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Forced Unfolding of the Coiled-Coils of Fibrinogen by Single-Molecule AFM ANDRE BROWN, RUSTEM LITVINOV, DENNIS DISCHER, JOHN WEISEL, University of Pennsylvania — A blood clot needs to have the right degree of stiffness and plasticity for hemostasis, but the origin of these mechanical properties is unknown. Here we report the first measurements using single molecule atomic force microscopy (AFM) to study the forced unfolding of fibrinogen to begin addressing this problem. To generate longer reproducible curves than are possible using monomer, factor XIIIa cross-linked, single chain fibrinogen oligomers were used. When extended under force, these oligomers showed sawtooth shaped force-extension patterns characteristic of unfolding proteins with a peak-to-peak separation of approximately 26 nm, consistent with the independent unfolding of the coiled-coils. These results were then reproduced using a Monte Carlo simulation with parameters in the same range as those previously used for unfolding globular domains. In particular, we found that the refolding time was negligible on experimental time and force scales in contrast to previous work on simpler coiled-coils. We suggest that this difference may be due to fibrinogen's structurally and topologically more complex coiled-coils and that an interaction between the alpha C and central domains may be involved. These results suggest a new functional property of fibrinogen and that the coiled-coil is more than a passive structural element of this molecule.

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