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Significant Impact of Host-Guest Stoichiometry on the Extensibility of Polyrotaxane Gels

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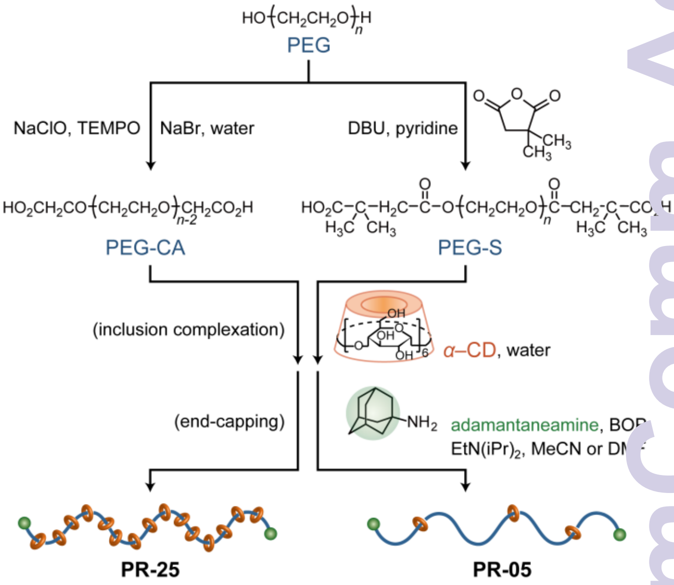
Kazuaki Kato, Yoshinori Okabe, Yuya Okazumi and Kohzo Ito

Modification of the guest polymer ends efficiently and substantially decreases the density of the threaded rings. The minimized ring density drastically facilitates chain sliding through the cross-links in polyrotaxane gels. This molecular design is like regulating the "pressure" of the rings confined in the interlocked architecture, which counteracts the sliding.

Controlling the stoichiometry of host-guest complexes is critical to the designed function and properties of the material, particularly when the guests are polymers. Systematic research on the complexation between diverse polymer guests and cyclodextrins (CD) as host molecules revealed several correlations between the stoichiometry and their molecular structures.[1] For instance, inclusion complexes wherein threaded CDs cover the guest densely or sparsely can be selectively obtained from short (low MW) or long (high MW) polymers, respectively.[2] Densely threaded complexes achieved high conductivity in guest polymers due to efficient insulation by CDs.[3] However, sparsely threaded complexes, with a low CD density in their backbone, enable motion (such as sliding and rotation) between threaded CDs and guest polymers. The intramolecular mobility in sparse polyrotaxanes can be confined by end-capping of the inclusion complex to form a polyrotaxane,[4] and various functionalizations have been demonstrated based on a common molecular design that integrates function and mobility by modification of the functional groups on the ring component.[5] In addition to such design for single-molecular function in solution, the mobility appears even macroscopically as a difference in the mechanical properties of the cross-linked materials, or so-called polyrotaxane gels.[6,7] The high extensibility of polyrotaxane gels is a direct reflection of the chain sliding through the cross-links. However, this effect only appears when relatively long guest polymers (PEG) are employed ($M_w >$ 3.5×10^5).[8] Recently, unknown mechanical behaviors were revealed and the possible contribution of the entropy of the ring components to the mechanical properties was proposed.[9,10] This hypothesis suggests that the control of host–guest stoichiometry, or the ring density of polyrotaxane gels, could become a significant method for controlling and diversifying the mechanical properties of polyrotaxane gels. This method has the potential to change the long-standing perception that chain sliding is the single most important feature in polyrotaxane gels, although experimental results have not directly confirmed the exact contribution of the rings. Here, we report the simple and efficient synthesis of polyrotaxanes with a considerably low density of CDs threaded on PEG with $M_w = 3.5\times10^4$ and demonstrate the effects of ring density on the mechanical properties of polyrotaxane gels.



Scheme 1. Synthetic schemes for two sparsely covered polyrotaxanes. Introduction of methyl groups at the ends of polyethylene glycol (PEG) (PEG-S) results in a reduced ring density on the polyrotaxane (**PR-05**) as compared to the conventional one (**PR-25**).[11]

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[a] *Department of Advanced Materials Science, Graduate School of Frontier Sciences, The University of Tokyo, 5-1-5 Kashiwanoha, Kashiwa, Chiba, 277-8561, Japan*

Electronic Supplementary Information (ESI) available: synthesis of polyrotaxane, detail of measurements, a tensile data at higher strain and a stress relaxation data. See DOI: 10.1039/x0xx00000x

The polyrotaxane ring density was minimized by modifying the end groups of the guest polymer prior to complexation with CDs, as shown in **Scheme 1**. The subsequent processes, namely complexation and end-capping, were essentially the same as those in the established and industrialized synthesis,[11] which produces sparsely threaded polyrotaxanes with 25% coverage (**PR-25**) from PEG with M_n = 3.2×10^4 and M_w = 3.5×10^4. **Figure 1a** shows SEC chromatograms of the product (**PR-05**), **PR-25**, and their components as detected by a differential refractometer. **PR-05** had a smaller molecular weight than **PR-25**, but a larger molecular weight than PEG. In addition, the refractive index of **PR-05** was smaller than that of **PR-25**. It indicates that **PR-05** had less CDs, because CD has considerably higher refractive index than that of eluent and PEG has similar index to that of eluent. The molecular weight of **PR-05** was estimated using PEG standards (M_n = 5.6×10^4, M_w = 8.5×10^4) and was about half of that of **PR-25** (M_n = 7.0×10^4, M_w = 1.1×10^5). All product components were detected by ^{1}H NMR and the signal assignments are shown in **Figure 1b**. The spectrum of **PR-05** mainly consisted of the *α*–CD and PEG protons, and their chemical shifts were essentially the same as those of **PR-25**. The only difference was in the ratio of the integral values of the two components. From that ratio, the coverages of **PR-05** and **PR-25** were calculated to be 5.6% and 25%, respectively, based on the definition that a single *α*–CD covers two repeating units of PEG in the full-coverage state.[12] The substantial reduction in ring density also appeared to have an effect on solubility; **PR-05** could be dissolved in DMSO, water, and DMF, whereas **PR-25** was only soluble in DMSO owing to the robust crystal formation by threaded CDs (see next paragraph for details). The yield of **PR-05** was 69% based on PEG.

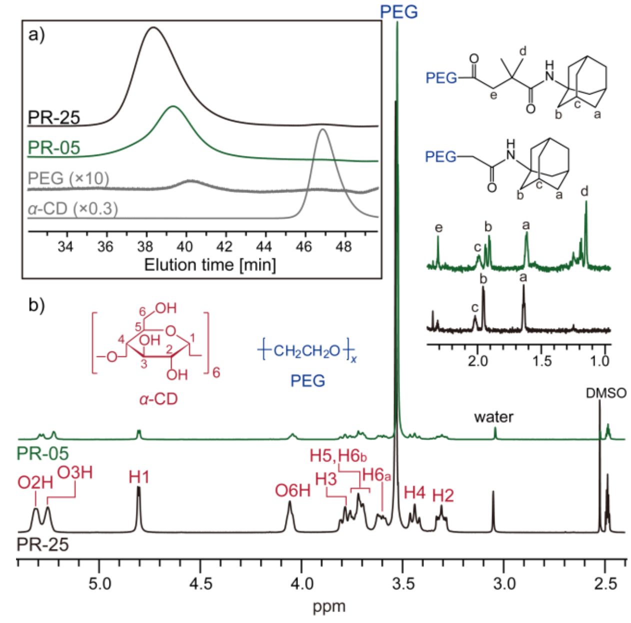

Figure 1. a) SEC traces (RI detector, eluent: DMSO/LiBr) and b) ^{1}H NMR spectra (400 MHz, DMSO-d_6, 80 °C) of **PR-05** and **PR-25**. SEC traces of common components of both polyrotaxanes, PEG, and α-CD are also shown for comparison.

Notably, a polyrotaxane with low coverage was efficiently synthesized; previous strategies based on either the dissociation of the inclusion complex during end-capping[13] or end-capping during halfway complexation[14] lead to a drastic decrease in yield. In addition, we confirmed the reproducibility seven times, and the coverage was 5.1±0.5%. The coverage was not affected by the reaction time for complexation (see ESI for details). The high yield and reproducibility indicate that the complexation between *α*–CD and PEG dimethylsuccinate (PEG-S) reached an equilibrium, where considerably fewer *α*-CDs were threaded, as compared to that between *α*–CD and PEG carboxylated (PEG-CA). As the complexation progressed, the solution of *α*–CD/PEG-S became turbid and precipitates were generated, whereas the *α*–CD/PEG-CA solution exhibited gelation, which was induced by the cross-links that were formed by crystalline *α*–CDs threaded with PEG.[15] Presumably, the crystalline cross-links were hardly formed because fewer threaded CDs were present in the *α*–CD/PEG-S system. Incidentally, the interaction between the end-groups of PEG-S and *α*–CD seemed to be significant; the *α*–CD/PEG-S complex remained in the solvent for several hours as noted by SEC, whereas *α*–CD/PEG immediately dissociated (data not shown). It is known that the bulkiness of end-groups can lead to varied inclusion kinetics.[16] The resultant phase separation induced by the crystal formation of threaded CDs is thought to govern the complexation.[17] As such, we speculate that the decelerated complexation could enable the phase separation with fewer threaded CDs. The relationship between complexation kinetics and threaded CD density is currently being evaluated in our laboratory.

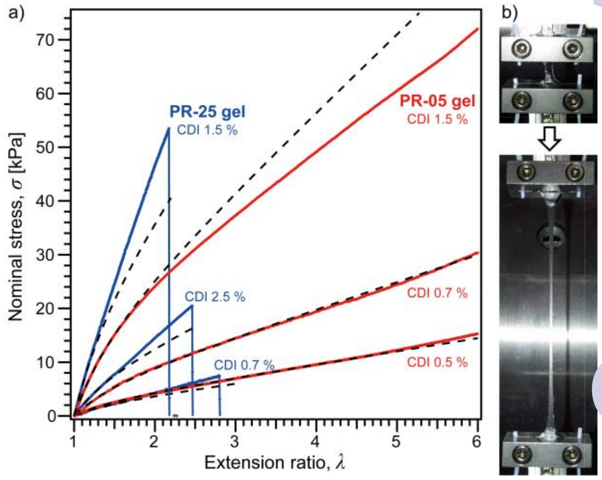

Figure 2. a) Stress-strain curves of two series of polyrotaxane gels prepared from **PR-05** and **PR-25**. Curves of three gels prepared with different cross-linker (CDI) concentrations are shown for each series of gels. Dashed lines represent the fitting curves with the neo-Hookean model. b) Photograph of a **PR-05** gel extended 10 times.

The two polyrotaxanes with substantially different coverages were cross-linked in DMSO with carbonyldiimidazole (CDI) to obtain polyrotaxane gels with different ring densities. DMSO dissociates the hydrogen bonds between CDs, which was the major driving force for complexation between PEG and CDs,[15,18] to dissolve polyrotaxanes homogeneously (details are discussed later). **Figure 2a** shows the stress-strain curves of three gels with different elastic moduli in each series of gels. In the series of **PR-25** gels, the softest gel was extended 2.8 times at most and the harder gels showed less extensibility, as is generally observed in polymer gels. On the other hand, **PR-05** gels could be extended by six times in length, even though their elastic moduli were similar to those of **PR-25** gels. One of the **PR-05** gels (CDI 0.7%) was extended at least 10 times in length (Figure S1a), though the stress-strain curve could not be accurately measured because of a slight slip from the fixture. Notably, the **PR-05** gels were also elastic with negligible stress relaxation (Figure S1b). Although larger stress with larger strain leads to inaccurate measurements, it is obvious that **PR-05** gels can be extended at least 10 times, as shown in **Figure 2b**.

The difference in the stress-strain behaviors between **PR-05** and **PR-25** gels became evident upon comparison to the predicted behaviors for ideal elastic bodies. The stress-strain behavior of an ideal elastic body is represented by the neo-Hookean model:[19]

$$\sigma = \frac{E}{3}\left(\lambda - \frac{1}{\lambda^2}\right) \qquad (1)$$

where σ is nominal stress, λ is strain, and E is the elastic (Young's) modulus. Ideal behavior is generally observed only in the small-strain regime, and the behavior of **PR-25** was almost fitted by Equation 1 until λ = 1.2–1.7. As the strain increased, hardening occurred due to the finite extensibility of the polymer network, and then the gels were fractured. On the other hand, **PR-05** gels behaved like ideal elastic bodies under much higher strain. For instance, the stress-strain of the softest **PR-05** (E = 7.3 kPa) was fitted by Equation 1 until λ = 5, whereas that of **PR-25** with a similar modulus (E = 6.2 kPa) deviated from neo-Hookean around λ = 1.7. The neo-Hookean model ignores not only the finite extensibility, but also the interaction of strains in different directions, or so-called strain-coupling. Because of the strain-coupling, the stress-strain behavior generally deviates from the model much earlier than the beginning of chain extension.**Error! Bookmark not defined.** Thus, the neo-Hookean-like behavior indicates that **PR-05** gels have negligible strain-coupling. Such negligible strain-coupling has been observed by biaxial stretching tests for other polyrotaxane gels with much longer PEG (M_w = 3.8×10^5), and it was considered that the chain sliding through the cross-links could minimize the strain-coupling.[20] Therefore, the observed high extensibility with neo-Hookean-like stress-strain behavior indicates effective chain sliding in **PR-05** gels, whereas the sliding in **PR-25** gels was significantly limited.

However, the limited chain sliding in **PR-25** cannot be explained by the conventional idea that the sliding is valid until CDs get stuck between cross-links (**Figure 3c**). This indicates that the potential sliding distance is determined by the length of uncovered chains: 75% and 95% for **PR-25** and **PR-05** gels, respectively. This difference is unlikely to significantly contribute to the ability to slide, and **PR-25** gels also exhibited high extensibility, even though it was slightly inferior to that of **PR-05** gels. Originally, the sparsely covered polyrotaxane **PR-25** was designed to make sufficient room for chain sliding, in contrast to densely packed polyrotaxanes (PR-100).[6] In addition, there is hardly any contribution from any of the interactions to the significant mechanical difference. As mentioned above, the hydrogen bonds between threaded CDs are crucial for the complexation between polymers and CDs. Because of the robust channel crystals formed by hydrogen bonds, polyrotaxanes are insoluble in water and DMSO, although their components (PEG and CD) are soluble. However, once the hydrogen bonds are dissociated by solvents such as DMSO and NaOH(aq), polyrotaxanes are dissolved homogeneously in those solvents. Indeed, in DMSO, threaded CDs were distributed randomly along the backbone without aggregation.[21] The consideration that dissociation of the hydrogen bonds is crucial for dissolving polyrotaxanes was also supported by the good solubility in special solvents used for the dissolution of polysaccharides.[22] Besides, the elastic modulus of **PR-25** gels increased with temperature, indicating entropic elasticity similar to that of rubbers and chemical gels with negligible interactions.[10] The contribution of interactions to the mechanical properties of **PR-05** gel should be weaker than that for **PR-25 gel**, as expected from the improved solubility. Incidentally, the difference in the persistence length of backbone induced by the different densities of threaded CDs, which is twice at the maximum from the fact that PR-25 has only twice longer persistence length than PEG,[21] cannot be a main reason for the drastically improved sliding ability.

This discrepancy seems to arise from the static picture of the ring components. In fact, the rings that are confined between cross-links are constantly sliding on the polymer backbone. Because various arrangements of the rings are possible on the backbone, such rings can theoretically generate an entropic force to spread the cross-links, as if they behave like gas molecules confined in cylinder.[9] Chain sliding induced by the extension of gel leads to a change in the length

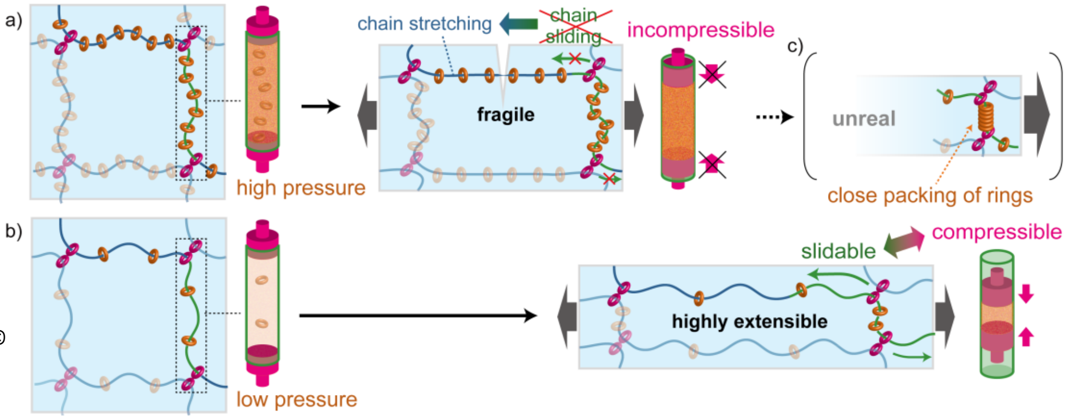

Figure 3. ... components generate an entropic force as if they behave like gas molecules confined in a cylinder to counteract the chain sliding through the cross-links. The high ring density in **PR-25** gels disables the chain sliding under small strains, although the chain has enough space to reach c) the unreal close packing state under the maximum

of the backbone between cross-links; this is analogous to a change in the distance between pistons in a cylinder, as illustrated in **Figure 3**. In short, the sliding competes against the entropy of the rings. In this way, the extension of polyrotaxane gels increases the "pressure" of the rings. With **PR-25**, although there was sufficient room for sliding, the "pressure" of the rings became high enough to compete with the chain sliding under very small strain (**Figure 3a**). The sliding is inactivated due to the high pressure of the rings, then the polymer chains must be stretched instead, similarly to conventional chemical gels that have fixed cross-links. Thus, the chain sliding and the corresponding extensibility were significantly limited in **PR-25**. On the other hand, in **PR-05**, the chain sliding was active until a higher strain because of the low ring "pressure" that arises from the low ring density (**Figure 3b**). Based on the analogy to gas pressure, the fivefold difference in the density of CDs corresponds to a fivefold difference in the "pressure". The considerably decreased counteraction can facilitate the sliding and lead to high extensibility and an ideal elastic body behavior until the high strain regime. In this way, the density of the ring component significantly affects the entropic force that counteracts the sliding, whereas the increased room for sliding is rather limited.

We demonstrated here that the ring density of polyrotaxanes can have a significant effect on the extensibility of polyrotaxane gels. Analysis of the stress-strain behaviors revealed that the high extensibility of the gels with 5% coverage was due to efficient chain sliding through the cross-links. On the other hand, the sparsely covered polyrotaxane with 25% coverage hardly showed the effect of chain sliding in the gels, even though there was sufficient room for chain sliding. This was because the ring density was already high enough to generate significant entropic force that could counteract the sliding. Intramolecular motions in polyrotaxanes have fascinated many scientists and have prompted the design of various functional molecules and materials to date. In such designs, the single most important issue was that the polyrotaxane rings were sparse enough to provide sufficient rooms for sliding. Therefore, the designs were satisfactory as long as the threaded CDs did not densely cover the backbone, and thus the stoichiometry between the cyclic host molecules and the guest polymer in such sparse polyrotaxanes was rarely investigated. However, this study clearly shows the considerable contribution of the ring components to the mechanical properties of polyrotaxane gels. Understanding that the rings behave like gas molecules confined in the backbone polymer will transform the designs of mechanically interlocked molecules. Although polyrotaxane gels are currently the only example of systems in which inherent "pressure" is converted into macroscopic stress, we believe that various functions will be realized based on this understanding.

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