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Supramolecular Polymeric Materials via Cyclodextrin–Guest Interactions

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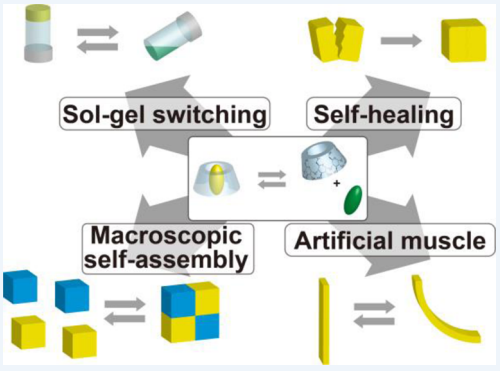
CONSPECTUS: Cyclodextrins (CDs) have many attractive functions, including molecular recognition, hydrolysis, catalysis, and polymerization. One of the most important uses of CDs is for the molecular recognition of hydrophobic organic guest molecules in aqueous solutions. CDs are desirable host molecules because they are environmentally benign and offer diverse functions.



This Account demonstrates some of the great advances in the development of supramolecular materials through host–guest interactions within the last 10 years. In 1990, we developed topological supramolecular complexes with CDs, polyrotaxane, and CD tubes, and these preparation methods take advantage of self-organization between the CDs and the polymers. The combination of polyrotaxane with αCD forms a hydrogel through the interaction of αCDs with the OH groups on poly(ethylene glycol). We categorized these polyrotaxane chemistries within main chain type complexes. At the same time, we studied the interactions of side chain type supramolecular complexes with CDs. In these systems the guest molecules modified the polymers and selectively formed inclusion complexes with CDs. The systems that used low molecular weight compounds did not show such selectivity with CDs. The multivalency available within the complex cooperatively enhances the selective binding of CD with guest molecules via the polymer side chains, a phenomenon that is analogous to binding patterns observed in antigen–antibody complexes.

To incorporate the molecular recognition properties of CDs within the polymer side chains, we first prepared stimuli-responsive sol–gel switching materials through host–guest interactions. We chose azobenzene derivatives for their response to light and ferrocene derivatives for their response to redox conditions. The supramolecular materials were both redox-responsive and self-healing, and these properties resulted from host–guest interactions. These sol–gels with built in switches gave us insight for creating materials that were self-healing or could serve as artificial muscle.

Furthermore, we developed another self-healing material with CD inclusion complexes that showed selective self-healing properties after its surface was cut. These CD self-healing materials do not include chemical cross-linkers; instead the inclusion complex of CDs with guest molecules stabilized the material's strength. However, by introducing chemical cross-linkers into the hydrogels, we produced materials that could expand and contract. The chemical cross-linked hydrogels with responsive groups bent in response to external stimuli, and the cross-linkers controlled the ratio of inclusion complexes. Furthermore, we used the molecular recognition of CDs to achieve macroscopic self-assemblies, and this chemistry can direct these macroscopic objects into even larger aggregated structures. As we have demonstrated, reversible host–guest interactions have tremendous potential for the creation of a wide variety of functional materials.

1. INTRODUCTION

In biological systems, enzyme–substrate complexes, antigen–antibody complex reactions, and DNA express essential functions through recognition of small molecules and macromolecules. In the past 30 years, molecular recognition chemistry[1] and supramolecular chemistry[2,3] have received much attention. Macrocyclic molecules (crown ethers,[1] cyclophanes,[2] cryptands,[3] and cucurbiturils[4]), which are used as host molecules, form diverse supramolecular structures through molecular recognition.

To develop real-world functional materials using supramolecular polymers, molecular recognition should realize unique macroscopic structures with novel properties.[5,6] Our research aims to realize "macroscopic molecular recognition" using artificial host–guest systems with an emphasis on the formation of supramolecular complexes by macrocyclic host molecules. Macroscopic molecular recognition can be categorized by three types of interactions: main chain (polyrotaxane), side chain, and sequential complexes (Figure 1).

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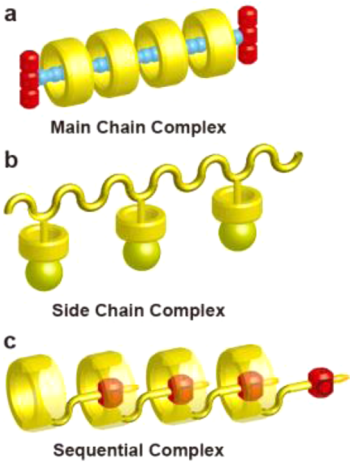
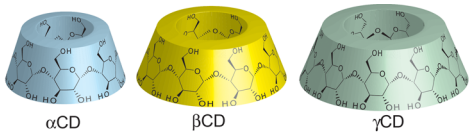
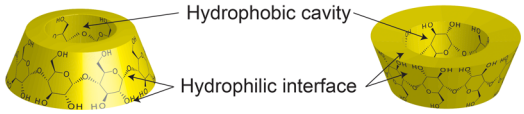


Figure 1. Supramolecular complexes with macrocyclic host molecules through macromolecular recognition.

Table 1. Chemical Structures, Approximate Geometric Dimensions, and Physical Properties of α, β, and γCD



	αCD	βCD	γCD
No. of Glucose Units	6	7	8
Cavity Diameter (Å)	4.7	6.0	7.5
Height of Torus (Å)	7.9	7.9	7.9



Our research employs cyclodextrins (CDs) as cyclic host molecules to construct supramolecular materials. For 15 years, we have studied the catalytic properties of polymers modified with CDs in the hydrolysis of ester compounds.[11] Additionally, we have examined the formation of polypseudorotaxanes in which CDs are incorporated using an axis polymer because reports on the formation of inclusion complexes with polymers and CDs were nonexistent.[9,10] Table 1 shows the physical properties of CDs.[7,8] Hydrophobic and van der Waals interactions between the inner surface of the CD ring and the hydrophobic guests with a suitable molecular size for the CD cavity are responsible for realizing CD inclusion complexes. Polypseudorotaxanes were initially formed in 1990 using water-soluble polymers and CDs in aqueous solutions. In 1997, complexation between CDs and the alkyl side chains on the poly(acrylamide) backbone was reported.[12] Introducing CDs onto the polymer side chains amplifies the selectivity toward guest units, and CD derivatives with hydrophobic guest groups spontaneously form supramolecular polymers via host−guest interactions in solution or in a solid.[13] These supramolecular complexes (main chain type, side chain type, and sequential type complexes) have realized various functional properties, including sol−gel switching, macroscopic self-assembly, self-healing, and artificial muscle properties.

Previously, main chain type supramolecular complexes and materials have been summarized in some reviews.[14−16] In this Account, we summarize our recent results on the molecular recognition properties of polymer side chains and the creation of functional supramolecular materials using intermolecular interactions between polymer side chains.

2. SIDE CHAIN MOLECULAR RECOGNITION BETWEEN POLYMERS

In addition to macromolecular recognition through the main chain, side chain molecular recognition similar to proteins and DNA must occur. Because host molecules precisely identify guest molecules on polymer chains through side chain molecular recognition, some polymers with CDs use this type of recognition to display attractive functions such as self-healing and stimuli-responsiveness. This section introduces side chain interactions between guest polymers and CDs (or CD polymers) and their properties.[17]

2.1. Side Chain Molecular Recognition on Polymers

Tables 2 and 3 summarize the interactions between CDs and side chain groups on polymers. αCD mainly interacts with linear alkyl chains (*n*-butyl, *tert*-butyl, hexyl, octyl, decyl, and dodecyl), whereas βCD selectively interacts with branched alkyl chains (isobutyl, isohexyl, and iso-octyl).[12] These copolymers can be prepared by radical copolymerization of acrylamide and guest molecules modified on methacrylate.

The interactions of CDs with aromatic groups (benzyl, 1- and 2-naphthyl groups) modified on an (acrylamide-*co*-acrylate) copolymer have been investigated.[18,19] βCD includes the 1-naphthyl group shallowly, but it includes the 2-naphthyl group deeply. X-ray crystallography of an inclusion complex of βCD with 2-naphthylmethanol shows that the longer axis of the 2-naphthyl group and the rotation axis of βCD are parallel.

CD interacts with poly(*N*-methacryloyltryptophan) (pMTrp) and with poly(*N*-methacryloylphenylalanine) (pMPhe) (Table 3). The association constants (K_a) of CDs with model compounds (sodium salts of tryptophan and phenylalanine) and pMPhe are comparable, but the K_a of CDs with pMPhe differ significantly.[20]

Poly(acrylic acid) (pAA) with dodecyl (C_{12}) groups as side chains forms a gel due to intermolecular hydrophobic interactions. However, the gel turns into a sol upon addition of αCD because αCD includes a C_{12} group, which decreases the hydrophobic interactions between the dodecyl groups.[21] Adding azobenzene (Azo) into this solution restores the gel because αCD includes Azo instead of the C_{12} group, which allows the dodecyl groups to associate to form a gel. Mixing αCD with pAA having a docecyl Azo group (pAA-Azo) forms a side chain polyrotaxane through a unidirectional inclusion in an aqueous medium.[22] To investigate the correlation between viscosity in semidilute solutions and the affinity in dilute solutions, Tribet and co-workers have studied the binding of pAA-Azo to βCD or βCD polymers and their photo-responsiveness.[23] Stoddart and Zhao have reported photo-stimuli responsive supramolecular hydrogels based on a deoxycholic acid-modified βCD derivative and an Azo-branched poly(acrylic acid) copolymer. They demonstrated that irradiation with visible light recovers the hydrogel from the sol phase.[24]

Similarly, a combination of βCD, dodecyl-modified pAA, and ferrocenecarboxylic acid as a redox-responsive guest achieves a redox-responsive sol−gel system.[25] Variations in the redox potential can induce a reversible host−guest interaction. The K_a of ferrocene (Fc) in its reduced state for βCD is larger than that for αCD (Fc/αCD, $K_a = 0.14 \times 10^3$ M^{-1}; Fc/βCD, $K_a = 17 \times 10^3$ M^{-1}).[26,27] The K_a of βCD for the Fc group on poly(acrylic

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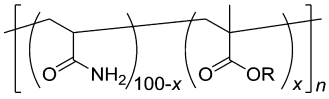
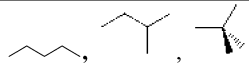
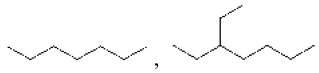
Table 2. Chemical Structures of Guest Polymers That Form Host−Guest Complexes on Polymer Side Chains

Main-chain structure	Side-chain structure	Ref.
		12
		12
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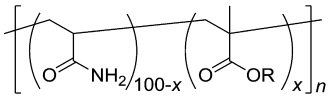
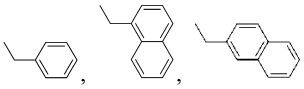
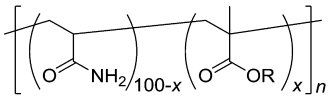
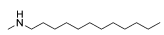
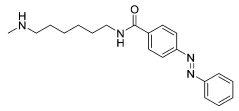
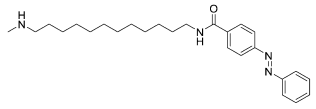
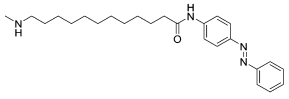
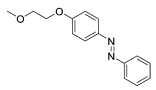
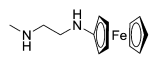
		18, 19
		21, 25
		22
		22
		23
		24
		25

acid) is 1.1×10^3 M^{-1}.[28] Ritter has reported the radical initiated homopolymerization of a soluble vinylferrocene−CD complex and copolymerization starting from CD complex with vinylferrocene and *N*-isopropylacrylamide (NIPAAM) in water.[29]

Ritter et al. recently reported a new type of side chain polyrotaxane in which inclusion complexes of di(meth)acrylates of butan-1,4-diol and hexan-1,6-diol are polymerized with αCD and methylated βCD using a redox initiator system in aqueous media.[30]

An alternating copolymer of sodium maleate and dodecyl vinyl ether ($pC_{12}MA$) forms micelle-like aggregates in aqueous media. Upon adding CD to the copolymer, an inclusion complex between CDs and the C_{12} groups forms and the dodecyl group synchronously self-associate in aqueous solutions. Due to the molecular weight dependence of the cooperative complexation of αCD,[32] the dodecyl groups in $pC_{12}MA$ interact significantly with αCD but not β or γCD[31] (Table 2).

CDs show molecular recognition for specific types of guest molecules on a polymer chain. βCD mixed with alternating copolymers of sodium maleate possessing an adamantyl (PAdMA) group or with the adamantylphenyl (PAdPhMA) in an aqueous solution selectively forms an inclusion complex with PAdMA. However, the K_a of βCD with the AdPh model compound is higher than that with the Ad model compound (Table 3).[33]

An alternating copolymer of sodium maleate with a heptyl carboxylic acid sodium salt group (C_7) and an Azo group connected with oligo(ethylene glycol) on the side chain forms a photoresponsive heteropolypseudorotaxane. αCD includes both the C_7 and *trans*-Azo group to form a side chain polypseudorotaxane. After UV irradiation to induce photoisomerization into *cis*-Azo, one αCD dethreads from the Azo group, while another αCD interlocks on the side chain. Furthermore, adding βCD to the side chain polyrotaxane gives an αCD−βCD heteropolypseudorotaxane (Figure 2).[34]

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Table 3. Chemical Structures of Guest Polymers Forming Host–Guest Complexes on Polymer Side Chains

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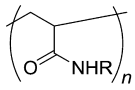
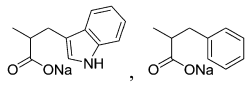
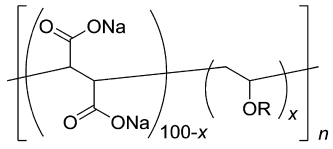
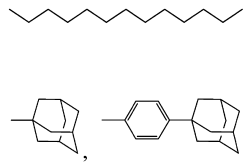
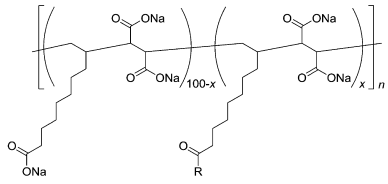
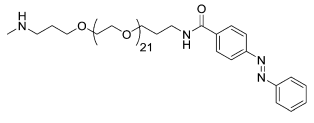
		20
		31 32 33
		34

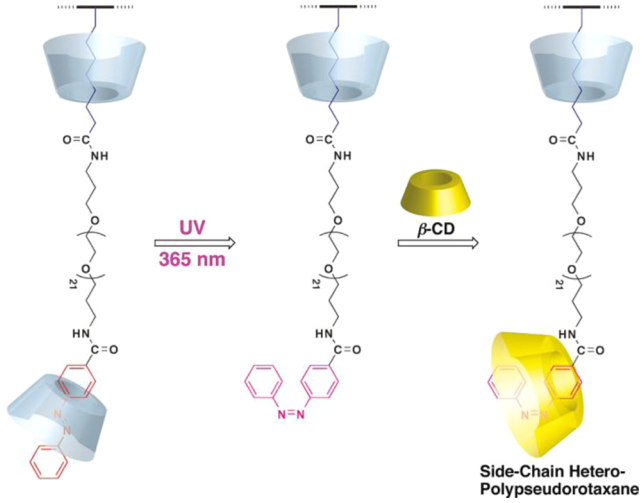


Figure 2. Schematic illustration of side chain formation in heteropolypseudorotaxane composed of α- and βCDs. Reproduced from ref 34. Copyright 2010 American Chemical Society.

2.2. Formation of Hydrogels through Side Chain Molecular Recognition

Adamantyl (Ad) groups are included and held strongly in βCD. To obtain noncovalently cross-linked gel structures, Ritter has used a CD dimer and Ad-containing polymers. Guest copolymers contain 1-adamantylacrylamide or 6-acryloylaminohexanoic acid 1-adamantylamide based on NIPAAM or *N*,*N*-dimethylacrylamide (DMAA) (Table 4). The formation of inclusion complexes between Ad-containing copolymers and βCD dimers give supramolecular hydrogels.[35] Furthermore, hydrogels based upon epichlorohydrin cross-linked CD polymers and adamantyl guest copolymer can be synthesized based on 2-acrylamido-2-methyl-1-propanesulfonic acid sodium salt. The concentration of both polymers affects the viscosity of the supramolecular hydrogel.[36]

Lincoln and co-workers have studied polymer networks constructed by inclusion complexes between βCD and 1-(2-aminoethyl)amidoAd substituents on PAA. Mixing βCD-substituted PAA and Ad-substituted PAA increases the viscosity at a 1:1 unit ratio.[37−39]

2.3. Photoresponsive Supramolecular Sol–Gel Transition Materials

Azo shows photoisomerization with UV or visible light irradiation.[40,41] αCD or βCD selectively forms an inclusion complex with the *trans*-isomer but not the *cis*-isomer because the K_a of CDs with *trans*-Azo is higher than that of *cis*-Azo.

Sol–gel transition systems have been constructed by complexation of αCD with dodecyl side chains on the poly(sodium acrylate) backbone.[18] The viscosity drastically decreases upon adding αCD to a hydrogel of poly(sodium acrylate) modified with 5 mol % of dodecyl side chains (p(AA/C_{12})). The viscosity of the solution with 4,4′-diazobenzoic acid (ADA) as a photoresponsive competitive guest increases with the concentration of ADA. Photoisomerization of ADA controls the association and dissociation of the dodecyl side chain with αCD, leading to photoresponsive sol–gel transitions (Table 5).

Mixing βCD modified poly(allylamine) with *trans*-Azo modified poly(acrylamide) yields supramolecular hydrogels. The K_a of *trans*-Azo with βCD is larger than that of *cis*-Azo. However, the *cis*-Azo copolymer does not form supramolecular hydrogels with βCD copolymers in water because the host–guest interaction between βCD and the *trans*-Azo group acts as a cross-linker between polymers.[42]

To estimate the change in the cross-link density of the mixed solution by photoirradiation, the change in viscosity of a mixture of αCD-modified pAA and Azo-modified pAA (pC_{12}Azo) under UV irradiation has been investigated by steady-shear viscosity measurements by attaching αCD to the side chain of pAA at the wider rim of αCD (p3αCD). Irradiating with UV light decreases the viscosity of p3αCD/pC_{12}Azo by nearly an order of magnitude, whereas subsequently irradiating with visible light recovers the initial viscosity value.[43]

Curdlan modified with αCD (CD-CUR) and pC_{12}Azo realizes a continuously variable photoresponsive supramolecular hydrogel because the difference between K_a of αCD with

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Table 4. Chemical Structures of Guest Polymers That Form Supramolecular Hydrogels with CD Polymers

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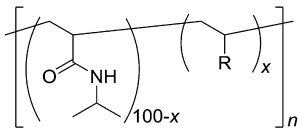
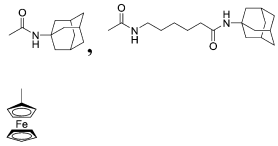
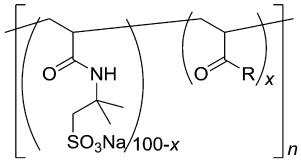
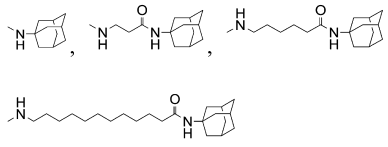
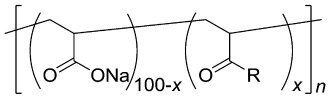
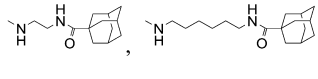
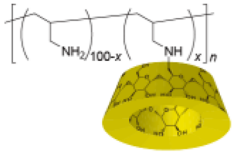
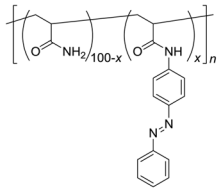
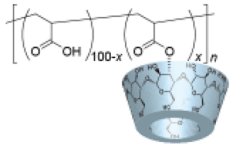
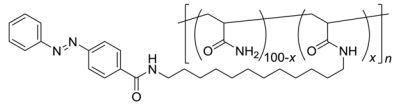
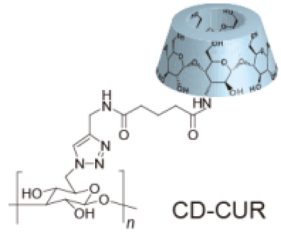
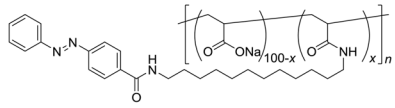
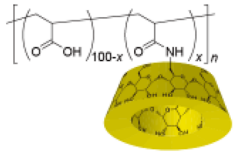
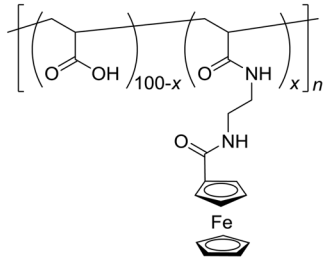
		35 29
		36 37-39
		31-34

Table 5. Chemical Structures of Host and Guest Polymers That Demonstrate a Stimulus-Responsive Sol−Gel Transition

CD host polymer	Guest polymer	Ref.
		42
		43
		44
		28

trans-Azo and that with *cis*-Azo is larger than those of βCD. A mixture of CD-CUR and pC_{12}Azo in an aqueous solution forms a supramolecular hydrogel. Irradiating with UV light (λ = 365 nm) converts the gel into a sol. However, visible light (λ = 430 nm) or heating (60 °C) induces back isomerization of the *cis*-Azo group to the *trans*-Azo group (Figure 3a). The viscosity changes of CD-CUR/pAC_{12}Azo can be repeatedly induced using UV and visible lights (Figure 3b).[44]

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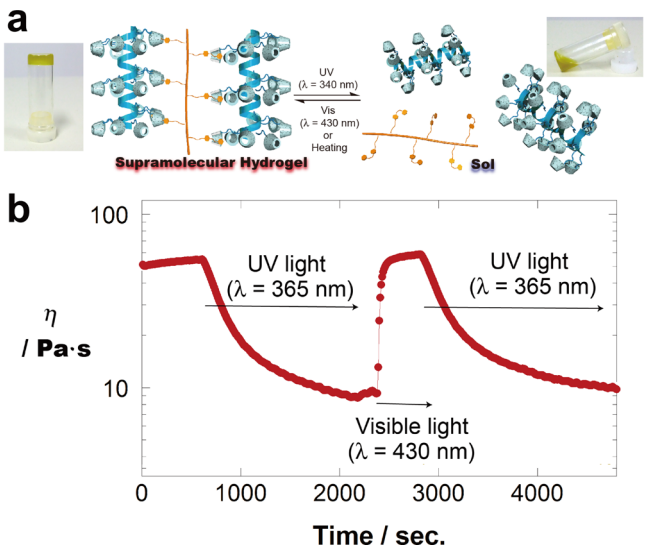

Figure 3. (a) Schematic representation of a photoresponsive sol–gel transition material with CD-CUR and pC12Azo upon irradiating with UV light (365 nm) and visible light (430 nm) or heating at 60 °C. (b) Zero shear viscosity (η_0) change for CD-CUR/pAC$_{12}$Azo after repeatedly photoirradiating with UV (λ = 365 nm) and visible light (λ = 430 nm). Reproduced with permission from ref 44. Copyright 2010 WILEY-VCH Verlag GmbH & Co. KGaA.

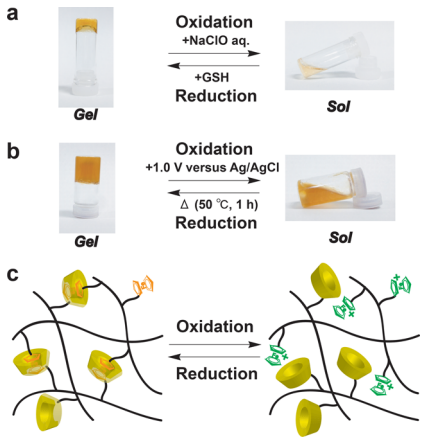

Figure 4. Redox-responsive sol–gel switching. Reprinted by permission from Macmillan Publishers Ltd: *Nature Communications* (ref 28), copyright 2011.

2.4. Redox-Responsive Supramolecular Sol–Gel Transition Materials

As mentioned above, βCD forms a 1:1 inclusion complex with ferrocenecarboxylic acid (FCA), whereas oxidized FCA weakly interacts with βCD. Taking advantage of the redox-responsive complex formation, gel-to-sol transition systems have been constructed by complex formation of βCD with the dodecyl side chains of p(AA/C$_{12}$).[25] Adding βCD to a hydrogel of p(AA/C$_{12}$) decreases the viscosity drastically to give a sol. However, the viscosity of the sol with FCA as a redox-responsive competitive guest increases as the FCA concentration increases. After oxidation with sodium hypochlorite, the gel state changes to the sol state.

A mixture of pAA with βCD and pAA with Fc forms a hydrogel with a self-standing property. Treating the gel with an oxidizing agent (sodium hypochlorite) produces the sol (Figure 4a) due to changes in the ferrocenium cation (Fc$^+$) upon oxidation. The βCD cavity does not include Fc$^+$, eliminating the cross-linking and converting the gel into a sol (Figure 4c). Treating the sol with a reducing agent [glutathione (GSH)] restores the gel. Additionally, the gel–sol transition can be induced via an electrochemical redox (Figure 4b).[28]

3. SELF-HEALABLE SUPRAMOLECULAR HYDROGELS FROM HOST AND GUEST POLYMERS

3.1. Conventional Self-Healing Materials

Recently, synthetic methods have been used to design and construct self-healing polymeric materials.[45−48] Various noncovalent interactions and dynamic covalent bonds have been utilized as a "binder" to unite synthetic polymers to form self-healing materials (Figure 5). In particular, host–guest interactions are advantageous due to their reversibility and responsiveness to various external stimuli. Supramolecular hydrogels based on water-soluble polymers using molecular recognition have great potential for medical approaches, such as cell scaffolds, drug delivery, prostheses, etc. We have developed self-healing supramolecular hydrogels based on host–guest interactions at the side chain of water-soluble polymers. We have proposed two different effective approaches to prepare supramolecular self-healable materials through host–guest interactions: (1) from a mixture of host and guest polymers and (2) from polymerization of host and guest monomers (Figure 6).

3.2. Redox-Responsive Self-Healing

We initially investigated the self-healing ability of supramolecular hydrogels based on the host and guest polymers

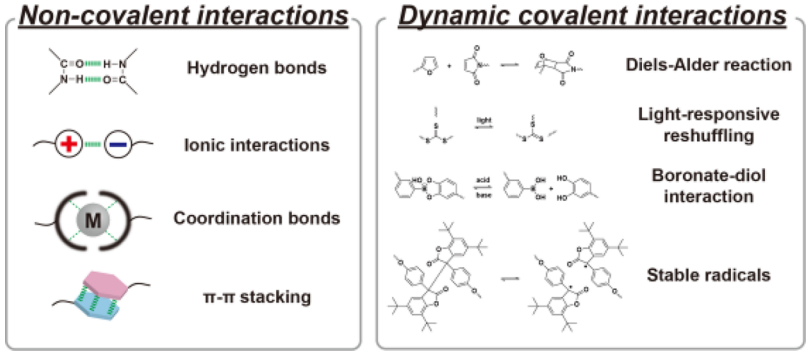

Figure 5. Examples of noncovalent and dynamic covalent interactions utilized in polymeric self-healing materials.

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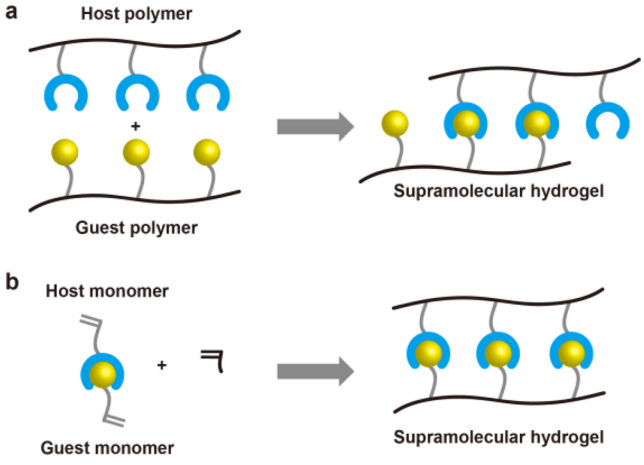

Figure 6. Conceptual illustrations of the preparation methods for self-healing polymeric materials using two different approaches: (a) mixing host and guest polymers and (b) copolymerization of host–guest inclusion complexes via a supramolecular cross-linker.

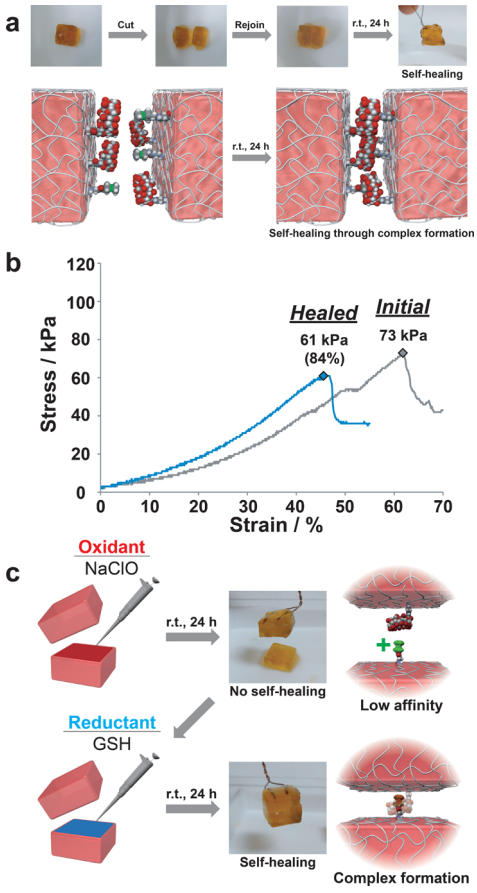

Figure 7. Redox-responsive self-healing hydrogels. (a) Self-healing of a hydrogel composed of a host polymer modified with βCD and a guest polymer modified with ferrocene. (b) Stress–strain curves of pAA-6βCD/pAA-Fc hydrogel (3 wt %) after standing for 24 h. (c) Redox-responsive switching of the self-healing ability. Coating the cut surface with an oxidant (NaClO) inhibits self-healing, but subsequent treatment with a reductant [glutathione (GSH)] restores the self-healing ability. Reprinted by permission from Macmillan Publishers Ltd: *Nature Communications* (ref 28), copyright 2011.

(Figure 6a). The gel mentioned in section 2.4 formed from a βCD polymer and Fc polymer exhibits a redox-responsive sol–

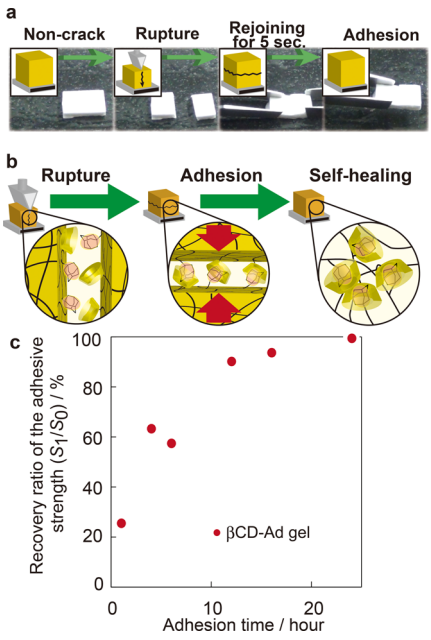

Figure 8. Self-healing hydrogels formed by host–guest polymers. (a) Self-healing of the hydrogel composed of a host (βCD)–guest (adamantane) polymer. (b) Schematic illustration of the rapid and complete self-healing between cut surfaces. (c) Recovery ratio, which is ratio of the initial stress strength (S_0) to the adhesion strength (S_1) of βCD-Ad gel(7,6), as a function of time. Reproduced with permission from ref 49. Copyright 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

gel transition. Even if the gel is cut in two using a razor, the contact surface disappears and self-healing is complete in several hours (Figure 7a).[28] After 24 h, the gel recovers almost 85% of the initial strength (Figure 7b). Treating the cut surface with an oxidizing agent (sodium hypochlorite) prevents the pieces from readhering. However, treating the cut surface with a reducing agent improves the ability of the pieces to readhere, and a single piece is produced. Thus, the self-healing process can be regulated by external stimuli, which, in this case, are redox reactions (Figure 7c).

3.3. Self-Healing Materials through Host–Guest Complexes

Furthermore, host–guest interactions should realize improved self-healing materials with higher healing efficiencies. To obtain effective self-healing materials, we adopted the host–guest containing polymer approach (Figure 6b). In this case, Ad and βCD are used as a guest and host, respectively.[49] Formation of an inclusion complex with βCD solubilizes the Ad monomer. This complex can be copolymerized with acrylamide to give a self-healable hydrogel. When two freshly cut surfaces come into contact, the two pieces adhere to form a single gel (Figure 8a), and the initial gel strength is almost completely recovered after 24 h (Figure 8b). Additionally, the recovery ratio of the rupture strength increases with adhesive time (Figure 8). Interestingly, the cut surfaces of the obtained hydrogel show a selective self-healing property.

4. MACROSCOPIC SELF-ASSEMBLY THROUGH MOLECULAR RECOGNITION

Although the formation of supramolecular structures using simple nanometer-sized molecules has been well investigated, supramolecular polymers cannot be directly observed without

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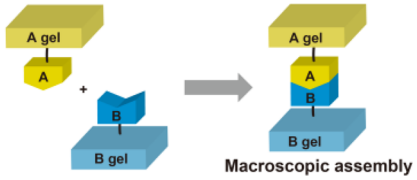
Table 6. Macroscopic Self-Assemblies between Host Gels and Guest Gels and K_a's of CDs (αCD, βCD, and γCD) with Guest Units



A	B	Interaction	K / M^{-1} α	β	γ	Ref
α β		Host-Guest	98	1500		50
α		Host-Guest	57			50
β		Host-Guest		170		50
α		Host-Guest	290			51
β		Host-Guest		6670		51
α		Host-Guest	1200			51
α		Host-Guest	330			51
β γ		Host-Guest		84	310	51
α β γ		Host-Guest	13	84	-	53,58
β		Host-Guest		43		53
β		Host-Guest		120		52
β		Host-Guest		270		52,53
β γ		Host-Guest		110	-	53
γ		Host-Guest			350	53
β γ		Host-Guest		-	340	53,56
β		Host-Guest		122		57
α β		Host-Guest	2000[a]	280[b]		54
β		Host-Guest		1100		55
		Ionic		-		55

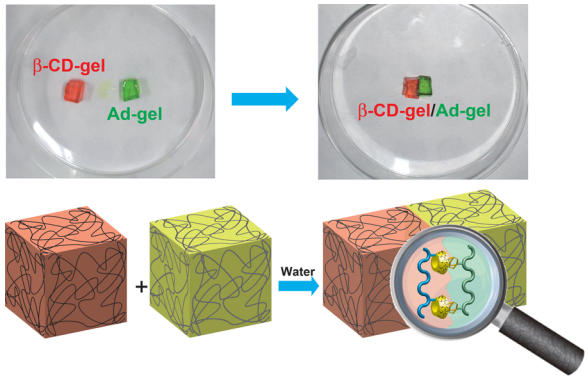


Figure 9. Macroscopic self-assembly between the βCD-gel (red) and the Ad-gel (green). Reprinted by permission from Macmillan Publishers Ltd: *Nature Chemistry* (ref 50), copyright 2011.

special equipment. However, if a gel is considered as a gigantic molecule composed of macromolecules joined by short cross-linking reagents, it may be possible to directly observe molecular recognition with the naked eye. To this end, a poly(acrylamide) gel (pAAm gel) is used as a scaffold because the pAAm gel does not interact with proteins, DNA, and polysaccharides, including CDs.

We prepared CD host gels and guest gels by copolymerization of acrylamide, the functional monomer, and *N*,*N*′-methylenebis(acrylamide) (MBAAm). Table 6 summarizes the macroscopic interactions between the host and guest gels.

4.1. Gel Self-Assembly through Host–Guest Interactions

As the first example of adhesion of macroscopic materials via molecular recognition, a βCD gel adheres strongly to an Ad guest gel, and separation is difficult (Figure 9). Although we tried to separate the assembly using a creep meter, the gel would not separate. However, the gel did break, just not at the contact surface.

If an αCD gel is added to a guest gel mixture of *n*-butyl gel and *t*-butyl gel, αCD only binds to the *n*-butyl gel. In contrast, adding a βCD gel to the same mixture of guest gels results in the βCD gel binding with only the *t*-butyl gel. Hence, CD gels can discriminate guest gels by molecular recognition;[50] αCD gels selectively bind to linear alkyls, while βCD and γCD gels bind to cyclohexyl gels and cyclododecyl gels (Table 6).[51]

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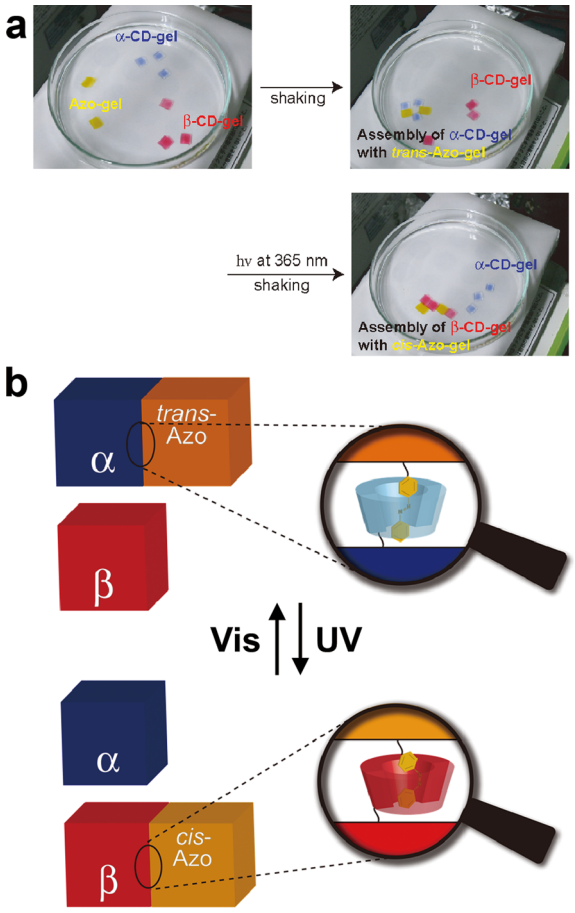


Figure 10. Schematic illustration of a photoresponsive macroscopic self-assembly through host–guest interactions. Reprinted by permission from Macmillan Publishers Ltd: *Nature Communications* (ref 54), copyright 2012.

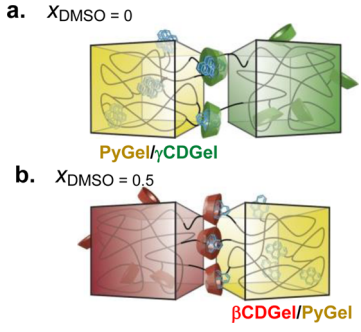


Figure 11. Schematic illustration of selectivity switching of Py gel as a function of x_{DMSO}. Reprinted by permission from Macmillan Publishers Ltd: *Nature Communications* (ref 56), copyright 2012.

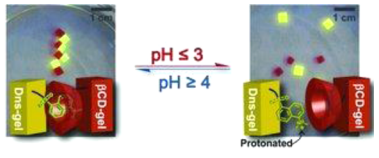


Figure 12. Schematic illustration and photographs of a pH-responsive assembly of Dns-gel and βCD-gel. Reproduced with permission from ref 57. Copyright © 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim

4.2. Photoswitchable Gel Self-Assembly

The Azo gel and the αCD gel form an assembly in water because *trans*-Azo is included in the αCD cavity. However, UV light causes the assembly to dissociate. Irradiating the *cis*-Azo gel with visible light converts *cis*-Azo into *trans*-Azo, enabling the Azo gel and the αCD gel to rebind. Irradiating a gel assembly of αCD and *trans*-Azo with UV light in the presence of the βCD gel causes the Azo–αCD gel to dissociate, and then the Azo gel forms an assembly with βCD because the K_a of *cis*-Azo with βCD is larger than that with αCD (Figure 10).[54]

4.3. Redox-Switchable Gel Self-Assembly

We investigated a redox-responsive gel assembly using Fc as a redox-active probe molecule with a βCD gel, a Fc gel, and an anion (*p*-styrenesulfonic acid sodium salt (SSNa)) gel. Under reductive conditions, the Fc gel selectively adheres to the βCD gel. The Fc^+ gel, which is prepared by the oxidation of the Fc gel, does not form a gel assembly with βCD, but the Fc^+ gel selectively adheres to the SSNa gel through ionic interactions. These two discrete noncovalent interactions can control the gel assemblies using Fc as an intelligent recognizer and a suitable adhesion partner.[55]

4.4. Solvent-Switchable Gel Self-Assembly

Pyrene (Py) easily forms dimers and aggregates in aqueous media but remains a monomer in organic solvents such as dimethyl sulfoxide (DMSO). Varying the volume fraction of DMSO (x_{DMSO}) in a mixed solvent system alters the macroscopic assembly between CD gels and Py gels. In pure water (x_{DMSO} = 0), the Py gel aggregates only with the γCD gel through host–guest interactions between γCD and the Py dimer on the gel surfaces. At x_{DMSO} = 0.5, only the βCD gel adheres to the Py gel to form an aggregate (Figure 11). Thus, the Py gel can discriminate between αCD, βCD, and γCD gels based on the external environment, such as the solvent composition.[56]

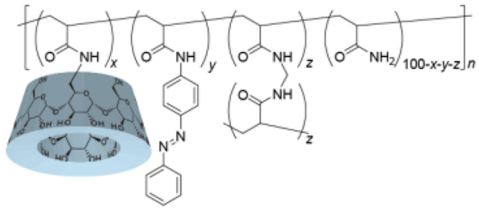
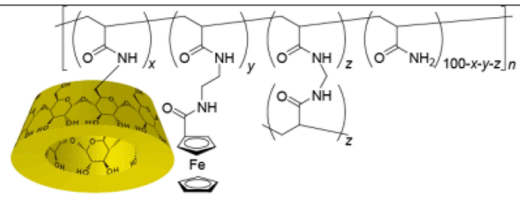
4.5. pH-Switchable Gel Self-Assembly

We have also developed a pH-responsive gel assembly based on host–guest interactions between CDs and dansyl (Dns) residues. The βCD gel forms an aggregate with the Dns gel at neutral pH but not at a lower pH (≤3.0). The Dns moiety exists in its protonated form at an acidic pH, but the protonated Dns moiety is too hydrophilic to form an inclusion complex with βCD. These results indicate that the gel assembly is formed due to complexation between neutral Dns and βCD on the surfaces of the gels. The association and dissociation of both gels are reversible by altering the pH of the external aqueous medium using an acid (HCl aq.) or base (NaOH aq.) (Figure 12).[57]

4.6. Temperature-Sensitive Gel Self-Assembly

The formation of macroscopic assemblies can also be controlled by temperature.[58] pAAm gels modified with a benzyl (Bz) moiety (Bz gel) form assemblies only with the βCD gel at room temperature (23 °C), but cooling the external solution to 15 °C begins to induce assemblies between the αCD gel and the Bz gel. Further cooling down to 5 °C also results in an assembly between the Bz gel and the γCD gel. Consequently, one large aggregate composed of the Bz, αCD, βCD, and γCD gels is formed, and the stability of the inclusion complex controls the interaction strength between the Bz and CD gels (βCD gel > αCD gel > γCD gel).[58]

Table 7. Chemical Structures of Stimuli-Responsive Supramolecular Materials

External stimuli	Chemical structures	Ref.
Photo (UV & Vis lights)		59
Redox		60

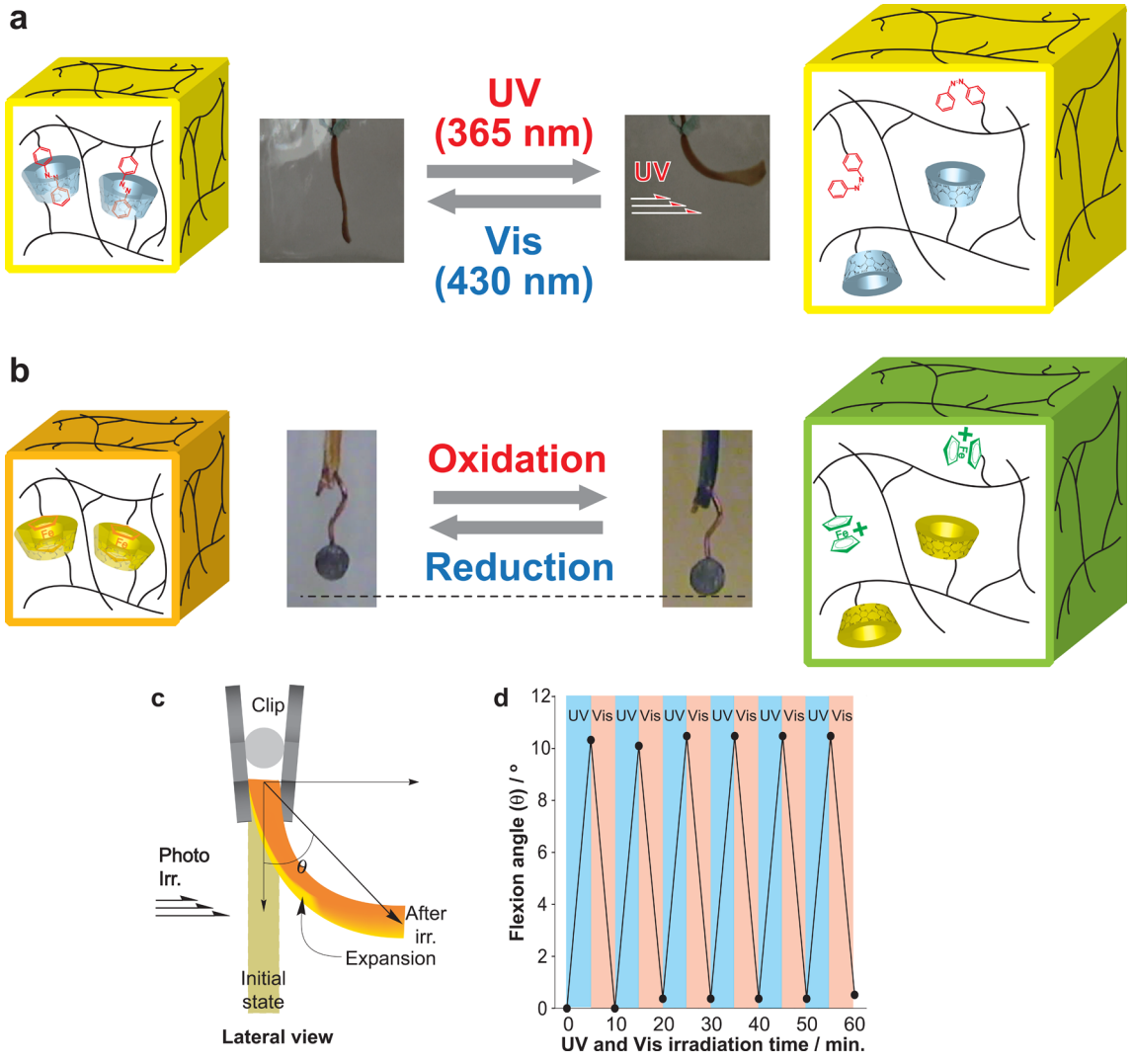


Figure 13. Schematic illustrations of (a) photoresponsive and (b) redox-responsive supramolecular actuators. (c) Lateral view of αCD−Azo gel (2,2) hung with a clip. Flexion angle (θ) is defined here. (d) Repetition experiment of αCD−Azo gel (2,2) irradiated with UV and visible lights for 5 min. Plots show the correlation between irradiation time and flexion angle (θ). Panels a, c, and d reprinted by permission from Macmillan Publishers Ltd: *Nature Communications* (ref 59), copyright 2012. Panel b reproduced with permission from ref 60. Copyright 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

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5. ARTIFICIAL MUSCLES

5.1. Conventional Artificial Muscles

To realize artificial muscles (actuators), many works have examined muscle-like movements in actuators that convert input energies (electric, thermal, change, and photo energies) into visualized movements (deformation, transformation, pressure, etc.). It has been found that polymer-based actuators show reversible shape deformations in response to external stimuli. We reported that sol−gel switching materials are formed by mixing an aqueous solution of a host polymer containing CD with that of a guest polymer containing Azo[42−44] or Fc[28] (Table 5). A sol−gel transition occurs when an external stimulus alters the cross-link density. If the covalent bonds partly cross-link polymer chains, then external stimuli should induce an expansion−contraction behavior instead of a sol−gel transition. This section examines stimuli responsive supramolecular actuators through CD−guest interactions. Table 7 summarizes the chemical structures of supramolecular materials with CDs and stimuli responsive groups based on pAAm gels.

5.2. Gel Actuator Containing αCD and Azobenzene

A host−guest gel (αCD−Azo gel) with αCD and Azo creates a photoresponsive contraction−expansion materials. Irradiating αCD−Azo gels with UV light increases the weight, but irradiating with visible light restores the initial weight and volume due to the formation of an inclusion complex between the αCD and Azo units. Because the αCD−Azo gel bends in the same direction as the incident light, the volume of the surface exposed to UV light increases, while nonexposed surface remains constant. Hence, the αCD−Azo gels show a flex-like behavior due to strain deformation (Figure 13a).[59] Figure 13c defines the flexion angle (θ). The gel clearly shows a back-and-forth motion, which depends on the wavelength regardless of the irradiation history (Figure 13d).

5.3. Gel Actuator Containing βCD and Ferrocene

When a gel containing βCD as a host molecule and Fc as a guest molecule is oxidized, the gel expands as Fc changes to Fc^+. Fc^+ has low affinity for βCD, and the inclusion complex dissociates. Reducing Fc^+ back to Fc shrinks the gel because Fc is included in the βCD, restoring the cross-linking parts.

When a gel strip containing βCD and Fc is oxidized, the gel strip expands, decreasing the weight. Subsequent reduction of Fc^+ shrinks the gel to restore the original weight, and eventually the chemical energy is converted into mechanical energy (Figure 13b).[60]

6. CONCLUSION

Thirty years ago, the chemistry of CDs was actively studied as an enzymatic model. Beginning in 1990, rotor molecules have become commonplace to prepare supramolecular complexes, including polyrotaxane, CD tubes, and supramolecular polymers, and in the last five years, functional supramolecular materials, including macroscopic self-assemblies, self-healing materials, and actuators, have been exploited. Although diverse molecular recognition properties with CDs produce interesting material functions, molecular recognition of CDs in supramolecular materials has yet to be completely understood in molecular dynamics, surface science, and statistical analysis. However, through selective molecular recognition, supramolecular materials using CDs should help advance science and technology involving supramolecular materials.

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Notes

The authors declare no competing financial interest.

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