Protein hydrogels based antibody purification columns ($51,000)

Ionel Popa, Ph.D., Assistant Professor, Department of Physics

Dr. Popa's research focuses on developing and implementing new techniques to study the mechano-chemistry of proteins. He uses a tool known as single molecule force spectroscopy to apply force to proteins to better understand their responses to mechanical perturbation. In this proposal, he has utilized this knowledge to create a protein-based hydrogel made of pure soluble proteins in which the proteins utilized contain regions that bind strongly to antibodies. This technology aims to be faster and less expensive compared to current options on the market.

Problems with Antibody Purification. Affinity based antibody purification techniques used for research and phamaceutical production have largely remained unchanged since the 90s. Current formulations rely on proteins derived from bacteria known as proteins A, G, L, and M which evolved to disrupt the immune response in animals. Products today immoblize these antibody-binding domains on the surface of support materials or embedded in semiporous materials. The efficiency is thwarted by the available protein binding sites and concentration. Dr. Popa's team has created a hydrogel using repeats of protein L in order to optimize binding and retention capacity of antibodies. This allows for a reduction in the purification time from hours or days to ~10 minutes. The materials being used are not expected to exceed the production costs of current competitive products.

Market for Antibody Purification. The global antibody market is in excess of $80 B and continues to expand. The major sectors are therapeutic applications, diagnostic testing, and research use. The research use market alone generates $2.2 to $2.7 B per year in revenue. A number of antibody-based therapeutics have been FDA approved in recent years including Humira at $13 B, the number one selling drug in the U.S. Nine antibody-based drugs were approved by the FDA in 2015. The protein purification and isolation market is expected to reach $6.4 B by 2020 due to the increased research in the pharmaceutical and biotech fields and the growing need for rapid purification kits to screen, prepare, purify, and concentrate the protein samples.

Project Objective – Optimize, Develop Prototypes, and Compare to Competitors. The Popa lab already has obtained promising results showing that their protein L version can strongly bind the light chain domains of antibodies in a short time period, and that these antibodies can then be easily eluted from the columns. A protein A and Protein G version will be optimized next. They have also found that linking their hydrogels to a particular sponge-like matrix allows even further surface contact and prevents clogging, a common problem with column systems. To further prevent clogging they will mechanically break the hydrogels into a slurry format and create hydrogel beads of various sizes. Further optimization is required to determine the most effective size and type of hydrogel for the column. Lastly, the shelf-life of the hydorgels must be tested to understand their commercial viability. Ultimately, these studies will lead to prototypes for the creation of a kit for users in both research and industry.

Customer Discovery and Icorps. Dr. Popa and his co-inventor participated in the Milwaukee I-Corps program and conducted 37 customer discovery interviews to explore the academic, biopharmaceutical, antibody production, and blood testing markets. The interviews confirmed that academics are looking for better tools, and that biopharma finds the purification step to be one of the most expensive in the creation of drugs. Antibody production companies were interested in a faster column method. The I-Corps process has been instrumental in training the inventors to think deeply about the commercialization of his invention and the key experiments needed to find licensing partners to bring this technology to market.

Developing an Online Self-administered Psychiatric Diagnostic Program
($50,000)

Hanjoo Lee, Ph.D., Associate Professor, Department of Psychology

Dr. Lee's research focuses on adult psychopathology of anxiety disorders with an emphasis on obsessive-compulsive disorder, social anxiety disorder, and post-traumatic stress disorder. His current research includes several randomized controlled trial studies that aim to develop computer-based cognitive retraining programs for various types of anxiety, and examine their underlying therapeutic mechanisms. He is developing several online assessment systems, and his Catalyst proposal focuses on diagnostic interview software that performs a self-assessment before a visit to their doctor. This system can also help streamline the patient's visit and provide a thorough assessment of their problems related to anxiety.

Problems with Mental Health Assessment. Reliable psychiatric diagnosis is a prerequisite for effective planning and implementation of clinical interventions. Structured diagnostic interviews (e.g., Structured Clinical Interview for DSM-5: SCID-5) are regarded as the gold standard to examine patients' psychiatric statuses. Despite their diagnostic value, structured diagnostic interviews have been virtually discarded or severely underutilized in most clinical settings due to a lengthy administration time (e.g., taking a few hours for complex cases), cost (insurance companies unwilling to reimburse for an interview longer than an hour), and a mechanistic and lengthy process that is perceived as potentially harmful for a therapeutic relationship. Consequently, most clinicians rely on unstructured clinical interviews or subjective impressions to make a diagnostic decision, which may negatively impact the adequate planning of treatment and undermine overall clinical outcomes.

Self-Administered Diagnostic Interview Solution. To overcome these barriers, this project proposes to develop a cost and time efficient self-administered diagnostic interviewing program that can produce reliable diagnostic data for mental health care providers and patients. The preliminary version, OSDI (online self-administered diagnostic interview), has been developed for 21 modules of major depressive and anxiety disorders in DSM-5. The interview process can be tailored to each participant's prescreening response and will last 10-60 minutes, depending on the number of problems presented. The clinician can review the interview results before the visit and track interview outcomes over time. The Catalyst funding will be used to complete programming of the OSDI, recruit 400 patients with various disorders, compare the OSDI interviews with clinician-administered SCID-5, and compare the results.

Commercial Potential for Mental Health Care Providers. This technology is expected to offer mental health care providers, employed at various settings, the ability to efficiently and effectively acquire reliable diagnostic information that will ultimately enhance a patient's treatment planning and overall outcome. Through interviewing psychologists, supervisors, and a director of outcome assessment, Dr. Lee confirmed that his system could reduce time and costs for facilities as well as improve the quality of assessment and treatment of their patients. Either a start-up company created to operate the OSDI system, or a license to a business currently in the field of web-based psychological services, would be the most likely pathway to commercialization. The OSDI technology is expected to enhance the overall quality of mental health care by enabling clinicians to incorporate accurate diagnostic information into their treatment planning and evaluation processes, which would not be feasible using traditional face-to-face clinician-administered structured diagnostic interview methods.

Lightweight, Powered Hand Rehabilitation Glove, ($45,000)

Mohammad Rahman, Ph.D., Assistant Professor, Department of Biomedical Engineering/Mechanical Engineering

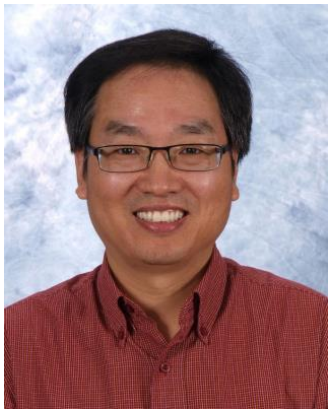
Dr. Rahman's laboratory conducts research on a variety of robots for use in biomedical applications. Examples include wearable robots, rehabilitation robotics, exoskeleton robots (for rehabilitation & motion assistance), human-assist robots, service robots, surgical robots, and medical robots. A second line of research involves intelligent system and control which includes nonlinear control, artificial intelligence, neural networks, fuzzy systems, fuzzy-neuro control, adaptive control, control using bio-logical signals (such as electromyogram signals), autonomous navigation, and tele-robotics. Dr. Rahman's team has been very active in our Milwaukee I-Corps program. He has participated on two teams that have explored robotics-based technologies. This proposal focuses on a new device for physical therapy of the hand.

Lack of Sufficient Therapy Devices. Finger impairment following stroke, trauma, sports injuries, occupational injuries, spinal cord injuries, and orthopedic injuries, results in significant deficits in hand manipulation and the performance of everyday tasks. The conventional therapeutic approach requires a long commitment by a therapist or clinician. Unfortunately, there is a consistent shortage of qualified physiotherapists/clinicians. Besides this factor, the treatment duration is usually very long, requiring many hours of the therapist's time for each individual patient. Moreover, the number of such cases continues to grow. Therefore, an alternative to these conventional treatments is essential. One of the novel and rapidly expanding technologies in rehabilitation, that enhances the recovery process and facilitates the restoration of function, is the use of robotic rehab devices. Current devices for the hand, however, lack the capacity to fully explore the space of possible training paradigms. Particularly, they cannot provide the independent joint control and levels of velocity and torque required**.**

A Novel Device for Hand Rehabilitation. In this research, a portable, lightweight, low cost, and novel powered-hand rehabilitation glove (PHRG) will be developed to be used at home and/or clinics to provide every variety of therapeutic finger movements to a wide group of patients with different degrees of fingers impairments. The proposed PHRG will be controlled with five linear actuators. A pilot study will be conducted to evaluate the proposed PHRG where the subject will be trained to use the developed PHRG and the hand-held controller to perform/choose the therapeutic exercise recommended by the therapists. An OT (occupational therapist) will evaluate the subject and train that subject to use the developed PHRG. After successful completion of training, the PHRG will be given to the subject to use for one week at home to perform the exercises as recommended by the OT. One week later, the subject and the OT will meet again to evaluate the recovery progress. It is expected that the proposed PHRG will significantly improve a subject's finger joint movements and strengths.

Customer Discovery and Value Proposition. Dr. Rahman's team conducted 42 interviews with therapists, clinicians, and disabled individuals and discovered extensive results and key conclusions. They determined that OTs are the key customer demographic in the therapy field. The team learned that a rehab device may be covered by insurance if justified by OT and the cost is below $2000. OTs below age 35 are interested in new, customizable therapy technology. In speaking to patients, the biggest concerns are cost of therapy. In many cases, high costs of therapy visits lead to dropout. Providing home therapy was a top preference throughout the interviews. There is a definitive need for portable therapeutic devices catered to individual finger joint movement. The unique value proposition for this device is better patient compliance, faster rehab, use in the home, lower cost for patient and insurance, increased convenience and independence of the patient, and greater throughput for clinicians.

A new two-line male sterility system for sorghum hybrid breeding, ($45,000)



Dazhong (Dave) Zhao, Ph.D., Professor, Department of Biological Sciences

Dr. Zhao's lab has a long-term goal of understanding the molecular mechanisms regarding cell differentiation and plant development using molecular, genetic, cell biological, and systems biology approaches. Specifically, his laboratory is looking at the anther, the male part of a flower which produces pollen, to elucidate how somatic and reproductive cells differentiate. They are also studying microRNAs, which have emerged as crucial regulators of gene expression, and the role that they play in controlling the auxin signaling network during plant development. This project is a collaboration with a co-inventor from the USDA (United States Department of Agriculture) in which a new male sterile mutant was discovered in sorghum. This mutant will be utilized to create a new sorghum breeding system.

Current Limitations in Sorghum Breeding. Cytoplasmic Male Sterility (CMS) is exclusively employed in sorghum hybrid breeding; however, the CMS hybrid breeding system requires three lines (or genetically distinct varieties) simultaneously, which is complicated and expensive. In addition, the CMS hybrid breeding system is not able to breed hybrids that are 1) resistant to some devastating diseases or 2) suitable for bioenergy production. The Nuclear Male Sterility (NMS) based two-line hybrid breeding system can be employed to solve these problems in some crops, such as rice, however, no NMS hybrid breeding system has been used to produce hybrid seeds in sorghum. Furthermore, the presence of A1 cytoplasm (a type of male sterile cytoplasm predominantly used in sorghum breeding) in almost all commercial hybrids may predispose sorghum to devastating diseases, like the outbreak of Southern Blight disease to maize hybrids in the 1970s.

New Solutions for Sorghum Breeding. Dr. Zhao and his collaborator found an easily recognizable sorghum male sterile mutant, *ms8*. Their goal is to develop a new two-line NMS hybrid breeding system for breeding sorghum hybrids via bioengineering approaches. A novel transgene construct is being designed to ultimately create a bridge plant harboring the ms8 mutation in both copies of the gene, and thus capable of being used for the production of pure male sterile plants for the breeding of any lines. A key benefit is also found after breeding; any progeny will be transgene free. Another safeguard of this system includes a marker of the transgenic seeds. This marker produces a red fluorescent protein making it easier to sort and separate the transgenic seeds. The successful implementation of this technology will substantially simplify sorghum breeding and make it possible to breed all types of sorghum hybrids.

Commercial Opportunity for Sorghum. Sorghum is the fifth most important grain crop in the world. Moreover, sorghum has emerged as a dedicated bioenergy feedstock for sugar, biomass, and biofuel production. The market value of sorghum was $15.5 B in 2015 and is projected to reach $26.6 B in 2017, making the U.S. the largest producer of sorghum in the world. Compared to maize and rice, the lack of widely applicable hybrid breeding systems cannot meet rapidly increasing demands for sorghum production. Many sorghum producers are providing healthier product offerings based on the increasing demand for sorghum as a better substitute in a variety of food products. Sorghum's versatility gives it the elasticity to reach beyond traditional markets, further enhancing a producer's productivity. Companies are forming joint ventures and making agreements to meet the rising sorghum demand. Investors are strengthening its presence in sorghum industry through mergers and acquisitions.