Journal of Materials Chemistry B

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/materialsB

Stiff, strong, and tough hydrogels with good chemical stability

Jianyu Li,[a] Zhigang Suo[ab] and Joost J. Vlassak[a]

Abstract

Most hydrogels have poor mechanical properties, severely limiting their scope of applications. Here a hybrid hydrogel, consisting of hydrophilic and crystalline polymer networks, achieves an elastic modulus of 5 MPa, a strength of 2.5 MPa, and a fracture energy of 14,000 Jm^{-2}, while maintaining physical integrity in concentrated electrolyte solutions.

Recent developments in the area of hydrogels promise to greatly expand their scope of applications.[1] Many applications require hydrogels to endure significant mechanical loads in aggressive environments. Examples range from biomedical applications such as artificial cartilage in tissue engineering,[2] to engineering applications such as swellable packers in the oil industry,[3] or artificial nerves and muscles in the nascent field of soft machines.[4] Substitutes for cartilage require high stiffness (1 MPa), high toughness (1,000 Jm^{-2}), and high water content (60-80 %).[5] Materials for oil packers require high stiffness, high strength, and chemical stability; they need to resist deformation, sustain sealing pressure (up to 34 MPa) and be stable in saline water.[3] Materials for artificial nerves and muscles require high resistance to mechanical damage,[6] and tolerance of concentrated electrolyte for ionic conductance.[4] Most hydrogels have low stiffness (10 kPa), strength (100 kPa) and toughness (10 Jm^{-2});[7] and some of them degrade in electrolyte solutions.[8] There is a strong need for mechanically robust hydrogels with good chemical stability.

Despite recent progress, developing hydrogels that are both mechanically robust and chemically stable is still a challenge.[7, 9] Breaking covalent bonds in double network gels results in permanent and irreversible damage to the network.[10] Formation of hydrophobic associations is limited by low solubility of the hydrophobes.[11] Hydrogen bonds have very low association strength in hydrogels due to competition of water for binding sites.[12] Ionic cross-links are particularly effective in toughening hydrogels – alginate-polyacrylamide hydrogels in which the alginate is cross-linked with calcium ions exhibit remarkably high toughness.[1c, 13] The ionic cross-link is, however, vulnerable to mobile ions, which are often encountered under physiological and engineering conditions,[2, 4] and the performance of ionically cross-linked hydrogels degrades markedly in electrolyte solutions.[1b, 8]

As an alternative to ionic cross-links, the use of crystallites to cross-link a network has great potential to overcome these limitations: crystallites serve as physical cross-links that are both reversible and stable when exposed to mobile ions. Polyvinyl alcohol (PVA) is an example of a polymer that can form crystallites. PVA is widely used and has seen extensive development for biomedical applications.[14] In 1975, Peppas discovered that a sequence of freeze and thaw cycles could produce PVA hydrogels where crystallites serve as cross-links.[14a] Unfortunately, hydrogels synthesized using this method are compliant and brittle.[15] It is possible to achieve higher stiffness and toughness using a dry-anneal method, but only at the expense of a much lower water content (Supplementary Information, Fig. S1).[16] Muratoglu and coworkers polymerized acrylamide monomers in the pores of a PVA hydrogel to form uncross-linked chains, and showed that the equilibrium water content of the resulting gels increased with acrylamide content, while the coefficient of friction, tear strength and creep resistance decreased.[14b]

Here we propose that a hybrid network of a crystalline polymer and a covalently cross-linked hydrophilic polymer may form a hydrogel with robust mechanical properties and good chemical stability: the crystalline polymer can generate a large number of crystallites to serve as physical cross-links that are both stable and reversible; the covalently cross-linked hydrophilic polymer maintain the elasticity of the network during deformation and controls the swelling of the hydrogel. We describe one such hybrid hydrogel that combines extremely high stiffness, strength, and toughness. The hydrogel consists of a hydrophilic polyacrylamide (PAAm) network that is covalently cross-linked and a PVA network that forms crystallites. We show that the PVA crystallites result in a high cross-link density, thus producing a hydrogel of remarkable stiffness and strength. The crystallites unzip under deformation, dissipating energy in the process and yielding a hydrogel with exceptional toughness. After deformation, unzipped crystallites recover at room temperature due to the incompatibility of the two polymers in the hydrogel. The hybrid hydrogel can achieve an elastic modulus of 5 MPa, a strength of 2.5 MPa, and a fracture energy of 14,000 Jm^{-2}. Moreover, these properties are stable, even in concentrated electrolyte solutions.

We prepared the hybrid hydrogels in a simple three-step protocol (Fig. 1). First we form a cross-linked network of PAAm in the presence of PVA chains. Second, we dry and anneal the gel at 120^{o}C. The drying process removes water and concentrates the PVA in the mixture. The annealing process enhances the mobility of PVA chains and promotes crystallization.[14b, 16] This step generates a much higher density of PVA crystallites than the freeze-thaw method developed by Peppas (Supplementary Information, Fig. S2).[14a] The resulting dry gel is translucent, indicative of phase separation (Supplementary Information, Fig. S3); evidently PAAm and PVA are not mutually soluble.[18] X-ray diffraction measurements confirmed the formation of crystallites (Supplementary Information, Fig. S4). In the final step, we re-hydrate the gel by immersing it in water for at least 3 days. The gel absorbs water and swells until it reaches equilibrium. Fourier transform infrared spectroscopy confirmed that the PVA-PAAm hydrogel is essentially a superposition of PVA and PAAm hydrogels (Supplementary Information, Fig. S5). Different from the semi-interpenetrating PVA-PAAm gel prepared by Muratoglu et al,[14b] the PVA-PAAm gel in this work contains both physical and covalent cross-links. Our design is to toughen the gel before introducing physical cross-links by crosslinking the PAAm, to increase the retraction force of the network, and to prevent leakage of PAAm chains.[17]

To evaluate the mechanical behavior of the hybrid hydrogels, we performed tensile experiments on two types of hydrogels: an entangled PVA-PAAm hydrogel and a crystallized PVA-PAAm hydrogel. The former was not subject to the dry-anneal step and the PVA chains in this hydrogel were simply entangled in the cross-linked polyacrylamide network; the latter went through the standard three-step protocol. The water contents of both gels were fixed at 66%. Samples of both gels were stretched to rupture (Fig. 2a). The nominal stress is the loading force divided by the cross-sectional area of the undeformed sample. The stretch ratio is the current length divided by the initial length of undeformed sample. The entangled PVA-PAAm hydrogel is compliant and soft. In contrast, the crystallized PVA-PAAm hydrogel is stiff and strong, evidently the result of a high density of physical cross-links. Each sample was stretched to a stretch ratio of 2.5 and then unloaded to its initial length (Fig. 2b). In the entangled PVA-PAAm hydrogel, the absence of crystallites results in relatively little hysteresis, and the sample behaves more or less elastically. In the crystallized PVA-PAAm hydrogel, on the other hand, the crystallites unzip and dissipate a significant amount of energy. This dissipated energy manifests as significant hysteresis in the stress-stretch curve, indicative of a very tough hydrogel. This behavior is similar to that of pure PVA, for which the evolution of crystallites under deformation has been characterized with small-angle X ray scattering and is well documented in the literature.[19] The unzipping of crystallites was further confirmed by the anisotropic swelling of hydrogels after uniaxial deformation and the resulting anisotropic microstructure as revealed by confocal microscopy (Supplementary Information, Fig. S6): the crystallites unzip preferentially in the deformation direction, allowing the gel to further expand in this direction on swelling.

To evaluate the stability of the hydrogels in electrolyte solutions, we performed tensile experiments on the PVA-PAAm hydrogel and an alginate-PAAm hydrogel, before and after soaking overnight in a saline solution (NaCl 9 $\mathrm{gL^{-1}}$). The results are shown in Fig. 2c. The alginate-PAAm hydrogel is a tough gel formed by covalently and ionically cross-linked polymers. The electrostatic interactions between alginate chains and calcium ions form ionic cross-links that unzip and dissipate energy under deformation.[1c] When an alginate-PAAm hydrogel swells in a saline solution, ion exchange takes place between the saline solution and the hydrogel; sodium ions compete with calcium ions for the binding sites on the alginate chains, resulting in an unzipping of the ionic cross-links. After soaking, the water content of the alginate-PAAm hydrogel has increased from 86% to 98%, its strength is significantly reduced, and the gel has lost its energy dissipation mechanism – the stress-stretch curve no longer shows any hysteresis. By contrast, soaking in saline has no effect on the stress-stretch curves of the PVA-PAAm gels, even in highly concentrated electrolyte solutions ($CaCl_2$ 1.0 M, Supplementary Information, Fig. S7). Unlike ionic cross-link, the crystallites in PVA do not rely on electrostatic interaction and remain intact in electrolytes with a high content of monovalent ions. Furthermore, unlike alginate, the PVA network is not susceptible to hydrolysis: the mechanical properties of the PVA-based gel do not degrade after storing in distilled water for as long as three months (Fig. 2d).

Recovery of the PVA-based hydrogels was investigated by performing compression tests on cylindrical samples with a diameter of 5 mm. Each sample was first compressed to a stretch ratio of 0.2 and then unloaded. The sample was then stored at room temperature for various durations of time and subjected to another compression test (Fig. 2e). We quantify the ability of the crystallites to reform by the recovery ratio, i.e., the work performed during the second compression test normalized by the work performed during the first test. The recovery ratio increases to more than 90% in less than 24 hours (Fig. 2f). The phenomenon is understood as follows. As the crystallites unzip under deformation, the covalently cross-linked network provides the force to re-store the original shape of the gel. Since PAAm and PVA are incompatible, there is a driving force for phase separation; the PVA chains aggregate and reform the crystallites at room temperature.[20] This process is relatively slow because of the large molecular weight of the PVA, but the rate of recovery increases with increasing covalent cross-link density (Supplementary Information, Fig. S8). A similar phenomenon is also observed in entangled PVA-PAAm hydrogel, which is initially transparent, but slowly turns translucent after storing at room temperature (Supplementary Information, Fig. S9).

To evaluate the effect of acrylamide on the properties of the dry-annealed PVA-PAAm gel, we prepared a series of hydrogels with various ratios of acrylamide to (acrylamide plus polyvinyl alcohol) and performed tensile tests. The results are summarized in Fig. 3. As the acrylamide content increases, both the strength (Fig. 3a) and stiffness (Fig. 3b) of the hydrogel decrease. The fracture energy was measured by performing tensile tests on notched samples using a geometry known as the pure shear test.[1c, 21] Similar to the other mechanical properties, the fracture energy of the hydrogels decreases with increasing acrylamide content (Fig. 3c). This trend is inversely correlated with the equilibrium water content (Fig. 3d): as the acrylamide content of a gel increases, so does its affinity for water, and the gel absorbs more water.[22] In the limit of no acrylamide, the gel has very good mechanical properties, but a water content of only 42%. At 25% acrylamide, the hydrogel has a relatively high water content of 62%, while maintaining a good combination of mechanical properties: an elastic modulus of 5 MPa, a strength of 2.5 MPa and a fracture energy of 14,000 Jm^{-2}. The mechanical behavior of these hybrid gels is well described by the rule of mixtures applied to the PVA and PAAm phases (Supplementary Information, Fig. S10), and varies with the covalent cross-link density of the

PAAm component (Supplementary Information, Fig. S11). The properties of PVA/PAAm hybrid gels can be tailored over a broad range. The swelling behavior of the hydrogel can be tuned by controlling the hydrophilicity of the covalent network. For instance, sodium acrylate can be copolymerized with acrylamide to provide a large ionic osmotic pressure and so increase the equilibrium water content of the gel (Supplementary Information, Fig. S12).

In Figure 4, we present two Ashby charts for a variety of soft materials. In terms of strength and stiffness, PVA-PAAm hydrogels outperform most hydrogels, including alginate-polyacrylamide hydrogels and polyampholyte hydrogels (Fig. 4a). Traditional PVA hydrogels prepared using freeze/thaw cycles are strong, but compliant and brittle with a toughness of only 500 Jm^{-2}, due to relatively low density of crystallites.[15] Bacterial cellulose-gelatin hydrogels have high strength, but are brittle and rupture at small strains.[23] With respect to stiffness and fracture energy, PVA-PAAm hydrogels do better than all other hydrogels (Fig. 4b). Considering that these gels contain 60-80% water, such high stiffness and fracture resistance are quite remarkable.

Conclusions

Our results suggest that hydrogels with excellent mechanical performance and chemical stability can be prepared by combining hydrophilic and crystalline polymers. With appropriate processing, the crystalline polymer can form a high density of crystallites that serve as cross-links resulting in high stiffness, strength, and toughness; the network formed by the hydrophilic polymer maintains the shape of the hydrogel, provides a strong driving force to reform crystallites, and increases the equilibrium water content. The hydrogels remain stable in electrolyte solutions. This strategy has a large pool of material candidates. Beside polyvinyl alcohol, a variety of other crystalline polymers can be used, including polyurethane,[24] poly-lactic acid and polyethylene glycol.[25] The combination of high stiffness, high strength, fracture resistance and recoverability along with chemical stability, biocompatibility, facile synthesis, and low cost make these materials ideal candidates for load-bearing applications.

Experimental method

Hydrogel synthesis. The polyvinyl alcohol-polyacrylamide hydrogel was synthesized using the following protocol. Polyvinyl alcohol powder (PVA, Mw 89000-98000, hydrolysis >99%) was dissolved in distilled water at 90 ^{o}C; the mixture was stirred overnight until the solution became homogeneous. The PVA solution was then mixed with acrylamide (AAm), N,N'-methylenebisacrylamide (MBAA), tetramethyl-ethylenediamine (TEMED) and ammonium persulfate (APS) in this sequence. The weights of TEMED and APS were fixed at 0.0055 and 0.006 times that of AAm, while the weight ratio of PVA versus AAm was varied. The mixture was placed in a glass mold (75 x 45 x 3 mm^3), and kept at room temperature overnight to complete the reaction.

Crystallization and rehydration. After synthesis, the hydrogels were dried at room temperature. The dry gels were subsequently heated in a vacuum furnace (Symphony, VWR). The temperature was kept at 80^{o}C for 3 hours and then increased to 120^{o}C for 1 hour. The gel was then fully rehydrated in distilled water, which took approximately three days. The mass of the gel was measured before and after rehydration (m_{dry}, m_{wet}) using an analytical balance. The equilibrium water content was calculated using $1 - m_{dry} / m_{wet}$.

Tensile tests. A rectangular strip of gel (75 x 45 x 3 mm^3) was glued to two rigid acrylate clamps (75 x 20 x 1.5 mm^3). Both unnotched and notched samples were prepared for tensile tests. For notched samples, an edge crack of length 35mm was cut using a razor blade in the middle of the gauge section of the sample. An Instron machine (model 3342 with a 1000 N load cell) was used.

The stretch rate was fixed at 2 min^{-1}. The signals of force and extension were recorded throughout the experiment.

Compression tests. Uniaxial compression tests were performed on gel cylinders of 5 mm diameters using the Instron machine. The upper platen approached the sample slowly until a rise in force was detected, indicating contact between the platen and the gel. Upon contact, the displacement rate of the platen was increased to 1 mm min^{-1} until a pre-determined stretch ratio was achieved. The entire loading process was finished in less than five minutes to avoid any redistribution of solvent inside the gel, and thus maintain incompressibility. Both force and displacement were recorded continuously throughout the experiment.

Acknowledgements

This work was supported by the MRSEC (DMR-0820484) at Harvard University and by the National Science Foundation through grant CMMI-1404653. It was performed in part at the Center for Nanoscale Systems at Harvard University. The authors thank David A. Weitz for providing the rheometer and confocal microscopy, and David J. Mooney for providing the Instron machine.

Notes and references

[a] *School of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138, U.S.A.*

[b] *Kavli Institute for Bionano Science and Technology, Harvard University, Cambridge, MA 02138, U.S.A.*

† Electronic Supplementary Information (ESI) available. See DOI: 10.1039/c000000x/

1. (a) J. P. Gong, Y. Katsuyama, T. Kurokawa and Y. Osada, *Adv. Mater.*, 2003, **15**, 1155; (b) T. L. Sun, T. Kurokawa, S. Kuroda, A. B. Ihsan, T. Akasaki, K. Sato, M. A. Haque, T. Nakajima and J. P. Gong, *Nat. Mater.*, 2013, **12**, 932; (c) J. Y. Sun, X. H. Zhao, W. R. K. Illeperuma, O. Chaudhuri, K. H. Oh, D. J. Mooney, J. J. Vlassak and Z. G. Suo, *Nature*, 2012, **489**, 133; (d) K. Haraguchi and T. Takehisa, *Adv. Mater.*, 2002, **14**, 1120; (e) S. E. Bakarich, S. Beirne, G. G. Wallace and G. M. Spinks, *J. Mater. Chem. B*, 2013, **1**, 4939; (f) K. J. Henderson, T. C. Zhou, K. J. Otim and K. R. Shull, *Macromolecules*, 2010, **43**, 6193; (g) T. Sakai, T. Matsunaga, Y. Yamamoto, C. Ito, R. Yoshida, S. Suzuki, N. Sasaki, M. Shibayama and U.-I. Chung, *Macromolecules*, 2008, **41**, 5379.

2. D. J. Huey, J. C. Hu and K. A. Athanasiou, *Science*, 2012, **338**, 917.

3. M. Kleverlaan, R. H. van Noort and I. Jones, in *SPE/IADC Drilling Conference*, Society of Petroleum Engineers, Houston, Texas, 2005.

4. C. Keplinger, J. Y. Sun, C. C. Foo, P. Rothemund, G. M. Whitesides and Z. G. Suo, *Science*, 2013, **341**, 984.

5. M. V. ChinPurcell and J. L. Lewis, *J. Biomech. Eng.*, 1996, **118**, 545.

6. R. V. Martinez, A. C. Glavan, C. Keplinger, A. I. Oyetibo and G. M. Whitesides, *Adv. Funct. Mater.*, 2014, **24**, 3003.

7. P. Calvert, *Adv. Mater.*, 2009, **21**, 743.

8. (a) H. Kamata, Y. Akagi, Y. Kayasuga-Kariya, U.-I. Chung and T. Sakai, Science, 2014, 343, 873; (b) D. A. De Silva, P. J. Martens, K. J. Gilmore and M. in het Panhuis, *J. Appl. Polym. Sci.*, 2014, DOI: 10.1002/APP.41216.

9. X. H. Zhao, *Soft Matter*, 2014, **10**, 672.

10. J. P. Gong, *Soft Matter*, 2010, **6**, 2583.

11. D. C. Tuncaboylu, M. Sari, W. Oppermann and O. Okay, *Macromolecules*, 2011, **44**, 4997.

12. E. A. Appel, J. del Barrio, X. J. Loh and O. A. Scherman, *Chem. Soc. Rev.*, 2012, **41**, 6195.

13. (a) J. Y. Li, W. R. Illeperuma, Z. G. Suo and J. J. Vlassak, *ACS Macro Lett.*, 2014, **3**, 520; (b) D. M. Kirchmajer and M. in het Panhuis, *J. Mater. Chem. B*, 2014, **2**, 4694.

14. (a) C. M. Hassan and N. A. Peppas, in *Biopolymers· PVA Hydrogels, Anionic Polymerisation Nanocomposites*, Springer, 2000, 37; (b) H. Bodugoz-Senturk, C. E. Macias, J. H. Kung and O. K. Muratoglu, *Biomaterials*, 2009, **30**, 589.

15. L. Zhang, J. Zhao, J. T. Zhu, C. C. He and H. L. Wang, *Soft Matter*, 2012, **8**, 10439.

16. W. I. Cha, S. H. Hyon, M. Oka and Y. Ikada, *Macromol. Symp*., 1996, **109**, 115.

17. H. Bodugoz-Senturk, J. Choi, E. Oral, J. H. Kung, C. E. Macias, G. Braithwaite and O. K. Muratoglu, *Biomaterials*, 2008, **29**, 141.

18. S. Mishra, R. Bajpai, R. Katare and A. Bajpai, *Microsystem Technologies*, 2008, **14**, 193.

19. T. Miyazaki, A. Hoshiko, M. Akasaka, T. Shintani and S. Sakurai, *Macromolecules*, 2006, **39**, 2921.

20. J. L. Holloway, A. M. Lowman and G. R. Palmese, *Soft Matter*, 2013, **9**, 826.

21. G. J. Lake and A. G. Thomas, *Proc. R. Soc. London, Ser. A*, 1967, **300**, 108.

22. J. Y. Li, Y. H. Hu, J. J. Vlassak and Z. G. Suo, *Soft Matter*, 2012, **8**, 8121.

23. A. Nakayama, A. Kakugo, J. P. Gong, Y. Osada, M. Takai, T. Erata and S. Kawano, *Adv. Funct. Mater.*, 2004, **14**, 1124.

24. J. Wu, Q. Ge and P. T. Mather, *Macromolecules*, 2010, **43**, 7637.

25. A. K. Gaharwar, P. J. Schexnailder, A. Dundigalla, J. D. White, C. R. Matos-Perez, J. L. Cloud, S. Seifert, J. J. Wilker and G. Schmidt, *Macromol. Rapid Comm.*, 2011, **32**, 50.

26. M. A. Haque, T. Kurokawa, G. Kamita and J. P. Gong, *Macromolecules*, 2011, **44**, 8916.

27. L. Zhang, Z. Wang, C. Xu, Y. Li, J. Gao, W. Wang and Y. Liu, *J. Mater. Chem.*, 2011, **21**, 10399.

28. U. G. K. Wegst and M. F. Ashby, *Philos. Mag.*, 2004, **84**, 2167.

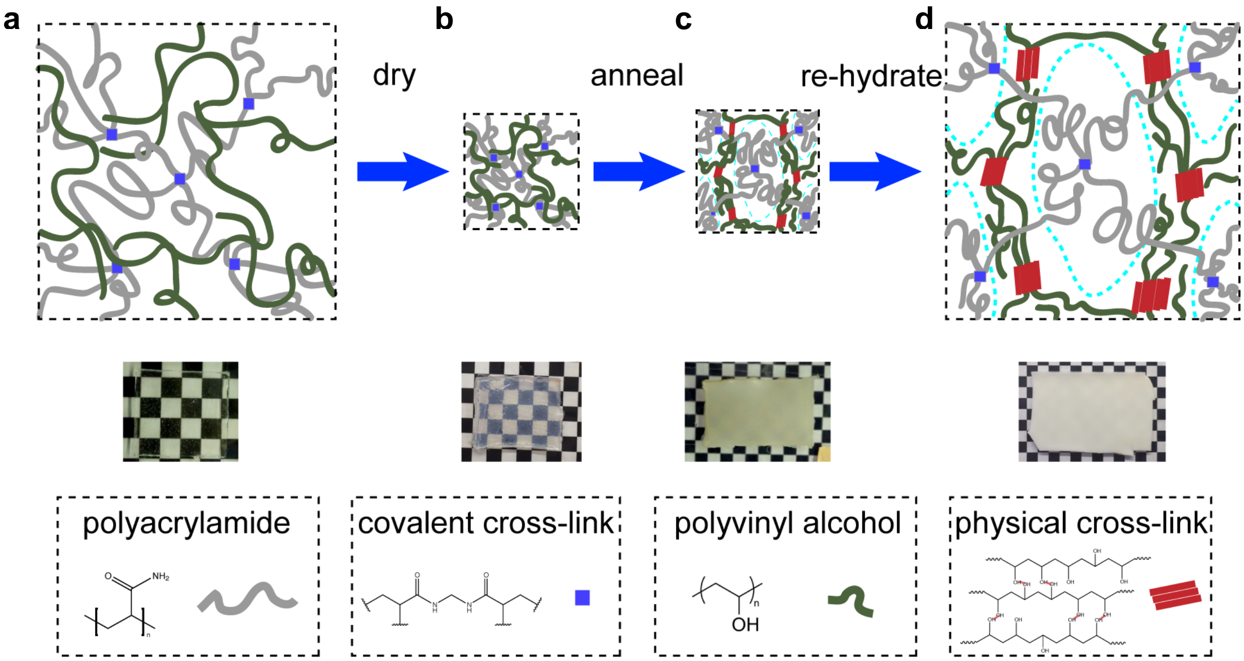

Figure 1. Synthesis and structure of the hybrid hydrogel. **a**, Acrylamide forms a covalently cross-linked network (PAAm, gray lines) with N,N'-methylenebisacrylate (MBAA, blue squares). The gel is dried at room temperature (**b**), and then annealed at elevated temperature **(c)**. Phase separation occurs (dashed cyan lines). Polyvinyl alcohol (PVA, green lines) forms a physically cross-linked network with crystallites (red blocks). **d**, On rehydration in distilled water, the crystallized PVA-PAAm gel forms a hydrogel. Optical photographs of the gels were placed beneath the corresponding schematics.

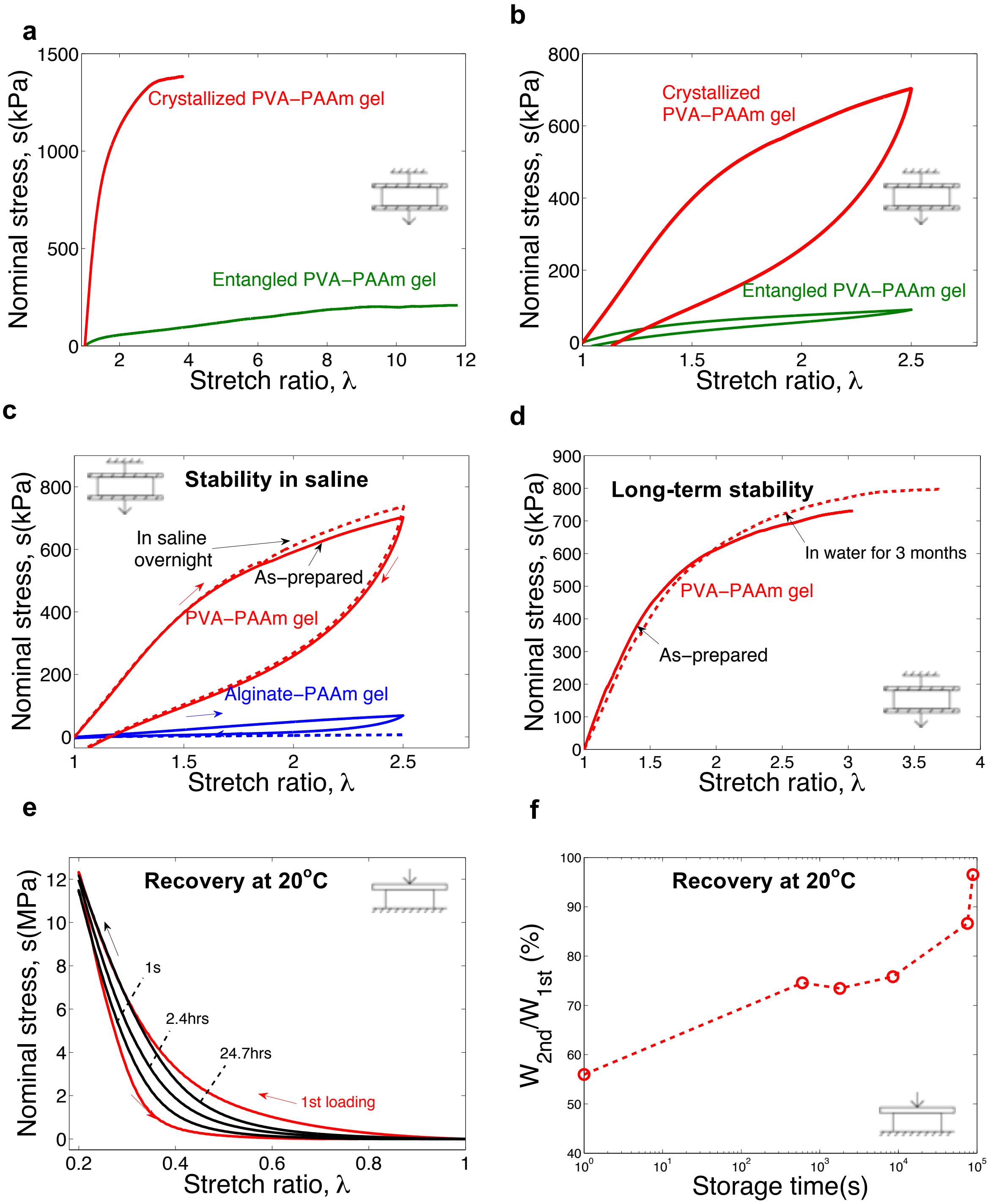

Figure 2. Crystallites as stable and recoverable cross-links. **a**, Stress-stretch curves of two types of gels. Each sample is stretched to rupture. The nominal stress is the applied force divided by the cross-sectional area of the undeform sample. The stretch ratio is the length of deformed sample divided by the initial length. **b**, Loading-unloading curves of both gels. Each sample is

stretched to a stretch ratio of 2.5. **c**, Effect of the saline solution. The loading-unloading curve of the gels stored in a saline solution (NaCl 9 gL^{-1}) overnight (dashed line) is compared with that of the as-prepared gels (solid line). **d**, Long-term stability of the gels in water. The gels are stored in distilled water for a long period (3 months). **e**, Recovery of samples stored at room temperature for different durations, as labeled. The samples are compressed to a stretch ratio of 0.2 (compressive strain 80%). **f**, Recovery ratio, i.e., work of the second loading, W_{2nd}, divided by that of the first loading, W_{1st}.

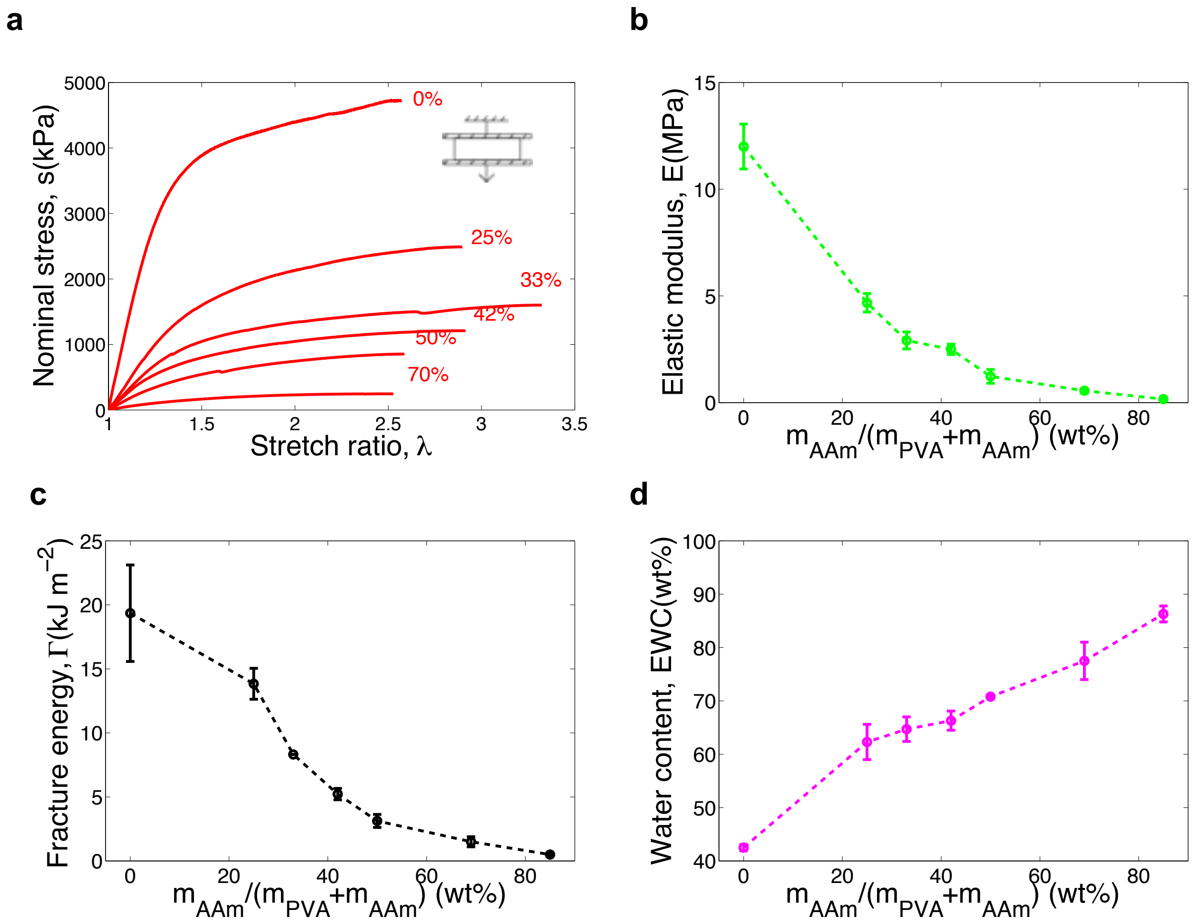

Figure 3. Composition greatly affects the properties of the hybrid gel. **a**, Stress-stretch curves of hybrid gels of various weight percentages of acrylamide to (acrylamide plus polyvinyl alcohol), as labeled. **b**, Elastic modulus, *E*, derived from the initial slope of the stress-stretch curves. **c**, Fracture energy, Γ, as a function of the acrylamide content. **d**, Water contents of the gels fully swollen in distilled water, *EWC*, plotted against the acrylamide content.

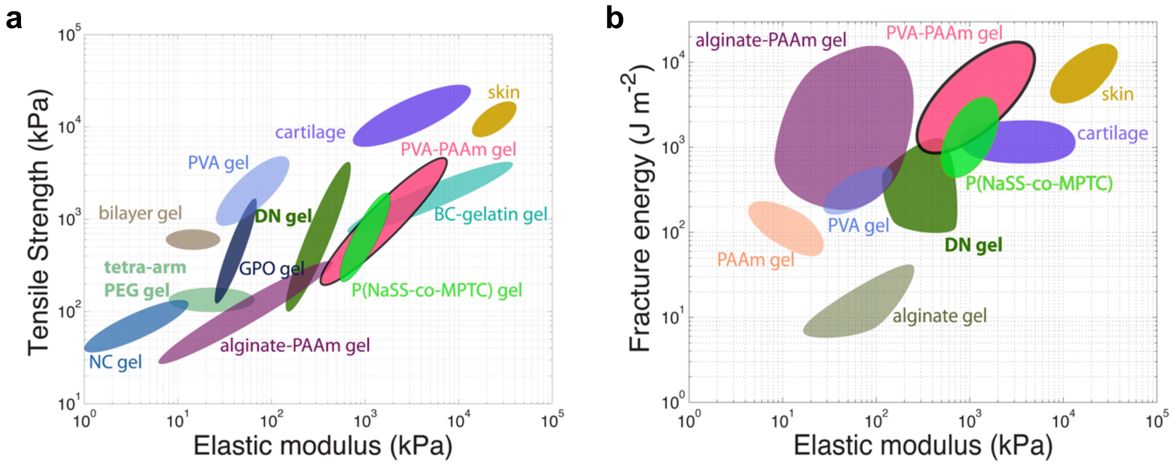

Figure 4. Material property charts for various soft materials. **a**, Tensile strength versus elastic modulus. **b**, Fracture energy versus elastic modulus. Materials include the gel prepared in this work (PVA-PAAm), polyvinyl alcohol gel (PVA),[15] double network gel (DN),[10] alginate-polyacrylamide gel,[1c] sodium p-styrenesulphonate-co-3-(methacryloylamino)propyl-trimethylammonium gel (NaSS-co-MPTC),[1b] polyacrylamide gel (PAAm),[1c] alginate gel,[1c] nano-composite gel (NC),[1d] tetra-arm polyethylene glycol gel (tetra-arm PEG),[1g] hydrophobic bilayer gel,[26] graphene peroxide gel (GPO),[27] bacterial cellulose-gelatin gel (BC-gelatin) along with cartilage and skin.[23, 28]