Physics Colloquium
Thursday, October 10, 2019
316 Lewis Lab.
4:25PM
Refreshments at 4:00PM

“Multiscale modeling of the human blood protein von Willebrand Factor”

Speaker: Edmund Webb
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The glycoprotein von Willebrand Factor (vWF) plays a crucial role in forming blood clots upon vascular injury. vWF molecules adopt a compact conformation in typical blood flow but, subject to hydrodynamic forces in regions where flow rate is high, they undergo significant elongation, revealing binding sites for platelets in blood and collagen exposed on damaged vessel walls. In this fashion, vWF molecules initiate clot formation. We have formulated a multiscale simulation platform of vWF, directly coupled to experimental investigation via single molecule force spectroscopy and microfluidic imaging. Herein, results from all-atom simulations of the A2 domain subject to external pulling forces will be presented. This domain has been identified as a possible governing unit for vWF binding to both collagen and platelets. Results from molecular dynamics simulations are used to parameterize hydrodynamic drag experienced by monomers in our coarse-grain model as well as the coarse-grain monomer’s mechanical behavior. Furthermore, all-atom simulations inform the coarse-grain model’s description of binding between vWF and collagen. Results from Brownian dynamics coarse-grain molecular simulations will be presented of vWF behavior in shear flow and when bound to model collagen. Results in shear flow provide strong evidence that scission of vWF molecules - critical to maintaining a functional size distribution of the protein - occurs preferentially near the center of vWF multimers. Coarse-grain simulations of vWF-collagen binding in shear flow permit a more detailed description of the possible role played by A2 domains in governing this reaction.

The Webb research group applies simulation techniques across multiple length and time scales to elucidate fundamental phenomena controlling the thermo-mechanical response of materials. Current studies include the coupling between protein conformation and flow conditions in human blood, capillary driven fluid flow, stress evolution in nanostructures and thin films, and mass and heat transport processes at interfaces between dissimilar materials. Prior to joining Lehigh in 2010, Webb spent 12 years with Sandia National Laboratories in Albuquerque, NM. As a national laboratory research scientist, Prof. Webb applied high performance computing resources to a range of materials and mechanics problems, including capillary driven fluid flow, friction mitigation, stress evolution in thin films, nanoscale thermal transport, and liquid droplet impacts.