

# RAPID COMMUNICATION

## Metal-Ion-Mediated Healing of Gels

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### INTRODUCTION

Self-healing is common in biological systems. A cut or a wound heals with time by cell migration from the adjacent tissues followed by cell proliferation and remodeling, leaving behind only a scar or weld line. Healing is also seen in synthetic linear polymers. Two pieces of polymers are welded by the reptation of chains across the interface at temperatures above the glass-transition or melting temperature.<sup>1,2</sup> Unlike linear polymers, crosslinked polymeric networks cannot heal naturally because of the lack of reptation ability of the network chains across an interface. However, several smart ways for healing crosslinked polymers have been reported in the recent past.<sup>3–6</sup> One of the techniques makes use of repair chemicals that are embedded in hollow fibers<sup>3</sup> or microcapsules<sup>5</sup> and that initiate self-repair when released during crack propagation. Another technique uses a reversible Diels–Alder chemistry, in which a furan and a maleimide react around 80 °C to reform a cracked network.<sup>6</sup> The aforementioned strategies cannot be used to heal lightly crosslinked and water-swollen polymer networks because of their soft nature and the presence of water. In this work, we meet the challenge of demon-

strating a healing phenomenon in hydrophilic gels. We show that certain hydrogels that have flexible hydrophobic side chains with a terminal carboxyl group undergo healing at the ambient temperature mediated by transition-metal ions. Healing occurs by the formation of coordination complexes that are much stronger than other noncovalent interactions such as chain entanglements and hydrogen bonding. The weld so formed then grows in strength with time, eventually leading to the process of metal-ion-mediated healing of the gels.

### EXPERIMENTAL

#### Synthesis of the Gels

The gels used in this work were synthesized from acryloyl derivatives of amino acids, which contain a hydrophobic alkyl chain (length =  $n$ ) and a terminal hydrophilic carboxyl group. More specifically, a gel based on acryloyl-6-amino caproic acid (A6ACA;  $n = 5$ ) was studied extensively. The procedure for preparing acryloyl derivatives of amino acids has been described elsewhere.<sup>7</sup> For comparative purposes, we also used gels synthesized from acrylic acid (AAc;  $n = 0$ ), poly(ethylene glycol) (PEG), and 2-acrylamido-2-methyl-1-propane sulfonic acid (AMPS). Gels were prepared by the free-radical polymerization of a 1 M aqueous solution of the monomers in the presence of  $N,N'$ -methylenebisacrylamide (10 mol %) as the cross-linker. Polymerization was carried out in double-dis-

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tilled water at 40 °C with ammonium persulfate as an initiator. The gels were washed thoroughly in deionized water for at least 48 h to remove any contamination of linear polymers and then dried to give approximately 0.5-cm-diameter cylindrical samples.

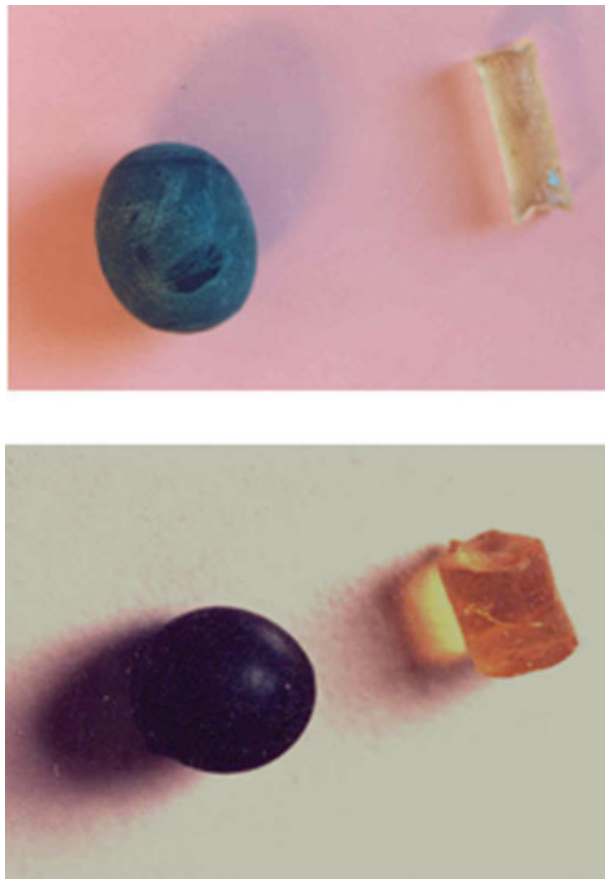
### Healing of the Gels

The gels were healed by the placement of the dried cylindrical pieces of the gels together in a dilute aqueous solution of 0.1 M  $\text{CuCl}_2$  at the ambient temperature. For mechanical testing, the cylindrical gels were butt-welded by the design of a small glass apparatus in which two dry gel pieces were inserted into a common chamber through opposing holes and their ends were juxtaposed. A small amount of  $\text{CuCl}_2$  was introduced into the chamber so that only the ends of the cylindrical gels came in contact with the  $\text{CuCl}_2$ . The portions of the gel pieces in contact with the  $\text{CuCl}_2$  drops absorbed most of the solution, and any small amount of excess solution on the gel surface was mopped off. Thus, the ends healed to form the butt weld.

### RESULTS AND DISCUSSION

We have shown before that when a single piece of a dry, solid, cylindrical A6ACA gel is placed in a  $\text{CuCl}_2$  solution, it transforms into a hollow ellipsoidal/spherical shape<sup>8</sup> (Fig. 1). Here at the beginning, the  $\text{Cu}^{2+}$  ions along with the water molecules start diffusing inside the gel and coordinate with the  $\text{COO}^-$  groups of the gel to form a monomeric complex. This slowly rearranges into a dimeric complex as more  $\text{Cu}^{2+}$  diffuses inside the gel. The dimeric complex first forms at the surface at which the  $\text{Cu}^{2+}$  concentration is the greatest, and as a result, the gel surface is rendered hydrophobic. Consequently, the cylindrical gel reorganizes into a spherical form to minimize the surface energy. With further diffusion of  $\text{Cu}^{2+}$ , the monomeric complex in the core of the gel rearranges layer by layer into a dimeric complex and deposits on the outer shell. This reorganization results in a buildup of high stresses in the core, causing the gel network to rupture, and a hollow interior is formed.<sup>8</sup>

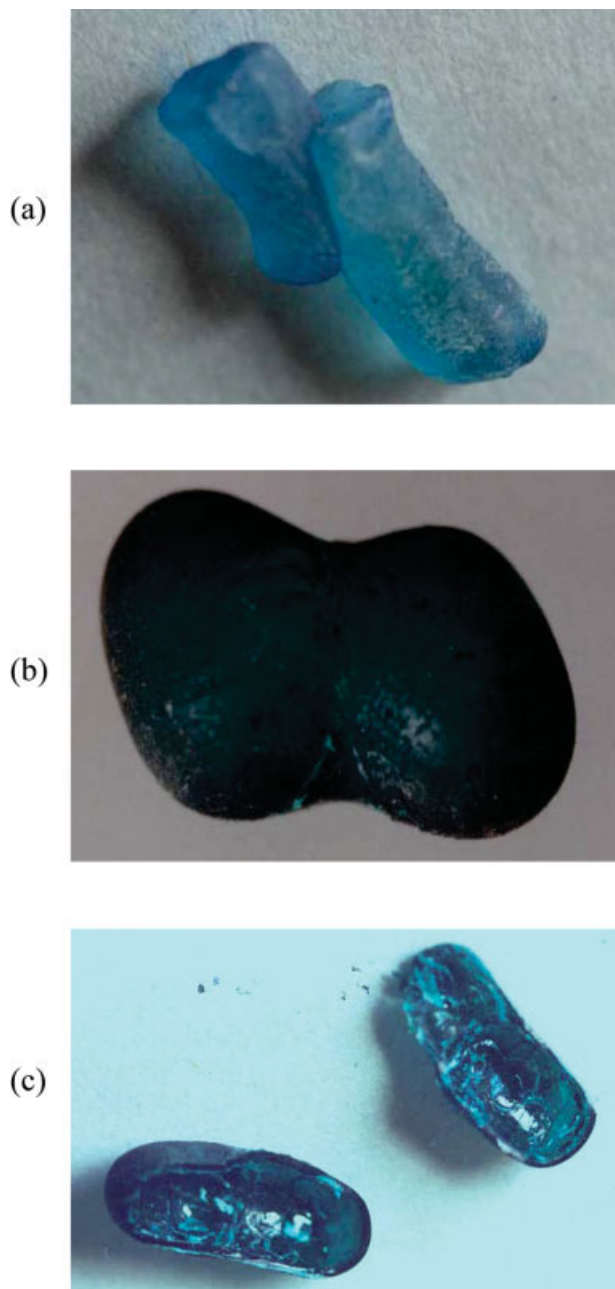
Now consider two dry cylindrical gel pieces of A6ACA that are held together in a 0.1 M  $\text{CuCl}_2$  solution at the ambient temperature. The immediate observation is that they stick to each other. Figure 2(a–c) shows the progress of the healing phenomenon in which two cylindrical gel pieces transformed into a single healed piece keeping a weld line; the healed gels finally transformed into a single hollow object. The two healed gels showed a continuous, hollow interior that connected them internally. This implies that the weld line that formed during healing was strong enough to bear the stresses that developed inside the gel during the formation of a single hollow, self-organized structure from the original two separate gel pieces. We also observed



**Figure 1.** A single cylindrical A6ACA dry gel (the object on the right), when placed in a  $\text{CuCl}_2$  solution, transforms into an ellipsoidal shape or a spherical shape according to the initial aspect ratio of the gel (the object on the left).

that when the two dry gel pieces were held together in deionized water (without  $\text{CuCl}_2$ ), no healing was observed, and the two gel pieces simply transformed into two distinct swollen samples. This clearly showed that the crosslinked gels were unable to heal in a manner similar to that of linear polymers because of the inability of the network chains to reptate across the interface.

A study of the progress of the healing process indicated that the welding improved with time over a period of few hours for gel pieces about 0.5 cm in diameter. This suggested that there was an increase in the strength of the welded joint. The strength of the joint was measured by a tensile peel test. Cylindrical gel pieces (0.5 cm in diameter  $\times$  20 mm long) were butt-welded as described earlier. This was done to prevent the entire gel from being converted into a self-organized, hollow object, for which tensile measurements would become impossible. By welding only a small volume of gels near their interface, we were able to prevent the formation of a hollow interior. Welding was allowed to take place for fixed time



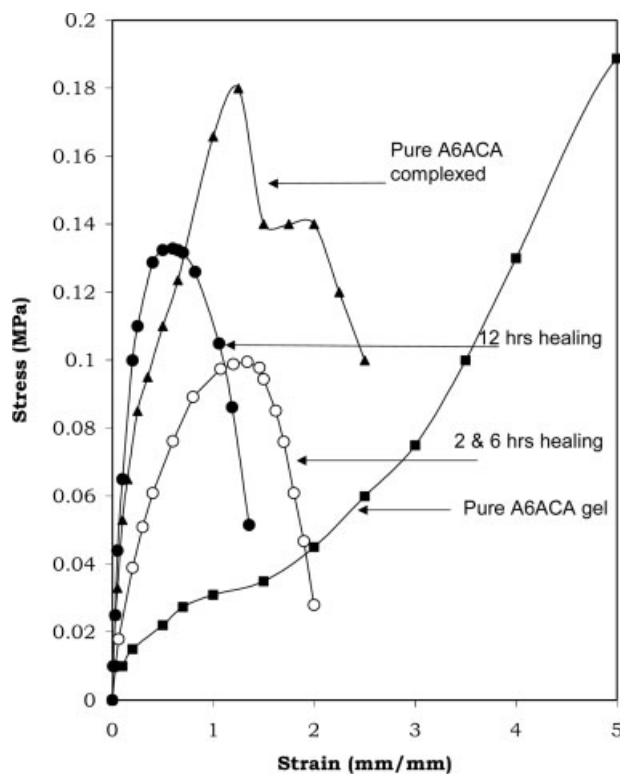
**Figure 2.** (a) Gel pieces welding instantaneously when dipped in a  $\text{CuCl}_2$  solution, (b) completely healed A6ACA gels with a thick interface, and (c) cross sections of the completely healed A6ACA gels showing a continuous, hollow interior.

intervals, after which the gel pieces were removed, dried, and then subjected to tensile testing.

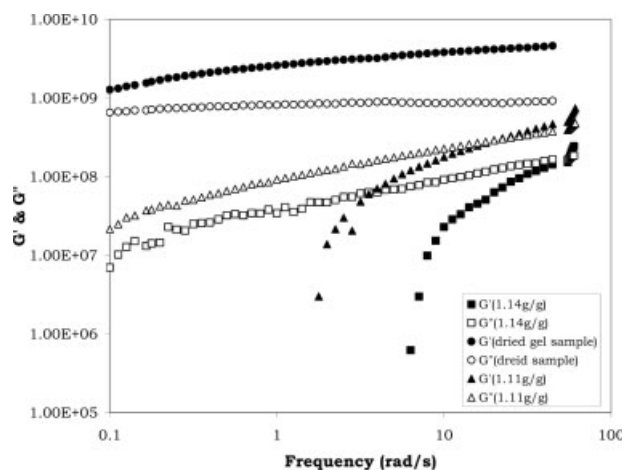
Figure 3 shows stress–strain graphs of A6ACA gels. The engineering stress was calculated as the tensile load per unit of initial area of the gel before deformation. An A6ACA gel containing 1.16 g/g of moisture showed an elastomeric response comprising an initial linear regime followed by a plateau of large

extension and finally a strain-hardening regime. In contrast, a single piece of  $\text{Cu}^{2+}$ -complexed A6ACA gel showed a brittle response characterized by a higher modulus, higher yield stress, and sudden fracture. This behavior corresponds to the expected increase in the crosslink density through the polymer–metal coordination complexation. The tensile behavior of the healed gels was similar to that of the single  $\text{Cu}^{2+}$ -complexed A6ACA gel. In the tensile tests of healed gels, the fracture always occurred at the weld line, and this indicated that the weld line was the weakest junction in the gel. The welded gels were not very brittle. This is seen from the fact that the stress–strain curve shows a distinct yield point after which there is a small but finite extension before the gel fractures. This behavior is indicative of the tenacity of the weld line. The weld-line strength, as characterized by the maximum stress at the yield point, was observed to increase as a function of the healing time (Fig. 3). Moreover, the yield stress values of the healed gels approached that of the original complexed A6ACA gel, indicating that the healing had progressed with time.

We observed that the metal-binding capacity of the gel, the nature of complexation, and the ability to deform under stress influenced the healing ability of the gel. For instance, a neutralized AAc gel, which had the same ionic functional group ( $\text{COO}^-$ ) as the



**Figure 3.** Stress–strain curves of A6ACA gels before and after healing for different time intervals.



**Figure 4.** Elastic ( $G'$ ) and viscous ( $G''$ ) moduli of A6ACA gels as a function of the moisture content.

A6ACA gel, did not heal. We have shown earlier that the stoichiometric binding capacity of A6ACA is greater than that of AAc gels because of the cooperative effects of hydrophobicity and metal binding and also that the A6ACA gel forms dimeric complexes with  $\text{Cu}^{2+}$ , whereas the AAc gel forms only monomeric complexes.<sup>7</sup> Other gels such as those made from PEG and AMPS, which did not form dimeric complexes with  $\text{Cu}^{2+}$ , also did not heal. In the case of AAc, PEG, and AMPS gels, healing was observed by visualization alone, and no mechanical measurements could be carried out because the samples did not heal.

We propose that when two dry A6ACA gel pieces are brought into contact with each other in the presence of  $\text{CuCl}_2$ , the long, flexible side groups carrying the terminal  $\text{COO}^-$  ions initially facilitate a monomeric complexation across the interface. The monomeric species rearranges with time into dimeric species as more  $\text{Cu}^{2+}$  and water diffuse into the interface. The formation of dimers would result in an increase in the crosslink density, which could then increase the weld-line strength. Figure 2(b) also shows that the gels deform considerably during healing, and this results in an increase in the weld area, which could also increase the load-bearing capacity of the weld line. The ability of the gels to deform was observed to be a strong function of the water content of the gel. Figure 4 shows the dynamic moduli of the A6ACA gel for different water contents. The dried sample in Figure 4 refers to a sample that was dried thoroughly to a constant weight. The other samples in Figure 4 were obtained by the exposure of the dried samples to ambient air for various time periods and by the gravimetric measurement of the water intake. Figure 4 shows that the moduli decreased with the water content (i.e., the gels softened), they exhibited a weak frequency dependence, and the viscous response dominated at lower frequencies. All of this suggests a viscoelastic creep behavior that can

facilitate macroscopic deformation during healing. We also found that an A6ACA gel containing a higher degree of crosslinking (e.g., 30% crosslinker) did not heal very well, and this agrees with the fact that the ability to deform decreases with an increase in the crosslink density.

That the healing occurred by coordination complexation alone was evident from the observation that the healed gel reverted back to the two original separate gel pieces when the complexed copper was leached out with HCl, with the exception of a microscopic fracture line roughly aligned along the axis of the cylinder.

## CONCLUSIONS

Successful efforts to demonstrate life-mimicking attributes such as sensitivity (to diverse stimuli),<sup>9–14</sup> selectivity (to diverse molecules),<sup>15,16</sup> mobility,<sup>17</sup> memory (for shape),<sup>18</sup> enzymelike activity,<sup>19</sup> and self-organization<sup>8</sup> have already been reported for smart hydrogels. In this work, we have presented the first experimental observation of yet another attribute, namely, metal-ion-mediated healing, in lightly cross-linked hydrophilic polymers gels. Our work could have several implications. The healing of gels as demonstrated here has some parallels with the adhesion of marine mussels to surfaces, to the extent that both processes occur in an aqueous environment and both involve coordination between macromolecules and metal ions.<sup>20,21</sup> Mussel adhesion, however, occurs by a much more complex process that involves metal-induced coordination and oxidative crosslinking of the protein.<sup>22</sup> The process of healing could have interesting applications in gel-based soft robotics,<sup>23</sup> in which gel arms can asymmetrically stretch or bend and attach themselves to objects through a healing process. Polymers comprising our gels could also find applications in self-healing paints and coatings; cracks in the coatings could be repaired by complexation-driven healing.

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