TEMPLE UNIVERSITY
Department of Mathematics

Applied Mathematics and Scientific Computing Seminar

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Nonlinear Structural Mechanics and Transport Properties of Blood Clots

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Abstract.

To restrict the loss of blood following rupture of blood vessels, the human body rapidly forms a clot consisting mainly of platelets and fibrin. Fibrin network is a major structural component of protective hemostatic clots an pathological obstructive thrombi that largely determines their mechanical stability in response to external loads including shear and compressive forces. In this work we show that fibrin displays unique mechanical and structural properties in response to external load and plays an important role in regulating transport of proteins in blood clots. We showed that fibrin networks revealed a unique nonlinear mechanical behavior characterized by a dual softening-stiffening transition as the networks were exposed to compressive loads, with softening occurring at small and intermediate compressive strains, while hardening developing at larger degrees of compression. Using a combination of confocal microscopy and rheological measurements, we demonstrated that these non-linear mechanical properties originated from structural rearrangements of the entire fibrin network, as well as alterations of individual fibers including fiber buckling, bending and reorientation. The network hardening strongly correlated with an increase in the number of intersecting fibers, resulting from densification of the compressed network and reorientation of the whole fibrillar network toward a planar structural architecture perpendicular to the direction of negative strain. We model this nonlinear behavior using a continuum theory of phase transitions and analytically predict the storage and loss moduli which are in good agreement with the experimental data. By integrating experiments in microfluidic devices with the hemodynamic thrombus model we also examined the role of the fibrin network in protein transport. We demonstrate that permeability of the fibrin network and protein diffusivity are important factors determining the transport of blood proteins inside the thrombus. It is shown that in in silico thrombus module the fibrin network does not dramatically limit the diffusion of thrombin but impaired flowing platelets in blood from reaching regions of high thrombin concentration thus, reducing the probability they are activated and stably integrated into the thrombus. This novel, counter-intuitive mechanism suggest that a fibrin network formed at early stages of thrombus initiation can prevent normally asymptomatic thrombi from developing into pathological clots.