Supplementary Information

Biphasic response of cell invasion to matrix stiffness in 3-dimensional biopolymer networks

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Collagen degradation after glutaraldehyde treatment

Collagen can be proteolytically degraded through matrix metalloproteinase (MMP) enzymes secreted by cells. The speed of collagen degradation in response to collagenase (2 mg/ml collagenase type IA, Sigma-Aldrich, Germany) was measured in gels that were treated or not treated with glutaraldehyde. A gel volume of 185µm x 185µm x 50µm (pixel size 361nm x 361nm x 370nm) was continuously imaged after addition of collagenase with confocal reflection microscopy using a 20x water immersion objective with 1.0 NA. The total reflected light intensity integrated over the imaged stack was taken as a measure of collagen fiber density. Our data show that the degradation rate of glutaraldehyde-treated gels is greatly reduced. The total intensity did not fall below 40% of its value before collagenase addition, because the dissolved collagen fibers formed aggregates that contributed to the reflection signal.

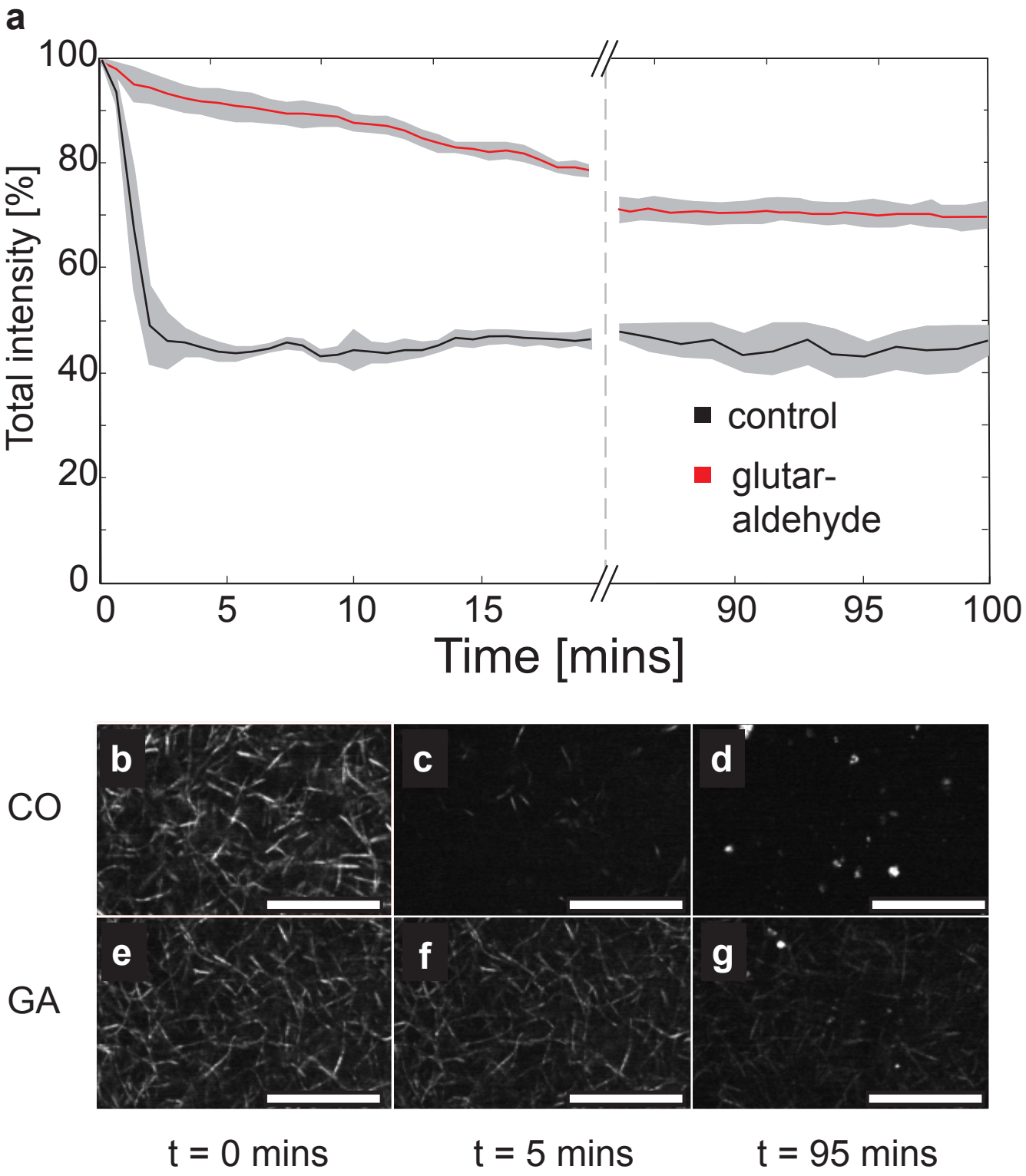

Figure S1 Collagenase digestion of control and glutaraldehyde-treated gels. (a) Integrated reflected light intensity of image stacks versus time (mean ± se of 3 different gels). At t=0, collagenase was added to the gels. Every 40 s, an image stack was recorded over a volume of 185µm×185µm×50µm. After collagenase treatment, collagen fibers disappeared faster in control gels (black line) compared to glutaraldehyde-treated gels (red line). (b-g) Confocal reflected microscopy images of control gels (top row) and glutaraldehyde-treated gels (bottom row) at different time points after collagenase addition. Scale bar is 20µm.

Fluidity of collagen gels from magnetic tweezer measurements

During the application of force steps from 1 to 10nN, the displacement of beads coupled to collagen fibers can be fitted with a power law [1, 2]. The power-law exponent β defines the dissipative properties of the material, where 0 corresponds to an elastic solid and 1 to a viscous fluid. Untreated collagen gels showed predominantly elastic behavior (β ~ 0.1), which was further enhanced by glutaraldehyde treatment (β < 0.05).

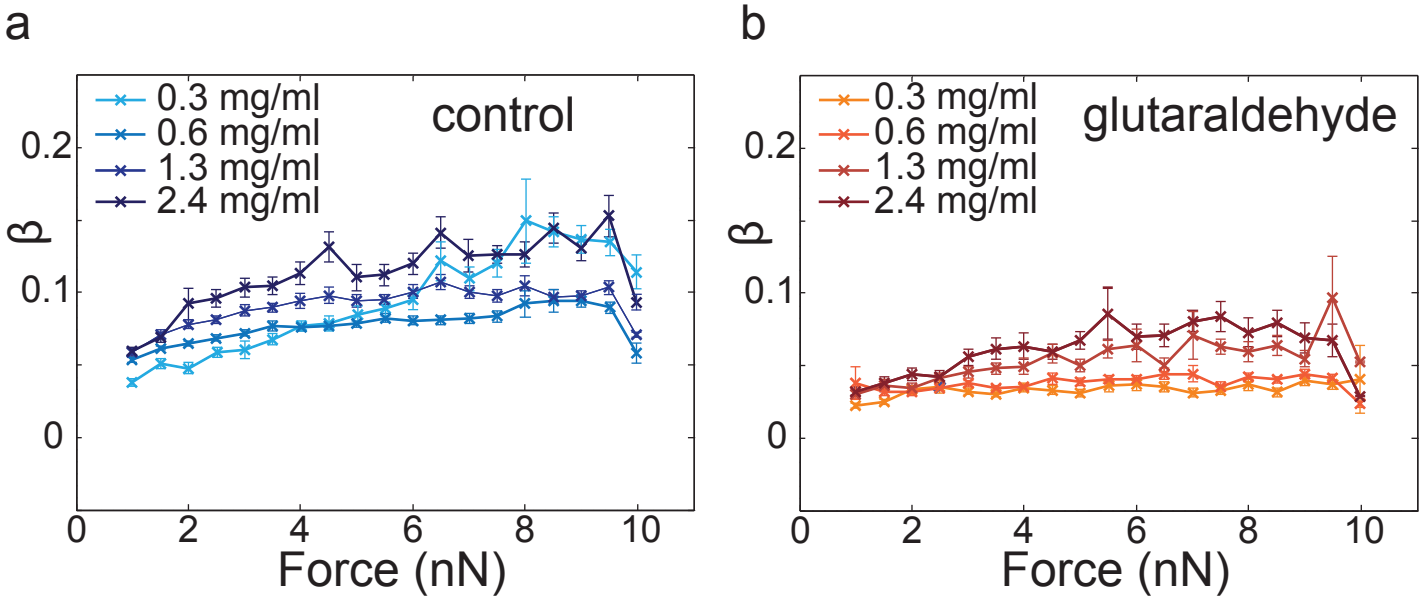

Figure S2 Power-law exponent versus applied force of untreated (a) and glutaraldehyde-treated (b) collagen gels measured from creep-experiments with magnetic tweezers.

References

[1] Kollmannsberger P, Fabry B. High-Force Magnetic Tweezers with Force Feedback for Biological Applications. Rev Sci Instrum. 2007;78:114301-1-6.

[2] Lautscham LA, Lin CY, Auernheimer V, Naumann CA, Goldmann WH, Fabry B. Biomembrane-mimicking lipid bilayer system as a mechanically tunable cell substrate. Biomaterials. 2014;35:3198-207.