



Regulation of Swelling Behaviour While Preserving Bulk Modulus in Hydrogels via Surface Grafting

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COMMUNICATION

Regulation of Swelling Behaviour While Preserving Bulk Modulus in Hydrogels via Surface Grafting

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This study presents a novel approach to control "linked property changes" in hydrogels. Specifically, we controlled the swelling behaviour without altering the bulk elastic modulus by grafting polymers selectively into the surface region of the gels, while varying the graft amount.

Hydrogels composed of three-dimensional cross-linked networks of water-soluble polymers and water are actively applied to a wide range of applications, such as soft actuators, cell-culture materials, and controlled release systems, owing to their flexibility and open system characteristics.^{1–7} In such applications, functional designs are needed to improve the strength of materials or systematically change the swellability and molecular permeability. However, altering the entire network structure to achieve a specific purpose often results in correlated changes in the elasticity, swellability, and molecular permeability of the gel, which pose negative effects to the materials. For instance, the strength should be improved, while maintaining the bulk flexibility and size when hydrogels are used as soft actuators, or the molecular permeability should be altered without changing the mechanical properties of the bulk when used as cell-culture materials. However, such needs are not often addressed.

"Linked property changes" present a significant problem in gel design as most gel properties are determined by a shared set of structural factors. The models predicting the elasticity of the gels, such as the affine and phantom network models, describe the effective chain density as a determinant of elasticity.^{8,9} The swelling degree is determined by the balance

between the resistance to mesh deformation and osmotic pressure difference inside and outside a gel, which are determined by the balance of the polymer concentration and crosslinking density of the gel. Molecular permeability of the gel is influenced by the polymer concentration and molecular weight between crosslinks.¹⁰ Elasticity, swellability, and molecular permeability of the gels are determined by their chemical and physical structures.

To date, examples to control "linked property changes" in gels have included the following approaches. First, biohybrid gels of heparin and four-arm star poly(ethylene glycol) do not exhibit a correlation between the heparin concentration in the gel and its elasticity.¹¹ Furthermore, the molecular weight and concentration of pentenoate-functionalized hyaluronic acid (PHA) and elasticity of the hydrogel can be successfully altered, while maintaining the other two variables constant in PHA hydrogels crosslinked with dithiothreitol.¹² Another approach involves the independent manipulation of the cell adhesive ligand density within the gel and its elasticity.¹³ However, these examples only attempt control between structural conditions and properties. To our knowledge, no control between characteristics has yet been reported.

One approach to achieving such control is the localized structural modification of the gel surface. Recently, various research groups have developed methods for grafting polymers onto localized regions of gels.^{14–16} Among these, the authors have established a method for grafting polymers only on the surface regions of bulk hydrogels.^{17–20} Specifically, surface-grafted hydrogels can be obtained by introducing an initiator of atom transfer radical polymerization (ATRP) into only the surface region of the hydrogel, followed by surface-initiated ATRP. This method is versatile in that a wide variety of polymers can be surface-grafted as long as polymerization by ATRP is possible. Furthermore, the grafting amount can be easily controlled.¹⁸ Prior studies on this surface-grafted gels have successfully demonstrated distinct manipulations, such as unique temperature-responsive control of a skin layer,¹⁷ formation of surface wrinkle structures,¹⁸ hydrophobization at

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the surface,¹⁹ and regulation of adhesiveness.²⁰ In this study, we used this method to regulate swelling behavior while preserving bulk modulus in hydrogels by systematically altering the surface grafting amount.

A base gel comprising a copolymer of *N,N*-dimethylacrylamide and 3-(*N*-aminopropyl)methacrylate was synthesized, and ATRP initiators were introduced into this gel surface through amide condensation. The density of the ATRP initiator was controlled by systematically reacting the base gel with ATRP initiators and a "sacrificial" initiator-like structural compound, which reacted with the base gel without initiator activity in different ratios.¹⁸ Subsequently, poly(1*H*,1*H*,5*H*-octafluoropentyl acrylate) (POFPA) was surface grafted by activators regenerated by electron transfer (ARGET) ATRP. The chemical reaction is shown in Fig. 1.

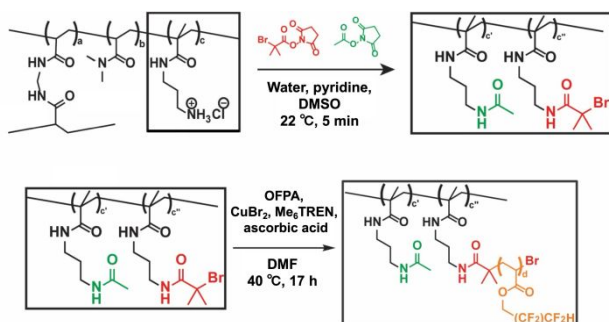


Fig. 1 Scheme for the preparation of the surface-grafted gels.

Table 1 presents the bromine contents of the initiator-introduced gels as determined by elemental analysis. The synthesis parameters for these gels were $[\text{initiator}]_0/[\text{initiator-like structural compound}]_0 = 0/100, 25/75, 50/50,$ and $100/0$ (mol/mol), abbreviated as IG0, IG25, IG50, and IG100, respectively. The results indicate the feasibility of fabricating gels with varying bromine quantities in relation to the gel mass. As the bromine quantity directly corresponds to the number of ATRP initiation points, gels with differing quantities of introduced ATRP initiator could be synthesized.

Table 1. Elemental analysis results for bromine in the initiator-introduced gels.

Sample	Br mass (%)	Proportion of Br mass per that of IG100 (%)
IG0	Not detected	—
IG25	0.27	17.0
IG50	0.73	45.9
IG100	1.59	100

Fig. 2 depicts the attenuated total reflectance (ATR)/Fourier transform infrared (FTIR) results of the POFPA-surface-grafted gels synthesized using IG0, IG25, IG50, and IG100, respectively; the POFPA-surface-grafted gels are abbreviated as FG0, FG25, FG50, and FG100, corresponded to the name of the IG gels used, respectively. Since the measurements are performed using the ATR method, these results reflect the chemical characteristics of the surface regions. The peak intensity of the C–F (1130 and 1169 cm^{-1}) and C=O associated with the ester (1760 cm^{-1}) from POFPA increased with increased levels of introduced ATRP

initiator. From this result, the POFPA graft amount could be controlled based on the initiator introduction density. Although it is not possible to distinguish whether the molecular weight of the grafted polymer or the graft density of the polymer increased from the FTIR results, it is likely that the graft density of the polymer increased depending on the density of initiator introduction. The intensity of the broad O–H peak from water ($3400\text{--}3200\text{ cm}^{-1}$) was comparable between FG0 and FG25. On the other hand, the intensity decreased with increasing polymer grafting in FG25–100. The results indicate that the water content on the gel surface is similar between FG0 and FG25 but decreases gradually among FG25, FG50, and FG100 as the amount of polymer grafted increases. Additionally, the wavenumber of the peak top remains almost identical between water and FG0 but shifts to higher values as the graft amount increases from FG0 to FG50, while showing little change between FG50 and FG100 (Fig. S1 in the Supporting Information). This indicates that the hydrogen bonding strength on the gel surface decreased when comparing FG0–50, although almost no difference in hydrogen bonding strength was observed between water and FG0 and between FG50 and FG100.²¹ These findings suggest that polymer aggregation in surface regions increased with the amount of POFPA chains grafted of FG0–50, while similar levels of polymer aggregation were considered to be occurred in surface regions of FG50 and FG100. The water peak at the low wavenumber side overlapped with the C=O peak of amide (1650 cm^{-1}).

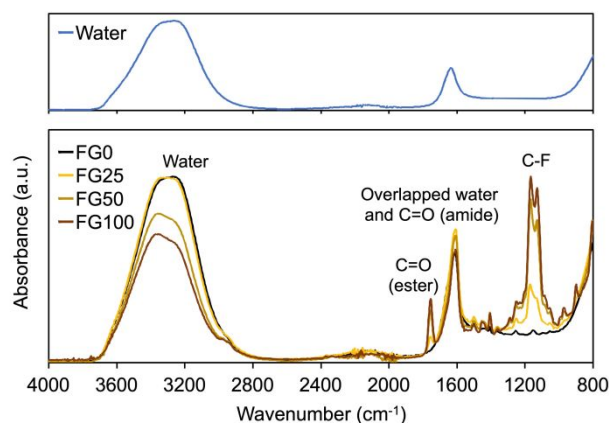


Fig. 2 ATR/FTIR spectra of water and the surface-grafted gels.

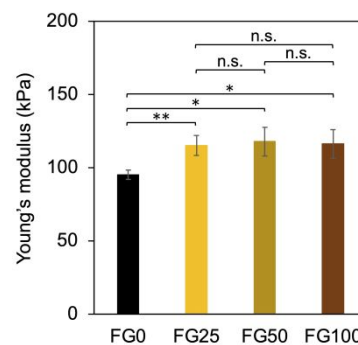


Fig. 3 Bulk Young's moduli of surface-grafted gels determined by tensile tests. Data from three separate experiments are expressed as mean \pm SD.

The comparison of Young's modulus in bulk of FG0-100, as obtained from the tensile tests, revealed significant differences between FG0 and FG25 ($P < 0.01$), FG0 and FG50 ($P < 0.05$), and FG0 and FG100 ($P < 0.05$). However, no significant differences were observed among FG25-100 ($P > 0.1$) (Fig. 3). Hence, the differences in the graft amount did not affect the bulk Young's modulus owing to the localized nature of the grafting sites.

The swelling behaviour during the 15-min immersion of dried FG0-100 in water are presented in Fig. 4a and b. In FG0-50, the gels first swelled with time, then contracted once and swelled again. This behaviour indicates the case II diffusion during the swelling of the gel, that is, the rate at which the polymer relaxes from a glassy state to a rubbery state through interaction with water is significantly slower compared to the rate of water penetration.^{22,23} It is considered that the rapid reduction in gel diameter denotes the complete relaxation of glassy polymer chains, relieving physical constraints and

subsequently facilitating extension along the longer axis. After immersion in water for 15 min, the difference in gel diameter observed between FG25-100 and FG0 was considerably larger than the difference seen among FG25, FG50, and FG100. This suggests that the presence or absence of grafts has a significant effect on water permeability. Fig. 4c shows the time at which the relaxation of glassy polymer chains was completed during the swelling experiment of FG0-50, in relation to the ratio of ATRP initiator used when preparing IG gels corresponding to FG gels, i.e., the surface graft amount. From this, the time required for complete relaxation of glassy polymer chains increased as the graft amount increased. FG100 exhibited no clear relaxation behaviour and showed a gradual increase in size (Fig. 4a and b). This can be attributed to the incomplete relaxation of the glassy polymer even after 15 min of immersion in water in the case of FG100.

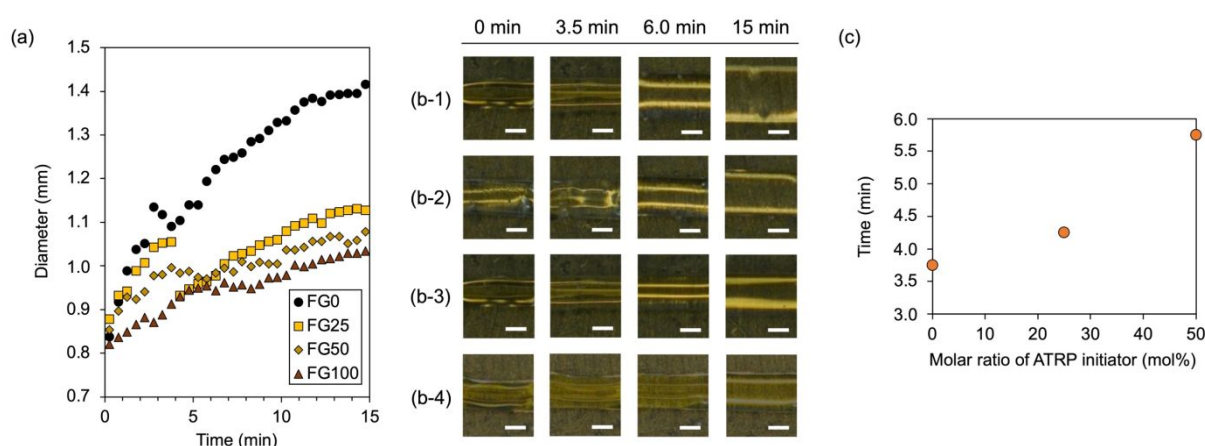


Fig. 4 (a) Swelling behaviour of dried FG0, FG25, FG50, and FG100 upon immersion in water for 15 min. Data are averages of the values obtained in three separate experiments. Time-dependent optical images of (b-1) FG0, (b-2) FG25, (b-3) FG50, and (b-4) FG100 after immersion in water. Scale bar: 500 μm . (c) Time at which the relaxation of the glassy polymer chains was completed during swelling in relation to the ratio of the ATRP initiator concentration used when preparing IG gels corresponding to FG gels.

The ATR/FTIR results suggested that dehydration and polymer aggregation in the surface region increased with the amount of POFPA chains grafted (Fig. 2). This is expected to cause stiffening of the gel surface and affect swelling behavior. Subsequently, we obtained the Young's moduli of the gel using high-speed atomic force microscopy (AFM) to confirm the stiffness of the surface. The Young's modulus obtained from force curve measurements using AFM represents the Young's modulus of the superficial surface regions, rather than the bulk, owing to the nature of the measurement. Measurements were conducted at numerous points in the x-y plane of the gel surface, and the results are presented as a histogram to illustrate the substantial variation in Young's modulus across the scanned area (Fig. 5). The average Young's modulus values were determined to be 77.0 kPa for FG0, 356 kPa for FG25, 663 kPa for FG50, and 729 kPa for FG100. These results demonstrate that Young's modulus increases with increasing polymer graft amount, especially significantly from FG0 to FG50. As can be seen from the ATR/FTIR results, surface regions of FG50 and FG100 are likely to have similar degrees of polymer

aggregation, resulting in little difference in the surface modulus of these samples.

As the grafting amount increased, the polymer chains on the gel surface aggregated, and stiffened in FG0-50. Therefore, in the swelling experiments, the relaxation rate of the glassy polymer chains slowed as the grafting amount increased and the degree of swelling after 15 min decreased as the graft amount of the gel increased in FG0-50. In comparing FG50 and FG100, the aggregation of polymer chains on the surface appears to be similar. However, there was a difference in surface water content, which may have affected the swelling behaviour. Taken together, the above results and discussion demonstrates that FG gel systematically controlled its swelling behavior depending on the amount of grafting.

In conclusion, while no significant difference in bulk Young's modulus was observed in surface-grafted gels with systematically varying amounts of POFPA chains grafted, significant differences were observed in the relaxation time of the glassy polymer chains when they were immersed in water in the dry state. These results indicate that surface grafting

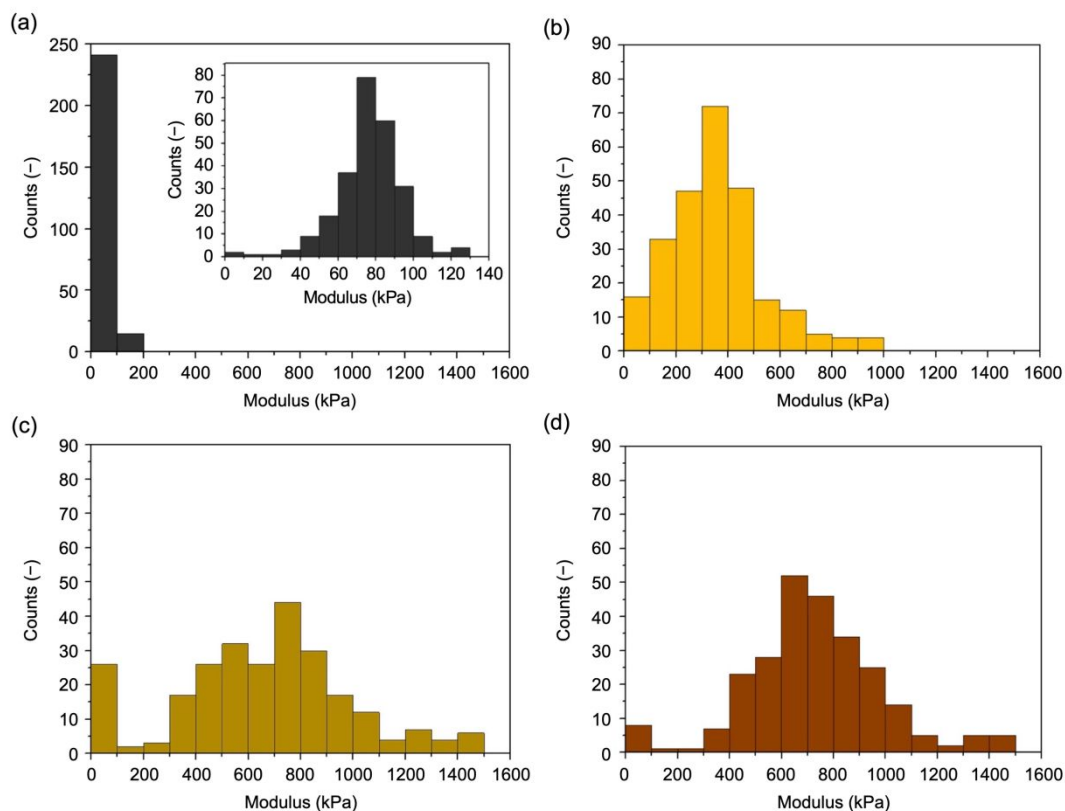


Fig. 5 Histograms illustrating the mapping results of Young's modulus obtained from force curve measurements using the high-speed AFM for (a) FG0, (b) FG25, (c) FG50, and (d) FG100.

method regulated swelling behaviour while preserving bulk modulus in hydrogels. Therefore, this study introduced a pioneering approach to address the critical challenge of “linked property changes” in the development of functional gels.

Conflicts of interest

There are no conflicts to declare.

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Data Availability Statement

Independent Regulation of Bulk Modulus and Swelling Behaviour in Hydrogels Through Surface-Grafting

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The data supporting this article have been included as part of the Supplementary Information.