Nonlinear mechanics of fibrin networks

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Fibrin is an insoluble polymer, the product of conversion of soluble plasma protein fibrinogen in response to damage of the vascular system. Fibrin forms a porous network of branching fibers that provides the scaffold of protective hemostatic blood clots and pathological obstructive thrombi. The structure and properties of the fibrin, including mechanical response to stresses generated by blood flow and during clot contraction, determine the course of pathological conditions, including bleeding, ischemic stroke or coronary heart disease.

Using precise dynamic microscopic and rheological measurements we have suggested a model for the fibrin network compression behavior based on the theory of foams. The compression stress-strain curve was measured in experiment along with the loss and storage moduli at various strains with simultaneous confocal microscopy of the fibrin network during the deformation. We showed that fibrin network compression response significantly depends on compression rate and protein concentration. Our results indicate a tri-phasic mechanical response of the network to compression. In addition to the non-linear behavior of storage and loss moduli, we were able to reveal the non-uniformity of the compressive deformation with formation of a "compression front" or "phase boundary" along the direction of compression. Combining collagen with fibrin resulted in formation of a composite hydrogel exhibiting synergistic mechanical properties compared to the isolated fibrin and collagen matrices. Specifically, the composite matrix revealed a one order of magnitude increase in elasticity in response to compression compared to the mechanical features of individual components.

Using a continuum theory of phase transitions, we explained the storage and loss moduli of the networks while accounting for the contributions of the moving phase boundary as well as the viscoelasticity of each phase. By implementing a discrete model approach we also demonstrated how structural characteristics such as length and orientation of individual fibers alter when the network is subjected to external tensile, shear and compressive stresses. Additionally, these simulations show how shape and volume of the entire network and its stress-strain response dramatically depends on the network initial alignment and mechanical properties of individual fibers. Predictive simulations successfully recapitulated the appearance of compression front in fibrin networks under unidirectional load as well as softening of the compressed fibrin gel. Our experimental and modeling results provide new insights into the structural biomechanics of the polymeric matrix that can help to create fibrin-based sealants, sponges, and tissue scaffolds with tunable and predictable mechanical properties.