

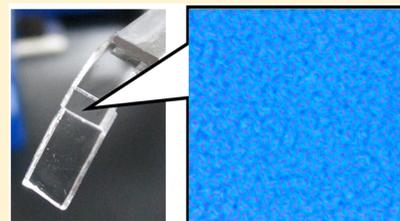
Hydrogel Adhesion with Wrinkle Formation by Spatial Control of Polymer Networks

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ABSTRACT: We prepared a novel wrinkled adhesive interface of hydrogels for strong adhesion via spatial control of polymer networks, including the density, distribution, and mobility of interactive units. A wrinkle structure was formed by the elasticity mismatch of hydrogels and adhesive polyion complex layers when electrophoresis was carried out between cationic and anionic semi-IPNs. The wrinkling wavelength of interfaces was controlled by Young's modulus of hydrogels. The role of wrinkle structure in adhesion was investigated by the measurement of the adhesive strength of hydrogels which were adhered under the compression, resulting in the disappearance of the wrinkle structure by compression that induced a decrease in adhesive strength. These results indicate that strong hydrogel adhesion was achieved by both the spatial design of interactive units and wrinkle formation.



INTRODUCTION

Wrinkled structures are often observed around soft and elastic interfaces such as fingers and the brain in the human body and play an important role of gaining surface area. It is well known that wrinkles are formed by the generation of a stress mismatch between two adhesive layers,^{1–5} indicating that a wrinkle structure has potential applications in the adhesion of two soft materials. Actually, the formation of such active wrinkles has previously been reported for a surface-treated elastomer^{1,2} and has been used for dry-adhesive substrates³ using the enhanced surface area.

On the other hand, hydrogels are similar to macromolecular-based constituents such as proteins, cells, and tissue; therefore, the adhesion of hydrogels has numerous applications in tissue engineering⁶ and drug delivery systems.⁷ It is well known that two hydrogels adhere to each other using interface interactions such as electrostatic,^{8–10} host–guest,¹¹ metal–ligand,^{12,13} and organic–inorganic^{14–18} interactions. Interactive units around the outermost surface of hydrogels play a key role in hydrogel adhesion.

However, the stoichiometric investigation of interactive units for the adhesion of hydrogels is the central part of a discussion. The spatial arrangement of interactive units based on network design is mostly unknown. Moreover, any wrinkle structure at hydrogel–hydrogel interfaces has not been reported, although swelling-induced hydrogel surfaces have been reported.^{4,5} There is no design guideline for effective hydrogel adhesion except for the chemical design of interactive units.

If a wrinkle structure is formed at a hydrogel–adhesive interface, it must contribute to the development of novel adhesive methods for soft materials with strong adhesion. In this study, therefore, we focused on the spatial control of

polymer networks such as the density, spatial distribution, and mobility of interactive units for making a wrinkle structure at hydrogel–hydrogel interfaces (Figure 1). Strong adhesion and a novel adhesive mechanism of hydrogels will be achieved by the wrinkle structure due to stress mismatch between hydrogels and the adhesive layer.

EXPERIMENTAL SECTION

Materials. *N,N*-Dimethylacrylamide (DMAAm) was purchased from Wako Pure Chemical Industries and used after distillation. 2,2'-Azobis[2-(2-imidazolin-2-yl)propane]-dihydrochloride (VA-044), ammonium persulfate (APS), *N,N'*-methylenebis(acrylamide) (MBAAm), *N,N,N',N'*-tetramethylethylenediamine (TEMED), and [3-(methacryloylamino)propyl]trimethylammonium chloride (TMA) were purchased from Wako Pure Chemical Industries (Osaka, Japan) and used as purchased without further purification. Sodium styrenesulfonate (SS), sodium poly(styrenesulfonate) (PSS), and poly(diallyldimethylammonium chloride) (PDDA) were purchased from Aldrich and used as purchased without further purification.

Preparation of Cationic and Anionic Hydrogels. The copolymerization of SS and DMAAm with MBAAm was carried out in water using 1 mol % APS as an anionic initiator and TEMED at 4 °C for 8 h. For the preparation of cationic TMA copolymer gels, VA-044 was used as a cationic azo-initiator and then gelation was carried out at 40 °C for 8 h. Semi-interpenetrating polymer networks (semi-IPNs) were prepared

Received: February 11, 2016

Revised: April 18, 2016

Published: May 17, 2016

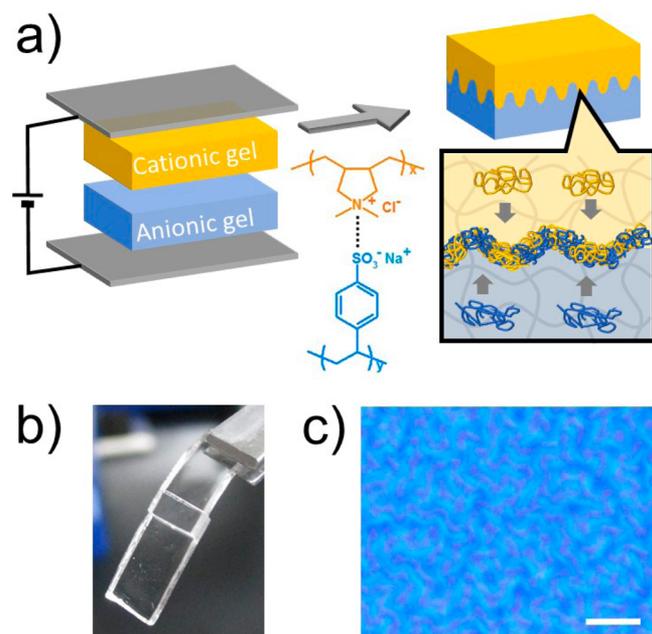


Figure 1. (a) Schematic illustration of wrinkle formation of adhered cationic and anionic gels by electrophoresis. (b) Macroscopic and (c) phase-contrast microscopic observation of adhered gel interfaces. (b, c) The gels were cut into $5 \times 15 \text{ mm}^2$ strips, with an adhesion area of $2 \times 5 \text{ mm}^2$. Ionic monomer units and the cross-linking ratio are 50 mmol L^{-1} and 1.0%, respectively. The scale bar is $10 \mu\text{m}$.

by the free-radical polymerization of DMAAm with MBAAm in the presence of PSS or PDDA by using an anionic or cationic initiator. The prepared hydrogel was washed with water for the removal of unreacted monomer. Young's modulus was measured using a tensile tester (Shimadzu EZ-S10) in an ambient atmosphere. They were loaded to failure at 3 mm min^{-1} in tensile mode.

Adhesion of Hydrogels. The preparation of the adhered hydrogels was performed in essentially the same way as described in our previous study.^{19–22} Briefly, electrophoresis was carried out between two Pt electrodes. The two gels were held in contact with each other between the Pt electrodes, and an electric field was applied. In this case, cationic gels were on the anode and anionic gels were on the cathode. The applied voltage and electrophoresis time were 5 V mm^{-1} and 3 s, respectively. The lap shear adhesion force was measured using a tensile tester in an ambient atmosphere. The adhered gels were loaded to failure at 3 mm min^{-1} in tensile mode, and the failure strain was measured.

RESULTS AND DISCUSSION

We prepared two types of hydrogels, (a copolymer gel and semi-interpenetrating polymer networks (semi-IPNs)), and then charged groups were chemically and physically fixed on the network.²³ The charge density of hydrogels was controlled by the amount of charged monomer and polymers. The adhesion of hydrogels was carried out by using our previously developed electrophoretic adhesion method (Figure 1a).^{19–22} During electrophoresis, cationic and anionic polymer chains move to the cathode and anode, respectively, and polyion complexes (PIC) were eventually formed at the hydrogel interface, causing adhesion. As shown in Figure 1b, two hydrogels quickly adhered within 3 s, and adhesive interfaces were visually transparent. Interestingly, wrinkle structure was

founded at adhesive hydrogel interfaces by phase-contrast microscopic observation (Figure 1c).

To investigate the relationship between the wrinkle structure and adhesive strength, the lap shear adhesion force was measured (Figure 2a). The adhesive strength of semi-IPNs and

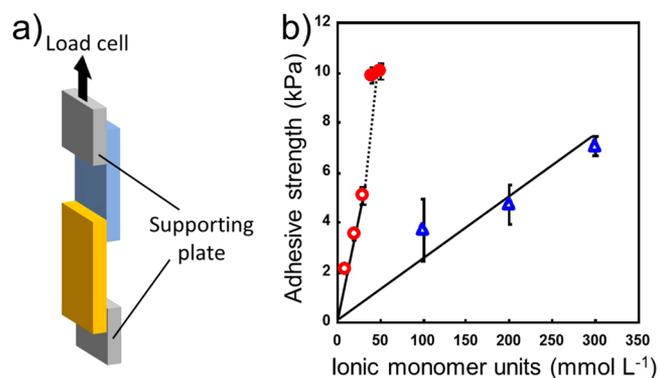


Figure 2. (a) Experimental procedure for lap shear tests on adhered cationic anionic gels. (b) Adhesive strength of semi-IPNs (circle) and copolymer (triangle) gels when electrophoretic adhesion was carried out for cationic and anionic gels. The closed symbol shows where the adhered gels have broken.

copolymers gels is shown in Figure 2b. The adhesive strength of both gels increased with increasing ionic monomer units inside polymer networks. The adhesive strength of semi-IPNs was stronger than that of copolymer gels in all cases. These results indicate that the adhesion of hydrogels was controlled by the amount of charged monomer and also depended on the network structure, especially on the local charge density of gel networks. The charge densities of both copolymer gels and semi-IPNs were normalized by the molarity of ionic monomer units. When the copolymer gels and semi-IPNs have the same extent of charge density, charged units inside the copolymer gels may be uniformly dispersed inside the PDMAAm networks. However, semi-IPNs have higher and lower local charge densities because of the presence of linear PSS or PDPA inside the networks. When the ionic monomer units have concentrations of 40 and 50 mmol L^{-1} for semi-IPNs, the adhesion interface with wrinkles was stronger than the gels themselves, and the gels were broken before the adhesion interface detached during a tensile strength test (Figure 2b, closed circle; Figure 1c). Stronger adhesion seems to be due to the formation of PIC films as an adhesive layer during electrophoresis. Therefore, wrinkle formation was observed for semi-IPNs with 30 mmol L^{-1} ionic monomer units, although a wrinkle was not formed for copolymers gel with 300 mmol L^{-1} ionic monomer units and semi-IPNs with 10 mmol L^{-1} ionic monomer units. These results indicate that a buckling instability did not occur because of an insufficient PIC layer due to lower polymer mobility and poor charge density. Moreover, similar behavior in adhesive strength was observed even though the concentration of ionic monomer units of copolymer gels is 10-fold higher than for semi-IPNs, indicating that the amount of charge, charge density, mobility of polymer networks, and wrinkle formation are important for the strong adhesion of hydrogels. In addition, such a wrinkle was not formed without electrophoresis in all cases. To confirm that a wrinkle consists of a PIC film and hydrogels, one side of the PSS gel was replaced with a PSS aqueous solution, and then electrophoresis was carried out at PDPA gels and the PSS

solution interface (Figure 3a). As expected, a wrinkle was formed on the PDDA gels (Figure 3b), indicating PSS/PDDA

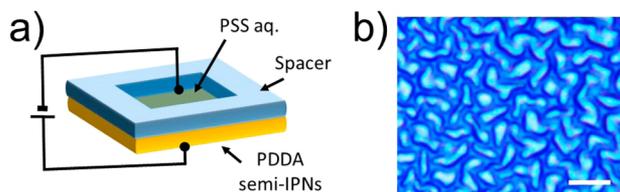


Figure 3. (a) Experimental procedure for PSS/PDDA PIC formation on the PDPA hydrogels and (b) phase-contrast microscopic observation. The scale bar is 10 μm .

PIC formation on the PDPA hydrogels. These results strongly suggest that the PIC layer as an adhesive interface was formed at a hydrogel interface, and then the wrinkle structure appeared by the elasticity mismatch of hydrogels and PIC layers.

Generally, the relationship between the wrinkling wavelength (λ) and Young's modulus of the substrate (E_s) and film (E_f) should be given by eq 1

$$\lambda = 2\pi t(E_f/3E_s)^{1/3} \quad (1)$$

where t is the film thickness. Therefore, the cross-linking ratio of hydrogels was changed to modulate E_s . When the cross-linking ratio of the hydrogel was changed from 1.0 to 0.3%, E_s was changed from 520 ± 90 to 115 ± 30 kPa. Actually, the size of the wrinkle was strongly affected by E_s (Figure 1c and Figure 4a,b), resulting in the wrinkling wavelength increasing from 3.6 ± 0.3 to 5.1 ± 0.5 μm with decreasing E_s . As shown in Figure 4c, the wrinkling wavelength can be well fitted with an inverse function of E_s ,

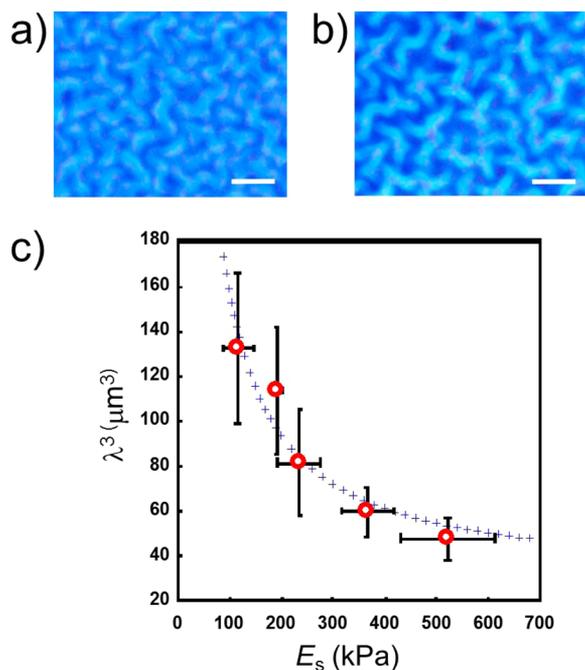


Figure 4. Phase-contrast microscopic observation of adhered (a, b) 50 mmol L^{-1} semi-IPNs gels. The cross-linking ratios of (a) and (b) are 0.5 and 0.3%, respectively. (c) Relationship between the wrinkling wavelength and Young's modulus of gels. Blue plus symbols trace the fitting curve. All scale bars are 10 μm .

$$\lambda^3 = A/E_s + B \quad (2)$$

where A is $(2\pi t)^3 E_f/3 = 1.3 \times 10^4$ and B is a fitting parameter equal to 28. In this study, the direct measurement of Young's modulus (E_f) and the thickness (t) of the PIC layers at the hydrogel–hydrogel interface are difficult. However, other researchers reported that Young's modulus of PDPA/PSS films, which were prepared by layer-by-layer methods, are 590 ± 90 MPa in water.²⁴ Therefore, the results will not contradict the theory when the thickness of the PIC layers is a few hundred nanometers. We also confirmed a three-dimensional structure of wrinkles by the cross-sectional observation of adhered gels because phase contrast images may just reveal a periodic variation in the refractive index of PIC layers and hydrogels. The no-wrinkle interface showed a flat cross-section (Figure 5a). However, a waving adhesive interface was observed



Figure 5. Phase-contrast microscopic observation of a cross-section of adhered (a) 10 and (b, c) 50 mmol L^{-1} semi-IPNs gels. Cross-linking ratio values for (a, b) and (c) are 1.0 and 0.3%, respectively. All scale bars are 20 μm .

at a cross-section of wrinkle interfaces and amplitude showing an increasing tendency with decreasing cross-linking ratio of hydrogels (Figure 5b,c). These results strongly suggested that wrinkles at interfaces had three-dimensional structure as shown in Figure 1a.

Finally, to investigate the role of wrinkle structure in adhesion, we measured the adhesive strength of hydrogels when electrophoretic adhesion was carried out under the compression of hydrogels because a wrinkle was formed by vertical growth with horizontal shrinking. We hypothesized that wrinkle formation was inhibited by the deformation of hydrogels as a result of vertical compression and horizontal stretching. Therefore, electrophoretic adhesion was carried out under compression, and adhesive strength was measured after stress release. The compression ratio was calculated from the height of two gels without (h_0) and with (h) compression (Figure 6a). We used 20, 30, 40, and 50 mmol L^{-1} semi-IPNs as shown in Figure 2. In the case of 20 and 30 mmol L^{-1} , a significant difference was not observed for adhesive strength with and without compression (Figure 6b, squares and inverse triangles). In the case of 50 mmol L^{-1} semi-IPNs, wrinkle structures were clearly observed from 0 to 23% compression, and then the gels were broken before the adhesion interface detached. When the hydrogels were compressed to 42%, the detachment of adhered gels and the disappearance of wrinkle structure was observed (Figure 6b, circles). The fracture of both the adhesive interface and gel itself occurred between 23 and 42% compression. These results indicate that wrinkle

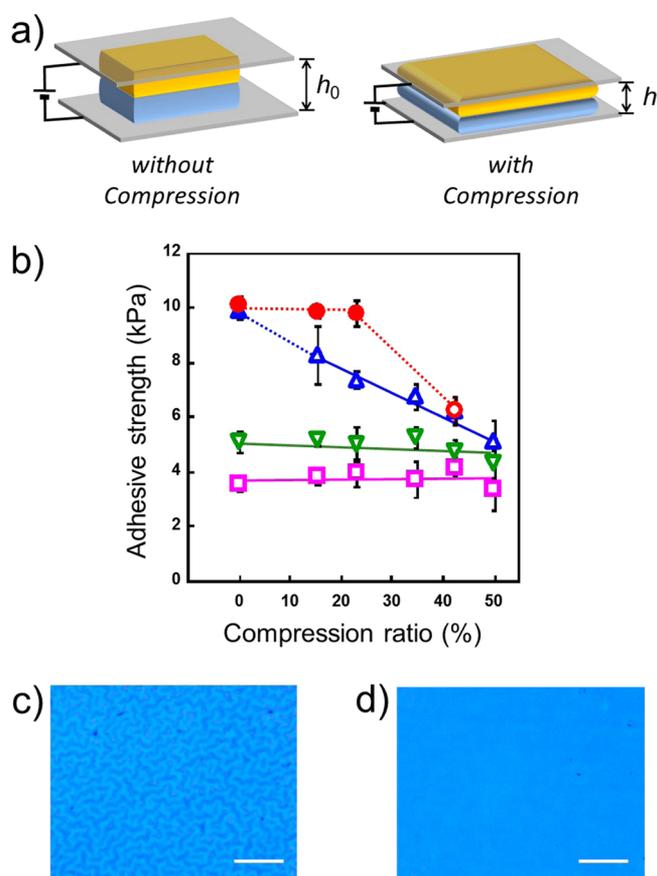


Figure 6. (a) Electrophoretic adhesion under the compression of gels and (b) adhesive strength of hydrogels as a function of the compression ratio. Circles, triangles, inverse triangles, and squares indicate 50, 40, 30, and 20 mmol L⁻¹ semi-IPNs. The closed symbols show where the adhered gels have broken. (c, d) Phase-contrast microscopic observation of adhered 40 mmol L⁻¹ semi-IPNs gels with (c) 0 and (d) 50% compression. All scale bars are 20 μ m.

formation is inhibited by hydrogel compression. Generally, two materials adhered by compression as a result of close contact with each other.³ On the contrary, in the present system, we found that the deformation of hydrogel networks inhibited wrinkle formation, and then the adhesive strength decreased. Therefore, increasing the compression ratio resulted in a decrease in the adhesive strength of 40 mmol L⁻¹ semi-IPNs in a continuous manner (Figure 6b, triangles) with the disappearance of wrinkle structure (Figure 6c,d). These results indicate that strong hydrogel adhesion was achieved by both the chemical design of interactive units and interface relaxation such as wrinkle formation.

CONCLUSIONS

We fabricated a novel adhesive interface of hydrogels with a wrinkle structure via spatial control of polymer networks. We confirmed that the wrinkle structure at adhesive hydrogel interfaces was formed by the elasticity mismatch of hydrogels and PIC layers. Wrinkling wavelengths were strongly affected by Young's modulus of hydrogels, resulting in the wrinkling wavelength increasing with a decreasing Young's modulus of hydrogels. Increasing the compression ratio of hydrogels resulted in a decrease in the adhesive strength with wrinkle disappearance. It was suggested that the presence of wrinkle structure strengthens the adhesive strength of hydrogels. The

discovery of wrinkle structure at the adhesive interface will contribute considerably to the development of a novel adhesion strategy and an understanding of interfaces of soft materials.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This study was supported by the Sasakawa Scientific Research Grant from The Japan Science Society and a Grant-in-Aid for Challenging Exploratory Research (no. 26560227) from the Japan Society for the Promotion of Science. We thank Profs. Tatsuya Shoji, Tetsuro Shinada, and Yutaka Amao at Osaka City University for helpful discussions.

REFERENCES

- (1) Kim, H. S.; Crosby, A. J. Solvent-Responsive Surface via Wrinkling Instability. *Adv. Mater.* **2011**, *23*, 4188–4192.
- (2) Tokudome, Y.; Suzuki, K.; Kitanaga, T.; Takahashi, M. S. Hierarchical Nested Wrinkles on Silica-Polymer Hybrid Films: Stimuli-Responsive Micro Periodic Surface Architectures. *Sci. Rep.* **2012**, *2*, 683.
- (3) Chan, E. P.; Smith, E. J.; Hayward, R. C.; Crosby, A. J. Surface Wrinkles for Smart Adhesion. *Adv. Mater.* **2008**, *20*, 711–716.
- (4) Guvendiren, M.; Yang, S.; Burdick, J. A. Swelling-Induced Surface Patterns in Hydrogels with Gradient Crosslinking Density. *Adv. Funct. Mater.* **2009**, *19*, 3038–3045.
- (5) Guvendiren, M.; Burdick, J. A.; Yang, S. Kinetic Study of Swelling-induced Surface Pattern Formation and Ordering in Hydrogel Films with Depth-wise Crosslinking Gradient. *Soft Matter* **2010**, *6*, 2044–2049.
- (6) Lee, K. Y.; Mooney, D. J. Hydrogels for Tissue Engineering. *Chem. Rev.* **2001**, *101*, 1869–1879.
- (7) Vermonden, T.; Censi, R.; Hennink, W. E. Hydrogels for Protein Delivery. *Chem. Rev.* **2012**, *112*, 2853–2888.
- (8) Tamagawa, H.; Nagato, F.; Umemoto, S.; Okui, M.; Popovic, S.; Taya, M. The Influence of Salt-Linkages on the Adhesion and Hardness Variance of Hydrogels. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 383–388.
- (9) Tamagawa, H.; Takahashi, Y. Adhesion Force Behavior between Two Gels Attached with an Electrolytic Polymer Liquid. *Mater. Chem. Phys.* **2008**, *107*, 164–170.
- (10) Abe, H.; Hara, Y.; Maeda, S.; Hashimoto, S. Surface Modification Method for Adhesion of Gels. *Chem. Lett.* **2014**, *43*, 243–245.
- (11) Harada, A.; Kobayashi, R.; Takashima, Y.; Hashidzume, A.; Yamaguchi, H. Macroscopic Self-assembly through Molecular Recognition. *Nat. Chem.* **2011**, *3*, 34–37.
- (12) Holten-Andersen, N.; Harrington, M. J.; Birkedal, H.; Lee, B. P.; Messersmith, P. B.; Lee, K. Y. C.; Waite, J. H. pH-Induced Metal-ligand Cross-links Inspired by Mussel Yield Self-healing Polymer Networks with Near-covalent Elastic Moduli. *Proc. Natl. Acad. Sci. U. S. A.* **2011**, *108*, 2651–2655.
- (13) Asoh, T.; Yoshitake, H.; Takano, Y.; Kikuchi, A. Fabrication of Self-Healable Hydrogels through Sol–Gel Transition in Metallo-supramolecular Aqueous Solution by Aeration. *Macromol. Chem. Phys.* **2013**, *214*, 2534–2539.
- (14) Haraguchi, K.; Uyama, K.; Tanimoto, H. Self-healing in Nanocomposite Hydrogels. *Macromol. Rapid Commun.* **2011**, *32*, 1253–1258.
- (15) Wang, Q.; Mynar, J. L.; Yoshida, M.; Lee, E.; Lee, M.; Okuro, K.; Kinbara, K.; Aida, T. High-Water-Content Mouldable Hydrogels

by Mixing Clay and a Dendritic Molecular Binder. *Nature* **2010**, *463*, 339–343.

(16) Rose, S.; PrevotEAU, A.; Elzière, P.; Hourdet, D.; Marcellan, A.; Leibler, L. Nanoparticle Solutions as Adhesives for Gels and Biological Tissues. *Nature* **2014**, *505*, 382–385.

(17) Meddahi-Pellé, A.; Legrand, A.; Marcellan, A.; Louedec, L.; Letourneur, D.; Leibler, L. Organ Repair, Hemostasis, and in vivo Bonding of Medical Devices by Aqueous Solutions of Nanoparticles. *Angew. Chem., Int. Ed.* **2014**, *53*, 6369–6373.

(18) Abe, H.; Hara, Y.; Maeda, S.; Hashimoto, S. Adhesion of Gels by Silica Particle. *J. Phys. Chem. B* **2014**, *118*, 2518–2522.

(19) Asoh, T.; Kikuchi, A. Electrophoretic Adhesion of Stimuli-responsive Hydrogels. *Chem. Commun.* **2010**, *46*, 7793–7795.

(20) Asoh, T.; Kawai, W.; Kikuchi, A. Electrophoretic Adhesion of Biodegradable Hydrogels through the Intermediary of Oppositely Charged Polyelectrolytes. *Soft Matter* **2012**, *8*, 1923–1927.

(21) Asoh, T.; Kikuchi, A. Rapid Fabrication of Reconstructible Hydrogels by Electrophoretic Microbead Adhesion. *Chem. Commun.* **2012**, *48*, 10019–10021.

(22) Asoh, T.; Kawamura, E.; Kikuchi, A. Stabilization of Electro-phoretically Adhered Gel Interfaces to Construct Multi-layered Hydrogels. *RSC Adv.* **2013**, *3*, 7947–7952.

(23) Wu, W.; Liu, J.; Cao, S.; Tan, H.; Li, J.; Xu, F.; Zhang, X. Drug Release Behaviors of a pH Sensitive Semi-Interpenetrating Polymer Network Hydrogel Composed of Poly(vinyl alcohol) and Star Poly[2-(dimethylamino)ethyl methacrylate]. *Int. J. Pharm.* **2011**, *416*, 104–109.

(24) Nolte, A. J.; Rubner, M. F.; Cohen, R. E. Determining the Young's Modulus of Polyelectrolyte Multilayer Films via Stress-Induced Mechanical Buckling Instabilities. *Macromolecules* **2005**, *38*, 5367–5370.