James and Lorna Mack Chair in Bioengineering
Caryn L. Heldt, Chemical Engineering
June 21, 2022

Heldt Bioseparations Laboratory


Caryn Heldt

This report summarizes activities of Caryn Heldt, the James and Lorna Mack Chair in Bioengineering, and her lab from January 1, 2022 through June 30, 2022.

Scholarship

The funding in the lab is strong. Last reporting period we completed three projects. We currently have nine ongoing (see Table 1) for a current total of $7.9M of active funding. All but one project has funding for lab personnel. The lab currently has two postdocs, one technician, five PhD students, one MS students, and four undergraduate students. Bianca Mercado Velez joined the lab as a new PhD student in January.

Table 1: Externally sponsored work in the Heldt Bioseparations Lab

Sponsor	Role	Total Funded	End Date
Ongoing			
Cottrell Foundation: Continuous Bioprocessing of Virus-Like Particles for Vaccine Manufacturing	PI	$435,000	12/31/2022
NIH R21: Dense Phase Electrolytes to Thermally Stabilize Viral Vaccines	PI	$428,620	02/28/2023
NSF DMR: Biomimetic Redox Chemistry for Antiviral Application	Co-PI	$302,958	06/30/2023
Industrial Collaboration	PI	$165,000	12/31/2022
NSF: Collaborative Research: DMREF: A computationally-driven predictive framework for stabilizing viral therapies	PI	$558,044	09/30/2025
Industrial Collaboration	PI	$154,000	09/30/2022
FDA R01: Integrated and Continuous Manufacturing of an Influenza Vaccine	PI	$1,500,000	08/30/2024
MDHHS: MI-SAPPHIRE	PI	$4,375,000	07/31/2024
Total		**$7.9M**	

The lab has published one peer-reviewed paper during the reporting period, as detailed in Table 2. This paper was in collaboration with RPI. Many papers will be submitted in the second half of the year.

Table 2: Publications either published or accepted during the report period
(*__undergraduate student under my supervision__, #graduate student/postdoc under my supervision, +corresponding author)

Sorci, M., Fink,T.D., Sharma, V.#, Singh, S.#, Arduini, B., Dovidenko,K., Heldt,C.L., Palermo,E.F.+, and Zha, R.H.+. (2022) Virucidal N95 Respirator Face Masks via Ultrathin Surface-Grafted Quaternary Ammonium Polymer Coatings. ACS Applied Materials and Interfaces. In Press. doi: 10.1021/acsami.2c04165

The work in the lab can be categorized into four themes that fit into the areas of biophysics, virology, biomaterials, and continuous manufacturing.

Physicochemical Characterization of Virus

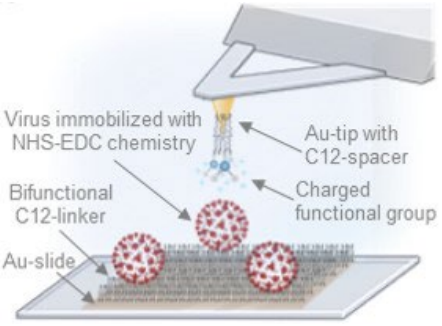

Figure 1: Single particle study of virus particles. An atomic force microscope (AFM) tip is functionalized with different chemical groups and the force between the chemical groups and the virus is measured. [Areo *et al.* 2021]

Most virus studies are either at the molecular scale or the bulk scale. We have developed a method to study virus particles at the single particle level, which is in between the traditional scales. We are learning how virus chemical surfaces change as you change the solution conditions using an atomic force microscope. We are using this method, which was developed using an NSF CAREER award, is now being applied to understand how viruses are stabilized for vaccine formulation, the differences between genetically empty and full viral capsids in gene therapy, how to develop better purification methods for viral particles and to understand how virus hydrophobicity controls adhesion properties. The main technique is shown in Figure 1. I presented on using this technique to study the difference between empty and full AAV particles at the Gordon Research Conference on Vaccines and Biotheraptuetics in Ventura, CA in March 2022. Empty AAV particles are likely a hinderance to the manufacturing of large quantities of AAV gene therapies. AAV has the potential to become a revolutionary cure to some single gene diseases, but manufacturing needs to provide a more pure product.

Stabilization of Viral Vaccines

The COVID-19 pandemic has exemplified the need for better stabilization of viral vaccines at room temperature, or even above, if we are to distribute vaccines across the globe. We understood this prior to the pandemic and received funding in March 2020 to study how polymeric peptides can be used to better thermally stabilize virus. In collaboration with Dr. Sarah Perry at the University of Massachusetts in Amhurst, we are better understanding how dense liquid phases formed by polypeptides can be a next generation vaccine formulation. We are also working with Dr. Perry and Dr. Sapna Sarupria, at the University of Minnesota, who will use machine learning techniques to help us discern the key aspects of compounds to better predict future vaccine formulations.

Antiviral Surfaces and Compounds

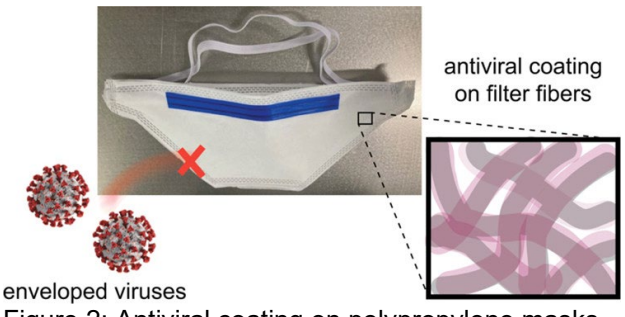

Figure 2: Antiviral coating on polypropylene masks [Sorci et al. 2022].

We have worked with many groups on campus and in industry to discern some key attributes that contribute to antiviral compounds, solution conditions, and surfaces. We are currently working with Dr. Bruce Lee in Biomedical Engineering. We are also working with Dr. Bowen Li in Material Science and Engineering and Dr. Edmund Palermo and Dr. Helen Zhu at RPI (paper published in Table 2 and shown in Fig. 2). We have several papers that will be submitted in the second half of the year on the effect of eco-friendly surfactants and copper ion materials on virus inactivation.

Continuous Manufacturing of Viral Vaccines

Current vaccine processes rely on batch manufacturing. This can cause stability issues with the viral vaccine during manufacturing and is expensive. To reduce the cost and increase the yield, we have several projects focused on the continuous manufacturing of viral vaccines. We have been developing methods to better understand the use of aqueous two-phase systems (ATPS) for the purification of viral particles. Since we have now developed methods to use ATPS to purify viral particles, we now want to develop methods to continuous purify viral particles with ATPS. Our collaboration with Dr. Michael Betenbaugh and Dr. Andrew Pekosz at Johns Hopkins University will expand our work and develop a continuous manufacturing process of a cell-based influenza vaccine.

Education

In January, we submitted an NIH T32 G-RISE trainingship that would provide graduate student funding for students studying in the Health Sciences in collaboration with Dr. Megan Frost in Kinesiology and Integrative Physiology and Dr. Wayne Gersie, Vice President of Diversity and Inclusion. Obtaining this grant will be a big step for Michigan Tech to expand health research and funding for graduate students. It will also provide valuable training for mentors in order to provide a sense of belonging and retain top graduate students.

Service

At Michigan Tech, my service as Director of the Health Research Institute (HRI) has been fruitful. The groundbreaking for the H-STEM building, which will be the first home space for HRI, was in April 2022. We look forward to occupying the building in 2024. We continue to work with MDHHS on genomic surveillance of SARS-CoV-2 variants and the future need to monitor pathogens, including the current avian influenza outbreak. As shown in Table 1, the MI-SAPPHIRE project will use our knowledge of medical testing to further provide valuable information to the state while increasing the capacity at Michigan Tech for genomic sequencing. Other activities as HRI Director include continued work to prepare for the NIH T32 training grant (mentioned earlier), preparing for the H-STEM building governance and safety protocols, and promoting health research and supporting health researchers on campus.

Mentoring faculty is one of my most enjoyable service activities. I currently mentor one Biomedical Engineering Assistant Professor as chair of her Early Career Mentoring committee. I also keep in touch with past mentees of this program as they grow in their careers. The most important thing I can spend time on is mentoring students at all levels and early career faculty. Their success is Michigan Tech's success.

Endowment Funding

Most of the endowment funds go towards funding a technician in my lab. Lynn Manchester has worked in my lab since Nov 2021. Due to the large number of projects, it is essential that Lynn keep everyone in supplies, keeps up to date records of trainings, and assists everyone in their projects. Lynn is involved with several of our projects and helps the students with infectivity assays.