Correlation of bulk degradation and molecular release from enzymatically degradable polymeric hydrogels

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Supporting Information

Rheology of polymer-peptide hydrogel starting materials

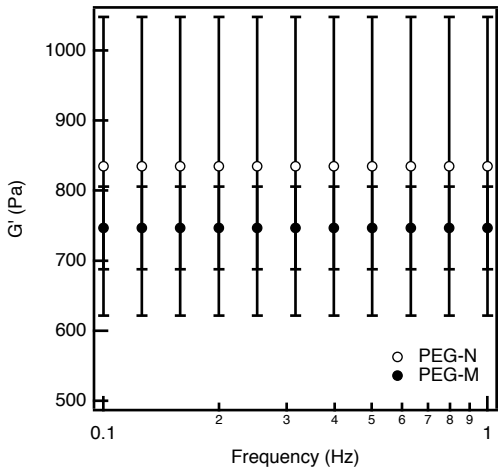

Figure S1: Bulk rheological measurements of the starting material properties for radical-initaited PEG-norbornene (PEG-N) and base-initiated PEG-maleimide (PEG-M) hydrogels. These gel compositions and equilibration times are chosen to ensure that both gels begin with similar initial G'_{eq}, which indicates they begin with similar cross-link densities.

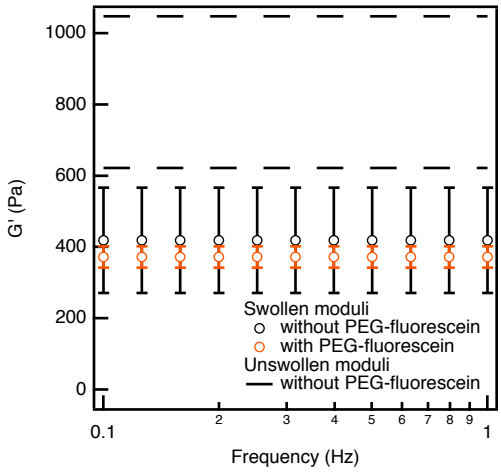

Figure S2: Swollen moduli for PEG-norbornene hydrogels with and without PEG-fluorescein tethered to the scaffold. Dashed lines are the unswollen moduli range for this hydrogel scaffold. Tethering PEG-fluorescein during network cross-linking does not change scaffold moduli.

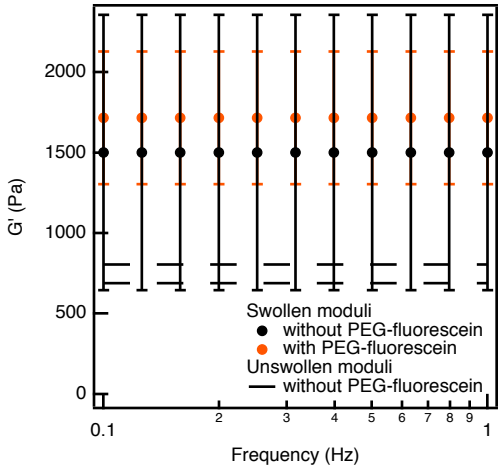

Figure S3: Swollen and unswollen moduli for PEG-maleimide hydrogels. Tethering PEG-fluorescein into the network during cross-linking does not change scaffold moduli. The swollen moduli is higher than the unswollen moduli in PEG-maleimide scaffolds.

Calibration curves for fluorescence intensity and PEG-fluorescein concentration

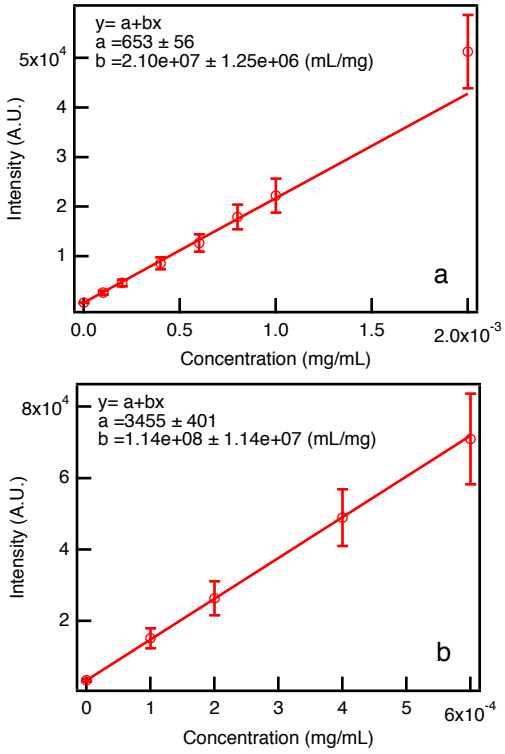

Figure S4: Calibration curves for an initial stock of PEG-fluorescein in 1 mg mL^{-1} collagenase. (a) Calibration curve used to calculate release from PEG-maleimide gels at 350 V. (b) Calibration curve used to calculate release from PEG-norbornene gels at 426 V.

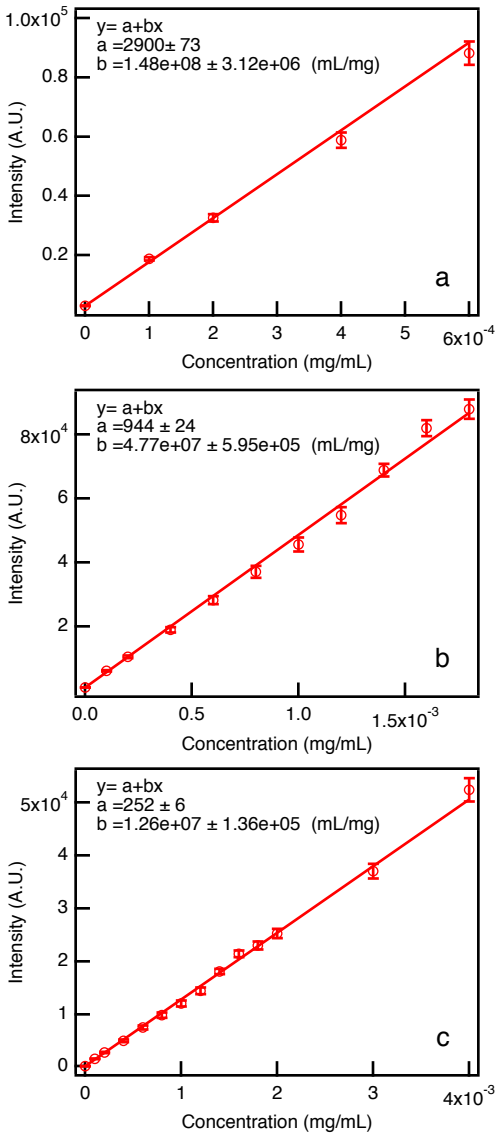

Figure S5: Calibration curve from second stock of PEG-fluorescein in 1 mg mL^{-1} collagenase at (a) 300 V, (b) 350 V and (c) 400 V. These curves are used to calculate release from PEG-maleimide and PEG-norborene hydrogels.

Additional molecular release studies

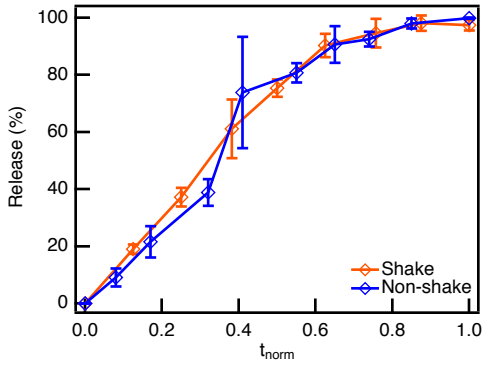

Figure S6: Molecular release from radical-initiated photopolymerized PEG-norbornene (PEG-N) hydrogels under constant (shake) or minimal (non-shake) shear during incubation. Cumulative mass release percentage is plotted as a function of normalized time, t_{norm}, when PEG-N gels are incubated in 1 mg mL^{-1} collagenase.

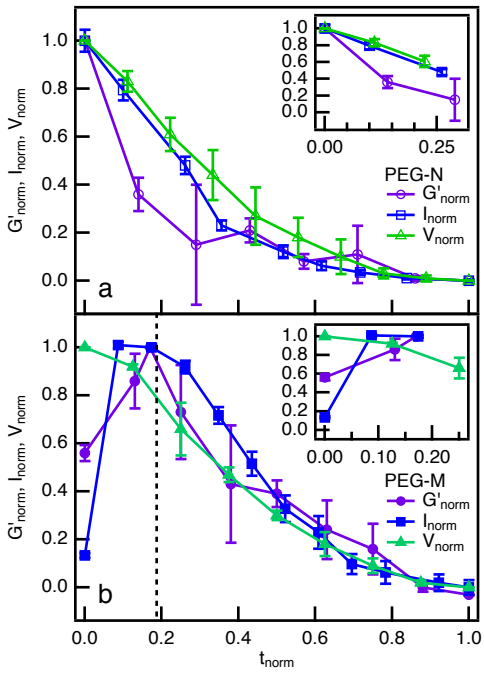

Figure S7: Normalized storage moduli (G'_{norm}), normalized gel intensity (I_{norm}) and normalized gel volume (V_{norm}) of (a) radical-initiated photopolymerized PEG-norbornene (PEG-N) and (b) base-initiated polymerized PEG-maleimide (PEG-M) hydrogels as a function of normalized time under minimal shear.

Correlation of release as a function of degradation

Data are fit to determine the kinetics of molecular release from both hydrogel scaffolds. All data in PEG-norbornene (PEG-N) photopolymerized hydrogels are used to fit the unreleased percentage of fluorescent molecules and normalized storage moduli. In PEG-maleimide (PEG-M) scaffolds the material begins by increasing cross-linking and then after a maximum moduli value degradation dominates. Only data when degradation is dominant is used to fit the kinetics. Data are fit from G'_{norm}=0.91 with corresponding $Unreleased\%$=77.87 % to G'_{norm}=0.00 and $Unreleased\%$=4.40 %. An example of data used for fitting is provided in Table S1. It should be noted that the bulk rheology and molecular release data are not taken at the same time during the degradation reaction. Therefore, we match the data with the closest normalized time.

Table S1: Change in unreleased mass percentage of fluorescent molecules and normalized storage moduli as a function of normalized time for PEG-maleimide hydrogels when the material is sheared during incubation. $t_{norm}(Unreleased\%)$ refers to normalized time used in release experiments and $t_{norm}(G'_{norm})$ refers to normalized time in bulk rheological measurements.

$t_{norm}(Unreleased\%)$	$Unreleased\%$	$t_{norm}(G'_{norm})$	G'_{norm}
0.00	100.00	0.00	0.38
0.13	90.77	0.12	0.97
0.23	77.87	0.25	0.91
0.31	70.21	0.31	0.78
0.39	50.31	0.37	0.63
0.51	24.76	0.50	0.39
0.60	17.68	0.56	0.30
0.69	14.77	0.69	0.16
0.79	7.89	0.81	0.07
0.89	2.98	0.87	0.04
1.00	4.40	1.00	0.00

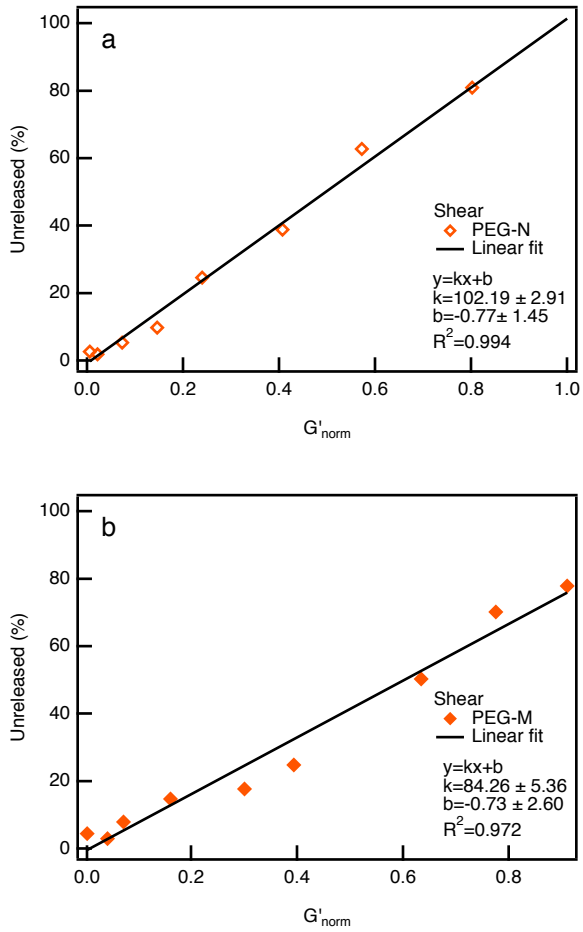

Figure S8: Unreleased mass percentage of fluorescent molecules in the incubation solution (sol-sample) as a function of normalized storage moduli for material under continuous shear or constant shaking. (a) For PEG-norbornene (PEG-N) photopolymerized hydrogels all data are fit. (b) For PEG-maleimide (PEG-M) hydrogels data are fit when degradation is dominant, which is after G''_{norm} reaches a maximum value.

Table S2: Results of linear fit of unreleased fluorescent molecules as a function of G'_{norm}. k is the slope and b is the intercept.

Type of cross-linked hydrogel	Shear		Non-shear	
	k	b	k	b
Radial-initiated PEG-norbornene hydrogels	99.92 ± 6.78	4.81 ± 4.90	94.75 ± 4.37	17.13 ± 4.12
Base-initiated PEG-maleimide hydrogels	86.11 ± 7.31	0.86 ± 2.71	88.78 ± 5.18	1.38 ± 2.86

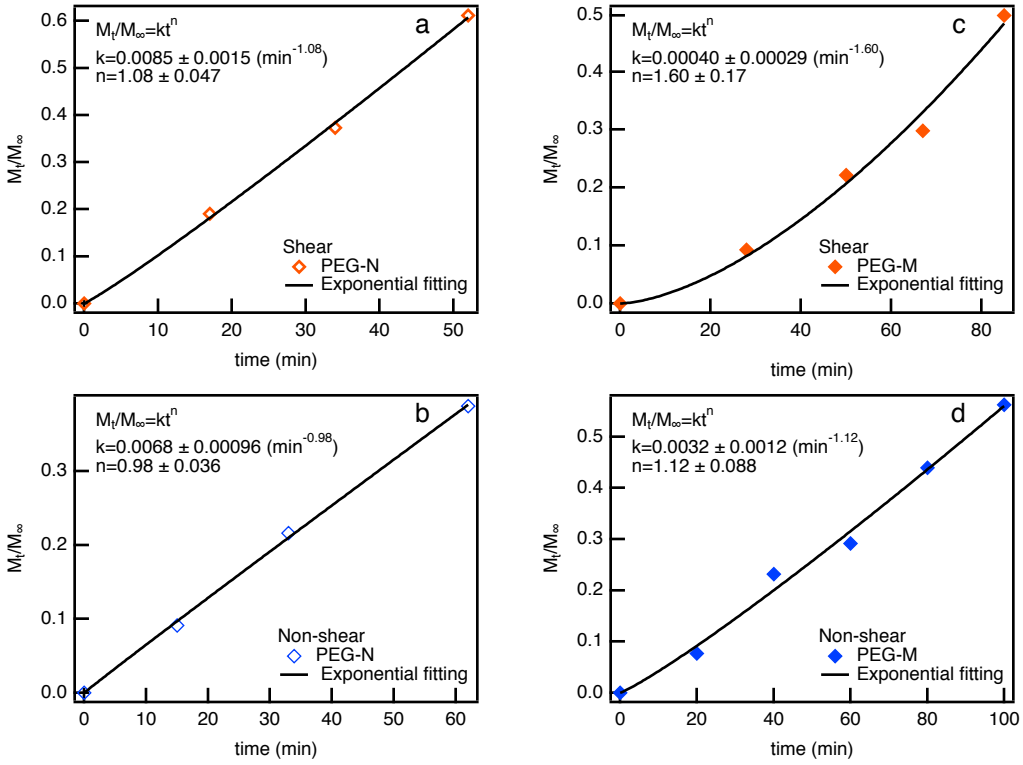

Figure S9: Fitting mass release percentage as a function of time to the Korsmeyer-Peppas-Ritger model, $\frac{M_t}{M_\infty} = kt^n$, where M_t is the amount of drug released at time t and M_∞ is the total amount of drug released. Both hydrogels under shear and minimal shear conditions are fit to determine the release exponent, n, which indicates the mechanism of molecular release. PEG-norbornene (PEG-N) hydrogels under (a) shear and (b) minimal shear. PEG-maleimide (PEG-M) hydrogels under (c) shear and (d) minimal shear. Both types of hydrogels have non-Fickian release.