Chemomechanics

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Direct Translation of Chiral Recognition into Mechanical Motion**

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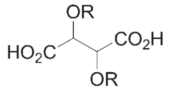
Chiral recognition is of fundamental importance in nature, and also for a manifold of chemical applications. Enantioselectivity is the landmark of many new synthetic strategies and the basis of separation techniques, for example, for drugs. In all these processes the recognition manifests itself in the predominant formation of one enantiomer, be it after the synthesis or after the separation. The direct translation of chiral recognition into mechanical motions has to the best of our knowledge never been reported. The influence of chiral effector compounds or constituents on gelation, on the structure of gel materials,[1] and on phase or sol–gel transitions[2] has received increasing attention. Until now, supramolecular reactions in chemomechanical polymers has been only known to be selective with respect to regioisomeric effector molecules.[3] We describe here how interaction of a chemomechanical hydrogel with chiral effector molecules in the aqueous surrounding can lead to a volume decrease of 95 %, whereas the optical isomer triggers a change of less than 20 %, depending on the effector concentration.

We used chitosan as the hydrogel as it contains aminoglucose units as chiral centers, and has been used, for example, for the separation of enantiomers.[4] The gel contains about 47 % water after preswelling with water; the gels exhibit additional volume expansion if exposed to anionic effector molecules which can bind to the protonated chitosan amino groups. Preliminary tests showed with *O*,*O*′-dibenzoyltartaric acids (DBTA, **1c**) that significant differences between the optical isomers already exist, and become smaller with increasing pH value (see the Supporting Information). Dramatically increased effects could be observed with gels containing acetic acid as cofactors. Investigations with other chemomechanical polymers have already shown that the cooperative action of different effector compounds in a gel can lead to significant alterations and enlargements of the volume changes.[5]



1a (TA) : R = H
1b (DPTA): R = CO-C(CH$_3$)$_3$
1c (DBTA): R = CO-C$_6$H$_5$

Treatment of chitosan first with 50 mM acetic acid yields a gel with higher water content (96 %). Exposure of this gel to a number of different anionic effectors then results in significant volume contraction instead expansion.[6] The volume differences of the resulting gels formed with L- or D-DBTA can amount to be almost a factor of ten, depending on the effector concentration (Figure 1). Noticeably, the D isomer triggers large motions at quite low concentrations, at which the L enantiomer is barely active. As expected, a racemic mixture ([D + L-DBTA] = 5 mM) leads to a slightly smaller effect (−93 %) than that of the D isomer (−95 %), as the L isomer binds to a lesser degree.

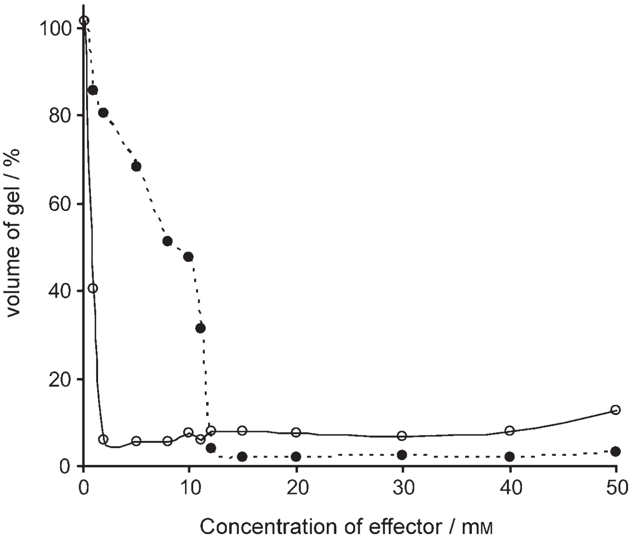


Figure 1. Volume contraction of the gel in the presence of acetic acid as a cofactor, induced either by L-DBTA (●) or by D-DBTA (○) at pH 3.5; starting volume of the gel particle (5 ± 0.3) mm^3.

At higher concentrations, in contrast, the L isomer has larger effects than the D enantiomer. The concentration profiles can be ascribed to a higher affinity of the D isomer, so that the L enantiomer is fully bound only at higher concentrations. The contraction is believed to be the result of ionic cross-linking by the two carboxylate groups of the DBTA, which can replace the existing acetic acid molecules within the gel.

In line with this the contraction, kinetic studies with D-DBTA show a significantly faster volume change than with the L isomer (Figure 2). Furthermore, the desorption profiles, observed by spectroscopic detection of effector-loaded polymer particles, show a faster release of L-DBTA, which is again in line with the smaller affinity of this isomer (see the

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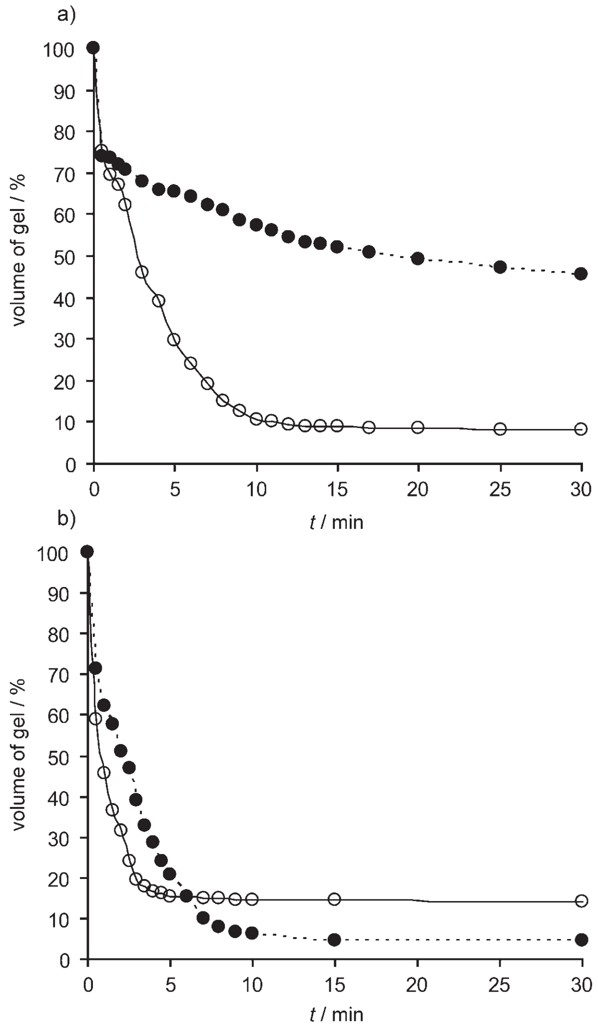


Figure 2. Kinetics of contraction of chitosan gels in the presence of acetic acid as a cofactor, induced either by L-DBTA (●) or by D-DBTA (○) at pH 3.5; starting volumes of the particles are around (5 ± 0.3) mm^3. a) with 10 mM DBTA, b) 50 mM DBTA.

Supporting Information). Interestingly, the desorption kinetics exhibit a two-phase behavior, thus indicating an absorption which amounts to more than that allowed through formation of an ion pair between one aminoglucose unit of the polymer and the effector (2.6- and 2.0-fold excess of L-DBTA and D-DBTA, respectively). This additional physisorption is clearly larger for the L isomer; after a longer reaction time, however, the desorption for both isomers reaches the concentration calculated for the formation of an approximate 1:1 ion pair between the gel monomer unit and the effector.

Comparison of the results with different enantiomeric effectors and in particular NMR analyses[7] provided insight into the underlying mechanisms. Unsubstituted tartraric acid (TA, **1a**) or DPTA (**1b**) induce smaller volume contractions than DBTA (to about 70% of the initial volume), and shows only negligible differences between the enantiomers. These observations indicate the important role of the phenyl groups for the chemomechanical effects, which is strongly supported by solid-state ^{1}H MAS NMR spectra of the DBTA-loaded gel (Figure 3). The spectra showed large upfield shifts of the aminoglucose signals of the polymer backbone only with the chemomechanically very active D enantiomer (the L isomer induced only negligible shielding effects). The shielding observed reaches up to $\Delta\delta = -2.5$ ppm, thus suggesting a strong interaction between the DBTA phenyl groups, with a face-to-face orientation between the glucose units and the effector aryl residues (Scheme 1). Such a geometry is in line with the shielding by the anisotropy cone of the phenyl rings, and is expected from the well-known cation–π interaction with the protonated nitrogen centers of the polymer backbone (supported also by CH–π interactions with the axial C–H protons of glucose). Comparison of the CH_3COOH signal areas in the NMR spectra also demonstrate the replacement of acetic acid molecules in the gel by the DBTA effector molecule.

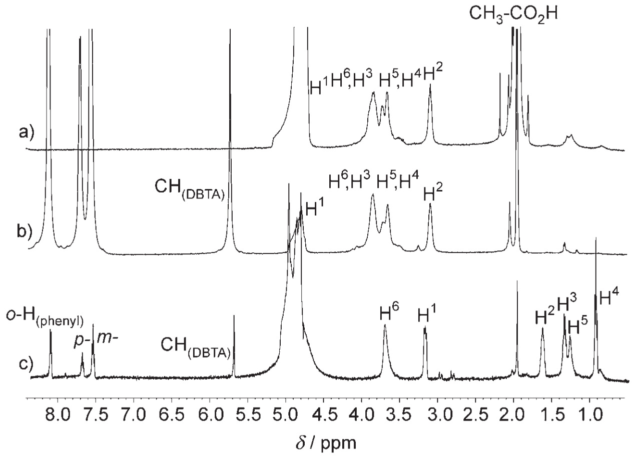
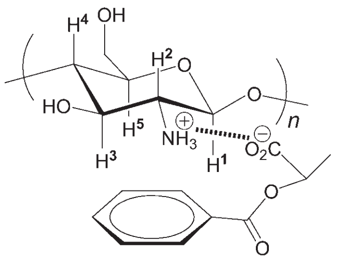


Figure 3. Solid-state ^{1}H MAS NMR spectra of chitosan gels in the presence of acetic acid as a cofactor: a) the swollen gel without any added DBTA; b) the gel treated with 5 mM L-DBTA; and c) the gel treated with 5 mM D-DBTA. All spectra were recorded with suppression of the water signal; all samples were prepared in D_2O solutions.



Scheme 1. The phenyl groups of the DBTA and the glucose units are ordered in the gels in a face-to-face arrangement.

Preliminary scanning electron microscopy (SEM) analyses of the gels showed few structural features unless the water was partially removed at high vacuum. The SEM pictures, however, again showed significant differences between gels loaded with either L- or D-DBTA (see the Supporting Information). The absence of nano- or microstructures in the SEM pictures of the gels is in line with the unusually sharp lines observed in the ^{1}H MAS NMR spectra, which indicate a solution-like mobility within these hydrogels. Previous studies have shown that thin films of chitosan doped with rare-earth metal ions do possess a homogeneous amorphous structure.[8]

Although significant enantiomer-selective motions could be already observed at millimolar concentrations of the effector, it would be desirable to increase the sensitivity furthermore. The chemomechanical response of a related polymer can increase significantly by decreasing the size of the polymer particles: as long as the affinity between the effector and the polymer units is sufficiently high, all the available effector molecules are bound fully to the host particles, independent of the concentration of the external effector.[9] Such a compartimentalization effect is seen in the present case; the chemomechanical response requires a much lower effector concentration as the polymer particles become smaller (Figure 4).

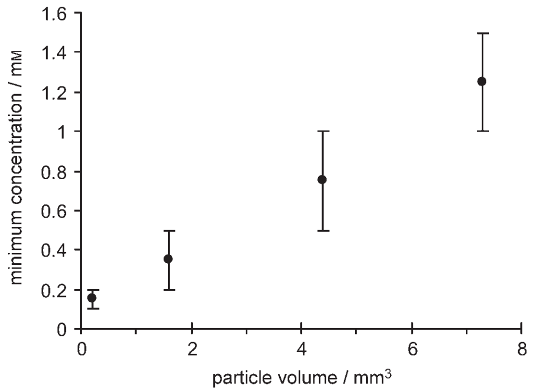


Figure 4. D-DBTA concentration necessary to obtain (20 ± 3) vol% of the starting gel as a function of the volume of the polymer particle. Measurements were made with chitosan gel in the presence of acetic acid as a cofactor, at pH 3.5.

In summary, the direct transduction of chiral recognition into large mechanical movements is now feasible, without the help of any additional devices. The application of micro-, or possibly nano-, particles should lead to even higher sensitivity and velocity of the response at very low effector concentrations.

Experimental Section

All chemicals, including chitosan (MW 190000–310000), were commercially available and used without further purification. The chitosan contained 14% *N*-acyl groups, as measured by integration of the signal in the ^{1}H NMR spectrum. The water content of the gel (determined by weight difference before and after drying) was (47±1)% after swelling chitosan in water for about 6 months. The particles showed a volume increase of (2200 ± 30)% with a water content of (95 ± 1)% after exposure to 50 mM acetic acid.

The changes in the size of the gel particles (generally 0.8 × 0.8 × 0.4 mm; volume 0.26 mm^3 after swelling in water) were determined as described earlier[10] with the help of a measuring microscope connected to a digital camera with suitable software. The changes in the length and width were used to calculate the volume changes. Changes in the thickness of the particles were also visible but not as accurate to follow. Measurements were usually performed at least three times and the values and errors are given from the average value.

MAS spectra (with a Bruker DRX 500 system at 500 MHz) were recorded in the absence of any solvent with suppression of the water signal. The gels were previously treated with D_2O solutions. The spectra are presented only with phase correction, without filtering for enhancing resolution. The decreased amount of CH_3COOH observed in spectrum Figure 3c is ascribed to partial removal by washing the sample prior to measurement.

SEM pictures of the wet gels were taken at −10°C in the field emission mode (using a fei quanta 400 feg system).

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