Microrheological characterization of covalent adaptable hydrogel degradation in response to change in pH that mimics the gastrointestinal tract

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Abstract
Covariant adaptable hydrogels (CAHs) dynamically change their structure in response to external stimuli. These dynamic covariant bonds reversibly break and reform when they are pushed out of equilibrium. This dynamically evolving structure makes CAHs promising in biological applications, such as oral delivery of therapeutics and nutrients. To study the potential of using CAHs as a platform for oral delivery, we characterize scaffold degradation in response to changes in environmental pH which mimic the gastrointestinal (GI) tract. The CAH we are characterizing consists of 8-arm polyethylene glycol (PEG)-hydrazide that covalently cross-links with 8-arm star PEG-aldehyde. Microrheology, multiple particle tracking microrheology (MPT), is used to mimic pH-dependent degradation in the GI tract. In MPT, fluorescent probes are embedded into the sample and Brownian motion is measured. Our microfluidic device enables the fluid environment to be changed around a single sample with minimal sample loss. μRheology is used to characterize degradation at a single pH (pH 4.3, 5.5, and 7.4), and temporal pH changes that mimic the pH in the entire GI tract. We quantitatively determine the gel-sol transition during degradation by characterizing the critical relaxation exponent, which is independent of degradation pH. In addition, we determine that degradation kinetics and material property evolution are not influenced by degradation history. However, the initial cross-link density of the scaffold at each pH exchange can be decreased by a single degradation history which reduces the time to the critical gel-sol transition. This result indicates degradation can be tuned by changing scaffold cross-link density which can be done by changing polymer concentration or the ratio of functional groups. This work will inform design of this scaffold for site-specific oral drug delivery.

Experimental design and apparatus
A previously designed two-layer microfluidic device enables changes in the fluid microenvironment around the sample with minimal sample loss to mimic pH changes in the digestive tract

Consecutive degradation with pH exchange
The scaffold is consecutively degraded at different pHs that mimics pH-dependent degradation in the GI tract

Degradation with single pH exchange
Degradation with single pH exchange

Comparing CAH degradation kinetics
The gel-sol transition during degradation is quantitatively determined by the critical relaxation exponent, which is independent of degradation pH

Degradation kinetics and material property evolution are not influenced by degradation history

Degradation induced by temporal pH changes through the entire GI tract

Dehydration

Acknowledgements

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