Redox-Generated Mechanical Motion of a Supramolecular Polymeric Actuator Based on Host-Guest Interactions

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Redox-Responsive Actuators

Redox-Generated Mechanical Motion of a Supramolecular Polymeric Actuator Based on Host–Guest Interactions**

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The expansion and contraction of natural muscles have inspired the design and construction of actuators capable of responding to external stimuli with controllable dimensions and shapes.[1–3] The development of actuators based on materials that reversibly change their shape in response to external stimuli should help improve people's quality of life in such areas as medical treatment and micromachine application. Recently, stimuli-responsive materials have been reported to create artificial muscles and actuators.[4–7] Stimuli-responsive materials using polymeric actuators[8–13] and crystal[14–16] and liquid-crystal[17–27] systems have achieved shape deformations in response to external stimuli, such as temperature,[28,29] chemicals,[30] pH,[31,32] ionic strength,[33,34] electric field/voltage/current,[8,35–38] and light intensity.[39,40] However, reports using redox responsive materials are relatively scarce.[41–44] Furthermore, supramolecular polymeric actuators with combination of redox responsiveness and host–guest interactions are extremely limited.

Previously, we reported supramolecular hydrogels possessing host and guest polymers with a self-healing property.[45] A supramolecular hydrogel consisting of a β-cyclodextrin (βCD) polymer and ferrocene (Fc) polymer cross-linked by host–guest interactions exhibits redox-responsive properties. The formation of inclusion complexes serving as cross-link points for the polymers yield self-healable hydrogels. In contrast, the dissociation of inclusion complexes results in transformation into a sol. We hypothesized that partial chemical bonds prevent a gel from changing to a sol, because the chemical bonds keep a gel structure. Changing cross-link densities (effective network chains) effects the expansion–contraction ability of hydrogels. Accordingly, the reversible complex formation by external stimuli may induce an expansion–contraction process. Although some previous reports have altered the expansion–contraction properties by ionic strength, adjustment of the cross-link density by a redox-responsive host–guest complex has yet to be reported. In particular, there have been no reports evaluating the mechanical work of host–guest supramolecular polymeric actuators by external stimuli.

Herein, we report a redox-driven supramolecular hydrogel actuator formed through a host–guest interaction. The hydrogel actuator consists of a poly(acrylamide) (pAAm) network cross-linked by *N,N′*-methylenebis(acrylamide) (MBAAm) and a complex of βCD-Fc, a redox-responsive host–guest pair. The actuator shows an expansion–contraction process in response to oxidation and reduction of the Fc moieties. We evaluate the mechanical work stored in the actuator.

Prior to preparing the host–guest gel (βCD-Fc gel), the Fc guest monomer (Fc-AAm) was dissolved by the βCD host monomer (βCD-AAm) in a mixed solvent of water and dimethyl sulfoxide (DMSO) (95:5 v/v) to form an inclusion complex. 2D NMR techniques demonstrated the association behavior between βCD-AAm and Fc-AAm as a model system. The 2D ROESY NMR spectrum of βCD-AAm/Fc-AAm in D_2O/[D_6]DMSO (95:5 v/v) is given in the Supporting Information, Figure S1. The protons of the inner cavity of βCD were correlated to the Fc protons, indicating complexation between the βCD and Fc moieties. The apparent association constant K between both monomers was determined to be $(9.3 \pm 0.5) \times 10^2\ \mathrm{L\,mol^{-1}}$ in a mixed solvent of D_2O/[D_6]DMSO (95:5 v/v) using ^{1}H NMR spectroscopy (Supporting Information, Figures S2, S3). This value indicated that about 72, 79, and 83 % of both monomers formed inclusion complexes before polymerization in cases of βCD-Fc gels(1,1,z), (2,2,z), and (3,3,z), respectively (see also Figure 1).

The βCD-Fc gel was prepared by homogeneous radical copolymerization of the inclusion complex with acrylamide (AAm) and MBAAm using 2,2′-azobis[2-(2-imidazolin-2-yl)-propane] dihydrochloride (VA-044) as a water-soluble radical initiator (Supporting Information, Scheme S1).[46] As reference gels, a host gel (βCD gel), a guest gel (Fc gel), and a blank gel (pAAm gel) were prepared by the similar methods as described above (Supporting Information, Schemes S2–S4). These hydrogels were purified by washing with DMSO and water to remove the unreacted compounds. Figure 1 depicts the chemical structures of the βCD-Fc gel(x,y,z), βCD gel(x,z), Fc gel(y,z), and pAAm gel(z). Here x, y, and z represent the mol % of βCD-AAm, Fc-AAm, and MBAAm units. ^{1}H Solid-state field-gradient magic-angle-spinning (FGMAS) NMR and FTIR spectroscopy characterized the chemical structures and content of each monomeric unit of

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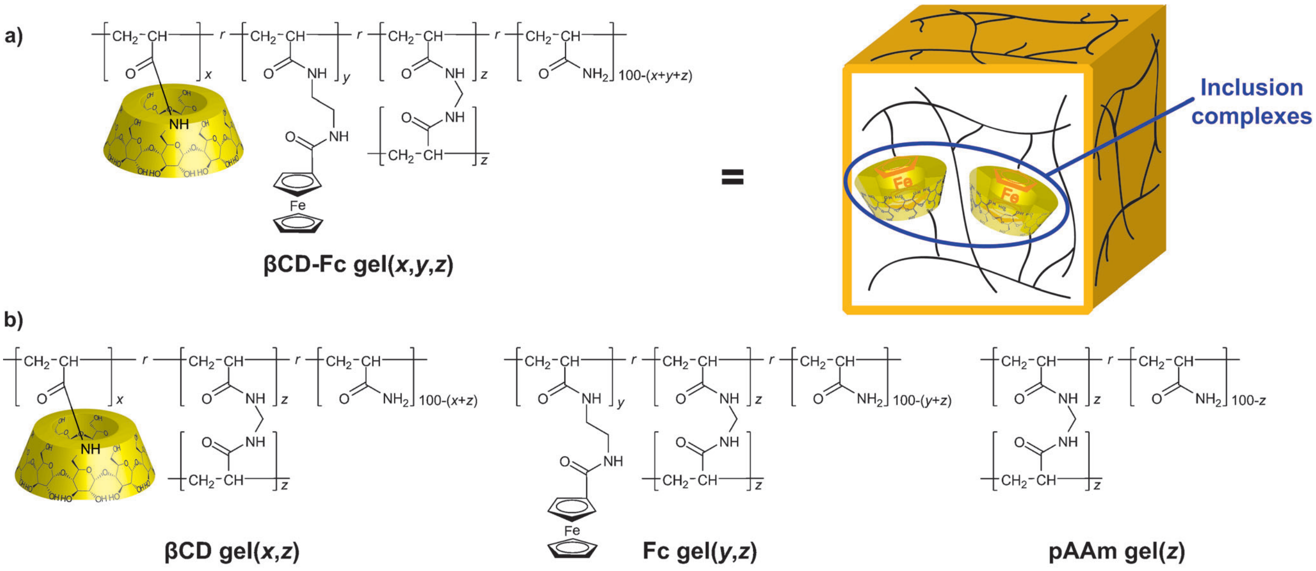

Figure 1. a) Chemical structure and illustration of the βCD-Fc gel(*x*,*y*,*z*). b) Chemical structures of reference gels βCD gel(*x*,*z*) (without the Fc unit), Fc gel(*y*,*z*) (without the βCD unit), and pAAm gel(*z*) (without βCD and Fc units). Here *x*, *y*, and *z* indicate the ratios of βCD-AAm, Fc-AAm, and MBAAm units, respectively.

the βCD-Fc gels, βCD gel(3,1), Fc gel(3,1), and pAAm gel(1) (Supporting Information, Figures S4, S5).

First, we investigated the formation of supramolecular complexes between the βCD and Fc units inside the hydrogel and the influence of competitive molecules on the size of the gel. The cube-shaped βCD-Fc gels (size: $1\times1\times1$ mm^3) were immersed in 3 mL of 0.1 M Tris/HCl buffer solutions (pH 7) of competitive molecules for two hours. We selected an adamantane carboxylic acid sodium salt (AdCANa) as a competitive guest and cyclodextrins (αCD, βCD, and γCD) as competitive host molecules. A digital inverted microscope measured the size changes of gels.[47] The ratio of the lengths r was determined as $r = L_f/L_i \times 100$ (%) (L_f: length of the hydrogel after equilibrium swelling, L_i: length of gel before swelling). Figure 2a,b shows photographs of the βCD-Fc gel(3,3,1) before and after immersion in 10 mM aqueous solutions of AdCANa and βCD. The size of βCD-Fc gel(3,3,1) increased after immersion into an aqueous solution of competitive molecules. Immersing the βCD-Fc gel(3,3,1) in 10 mM aqueous AdCANa increased the r value to 121 ± 1% of the original length (Figure 2c). When βCD-Fc gel(3,3,1) was immersed in 10 mM aqueous solutions of CDs (αCD, βCD, and γCD), r increased to 101 ± 1%, 106 ± 1%, and 102 ± 0.3%, respectively (Figure 2c). The r value for immersion in aqueous βCD was larger than those of αCD and γCD. Previous studies have suggested that the association constant of Fc for βCD was larger than those for αCD and γCD (Fc/αCD; $K = 0.14\times10^3$ L mol^{-1}, Fc/βCD; $K = 17\times10^3$ L mol^{-1}, Fc/γCD; $K = 0.90\times10^3$ L mol^{-1}).[48] The r value was larger for the AdCANa case than that for βCD because the association constant K of the adamantane derivative for βCD ($K = 35\times10^3$ L mol^{-1})[49] was much larger than that for Fc. These results indicate that βCD-Fc gels shrink in water owing to the formation of inclusion complexes between βCD and Fc units, which function as cross-linker inside the hydrogel before immersing in aqueous solutions of competitive molecules. After immersing, the addition of competitive molecules decompose the inclusion complexes to swell βCD-Fc gels (Figure 2).

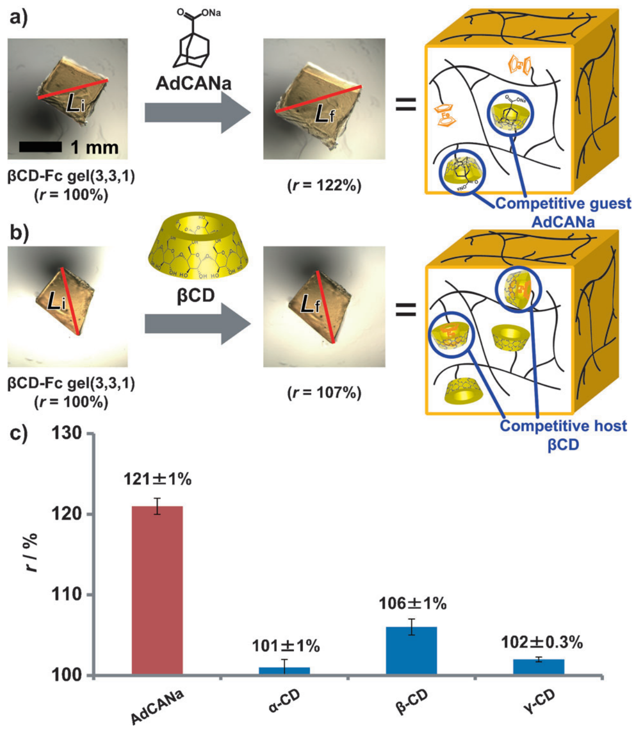

Figure 2. a,b) Photographs (left) and illustration (right) of the length change of βCD-Fc gel(3,3,1) by the addition of a) AdCANa and b) βCD. Red lines indicate the lengths of gels. Scale bar: 1 mm. c) The *r* value of the βCD-Fc gels immersed in solutions of competitive guest molecules (AdCANa) and competitive host molecules (αCD, βCD, and γCD). More than three independent studies confirmed the size change of the βCD-Fc gels.

Next, we regulated the size of the βCD-Fc gels using redox reagents. Cube-shaped gels were immersed in a 0.1 M Tris/HCl buffer (pH 7) before the redox reactions. The Tris/HCl buffer suitably controlled the cross-link density of the βCD-Fc gels by eliminating the electric repulsion between the oxidized ferrocenium cation (Fc^+) units. We chose ceric ammonium nitrate (CAN) as an oxidant. The following immersion procedure was used: 1) The βCD-Fc gel immersed in the Tris/HCl buffer (0.1 M) was placed into the Tris/HCl buffer with CAN (50 mM); 2) After standing for an hour, the oxidized βCD-Fc gel was returned into the Tris/HCl buffer. Figure 3a shows photographs of βCD-Fc gel(3,3,1) before and after the oxidation. The oxidized hydrogel changed from orange to green, which is a characteristic color of Fc^+. The redox reaction of the ferrocene moiety was traced by UV/Vis spectroscopy (Supporting Information, Figure S7). The oxidation with the Tris/HCl buffer with CAN increased the length of the hydrogel, whereas the continuous reduction of the βCD-Fc gel restored the initial length. This behavior was reversible for at least three oxidation-reduction cycles (Supporting Information, Figure S8). βCD showed a high affinity for the reduced state of the Fc group owing to its hydrophobic nature, but the oxidized state of the Fc group (Fc^+) exhibited a low affinity for βCD owing to the cationic nature, which resulted in dissociation of the inclusion complex of βCD/Fc.[50] In contrast, βCD gel(3,1), Fc gel(3,1), and pAAm gel(1) did not exhibit expansion behaviors in response to the CAN (Supporting Information, Figure S9). The stress–strain measurements clearly show the increase and decrease of the supramolecular cross-link density in response to redox stimuli (Supporting Information, Figure S12 and Table S1). The deformation of the inclusion complex between βCD and Fc decreases the cross-link density to swell the hydrogel, whereas the formation of the inclusion complex increases it to shrink, implying that the change in the cross-link density in response to the redox stimuli lead to the uptake and release of water from the gel, which altered the volume of the βCD-Fc gel (Figure 3b; Supporting Information, Table S2).

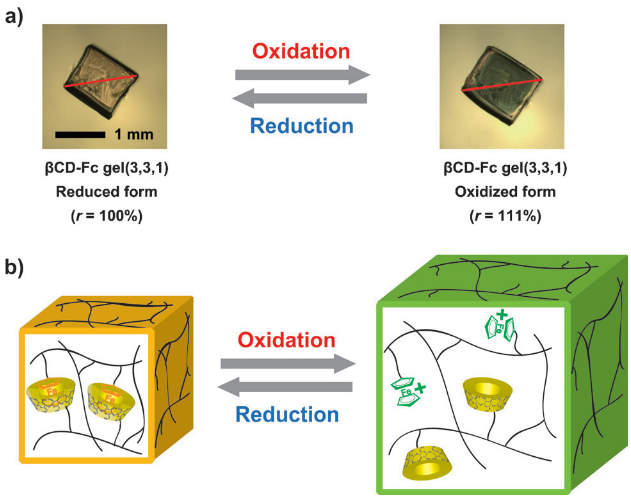

Figure 3. a) Photographs of the βCD-Fc gel(3,3,1) soon after immersion in Tris/HCl buffer with CAN (50 mM) (left) and after one hour (right). Red lines indicate the lengths of gels. Scale bar: 1 mm. b) Illustration of redox-responsive expansion–contraction of the βCD-Fc gel.

Finally, we estimated the mechanical work done by the βCD-Fc gel(3,3,1) through the redox-responsive contraction–expansion. A weight (291 mg) was attached to the bottom of a rectangular βCD-Fc gel (size: $10\times5\times1$ mm^3; Figure 4a).

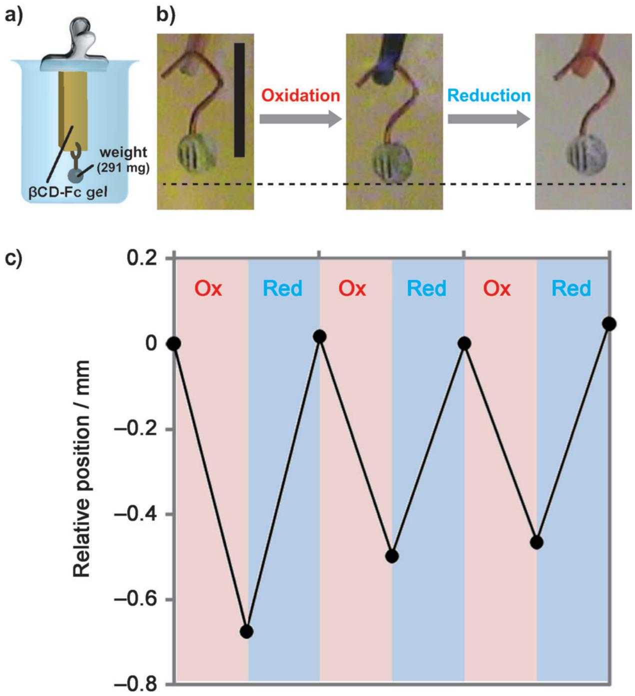

Figure 4. a) Illustration of the hydrogel actuator. b) Photographs of a βCD-Fc gel(3,3,1) actuator in response to redox stimuli. After immersion into the buffer with an oxidant (CAN), the length of the hydrogel increased and the attached weight was lowered. Subsequent immersion into the buffer restored the weight to the original position. Scale bar: 1 cm. c) Plot of the relative position of the weight versus immersion time in the case of βCD-Fc gel(3,3,1) with a weight (291 mg).

This hydrogel actuator was immersed into the Tris/HCl buffer with CAN (50 mM) as an oxidation and subsequently immersed into the Tris/HCl buffer as a reduction. Figure 4b shows photographs of an experiment conducted on the hydrogel actuator composed of βCD-Fc gel(3,3,1) with a weight (291 mg). Oxidation expanded the hydrogel and the position of the weight became down. Reduced βCD-Fc gel contracted and restored the weight to the original position (Figure 4b; Supporting Information, Movies S1 and S2). Figure 4c plots the position of the weight against immersion time. During the reduction step, the weight received mechanical work W, which was determined by $W=(m-\rho V)gx$ (m: mass of the weight, ρ: density of the buffer, V: volume of the weight, g: acceleration of gravity, x: length of the weight that was lifted). In this case, the mechanical work was estimated to be about 2.0 μJ. The same experiments were conducted with βCD-Fc gels(1,1,1) and (2,2,1) (Supporting Information,

Figure S13). The mechanical work of the hydrogel actuator increased in accordance with the amount of host–guest units. These results demonstrate that this hydrogel actuator acts like muscles in response to redox stimuli even in an aqueous buffer solution with high ionic strength.

In conclusion, we successfully achieved redox-responsive expansion and contraction of a hydrogel using inclusion complexes between βCD and Fc as supramolecular cross-links. βCD-Fc gel swells and shrinks by dissociating and re-forming supramolecular cross-links using redox stimulus even at a high ionic strength comparable to a physiological saline solution. Moreover, this expansion and contraction of the hydrogel was visualized as a motion on a macroscale using a hydrogel actuator, and the mechanical work was evaluated. We believe this type of hydrogel, which contains supramolecular cross-links, can be applied to artificial muscles.

Experimental Section

Preparation of βCD-Fc gels: To prepare a host–guest gel containing βCD and Fc moieties, βCD-AAm, Fc-AAm, AAm, and MBAAm were polymerized by radical copolymerization initiated by VA-044 in a mixed solvent of water/DMSO (95:5, v/v) after solubilizing Fc-AAm by βCD-AAm. The obtained gel was repeatedly washed with DMSO and water. Further details of the synthesis are given in the Supporting Information, Scheme S1.

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