1. **Nano-patterning Biomimetic ECM Cues to Engineer 2D Cardiac Tissue**
   Participating Labs/Departments: Feinberg lab, Biomedical Engineering, Materials Science and Engineering  
   Location: PTC  
   Primary Investigator: Adam Feinberg  
   Research Description: The goal of this project is to develop an improved 2D engineered cardiac muscle tissue using a biomimetic ECM micropattern based on ECM architecture in the embryonic heart. Previously work in the Feinberg lab has demonstrated that a first-generation biomimetic pattern of FN based on FN in the ventricular wall of the embryonic heart can be used to engineer 2D cardiac muscle with unique functional properties. The proposed research will develop a second-generation biomimetic pattern that more closely matches the length scale of FN fibers in the native heart. To do this we will use the Nanoscribe, a 3D laser lithography system that allows for sub-micron spatial resolution. A sub-micron resolution biomimetic pattern presents an improvement to the previously used microscale patterns and can be created using high-resolution images of the extracellular matrix (ECM) architecture of the chick embryonic heart. Since cardiomyocyte alignment in engineered tissue is dependent on directional ECM cues, a more accurate map of ECM in the native heart may yield increased alignment of such tissue. This second-generation biomimetic pattern will then be tested along with the first-generation pattern and a control 20x20 µm line pattern to show the variation in cardiomyocyte alignment. Cell actin alignment will be measured using immunostained images of cells and custom MATLAB software. These experiments will then be repeated using human induced pluripotent stem cell derived cardiomyocytes making this study more relevant to human cardiac therapies.  
   Major/Course/Skill Prerequisites: Cell culture, microcontact printing, immunofluorescent staining, confocal imaging, image analysis

2. **Project Title: Artificial Lungs for Destination Therapy**  
   Participating Labs/Departments: Cook lab (CMU BME) and the Allegheny Singer Research Institute  
   Location: Pittsburgh Technology Center and Allegheny General Hospital  
   Primary Investigator: Keith Cook  
   Research Description: The goal of this project is to develop an artificial lung for destination therapy. The project will combine artificial lung construction and in vitro and in vivo testing. This testing will focus primarily on blood-biomaterial interactions in these devices and their long-term viability. Accordingly, the student will examine the effect of various surface modifications on blood coagulation in the devices.  
   Clinical Exposure (Required for SURP in BME at CMU): Research rotations as required by the Carnegie Heart Program  
   Major/Course/Skill Prerequisites: The ideal student will study BME as well as either mechanical engineering, material science, or chemical engineering.

3. **Project Title: Cardiovascular Imaging Content Analysis**  
   Participating Labs/Departments: Cardiovascular MRI
4. **Project Title: Effects of fluid shear stress on endothelial cell structures leading to changes in gene expression**

Participating Labs/Departments: Kris Noel Dahl - Biomedical Engineering, Chemical Engineering
Location: Doherty Hall
Primary Investigator: Kris Noel Dahl
Research Description: Our laboratory investigates the role of mechanical forces on endothelial cells which line the inside of blood vessels. Specifically, we look at how fluid shear stress, both physiological levels and pathological levels influence the reorganization of cellular structures including the actin cytoskeleton and the nucleus. Using a combination of live cell fluorescence imaging, recombinant DNA expression, cellular manipulation with growth factors and shear flow and image analysis algorithms, we determine how the integrated mechanical structures of the cell turn mechanical forces in to a coordinated response in gene expression.
Major/Course/Skill Prerequisites: We are looking for students who have interest in tissue culture of human cells, microscope, computation and fluid dynamics to help in our studies of cardiovascular disease and endothelial cell function.

5. **Project Title: Controlled Release Systems for Improved Treatment of Intracranial Aneurysms**

Participating Labs/Departments: Bettinger (CMU) and Horowitz (AHN)
Location: Carnegie Mellon University
Primary Investigator: Chris Bettinger
Research Description: Brain aneurysms are a high risk condition in which bulging blood vessels in the brain are at risk of rupture. The mortality rate after rupture is 30-60% if no treatment is administered. Current treatment for both ruptured and unruptured aneurysms includes surgical clipping (exovascular therapy) and catheter based intervention (endovascular therapy). The latter, which is the focus of this work, places platinum coils into the aneurysm to induce clotting and sequestration of the aneurysm. The primary challenge associated with endovascular aneurysm therapy is the risk of aneurysm recurrence due to mechanical compaction and enzymatic digestion of the clot in the aneurysm sac. This proposal will produce a novel, cost-effective, clinically translatable strategy to improve the outcome of endovascular coiling of intracranial aneurysms. We posit that sustained release of naturally-occurring crosslinking agents delivered from coated endovascular coils will increase the mechanical stiffness of the clots and reduce fibrinolysis. Stabilized clots will be resistant to failure modes associated with coil compaction and enzymatic degradation. This approach will be validated in vitro during this project. Research activities will focus on characterizing the dosing and release of bioactive crosslinking agent from polymeric coatings. In vitro efficacy will be demonstrated using a model
aneurysm sac under flow of whole blood. The results from this project will be used to define specific formulations and dosing ranges for use in prospective in vivo experiments using a canine pouch model for intracranial aneurysms. Pre-clinical studies will establish safety and efficacy of drug eluting embolization coils. This technology has the potential to dramatically improve outcomes related to coil embolization of intracranial aneurysms.

Clinical Exposure (Required for SURP in BME at CMU): Will work closely with Horowitz on in vivo animal experiments.

Major/Course/Skill Prerequisites: MSE/BME with at least junior standing
6. Project Title: Apical Torsion Device for Circulatory Support

Participating Labs/Departments:
1. Circulatory Support Lab, Biomedical Engineering Dept., Carnegie Mellon Univ. (CMU)
2. Cardiothoracic Surgery Dept., Allegheny General Hospital (AGH)

Location: Carnegie Mellon University & Allegheny General Hospital, Pittsburgh, PA

Primary Investigators:
Dennis R. Trumble, PhD (Asst. Research Professor, CMU)
Walter E. McGregor, MD (Director, Robotic & Minimally Invasive Heart Surgery, AGH)

Research Description:
The technology under development is called an Apical Torsion Device (ATD), which is designed to enhance the pumping action of a failing heart by effectively ‘wringing’ blood from both the right and left ventricles concurrently. This is accomplished by attaching a rotary actuator to the apical aspect of the heart so that the apex can be turned counterclockwise (as viewed from the apex) with respect to the base of the heart. The applied torsion serves to restore the natural wringing motion observed to occur in healthy hearts—a contractile trait that is far less prominent in diseased hearts. The rotary actuator is placed on the epicardial surface of the heart so as not to contact the blood and can be used to provide supra-normal torsion (20 degrees or more) to improve ventricular emptying. Device actuation coincides with the systolic phase of the cardiac cycle and will increase ventricular ejection fraction directly by mechanical means and indirectly by lowering myocardial wall stress. The actuator can conceivably be powered electrically, pneumatically, or by low-volume hydraulics.

The primary objective of the research to be performed during the course of this Fellowship Program is to design a second-generation prototype device with special emphasis on optimizing cardiac interface surface characteristics (i.e., device fixation) and developing a minimally invasive transcostal deployment system.

Clinical Exposure:
During the course of this work the Fellowship recipient will have the opportunity to participate in the following clinical activities:
1. Open heart surgery observation to develop a technical appreciation of surgical methods, application of cardiopulmonary bypass, echo technology for cardiac imaging, and anesthesia technology for patient monitoring.
2. Patient rounds in the ICU to gain exposure to critical care technologies and also up-close encounters with ventricular assist devices, extracorporeal membrane oxygenation (ECMO), and cardiac transplantation.
3. Patient rounds on the floor to reinforce the human side of surgical medicine and medical device development.
Major/Course/Skill Prerequisites:
Fellowship recipients must have a firm understanding of global cardiac mechanics and a strong background in Computer Aided Design (CAD).
**Project Title:** Parallel Wire Robot for Epicardial Interventions  
**Participating Labs/Departments:** Surgical Mechatronics Lab, Robotics Institute  
**Location:** NSH A406  
**Primary Investigator:** Cameron Riviere (camr@ri.cmu.edu) / Michael Passineau (AHN)  
**Research Description:**

**Project Overview**

Gene therapies have emerged as a promising treatment for congestive heart failure, yet the lack a method for minimally invasive, uniform delivery. To address this need, we have developed Cerberus, a planar parallel wire robot for minimally invasive myocardial injections, shown in Fig. 1(a)-(c). The device is inserted using a subxiphoid approach that accesses the heart while avoiding the lungs. Flexible arms then allow the device to expand into a triangular shape and adhere to the surface of the beating heart with suction on its three bases, providing a stable platform with no motion relative to the heart. Wires from each base connect to an injector head that moves within the triangular support structure by changing the wire lengths. This design has the typical advantages of parallel wire robots, namely a large workspace and the ability to move quickly within this workspace. These advantages give the device the potential to deliver multiple injections accurately within the entirety of the workspace to the beating heart.

**Prior Work**

Work to date on this project has focused on the design, construction, and demonstration of prototype end-effectors and control hardware as well as the development of a hybrid control architecture that controls position and force simultaneously. While the device has been successfully demonstrated in live animal porcine models, there exists a significant need for the further development of the hybrid control scheme. Although the heart is a curved, and dynamic surface, the current control scheme assumes that the device is planar. This control scheme has been developed and demonstrated on a benchtop setup, shown in Fig. 1(d) below.

**Proposed Student Research**

The next step in moving this device towards clinical relevancy is to address the issues of the curved geometry of the heart as well as the dynamic nature of the heart. The first step in accomplishing these goals is to extend the forward kinematics and statics to arbitrary curved surfaces for the hybrid controller. Validation of this work will be carried out on a modified desktop set-up that must be designed and manufactured. These experiments will compare the performance of the curvature-compensating controller with the performance of assuming that the device is planar.

The next step in development will be to deploy the device on a rubber beating heart model in the laboratory, and to implement motion compensation into the control scheme. This will likely be achieved using feedforward control signals to account for the periodic deformation of the heart.

**Major/Course/Skill Prerequisites:** Controls, CAD, Matlab
Fig. 1. Triangular manipulator for rapid accurate myocardial injection for gene therapy. (a) The manipulator collapses for endoscopic insertion and removal. (b) After insertion, it deploys in triangular shape, with its three corners grasping the epicardium with suction. By pulling the 3 cables, injections can be rapidly and accurately placed anywhere within the dotted triangle. (c) Modified Cerberus geometry enables access to the entire left ventricle by placing distal suction bases on the anterior and posterior surfaces of the heart. (d) Desktop set-up with three bases fixed on a platform, where the left and right base can be set to various lengths, and a mounted camera.
8. Project Title: Interactive Neurorehabilitation
Participating Labs/Departments: Robotics, Design (and I hope) Bioengineering
Location: MM A1
Primary Investigator: Thanassis Rikakis (vice provost for design, arts and technology, professor of design, courtesy appointment in BME)
Research Description: The Interactive NeuroRehabilitation group at Carnegie Mellon University (INR@CMU) brings together computing, engineering design and arts knowledge to develop systems that evaluate and deliver feedback on a patient’s movement computationally to promote active learning and enhance the process and outcomes of sensorimotor rehabilitation. The group collaborates with medical and rehabilitation experts from Emory University, University of Pittsburgh and Rehabilitation Institute of Chicago, with engineering and arts faculty from Arizona State University and with perceptual computing colleagues from Intel.

Currently the group is developing a low cost/low power system for unsupervised home-based interactive rehabilitation of the upper extremity of stroke survivors. The system aims to improve functionality and movement quality in an integrative manner. It is highly adaptive so it can address all levels and types of impairment. The system is lightweight (consisting of one camera, a training mat, an array of training objects, a computer and a table interface) and can be adapted to be used on almost any table-top at the home with minimal disruption to the home environment.

Research issues being tackled by the team include:
- Precise and detailed computational tracking and understanding of upper extremity functional movements (including detailed tracking of end effector and digits and coarse tracking of torso movements) in high uncertainty contexts
- Quantifying movement quality evaluation and extracting relation of movement components to overall task performance
- Development of modular training object arrays that facilitate adaptive training
- Use of smart skins on training objects that can be combined with innovative computer vision approaches for tracking hand and finger activity
- Development of multimodal feedback structures that can assist self-assessment and promote active learning across multiple activity scales (from component to complex task) and time scales (from real time to aggregates of performance across multiple training days).
- Development of intuitive interfaces for system users (including the stroke survivor, the partner and the therapist)
- Use of participatory design for structuring effective, adaptive training experiences
- Development of semi-automated adaptive protocols for therapy that are informed by expert input and computational analysis and that customize dosage, sequence, challenge level and experience to user ability, performance, progress and preference.

Clinical Exposure (Required for SURP in BME at CMU): The system will be tested through clinical studies in our three partner clinical institutions: University of Pittsburgh Medical School, Emory University Medical School, Rehab Institute of Chicago/Northwestern
Major/Course/Skill Prerequisites: Bioeng or Mech or SCS or EE students: Students could do work in smart object development, clinical study development and implementation and related analytics, computer vision for interactive neurorehab, system design. Advanced undergraduate course experience in the area of interest is required.