. In turn, these insights will provide important leads to the development of novel therapeutics to combat bacterial diseases.

To meet our summer goals, we will closely follow this timeline. During weeks 1 and 2 [redacted] and [redacted] will learn to use the software programs LEaP and Packmol to build initial models of their filament system. They will learn to create input files for our simulation software, AMBER, and learn to perform simulations on TCNJ's High Performance Computing cluster ELSA. In addition to the training I provide them, they will also participate in the TCNJ ELSA supercomputer workshop that I organize and run due to my role as the Chair of the TCNJ HPC Committee along with Mr. Shawn Sivy (TCNJ supercomputer administrator). During weeks 3-5 they will learn to write computer scripts in the Tcl and Python languages to analyze their simulation data (for example, to calculate how much energy is required to extend a bacterial filament under tension). They will also learn how to use the simulation visualization software, Visual Molecular Dynamics. During weeks 6 and 7 they will use these scripts to carry out analysis and will compare the results to our previous work on other filament types. In the final week of MUSE, they will write up their results. This research will contribute towards a publication and will also help to support the submission of future NSF grants beyond my current funding. This research direction in my lab has led to many presentations, and a number of publications, related to bacterial filament work. [redacted] and [redacted] will also present their work at the MERCURY Conference on Computational Chemistry during the summer, and later at a national meeting of the American Chemical Society.

II. Role of Students and Mentor: I am requesting two students, [redacted] and [redacted], for MUSE. We will collaborate to design simulation protocols and scripts, and they will learn to use the tools and software described above in the timeline to set up, run, and analyze their simulations. They will learn how to use our campus supercomputer ELSA. As a chemistry student [redacted] has had little computational training so far. [redacted], a computer science major, will learn about many facets of chemistry, biology and physics that she would not have an opportunity to learn in her major. Therefore, MUSE will greatly broaden their experiences at TCNJ, and they will also learn much from each other. Multiple students are needed for this project, since we have a significant number of overall simulations to run (multiple filament types). I will set weekly goals and interact with both students daily to help them progress towards achieving those goals. They will learn to visualize simulation results using the program, Visual Molecular Dynamics. As MUSE progresses, I will encourage them to become increasingly research independent. We will hold weekly meetings to discuss problems and progress, and they will read and present literature articles to understand their project in a broader context. They will also present posters at the summer MERCURY Conference at Furman University and the fall MUSE poster session, increasing their training in science communication.

III. Broader Impacts: I am in my ninth year, and currently an Associate Professor in Chemistry at TCNJ. The proposed project is central to my overall research program goal of developing a fundamental molecular understanding of biomolecular systems. This project will contribute to strong collaborations I have with faculty at Umea University and Boston University School of Medicine. [redacted] and [redacted] will significantly broaden their scientific and computing knowledge, will present presentations of their work, and will be co-authors on figure papers related to the work. Additionally, women are underrepresented in the computational sciences, and this work will also support both of their interests in post-graduate education by exposing them to authentic mentored research. Furthermore, computational chemistry is an area of research within chemistry at TCNJ that was not represented before I was hired, and I am the only faculty in our department that specializes in this area.