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Strength and deformability of fibrin clots: Biomechanics, thermodynamics, and mechanisms of rupture

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ABSTRACT

Fibrin is the major determinant of the mechanical stability and integrity of blood clots and thrombi. To explore the rupture of blood clots, emulating thrombus breakage, we stretched fibrin gels with single-edge cracks of varying size. Ultrastructural alterations of the fibrin network correlated with three regimes of stress vs. strain profiles: the weakly non-linear regime due to alignment of fibrin fibers; linear regime owing to further alignment and stretching of fibers; and the rupture regime for large deformations reaching the critical strain and stress, at which irreversible breakage of fibers ahead of the crack tip occurs. To interpret the stress-strain curves, we developed a new Fluctuating Spring model, which maps the fibrin alignment at the characteristic strain, network stretching with the Young modulus, and simultaneous cooperative rupture of coupled fibrin fibers into a theoretical framework to obtain the closed-form expressions for the strain-dependent stress profiles. Cracks render network rupture stochastic, and the free energy change for fiber deformation and rupture decreases with the crack length, making network rupture more spontaneous. By contrast, mechanical cooperativity due to the presence of inter-fiber contacts strengthens fibrin networks. The results obtained provide a fundamental understanding of blood clot breakage that underlies thrombotic embolization.

Statement of significance

Fibrin, a naturally occurring biomaterial, is the major determinant of mechanical stability and integrity of blood clots and obstructive thrombi. We tested mechanically fibrin gels with single-edge cracks and followed ultrastructural alterations of the fibrin network. Rupture of fibrin gel involves initial alignment and elastic stretching of fibers followed by their eventual rupture for deformations reaching the critical level. To interpret the stress-strain curves, we developed Fluctuating Spring model, which showed that cracks render rupture of fibrin networks more spontaneous; yet, coupled fibrin fibers reinforce cracked fibrin networks. The results obtained provide fundamental understanding of blood clot breakage that underlies thrombotic embolization. Fluctuating Spring model can be applied to other protein networks with cracks and to interpret the stress-strain profiles.

1. Introduction

Fibrin, a naturally occurring biomaterial, is the main mechanical component of blood clots, and it plays a paramount role in stemming bleeding and wound healing. The gelation or coagulation of blood is an evolutionary mechanism geared to sealing the circulatory system and preventing blood loss in the event of injury. The formation of a blood clot that plugs a vessel wall injury results from enzymatic conversion of the soluble plasma glycoprotein, fibrinogen, into a polymeric insoluble fibrin clot, the reaction preserved across all vertebrate species from fish to mammals [1,2]. Fibrin formation begins with the thrombin-catalyzed cleavage of fibrinopeptides from fibrinogen, resulting in the conversion of fibrinogen into fibrin monomers. Fibrin monomers self-polymerize

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