



## Some hydrogels having novel molecular structures

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### ABSTRACT

Hydrogels are important materials for a variety of applications, particularly biomedical devices, but they generally have poor mechanical properties since they consist predominantly of water held in place by a relatively fragile polymer network. This brief review describes a few novel methods to control or improve the mechanical properties of hydrogels including slide-ring gels, double-network gels, nanocomposite gels, and photoactive gels. Our goal is to encourage more researchers to be aware of and to exploit these methods.

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### 1. Introduction

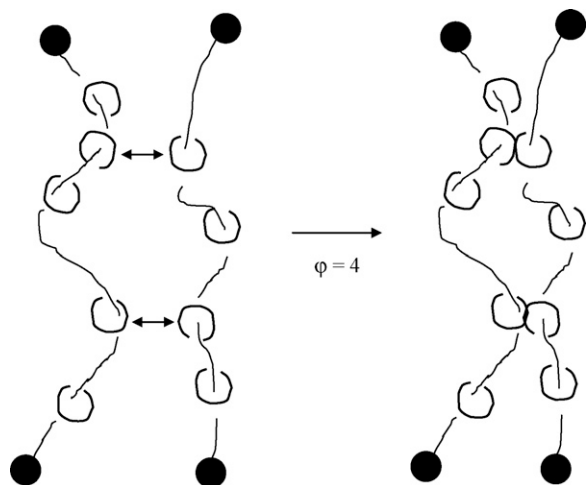
The materials of interest in this brief review are primarily hydrogels, which are polymer networks extensively swollen with water [1–5]. We place primary importance on four methods being developed to improve or control the mechanical properties of hydrogels. Materials possessing

biomimetic, collapsed crosslinks which unfold under stress and then refold reversibly upon retraction of the elastomer are not considered in this review but may be of interest to the reader [6–7].

### 2. Slide-ring gels

Slide-ring gels are topological networks with some similarities to linear rotaxane assemblies [8,9]. In these gels, a number of cyclic molecules are threaded onto a linear polymer chain and then trapped by placing bulky capping groups at the two ends of the chain. Some of the cyclics are

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**Fig. 1.** Sketch of the preparation of a slide-ring gel by connecting cyclics along the polymer chains to give tetrafunctional sliding junctions. Similarly connecting three cyclics would give a functionality of six, and so on.

then fused together to form mobile cross-links. In the case of two fused cyclics, the result is a figure-eight structure:  $\infty$  [10–17]. These cross-links are called slide rings, and act like pulleys for the chains threading through them. The structure is shown schematically in Fig. 1. The sliding motions are thought to equalize network stresses, cooperatively. This gives the gels unusual mechanical properties, in particular very high deformabilities and degrees of swelling.

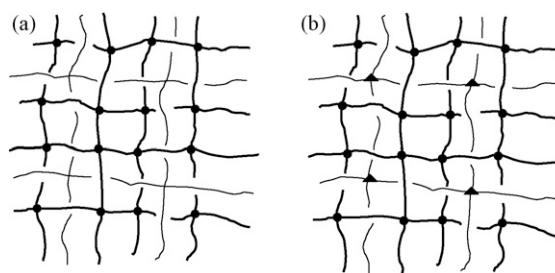
An example of a rotaxane used in these studies has a flexible polymer as the linear chain and  $\alpha$ -cyclodextrin units as the rings [10,13,18]. In some cases, ionic liquids have been used to facilitate their preparation [19]. In addition to studies of mechanical properties and swelling, the structures of these materials and their deformation mechanism [20] have been characterized by small-angle neutron scattering [11] and small-angle X-ray scattering [21].

There has long been a quest for materials of this type [12], and there has also been considerable interest in their theoretical treatment [22,23].

### 3. Double-network gels

Another class of hydrogels is generally called “double networks” [24–42], but this is an unfortunate choice of terminology since this name has long been applied to completely different elastomeric materials. The earlier use was for elastomers that had first been cross-linked in the undeformed state, elongated, and then cross-linked again in the elongated state. Upon retraction, the elastomer showed interesting behavior in that the stretching and disentangling of chains occurred during the second-stage cross-linking, with the resulting properties becoming anisotropic. Theoretical treatment of such materials goes back to 1960 [43], and research on them has continued to the present time [44–47].

The new materials going under this name generally consist of two independently cross-linked networks, one

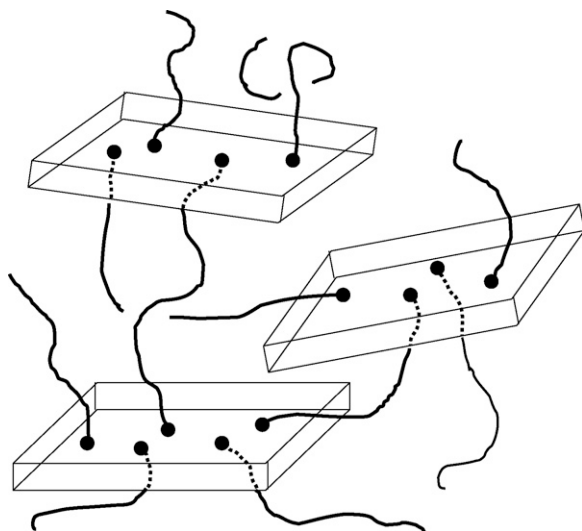


**Fig. 2.** A double-network gel in which the filled circles represent cross-links in the first network structure. In portion a of the figure, the second set of chains introduced simply reptate through the first network. In portion b, the second set is also a network, with its cross-links represented by the filled triangles.

consisting of a rigid polyelectrolyte and the other a flexible uncharged polymer. These hydrogels apparently exhibit the best mechanical properties when the first network is highly cross-linked and the second only lightly cross-linked (if at all). The two basic structures of double-network gels are illustrated in Fig. 2. The molar ratio of the second component to the first should be a factor as high as ten or more, which makes them rather different from most interpenetrating networks (IPNs) [48]. The enhanced mechanical properties of these double-network hydrogels are thought to be a result of the second network preventing cracks from growing to the point of producing catastrophic failure of the material. More specifically, this dissipation of crack energy may be facilitated by the second network appearing as clusters in voids occurring in what is apparently an inhomogeneous matrix of the first network. There is expected to be considerable entangling of the two types of chains in these domains. In some cases, a third component is used to form a triple network with, for example, uncross-linked polymer being added to reduce surface friction [49].

The structures of these materials have been studied by small-angle neutron scattering (SANS) [26] and there has been considerable modeling that has been carried out in attempts to establish the structure–property relationships of these double-network hydrogels [50–52]. There has been some interest in molecular dynamics simulations [50,51], and modeling of crack formation and growth [52,53]. In all cases, entanglements are apparently of critical importance [27,54], and one deformation mechanism includes the formation of voids as well [55].

Mechanical property studies have included measurements of strengths and fracture energies in compression and elongation [56,57], hysteresis and the Mullins effect [28], strain hardening [58], and necking [59]. In the area of dynamics, there have been reports on friction and lubrication [25,49], and wear [60]. Their impressive mechanical properties suggest their use in replacing biological tissues [61,62]. In many cases, the highly cross-linked polymer has been poly(2-acrylamido-2-methylpropane sulfonic acid), and the lightly cross-linked (or uncross-linked) polymer was polyacrylamide though other systems have been investigated, including some double networks based on cellulose [63].



**Fig. 3.** A nanocomposite gel in which the filled circles represent attachment points of polymer chains to the surfaces of clay platelets. When a chain has its ends attached to two different platelets, these platelets function as planar cross-links.

#### 4. Nanocomposite gels

Nanocomposite gels utilize nanoscopic inorganic materials such as clay to form crosslinking junctions [64–77]. For these clay nanocomposites, ends of the polymer chains adsorb strongly on the surfaces of the platelets, as is illustrated in Fig. 3, and enough of the chains attach to *different* platelets to provide the bridges that constitute a network structure. The fact that the cross-links are planar sheets of considerable dimensions and junction functionality somehow yields unusual mechanical properties, including very good toughness.

The structures of these nanocomposites have been studied by dynamic light scattering [78] and by SANS [70,79]. Of particular interest has been the mechanism of formation of these unusual structures [80]. Mechanical properties of interest have included necking [81], and sliding frictional behavior [82]. Of obvious importance have been the effects of composition [83] in particularly the clay content [68,84]. Some studies have focused on temperature responsiveness [85], including coil-to-globule transitions [86], and even porous nanocomposites of this type have been investigated [87]. The transparency of some of these materials could, of course, also be of importance in some applications [64].

Also of interest have been the control of cell cultivation and cell sheet detachment from poly(*N*-isopropylacrylamide)/clay hydrogels, and cell adhesion and proliferation were found to strongly depend on clay concentration [88]. With regard to optical properties, birefringence measurements showed that strain and gel composition had large effects on the optical anisotropies of these nanocomposite hydrogels in uniaxial deformation [89]. These types of hydrogels have also been employed in surface patterning by direct replication with subsequent changes in pattern size [90]. Their surfaces can also be made strongly hydrophobic, with abnormally high contact angles with water [91].

Alternatives to the above use of clay-type fillers would be to use reactive microgels as cross-linking agents [92] or to use aligned porous structures to suppress crack development [93].

#### 5. Photoactive hydrogels

Light is a truly unique chemical reagent which allows for exquisite temporal and spatial control over chemical transformations in a variety of settings. Light can be especially useful for selective cross-linking, alteration, and/or degradation of polymer networks [94] or for sensing of a network's properties. For example, Ikeda and coworkers [95] recently utilized the selective *cis/trans* isomerization of azobenzenes to photochemically drive a small engine. The Stoddart group [96] has used this same transformation to induce reversible hydrogel formation through the use of supramolecular interactions. The Sottos and Moore groups [97] recently reported mechanoresponsive materials which underwent a color change upon mechanical failure. Green-fluorescent protein (GFP) was incorporated into hydrogel materials, which were then shown to lose their fluorescence upon changes in temperature and pH, presumably due to denaturation of the GFP tertiary structure. The cornerstone of the microelectronics industry has been photo-initiated polymer cross-linking and degradation. Carter and Hawker [98–100] recently reported an oxygen-insensitive free-radical cross-linking procedure for the formation of sub-100 nm polymer patterns using thiolene click chemistry.

Surface patterning, as employed in the microprocessor industry, is spatially selective but not highly chemoselective, e.g. the cross-linking and/or degradation processes can occur anywhere along the precursor polymer chains. Recent work which utilizes light in the context of polymer networks pertains to molecule-specific photochemistry which typically relies on the following principle: if one chooses an appropriate chromophore which absorbs a specific wavelength, and polymers which do not absorb in that region, then it is possible to selectively address functionalities within a polymer network and thereby perform degradation, isomerization, or cross-linking at specific locations within that material. For example, Leblanc and coworkers reported the photocross-linking of polyethylene glycol (PEG) star polymers which possessed anthracene groups at their termini. Selective irradiation of the anthracene moieties with 365 nm light led to hydrogel formation by dimerization of the anthracene groups via 4 + 4 cycloaddition. The authors also showed degradation of the gels by irradiation with 254 nm light [101].

Light has perhaps been most exploited recently for site-selective degradation of cross-linked polymer materials. The Shoichet group pioneered the use of photo-protected moieties bound within hydrogels [102]. Using a nitrobenzyl-protected cysteine the authors were able to produce patterns of free cysteine within agarose hydrogels. These cysteines were then chemoselectively addressed using biologically active peptides for the study of neurite outgrowth. The same group later expanded this approach to three-dimensional patterns using two-photon patterning techniques along with coumarin-capped cysteines [103].

Johnson et al. [104,105] reported the synthesis of photodegradable cross-linked poly(*tert*-butyl acrylate) materials using copper-catalyzed azide-alkyne cycloaddition click chemistry. These gels possessed photocleavable nitrobenzyl groups at precise locations within the networks and could be degraded site-selectively to give soluble products of defined size and structure. Furthermore, these materials could be converted to poly(acrylic acid) materials by acidic hydrolysis to give photodegradable hydrogels.

The Anseth group [106,107] recently built on upon the work of Shoichet and Johnson to generate hydrogel materials which possessed both chemical and mechanical patterns through degradation. In their most recent work, the authors were able to control the migration of stem cells within the hydrogel network via temporal and spatial controls over photodegradation. These materials show great promise as tissue engineering scaffolds.

These examples show the utility of light as a reagent for the preparation of functional, stimuli-responsive materials through judicious choice of chromophores and polymer materials.

## 6. Conclusions

Techniques that have already been developed and are being refined are giving very impressive improvements in the mechanical properties of hydrogels and will certainly expand the range of applications of these materials. The same can be said of some of the new types of photoactive materials. Also, there is no obvious reason why at least some of these methods could not be used to improve the properties of other types of gels, specifically the wide variety of “organo-gels” (in which an organic solvent is the swelling component).

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