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A surface-grafted hydrogel demonstrating thermoresponsive adhesive strength change†

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Here, we designed a surface-grafted hydrogel (SG gel) that exhibits thermoresponsive changes in surface properties. Quantitative measurements using a self-made device showed that the adhesive strength between the SG gel surface and a Bakelite plate due to hydrophobic interaction changed significantly with temperature.

Hydrogels comprise a cross-linked polymer network structure and employ water as a solvent. In recent years, owing to the flexibility and oxygen permeability, hydrogels have attracted attention as stretchable biomaterials that are resistant to rashes.[1] In this context, several approaches, including the induction of covalent bonds,[2] electrostatic interactions,[3] specific molecular recognition,[4] and intermolecular interactions,[5] have been used to impart adhesive properties to hydrogels. When developing adhesive gel materials for skin applications as dressings, such as wearable devices and medical tapes, both the ease of detachment and adhesion properties are important considerations. This is because skin irritation due to the peeling of dressings can be an issue in clinical practice, often resulting in severe conditions, such as skin tears.[6] To address this issue, materials that have both strong adhesion and easy detachment properties need to be developed. Therefore, the development of adhesion/detachment mechanisms that respond to external stimuli is key to addressing the aforementioned issues. Although extensive efforts have been devoted to develop hydrogels with stimuli-responsive adhesion/detachment systems, such as light-responsive hydrogel systems,[7,8] it is essential to develop a thermoresponsive adhesion/detachment system that is less invasive to the living body, inexpensive, and simple to use.

On the surface of hard materials, the adhesion and detachment of drugs,[9,10] peptides,[11,12] proteins,[13] and cells[14–16] *via* thermoresponsive hydrophobicity changes have been realised by covalently modifying their surfaces with poly(*N*-isopropylacrylamide) (PNIPAAm). PNIPAAm is a thermoresponsive polymer with a lower critical solution temperature (LCST) of 32 °C. Below the LCST, PNIPAAm is hydrophilic and soluble in water; however, it is hydrophobic and forms aggregates above the LCST.[17,18] PNIPAAm is a non-toxic abiotic material, as cells exposed to PNIPAAm are practically used for clinical transplantation.[19] In this study, we designed a hydrogel surface with covalently modified PNIPAAm to control its surface adhesiveness by subjecting it to temperature changes. Although hydrogels composed of the PNIPAAm network show temperature-responsive changes in surface hydrophobicity,[20] they also exhibit volume phase transitions.[21] The volume change is undesirable when hydrogels are used as dressing materials because they may pull the skin. Additionally, when a typical PNIPAAm gel shrinks at a high temperature, it cannot recover its swelling state even if the temperature decreases below the phase transition temperature unless water is supplied. This issue has not been considered in previous studies on PNIPAAm-modified materials adhesion/detachment in aqueous solutions.[9–16] Therefore, this study focuses on this aspect and aims to control gel adhesion/detachment in air.

Based on the above discussion, we designed a surface-grafted hydrogel (SG gel) in which PNIPAAm was modified only in the surface region of a non-thermoresponsive base gel (NG gel) (Fig. 1). In this design, the polymer that shrinks or swells in response to temperature changes is present only in a localised small region of the gel. The synthesis scheme of the SG gel, based on our previously established method,[22,23] is shown in Fig. 2. Gel samples were prepared using a silicon sheet and a cylindrical mould to form discs 7 mm in diameter and 2 mm thick. Fig. 3(a) shows the results of confocal laser microscopy of the cross-section of the SG gel at 25 and 40 °C in an aqueous solution containing Nile Red, which accumulates and exhibits fluorescence in a hydrophobic environment.[24] The emission from Nile Red was observed only in the surface region of approximately 10 μm thickness at 40 °C, which was higher than the LCST of PINIPAAm (32 °C). This indicates that the thickness of the PNIPAAm-grafted gel surface is about 10 μm,

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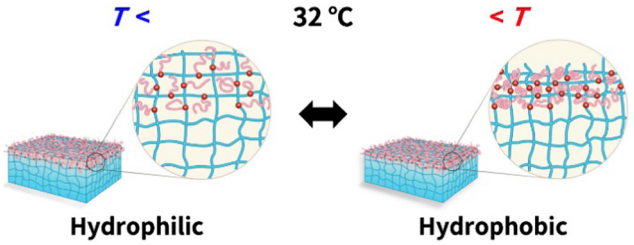

Fig. 1 Schematic of the surface-grafted (SG) gel.

and the gel surface shows temperature-responsive hydrophobicity change. When SG gel at 25 °C was placed on a stage heater set at 40 °C for 30 min, the surface of the SG gel adapted itself to the temperature changes and became fluorescent, suggesting that the surface became hydrophobic (Movie S1, ESI†).

To confirm the hydrophobicity changes of the SG gel surface according to the temperature, we performed water contact angle measurements on the SG and NG gels placed on heaters with the temperature set at 25 and 50 °C. The water contact angles on the NG gel at 25 and 50 °C are 51.7° and 56.8°, respectively, and no statistical difference is observed between them (Fig. 3b). These results indicate that the NG gel is a non-thermoresponsive hydrogel. The water contact angles on the SG gel showed a statistically significant difference between 25 and 50 °C (P = 0.00041), with the values of 68.4° and 92.7°, respectively. These results clearly prove that the thermoresponsive hydrogel surface was successfully constructed on the non-thermoresponsive NG gel by the surface grafting of PNIPAAm. We noted a difference of 24.3° in the contact angle between 25 and 50 °C.

The results motivated us to investigate whether the adhesiveness of SG gels depends on the temperature. However, the general tensile and peel test methods cannot be applied to determine the adhesive strength of the hydrogels prepared in this study because of their softness. Therefore, we developed a device that can quantitatively measure the peel strength per unit area when a hydrogel piece adheres to a solid material. The device is based on the principle of force curve measurements in atomic force microscopy (AFM).

The system of the device comprised a stainless-steel parallel plate spring used as a probe and a motorised stage on which the object to be adhered to the hydrogels was placed (Fig. 4). The parallel plate spring was equipped with a strain gauge sensor, and the sample was fixed to the top of the spring. First, the motorised stage rises, and the adherend contacts the hydrogel surface (Steps 1 and 2). The stage continues to compress the surfaces and reaches a predetermined position (Step 3). Subsequently, the stage starts to descend to apply the peeling force to the surface (step 4). Finally, a Bakelite plate is peeled off

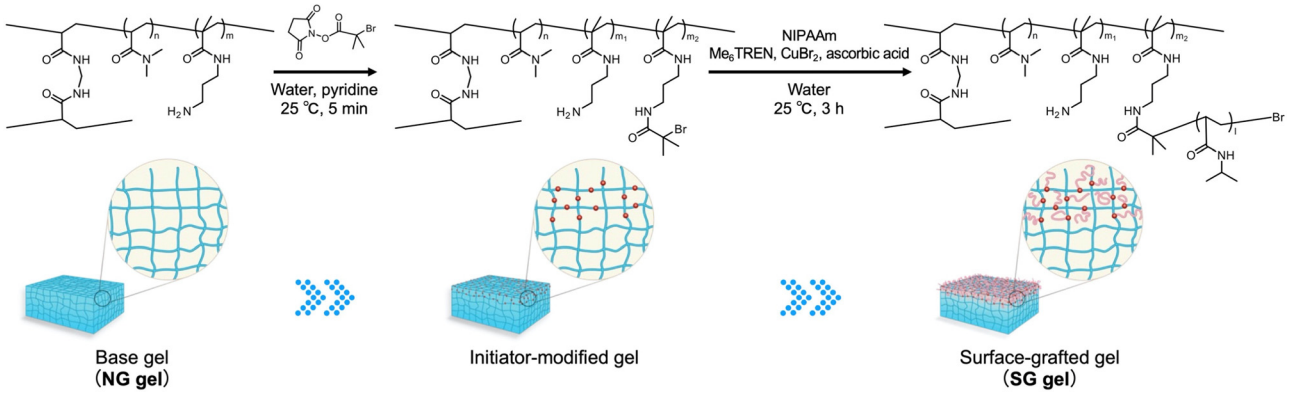

Fig. 2 Scheme for the preparation of the surface-grafted gel.

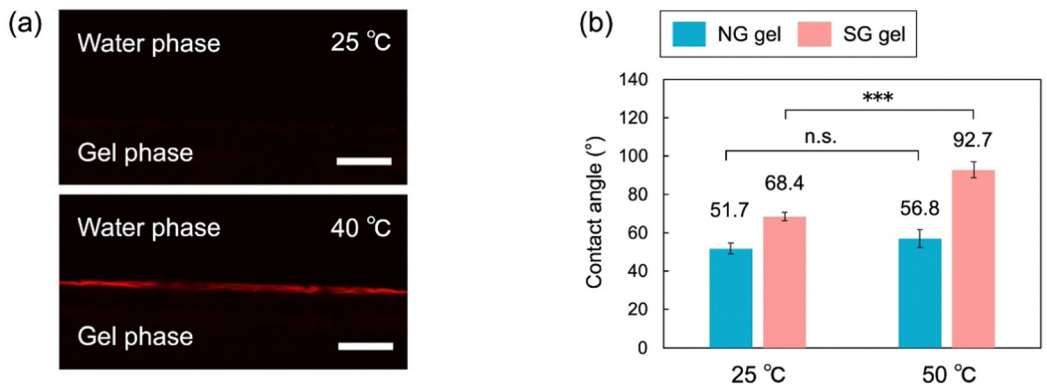

Fig. 3 (a) Confocal microscopy images of a cross section of the SG gel in an aqueous solution containing the Nile Red and (b) results of contact angle measurements of NG and SG gels. Scale bars: 100 μm. Data from three separate experiments are expressed as mean ± SD.

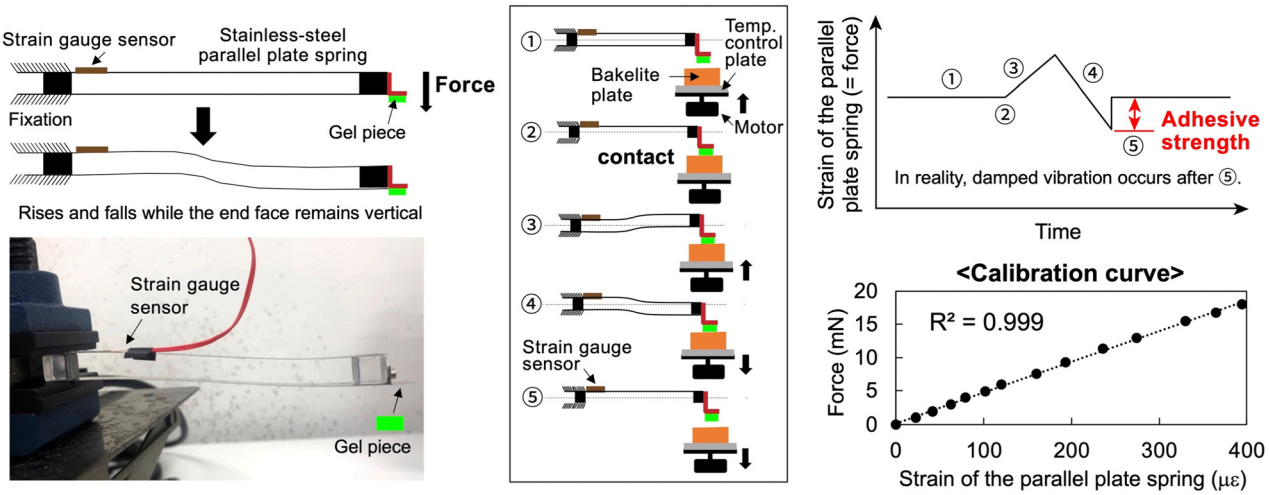

Fig. 4 Structure, mechanism, and calibration curve of the fabricated device to measure the adhesive strength of hydrogels.

from the gel (step 5). During this series of processes, strain of the parallel plate spring is measured with the strain gauge sensor to calculate the peeling force. We define the peeling force as the adhesive strength. The output of the strain gauge sensor was calibrated by placing weights at the top of the parallel plate spring. The calibration curve shown in Fig. 4 indicates that the device exhibited a good quantitative performance. Fig. 5 shows the adhesive strength of NG and SG gels to Bakelite plates, which are often used as synthetic skin models.[25] The measurements were made on placing the samples on a heater set at 25 and 50 °C. The water contents of the gel samples measured immediately before the adhesive strength measurement were 87.0% and 82.7% for the NG gel and the SG gel, respectively. Considering the NG gel, no significant differences are observed in the adhesive strength to the Bakelite plates between 25 and 50 °C (41.0 and 36.5 N m^{-2}, respectively), indicating no thermoresponsive changes in adhesiveness. However, a significant difference in the adhesive strength, exhibiting values of 21.0 and 65.8 N m^{-2}, was observed for the SG gel between 25 and 50 °C, respectively (P = 0.00104). This result indicates that the SG gel exhibited a thermoresponsive change in the adhesive strength to the Bakelite plates. The difference in the adhesive strength between 25 and 50 °C was 44.8 N m^{-2}. We assumed that the significant difference in the adhesive strength was due to the large difference in the hydrophobicity of the SG gel below and above the LCST of PNIPAm. Furthermore, the gel surface at 50 °C is expected to show high viscosity because of the coexistence of a hydrophilic PDMAAm network originated from the NG gel and hydrophobic grafted PNIPAAm chains above the LCST.[26] The viscous surface may enhance the adhesive strength to the Bakelite plate. However, only hydrophilic chains exist on the surface below the LCST. Therefore, we conclude that the thermoresponsive property of PNIPAAm grafted on the surface of the SG gel leads to thermoresponsive adhesive strength changes. On the other hand, although the contact angle of the SG gel was larger than that of the NG gel at 25 °C (Fig. 3(b)), the adhesive strength of the NG gel was larger than that of the SG gel at 25 °C (Fig. 5). The temperature-dependent change in adhesive strength of the SG gel with the same chemical composition is considered to be due to the change in hydrophobicity of PNIPAAm, but the cause of the difference in adhesive strength between NG and SG gels with different chemical compositions is currently unclear. We plan to examine parameters other than hydrophobicity in the future to clarify the cause. We believe that clarifying the parameters that influence adhesion phenomena is also important for the development of measurement systems that enable measurements with smaller error bars.

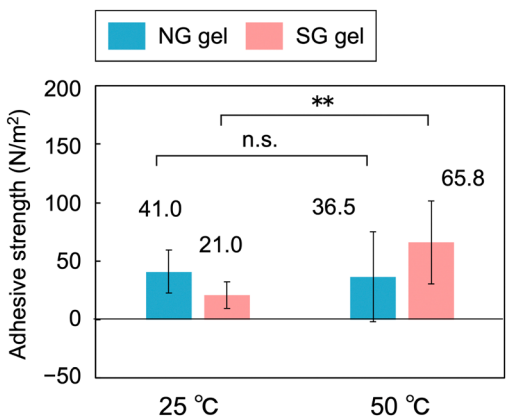

Fig. 5 Adhesive strength of NG and SG gels toward Bakelite plates. Data from ten separate experiments are expressed as mean ± SD.

In conclusion, we designed a surface-grafted hydrogel based on a non-thermoresponsive PDMAAm gel, which acts as a water reservoir and is modified with PNIPAAm only in its surface region. The hydrophobicity of the SG gel surface exhibited thermoresponsive changes below and above the LCST of PNIPAAm. We demonstrated that the adhesive strength of a gel surface toward a Bakelite plate changes in a thermoresponsive manner. This paper presents the first attempt to control adhesion of a hydrogel in a temperature-responsive manner by appropriate surface modification. Further optimisation of the

conditions may lead to the precise adhesion/detachment control of the hydrogel surfaces to the actual skin.

Author contributions

A. M. Akimoto contributed to directing the research, designing the system, and writing the paper. Y. Ohta contributed to designing the system. Y. Koizumi, T. Ishii, and M. Endo contributed to data collection. T. Enomoto, T. Nishimoto, and R. Yoshida contributed to the analysis and organization of the data.

Conflicts of interest

There are no conflicts to declare.

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