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Multiscale self-assembly of fibrin governs its polymerization kinetics, fiber and network structure, as well as nonlinear rheological properties

N A Kurniawan[1], J Grimbergen[2], K Jansen[1], I K Piechocka[3], J Koopman[2] and G H Koenderink[1]

[1]FOM Institute AMOLF, The Netherlands, [2]ProFibrix BV, The Netherlands, [3]ICFO-Institut de Ciencies Fotoniques, Spain

Fibrin is a fibrous biopolymer that forms a tough three-dimensional mesh and clots the blood in a wound site. This network needs to be sturdy yet extensible under shear to sufficiently protect the area during healing. At the same time, the structure of the self-assembled network needs to be precisely controlled to allow timely breakdown of the clot, which could otherwise present thrombotic complications. Studying the structure and mechanics of fibrin clots is therefore important not only in understanding the molecular origins of their behavior and regulation in various diseases, but also in designing hemostatic materials, particularly in surgical settings.

By monitoring and analyzing the scattering of self-assembling fibrin gels, we identified different temporal stages in which fibrils aggregate laterally to form floppy fibers, followed by slow compaction of the fibers. These stages are reflected in the fast (10 min) and slow (hours) development of the elastic modulus. Furthermore, we have found that fibrin gels stiffen nonlinearly with stress, and comparison to theoretical model reveals that the stiffening regimes are linked to the different deformation modes at fiber and network levels. Interestingly, the rheological response shows multiple plateau-stiffening steps, a behavior unique to fibrin gels. Moreover, the presence of Factor XIII, a natural cross-linker of fibrin, is found to alter both the polymerization kinetics and time-dependent rheological response. However, the behavior of uncross-linked and cross-linked gels collapse onto a single curve at large stresses, suggesting that single fibril mechanics dominates at large deformations. By combining rheological studies with microstructural characterization using microscopy and turbidity measurements, we propose a model to explain how the hierarchical structure of fibrin network is interconnected with its mechanics at multiple length- and time-scales.