As the underlying cause of 35% of all deaths in the United States and an annual cost of $500 billion, cardiovascular disease has tremendous societal impact. The recent evidence of relationships between cardiovascular disorders and hemodynamic stresses motivates the elucidation of cardiovascular pathology via a mechanobiological approach. This strategy, based on the exploration of the relationships between tissue biology and its hemodynamic environment, has the potential to limit this human and economic burden by enabling the discovery of new treatments, diagnosis tools and patient-specific treatment strategies.

In pursuit of this goal, my doctoral research will focus on the experimental and computational characterizations of the flow through native aortic valves (AVs) under physiologic and pathologic states. The AV is a dynamic trileaflet structure that regulates blood flow between the left ventricle and the aorta and that interacts closely with the surrounding hemodynamic environment. Calcification, the most common AV disease, results in the progressive stiffening of the valve leaflets and can lead, in turn, to a reduction of the effective valve orifice area. Although this condition is presumed to be triggered by pathological alterations in the local shear stresses experienced by the valve leaflets, the fluid stresses triggering the calcification pathway are still unknown. In order to fill this knowledge gap, this study will characterize the flow fields through realistic AV models mimicking the structure and mechanics of native AVs under physiologic (normal AV) and pathologic (bicuspid AV, stenotic AV) states.

The characterization of the valvular fluid mechanical environment is the first step toward the elucidation of the role played by the surrounding hemodynamics in disease initiation and progression. Ultimately, knowledge of the fluid shear stress alterations experienced by the valve during its transition from normal to diseased states could be exploited to establish the sequence of molecular events involved in the early stage of the disease. The integration of those relationships into the computational flow model developed in this research will permit the design of groundbreaking computer-aided diagnosis tools that will help anticipate the onset of the disease and guide the selection of the most appropriate treatment strategy on a patient-specific basis. The novel experimental flow diagnostic tools developed in this research could also be used for the assessment and optimization of heart valve prostheses such as percutaneous valve endografts, which show promise as a minimally-invasive AV replacement solution.

Part of my research project also contains two educational outreach components. During the course of my PhD, I will supervise undergraduate students who will assist me in my research. The second component will consist of designing and presenting an educational display for the local HealthWorks! Kids’ Museum aimed at demonstrating the effects of cardiovascular risk factors on health. The objective of this outreach initiative will be to expose children to cardiovascular risk factors, disease and treatments. For this purpose, I will develop a simplified portable circulatory flow loop mimicking the human circulation through the major organs and
arteries. The modular aspect of the design and the use of air bubbles will allow children to visualize the effects of different cardiovascular diseases (e.g., atherosclerosis, AV calcification, hypertension) on blood flow.

### AV Model Development
- Normal trileaflet
- Stenotic trileaflet
- Bicuspid
- Kinematic validation

### PIV Study
- Flow loop construction & validation
- Flow characterization

### FSI
- Tissue mechanic properties
- AV anatomy reconstruction
- Computational flow characterization

The first aim of the project is to design a flow loop that will allow an *in vitro* study on porcine AVs. This loop will represent the flow from the left ventricle through the AV into the aorta. Two other tissue valve models will also be studied: a stenotic (calcified) AV and a bicuspid valve (BAV) which has two leaflets and is known to be prone to calcification. Validating the loop will be done by comparing pressure and flow rates of the loop to well-documented physiological conditions. The AV models will be validated by comparing the kinematics of the leaflets to MRI scans of native leaflets provided by the local hospital.

In the second aim, stereo particle image velocimetry (PIV) measurements will be conducted to characterize the flow through the three valve models. Additionally, the experimental determination of the shear stress experienced by the leaflets will be achieved by developing new algorithms based on the interpolation of the velocity field in the boundary layer of the leaflet. The algorithm will be validated by implementing it on benchmark flows (e.g., Couette and Poiseuille flows).

In the third aim of this project, the new ANSYS Multiphysics Solver will be used to model the flow through the different AV anatomies. The approach will consist of a fluid-structure interaction (FSI) model that will account for the complex coupling between the blood flow and the associated leaflet deformations. Computed tomography scans of porcine AVs will be used to reconstruct the valve geometry and the material properties of the valve will be measured by a biaxial machine and used in the computational model. The FSI model will be validated with respect to the PIV and leaflet kinematics measurements. The model will then be implemented to predict the shear stress distribution on the surface of AV leaflets under normal and diseased states. This data will provide new insights into the hemodynamic stresses experienced by valve leaflets under pathologic conditions. Ultimately, this knowledge will be exploited to quantify the effects of pathologic hemodynamics on the onset and progression of valvular disease.

### References