Independent Control of Rigidity and Toughness of Polymeric Hydrogels

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ABSTRACT: Refined control over the mechanical properties of hydrogel-based materials has increased as these materials have found broader application. We investigated various aspects of gel cross-linking to independently regulate the elastic modulus (*E*) and toughness (*W*). Alginate hydrogels were chosen as a model system, since alginate can be gelled via ionic or covalent cross-linking, and its block structure dictates the structure of ionic cross-links. Increasing the density of covalent cross-links increased *E* but led to more brittle gels. In contrast, increasing the density of ionic cross-links and length of the blocks responsible for the cross-linking increased both *E* and *W*. Oscillatory shear measurements suggested that ionic cross-links and their length were important in dissipating the energy of deformation due to a partial and stepwise de-cross-linking. In contrast, covalently cross-linked gels underwent energy accumulation. This study demonstrates a novel approach to independently control different mechanical properties of gels.

Introduction

It is highly desirable to control the various mechanical properties of materials, including the mechanical rigidity and toughness, used for structural purposes. Cross-linking has typically been utilized to improve the mechanical properties of many materials (i.e., thermosetting resins). Increasing the cross-linking density generally makes materials more stiff but eventually increases the brittleness of the materials as well.[1,2] The most popular method to allow independent control of these two disparate mechanical properties has been to incorporate various reinforcements, such as fibers and microspheres into the polymer matrix.

In a same context, a need for refined control over the mechanical properties of hydrogel-based materials has been widely acknowledged, as these materials find broader application in a number of fields.[3] Specifically, sophisticated control of the mechanical properties is a critical factor for their successful utilization in tissue engineering.[4,5] The mechanical properties are key to protecting the encapsulated components (e.g., cells, macromolecules) from mechanical deformation at the transplantation site and also to controlling the gene expression of the encapsulated cells.[6] However, gels formed by cross-linking also typically exhibit an increase in both the moduli and brittleness with increases of cross-linking density,[7−9] similar to typical thermosetting polymers.

This study explored methods to raise both the elastic moduli and toughness of gels without incorporating reinforcing particles or fibers. For this purpose, we focused on modifying the properties of the cross-linked junctions responsible for gel formation, where the stress is likely to be localized.[10,11] We hypothesized that modifying the type of cross-linking (e.g., ionic or covalent bonding) and the length of cross-linked junctions would alter the mode of stress localization under deformation. This hypothesis was investigated with alginate, which consists of regions containing consecutive mannuronic acid (MA) residues (defined as MA blocks), regions containing consecutive guluronic acid (GA) residues (defined as GA blocks), and regions containing alternating residues of MA and GA (defined as MG blocks). This material can be formed into gels via both covalent and ionic cross-linking. Covalently cross-linked gels are typically formed by the reaction between carboxylic groups in two different alginate molecules and a cross-linking molecule possessing primary diamines.[12] In contrast, ionically cross-linked gels are formed by the binding of divalent cations (e.g., calcium) between GA blocks possessing more than 20 GA residues on different polymer chains.[13−15] Therefore, the length of the cross-linking junction can be readily adjusted by utilizing alginates having different lengths of GA blocks. This study investigated the macroscopic and microscopic mechanical properties of gels varied by those factors.

Experimental Section

Characterization of Alginate Molecules. Molecular weights of alginates (supplied from FMC Technologies), which have different fractions of mannuronic acid (MA) and guluronic acid (GA) residues, were determined with a size-exclusion chromatographic system equipped with a triple detector system (Viscotek) including a laser refractometer (LR 40), a differential viscometer (T60), and a right angle laser light scattering detector (RALLS). 0.1 M $NaNO_3$ buffer solution (pH 6.3) was used as a mobile phase, and the samples were dissolved in the mobile phase. A set of two TSK-gel columns ($G4000PW_{XL}$ and $G3000PW_{XL}$) was used to separate the alginate molecules with different molecular weights.

The fraction of MA and GA residues—two continuous MA or GA—in alginates was determined with a circular dichroism (CD) spectrometer (AVIV 202). The sample concentration was 0.4 mg/mL, and the absorbance of the solution was scanned at wavelengths from 250 to 190 nm at 25 °C. From the CD spectra, molar ellipticity values were acquired in units of deg cm^2/dmol. The ratio between MA and GA residues was calculated by dividing the height of the peak (MA residues at 200 nm) by that of the trough (GA residues at 220 nm), since both values were negative.[16]

To measure the length of GA blocks in alginate molecules, the poly(guluronic acid) blocks (GA blocks) were isolated using

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a thermal treatment in acid−basic condition, following the procedure described elsewhere.[17] Molecular weights of isolated polyguluronic acids were measured with size exclusion chromatography.

Preparation of Alginate Hydrogels. To prepare covalently cross-linked alginate hydrogels, 2% (w/w) alginates solutions prepared with 2-(*N*-morpholino)ethanesulfonic acid hydrate (MES, Sigma) buffer (at pH 6.5) were sequentially mixed with 1-hydroxybenzotriazole (HOBt, Aldrich), 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide (EDC, Sigma), and adipic acid hydrazide (AAD, Sigma). To alter the cross-linking density, the concentration of AAD was varied from 0.05 to 0.15 M, where M is the molar ratio between AAD and alginate. Ionically cross-linked alginate hydrogels were prepared by mixing 2% (w/w) alginate aqueous solutions with slurries containing different masses of calcium sulfate ($CaSO_4$, Sigma), varying from 8 to 20% (w/w). The resulting calcium:alginate sugar residue ratios used to form gels thus varied from 0.24 to 0.60. The mixtures were immediately cast between glass plates with 1 mm thickness after mixing, and after 2 h the gels were cut into disks (24 mm diameter) for compression and oscillatory shear tests or rectangular stripes (10 × 3 × 0.1 cm) for uniaxial tensile testing. The gels were stored at 25 °C in deionized (DI) water for a day before testing.

Characterization of Physical Properties of Hydrogels. To measure the elastic moduli of hydrogels, the gel disks were placed between parallel plates (gap distance at 1 mm) in a rheometer (VOR, Bohlin Instrument). The gels were deformed at a stress within the linear viscoelastic region, as determined using a frequency of 1 Hz. The complex moduli calculated from the resulting strain were utilized as the elastic moduli (E). Weights of incubated gels and dried solids were also measured to quantify the degree of swelling (Q), defined as the reciprocal of the volume fraction of a polymer in a hydrogel (ν_2)

$$Q = {\nu_2}^{-1} = \rho_p\left[\frac{Q_m}{\rho_s} + \frac{1}{\rho_p}\right] \tag{1}$$

where ρ_p was the polymer density (0.8755 g cm^{-3}), ρ_s was the density of water, and Q_m was the swelling ratio, defined as the mass ratio of absorbed water to the dried gel. From E and Q, molecular weights between cross-links (M_c) were calculated on the basis of the rubber elasticity theory[18]

$$M_c^{\ -1} = \frac{EQ^{1/3}}{\rho RT} + \frac{2}{M_n} \tag{2}$$

where R was the gas constant (8.314 J mol^{-1} K^{-1}), T was the temperature at which the modulus was measured, and M_n was the number-average molecular weight.

To evaluate the toughness of hydrogels, a test to quantify the work of fracture was utilized.[19−21] The total work to fracture W_{total} was expressed as the summation of the work dissipated at the process zone of fracture (W_p) and the work dissipated outside the process zone (W_o).

$$W_{total} = W_p + W_o \tag{3}$$

The essential work to fracture w_{total} (J/m^2), the essential work at the process zone (w_p, J/m^3), and the essential work dissipated outside the process zone (w_o) were attained from dividing the work of fracture by load-carrying area of gel strips.

$$w_{total} = W_{total}/lt = w_p + blw_o \tag{4}$$

where l was the width of sample between the two initial notches, t was the thickness (1 mm), and b was the shape factor. For this test, we introduced a notch in the gel strips with a razor blade. The length of the notch was varied from 1 to 3 mm. Then, the strips were extended at a constant deformation rate of 1 mm/min, and stresses were measured. The w_{total} was calculated from the area of stress (σ) vs displacement curve, and w_o was calculated from the slope of w_{total} vs l curve.

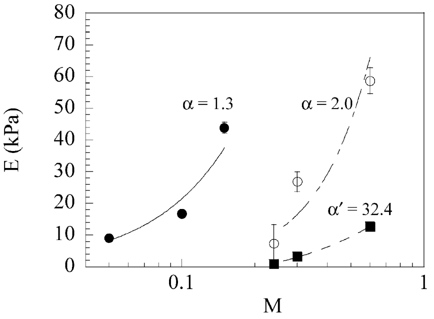

Figure 1. Increasing the concentration of cross-linking molecules (M) increased the elastic moduli (E) of alginate hydrogels: (●) high GA alginate hydrogels cross-linked with AAD; (○) high GA alginate hydrogels cross-linked with Ca^{2+}; (■) high MA alginate hydrogels cross-linked with Ca^{2+}. M = moles of cross-linking molecules per moles of alginate sugar residue. α is a constant from the fitting by a power law, and α′ is a constant from a linear fitting.

Table 1. Structure of Alginate Molecules

alginate	M_w (g/mol)	fraction of GA residues	number of GA residues
high GA	269 100	0.62	30
high MA	280 000	0.36	14

Dynamic oscillatory shear measurements were conducted by shearing the gel disks between the parallel plates in a rheometer. To quantify the viscoelasticity of hydrogels, gels were deformed at a stress within the linear viscoelastic region, while varying the frequency from 0.01 to 10 Hz. Resultant strains were measured, and the storage and loss moduli were calculated. Viscoelasticity was evaluated from dependency of storage moduli on the frequency, described by a power law. To investigate the oscillatory shear responses of hydrogels at a large deformation, hydrogels were deformed at constant frequency of 1 Hz, while varying the stresses from 10 to 100 Pa. Resultant strain was measured, and storage and loss moduli were also calculated. Dependencies of the storage moduli on the strain were calculated by fitting the curves to a power law.

Results

Analysis of Alginate Molecules. Alginate molecules possessing different block structures (i.e., fraction of GA residues and length of GA blocks), but comparable total molecular weights, were used in this study. Alginates rich in guluronic acid blocks (high GA) had twice the fraction of GA residues than alginate rich in mannuronic acid blocks (high MA), as analyzed with CD spectra (Table 1). The length of the GA blocks in high GA alginate was almost twice as long as those in the high MA alginates, indicating that the higher fraction of GA residues in high GA alginate is simply attributed to the longer length of GA blocks rather than a higher number of GA blocks.

Mechanical Properties of Hydrogels. Hydrogels could be formed via covalent cross-linking at much lower concentrations of cross-linking molecules than those required for the formation of ionically cross-linked hydrogels (Figure 1). The critical AAD concentration required to form a gel was 0.03 mol/mol of alginate sugar residue (M), while the critical Ca^{2+} concentration was 0.24 mol/mol of alginate sugar residue. Increasing the concentration of the cross-linking molecules increased the elastic moduli (E) of high GA alginate hydrogels, following a power law, $E \propto M^{\alpha}$, irrespective of the type of cross-linking. In contrast, the increased elastic moduli of high MA alginate hydrogels due to

Table 2. Summary of Cross-Linked Structure of Alginate Hydrogels Formed with Different Types of Cross-Linking, Concentration of Cross-Linkers, and Alginate Structure[a]

alginate	cross-linking molecules	M	M_c (g/mol)	w_o (J/m^3)	n	$-k$
high GA	AAD	0.05	5640	0.40	0.04 ± 0.02	
		0.10	2970		0.01	0
		0.15	1110		0.01 ± 0.003	
high GA	Ca^{2+}	0.24	4380	13.7	0.27 ± 0.007	0.80 ± 0.15
		0.30	1608	42.6	0.06 ± 0.005	1.23 ± 0.06
		0.60		80.4	0.07 ± 0.001	1.27 ± 0.06
high MA	Ca^{2+}	0.24	35649	1.7	0.94 ± 0.29	
		0.30	13249		0. 65 ± 0.22	0.90 ± 0.10
		0.60			0.12	

[a] The molecular weights between cross-links (M_c), essential work of fracture outside the process zone (w_o), and dependence of storage modulus of alginate hydrogels on frequency (n) and strain ($-k$) are shown. M is the moles of cross-linking molecules per moles of alginate sugar residue. Values for n and k represent mean ($n = 4$) and standard deviation.

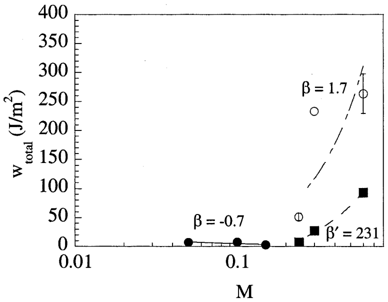

Figure 2. Type of cross-linking and concentration of cross-linkers altered the work of fracture (w_{total}) of alginate hydrogels: (●) high GA alginate hydrogels cross-linked with AAD; (○) high GA alginate hydrogels cross-linked with Ca^{2+}; (■) high MA alginate hydrogels cross-linked with Ca^{2+}. M = moles of cross-linking molecules per moles of alginate. β is a constant obtained from fitting by a power law, and β' is a constant obtained from a linear fit.

raising the ionic cross-linking density followed a linear relationship, $E \propto \alpha' M$. Thus, alginates rich in GA blocks led to higher elastic moduli at a given Ca^{2+} concentration than gels formed with high MA alginates.

Combined with the degree of swelling (Q), molecular weights between cross-links (M_c) were calculated from the elastic moduli following eq 2. In the ionically cross-linked hydrogels, M_c was regarded as the length of the non-cross-linking blocks between two cross-linked GA blocks. In addition, this calculation was limited to the gels formed with a Ca^{2+}:alginate sugar residue ratio less than 0.6, since multiple cross-linking between the GA blocks can develop at higher concentrations of calcium.[22] Calculation of M_c revealed that gels exhibited much lower M_c with covalent cross-linking than ionic cross-linking at given concentrations of cross-linking molecules (Table 2). This result was attributed to the much higher [Ca^{2+}] required to form an elastic network, as a minimum of 20 Ca^{2+} residues are believed to be necessary to form one ionic cross-link junction. In contrast, a single AAD molecule can form a covalent cross-link between two alginate chains.[14] Ionically cross-linked high MA alginates exhibited much higher M_c at any given calcium concentrations than high GA alginates, likely due to their longer MA or MG blocks.

To quantify the toughness of hydrogels, the fracture responses of gels formed with the various types of cross-linking, density, and polymer structure were investigated. The work to fracture (w_{total}) of the covalently cross-linked hydrogels was 2 orders of magnitude lower than the ionically cross-linked hydrogels (Figure 2), even though they exhibited comparable elastic moduli. Increasing the cross-linking density of the covalently cross-linked hydrogels led to a reduction in w_{total}, similar to other bulk polymer materials formed from a covalent cross-linking reaction. Indeed, it was not even possible to prepare the rectangular strips for this test when the gels were cross-linked with 0.15 M AAD, due to the high brittleness of these gels. In contrast, raising the calcium concentration significantly increased w_{total} of high GA alginate hydrogels, following a power law, $w_{total} \propto M^{\beta}$. In contrast, high MA alginate hydrogels followed a linear relationship, $w_{total} \propto \beta' M$, similar to the linear relationship between E and M. The variations in the toughness of the hydrogels were analyzed in more detail by examining the ultimate stress and strain to cause failure. The length of the notch in the gels was kept constant at 1 mm in this analysis. Increasing the concentration of AAD decreased the strain at break, although the slope of the curves increased (Figure 3a). In contrast, ionically cross-linked hydrogels exhibited increases in the strain at break as well as the slope of the curves upon increasing the concentration of calcium (Figure 3b). High GA alginates also exhibited a higher slope and strain at break than high MA alginates at any given calcium concentration (Figure 3c).

The contribution of the work to fracture dissipated outside the process zone (w_o) to the total work of fracture was calculated following eq 4 (Table 2). The w_p was very small for all gels irrespective of the type of cross-linking, suggesting that w_{total} of the gels was mainly determined by the capacity of the gels to dissipate energy outside the process zone. Thus, increasing the ionic cross-linking density of high GA alginate led to much higher w_o, similar to what was observed with w_{total}. The higher w_o implies that the ionically cross-linked high GA alginate gels have a decreased sensitivity to the notch, due to the formation of a larger plastic zone. These data suggest that the properties of the cross-linked junctions are important in decoupling the toughness and mechanical rigidity of these gels.

Responses of Hydrogels to Oscillatory Shear Deformation. Dynamic oscillatory shear measurement techniques were subsequently used to monitor the viscoelastic behavior of the gels. First, the response of hydrogels to small deformation was investigated in order to interpret the changes in the elastic moduli of hydrogels. In general, the magnitudes of storage moduli (G') of both covalently and ionically cross-linked hydrogels were varied by the concentration of cross-linking molecules, as shown in Figure 1. However, the dependence of the storage moduli on the frequency was greatly influenced by the type of cross-linking as well as the cross-linking density. Covalently cross-linked hydrogels demonstrated an independence of storage moduli on the

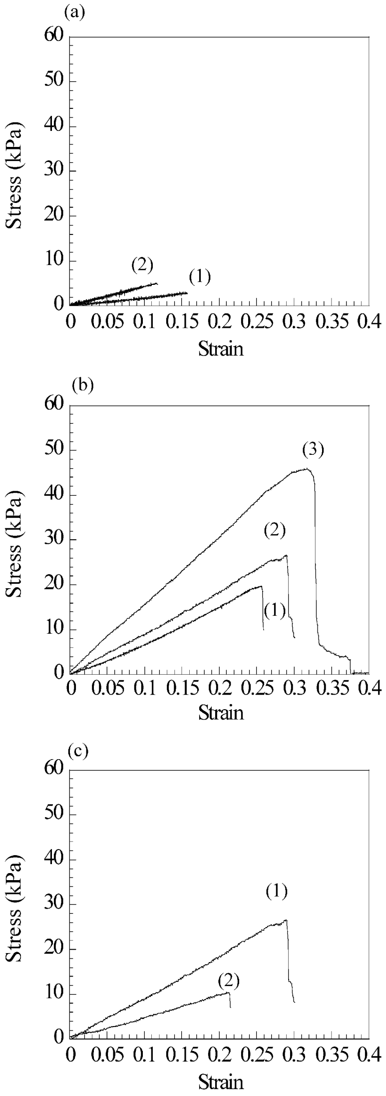

Figure 3. Detailed tensile stress vs strain curves of cross-linked hydrogels prepared with a 1 mm notch. (a) High GA alginate gels cross-linked with AAD at (1) 0.05 M and (2) 0.10 M. (b) High GA alginate hydrogels cross-linked with Ca^{2+} at (1) 0.24 M, (2) 0.30 M, and (3) 0.60 M. (c) Comparison of high GA (1) and high MA (2) alginate hydrogels cross-linked with Ca^{2+} at 0.30 M.

frequency, irrespective of the concentration of AAD. This independence indicated that the gels behaved like an elastic solid, even at a low cross-linking density (Figure 4a).[23] In contrast, ionically cross-linked hydrogels demonstrated more liquid behavior, as shown with the linear dependences of the storage moduli on the frequency (Figure 4b). However, increasing the concentration of calcium greatly reduced this dependency (n), quantified from the power law $G' \propto (\text{frequency})^n$ (Table 2). At high calcium concentration (0.6 M), n became almost zero, similar to the covalently cross-linked hydrogels. Use of high MA alginate greatly increased n at any given calcium concentration, although n also decreased with increases in the calcium concentration in these gels.

To interpret the changes in the cross-linked structure under large deformation, the responses of the gels to large-amplitude oscillatory shear deformation were also investigated. Although this analysis does not accurately quantify the viscoelasticity of hydrogels with increases of the strain to the nonlinear viscoelastic region, it still has been reported to provide valuable information on the deformation of cross-linked structures.[24,25] When the gels were deformed at a constant frequency of 1 Hz, the storage moduli of covalently cross-linked hydrogels were almost independent of the strain magnitude (Figure 5). In contrast, ionically cross-linked hydrogels showed a weak dependency of storage moduli on strain magnitude even at the low strain regime. Specifically, the storage moduli decreased significantly, as the strain exceeded 0.5%. The slopes of the curves ($-k$), quantified from the power law $G' \propto (\text{strain})^{-k}$, varied with calcium concentration and alginate structure (Table 2). These large dependencies of the storage moduli on the strain magnitude with ionic cross-linking agree well with findings that ionic cross-linking produces larger stress relaxation than covalent cross-linking.[26] Increases in the calcium concentration, which made the gels more elastic under small deformation, increased the slope at high

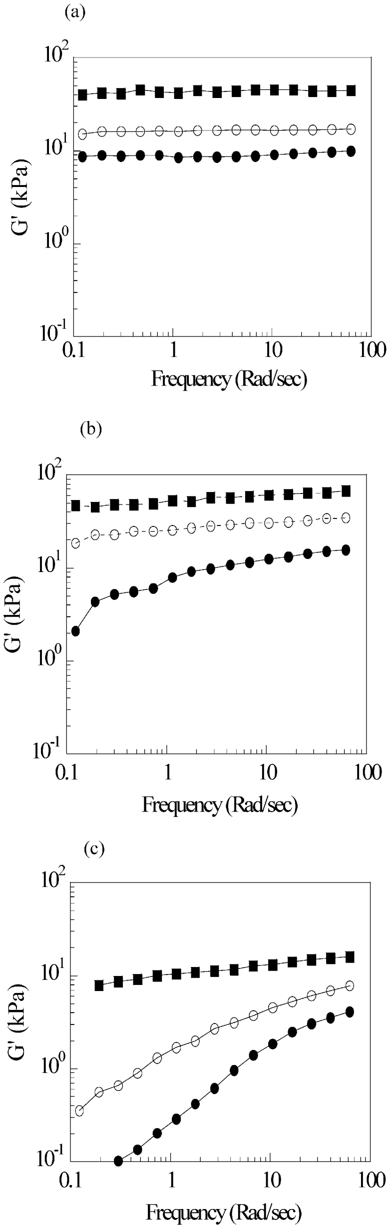

Figure 4. Viscoelastic properties of hydrogels cross-linked with AAD at 0.05 M (●), 0.10 M (○), 0.15 M (■) (a) and hydrogels cross-linked with Ca^{2+} at 0.24 M (●), 0.30 M (○), 0.60 M (■) (b, c). Graph b corresponds to the gels prepared from high GA alginates, and graph c corresponds to gels prepared from high MA alginates.

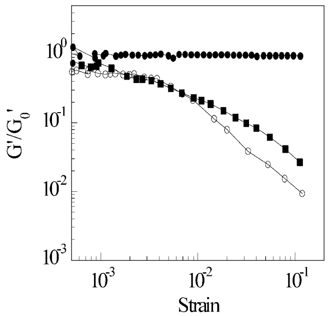

Figure 5. Large-amplitude oscillatory shear measurements demonstrated that hydrogels with higher toughness have increased plasticity with increases of deformation: (●) hydrogels formed by cross-linking high GA alginate with AAD at 0.05 M, (○) hydrogels formed by cross-linking high GA alginate with Ca^{2+} at 0.30 M, or (■) high MA alginates cross-linked with Ca^{2+} at 0.30 M. G_0' represents the storage modulus at plateau.

deformation, as illustrated with the higher k. The high GA alginates also had higher k values than the high MA alginates at any given calcium concentrations. These reductions in the storage moduli with an increase of strain were not attributed to irreversible breakdown of the cross-linked structures of hydrogels, since no reduction in the storage moduli was observed in second strain sweep measurements. In addition, the reduction in G' was not attributed to the slippage between the plates, as illustrated with different values of k. Therefore, we propose that the covalently cross-linked hydrogels behaved like an elastic solid material at both small and large deformations, while the ionically cross-linked hydrogels behaved in a different manner, depending on the magnitude of deformation.

Discussion

This study has demonstrated that the type and number of cross-linking and length of cross-linked junctions (i.e., length of GA blocks) controlled the elastic moduli and toughness of hydrogels. Specifically, the elastic moduli and toughness of gels both increased in ionically cross-linked gels with cross-linking density, while covalent cross-linking led to increases in the elastic moduli and brittleness with higher cross-linking densities. In the formation of ionically cross-linked hydrogels, the longer length of GA blocks, leading to longer cross-linked junctions, was advantageous in attaining a higher toughness as well as elastic modulus. These alterations in the mechanical properties were interpreted by the responses of hydrogels to dynamic oscillatory shear deformations at both small and large amplitudes. One of the striking findings in these experiments was that gels formed at high ionic cross-linking density behaved like an elastic solid at small deformation, while exhibiting a higher capacity to dissipate energy with larger deformations.

Increases in the elastic moduli of the hydrogels were simply attributed to the increase in the cross-linking density irrespective of the type of cross-linking, as illustrated with Table 2. A much higher critical concentration of cross-linking molecules was required to form ionically cross-linked hydrogels, as compared to covalent cross-linking, and this could be interpreted in terms of the egg-box model of ionic cross-linking.[27] This proposed model of alginate cross-linking indicates that a minimum of 20 Ca^{2+} residues are necessary to form one ionic cross-link junction. In contrast, a single AAD molecule can form a covalent cross-link between two alginate chains. The importance of the length of GA blocks in determining the elastic moduli was also confirmed by the comparison between high GA and high MA alginate gels.[13]

The varying fracture behavior of hydrogels formed with the two types of cross-linking can be explained in terms of the intermolecular bonding between the alginate and its cross-linkers. In an ionically cross-linked structure, the critical stress required to dissociate one cross-linked GA block completely can be expressed as the summation of the stresses to dissociate each cross-linked GA in the block. This infers that there likely exists a fraction of GA residues undergoing dissociation even at a lower stress or strain than that required to cause the complete de-cross-linking of GA blocks (Figure 6a). This partial de-cross-linking would significantly reduce the stress localized at the cross-linked junctions, and subsequent increases in the stress, upon increasing the displacement, would presumably induce another partial de-cross-linking in the neighboring GA blocks. Hence, the complete de-cross-linking in one GA block may be retarded by the stepwise energy dissipation occurring in surrounding GA blocks, which can be expressed as the formation of larger plastic zone around the crack tip. Subsequently, energy localization specifically at the process zone behind the notch is retarded, leading to slower propagation and less sensitivity to the preintroduced notch, as described in Figure 6c. In addition, the incomplete de-cross-linking in the ionically cross-linked alginate may be followed by a re-cross-linking process, which recovers the original cross-linked structure. In contrast, the de-cross-linking occurring in the covalently cross-linked hydrogels proceeds in a homogeneous manner, as the stress localized at a single cross-linked point exceeds the critical stress (Figure 6b). In consequence, the area of the plastic zone is limited to the process zone (Figure 6c), and crack propagation is much faster than in the ionically cross-linked gels. The higher w_0 of ionically cross-linked gels, which indicates the formation of a large plastic zone, clearly supports this possible mechanism. This toughening mechanism of ionically cross-linked gels may be similar to the enhanced toughening of brittle ceramic materials by the formation of multiple cracks outside the preintroduced process zone.[28]

The potential stepwise de-cross-linking processes in disparate GA blocks under loading were detected by the material response to oscillatory shear deformation. According to a Maxwell model, ionically cross-linked GA blocks can be described as a combination of a spring and damper. Under small deformations, only the spring component is utilized, leading to the independence of storage moduli on the frequency. As the deformation becomes larger, the partial de-cross-linking and subsequent expansion of the plastic zone dampen the energy accumulation. This is consistent with the reduction of storage moduli with strain, as illustrated in Figure 5. Note that this reduction of storage moduli within the small strain magnitude is likely related to very small degree of de-cross-linking, which can be readily recovered upon removing the deformation. In contrast, covalently cross-linked hydrogels can be described as a system possessing only the elastic spring component. Therefore, the stress is accumulated on the extended spring without any capacity to dissipate the energy. Consequently, storage moduli are independent of both

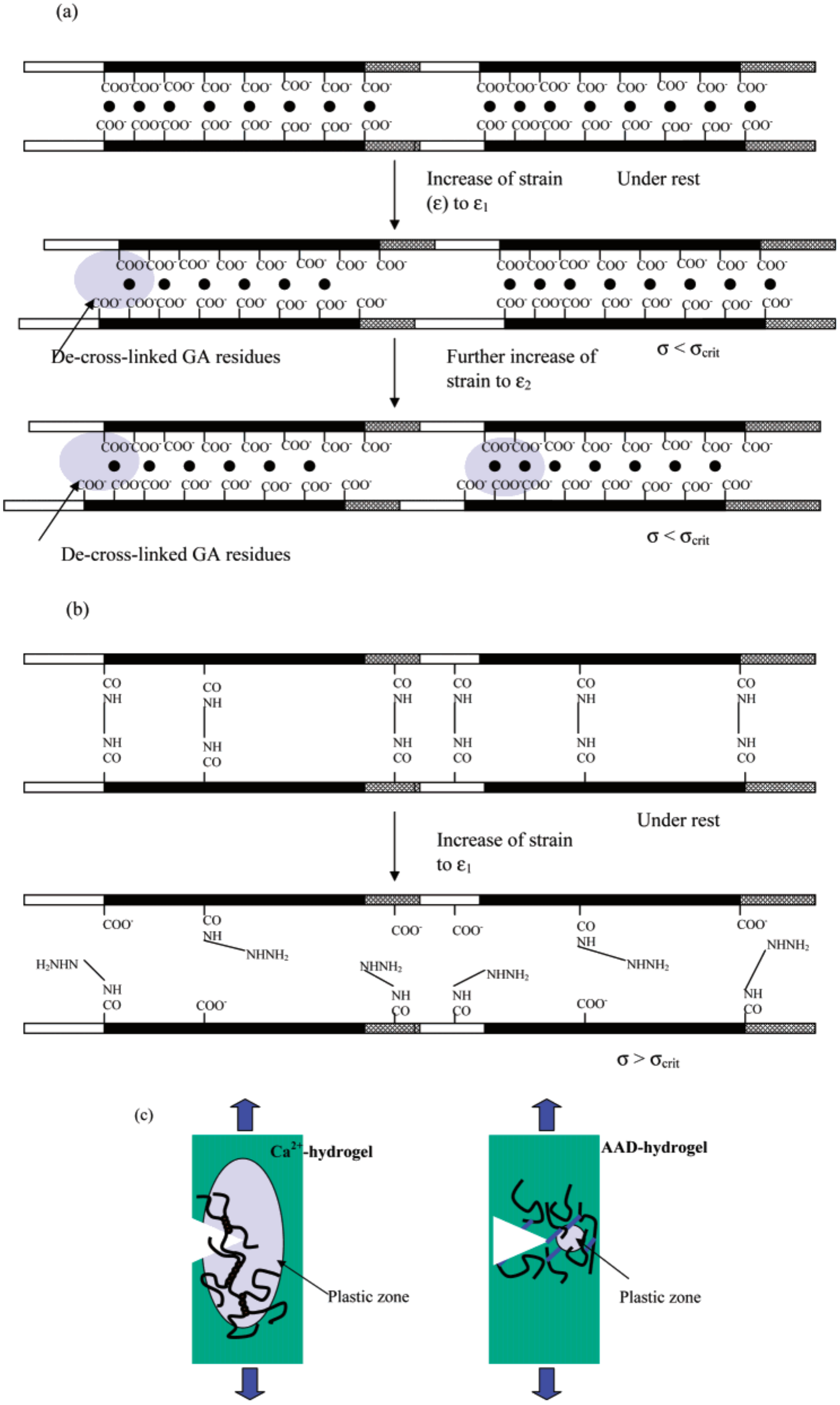

Figure 6. Schematic description of potential mechanism underlying different responses of the hydrogels under tension, Ca^{2+} cross-linked gels underwent partial and stepwise de-cross-linking (a), while AAD cross-linked hydrogels underwent a catastrophic de-cross-linking as the stress exceeded the critical stress (σ_{crit}) (b). In consequence, the area of the plastic zone in Ca^{2+} cross-linked hydrogel was much larger than that of AAD cross-linked hydrogels (c). ■, GA blocks; □, MA blocks; ⧄, MG blocks; ●, Ca^{2+}; H$_2$NHN—NHNH$_2$, adipic acid hydrazide.

frequency and strain magnitude. According to this model, increasing the density of ionic cross-linking can thus be related to increases in the number of springs and dampers in the gel. When tested at small deformation, the elastic properties of hydrogels at a higher cross-link density are increased due to a higher number of springs. Simultaneous increases in the number of dampers, which is realized by a larger plastic zone, results in a steeper drop in the storage moduli of hydrogels with increases of strain. In contrast, increasing the covalent cross-linking density only increases the number of springs. The stress accumulation becomes higher even at small strain, and the material becomes more brittle. The advantageous contribution of the length of the cross-linked junctions on improving the mechanical properties can be explained in terms of this model. Raising the length of GA blocks increases the spring constant and the capacity to dampen deformation energy, leading to the higher elastic moduli and the formation of a larger plastic zone, respectively. Subsequently, hydrogels prepared with high GA alginates possess higher resistance to both deformation and crack propagation. Non-cross-linkable blocks (i.e., MA blocks or alternating MG blocks) present between cross-linked GA blocks can be regarded as a component that allows extension of the system.[15] However, the contribution of these blocks to the ductile properties is likely limited, since the polymer molecules are already extended by the swelling of the gel. This qualitative interpretation may be more refined in the future by utilizing recently developed theoretical efforts.[29]

In summary, this study demonstrates the feasibility of controlling the mechanical properties of hydrogels in a sophisticated manner through alterations of cross-linking. In addition, these studies indicate that expanding the plastic zone in deformation by building in a stepwise and partial de-cross-linking process allows one to toughen a brittle material, and this concept may be applicable to both gels and bulk polymers.

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