ACS Macro Letters

Letter

pubs.acs.org/macroletters

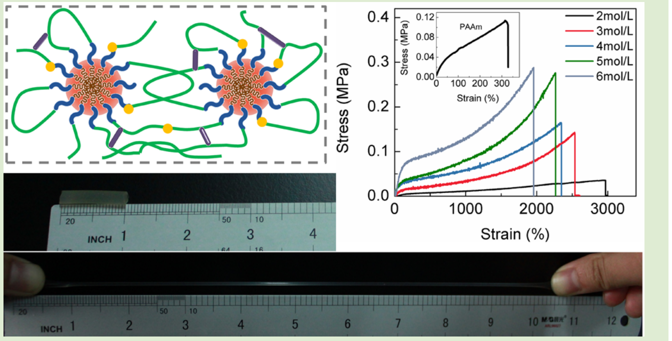
Super Tough, Ultrastretchable, and Thermoresponsive Hydrogels with Functionalized Triblock Copolymer Micelles as Macro-Cross-Linkers

Yuan-na Sun, Guo-rong Gao, Gao-lai Du, Ya-jun Cheng, and Jun Fu*

Polymers and Composites Division, Ningbo Institute of Materials Technology and Engineering, Chinese Academy of Sciences, 1219 Zhongguan West Road, Ningbo 315201, China

Supporting Information

ABSTRACT: Vinyl-functionalized thermosensitive Pluronic F127 micelles have been used as multifunctional cross-links for the synthesis of super tough, highly resilient and thermoresponsive nanomicelle (NM) hydrogels. Pluronic F127 diacrylate (F127DA) with vinyl groups on both ends self-assembled in aqueous solution into micelles. Such micelles served as multifunctional macro-cross-links to copolymerize with acrylamide (AAm) monomers, generating novel NM hydrogels with extraordinary tensile and compressive properties, without using any chemical cross-linkers. Uniaxial tensile tests demonstrated a fracture strain above 2265%, an ultimate stress of 276 kPa, and a fracture energy of 2.34 MJ/m^3. Under compression tests, these hydrogels did not fracture up to 98% strain and 62 MPa stress. Cyclic compressive loading−unloading tests at 90% strain showed no decay of the hyseteresis energy, indicating an unprecedented fatigue resistance.



Tough hydrogels capable of dissipating energy under cyclic loading have been widely pursued for potential applications to the replacement or engineering of load bearing tissues. Numerous strategies have been developed to introduce energy dissipation mechanisms in hydrogels aiming at improving the toughness and/or fatigue resistance.[1] Double network (DN) hydrogels utilized a sacrificial rigid network to dissipate energy through its fracture upon loading, showing a large hysteresis.[2] However, the permanent damage of the rigid network is irreversible and thus the gels are softened.[2] Based on the interpenetrating network concept, polymer microgels with strictly controlled size were used to cross-link and entangle soft PAAm chains, yielding highly resilient hydrogels with superior tensile properties.[3] Recently, tough and recoverable hydrogels based on polysaccharides including alginate[4] and agarose[5] have been reported. Another strategy utilizes dynamic physical interactions to create tough hydrogels. Multifunctional cross-linkers based on nanoparticles (e.g., silica,[6−8] clay,[9−11] graphene oxide,[12,13] or surfactant particles[14,15]) with chemical bonding or physical adsorption to polymer chains have been demonstrated effective in reinforcing polymer hydrogels. The sparsely dispersed cross-links, together with the extensive entanglements and physical interactions of the polymer chains are suggested to account for the high mechanical strength and/or resilience. Moreover, surfactant micelles based on hydrophobic associations[16] have offered additional energy dissipation of hydrogels, primarily due to the synergistic deformation of the micelles and the internal rearrangements of physical association.

$PEO_{99}-PPO_{65}-PEO_{99}$ (Pluronic F127) is a widely recognized amphiphilic triblock copolymer with excellent biocompatibility and thermoresponsiveness. The hydrophobic PPO block drives self-assembling of the copolymer chains into micelles in aqueous solution. The highly entangled assemblies of F127 at high concentration (e.g., 20 w/v%) have been used as physical network to host the cross-linking copolymerization of acrylic acid (AAc) and *N*,*N*′-methylenebis(acrylamide) (MBAA), yielding IPN hydrogels with pH- and thermosensitivity.[17] On the other hand, the strong adhesion of F127 chains to laponite platelets results in hydrogels with temperature-dependent sol−gel transitions[18] and improved mechanical strength and toughness.[19] Therein, the strong physical adsorption of polymer chains to laponite platelets imparts viscoelasticity to the originally weak hydrogels.

In this Letter, self-assembled F127 micelles with vinyl functional groups serve as multifunctional cross-linking centers for polymerization of acrylamide (AAm) monomers, yielding nanomicelle (NM) hydrogels with extraordinary tensile and compressive properties. Pluronic F127 chains were acrylated on both ends (Figure 1a). The resulted F127 diacrylate (F127DA) self-assembled in dionized water into nanomicelles with vinyl groups on surface (Figure 1a), which were copolymerized with AAm monomers chains to form a hydrogel with the micelles as

Received: April 11, 2014
Accepted: May 8, 2014
Published: May 9, 2014

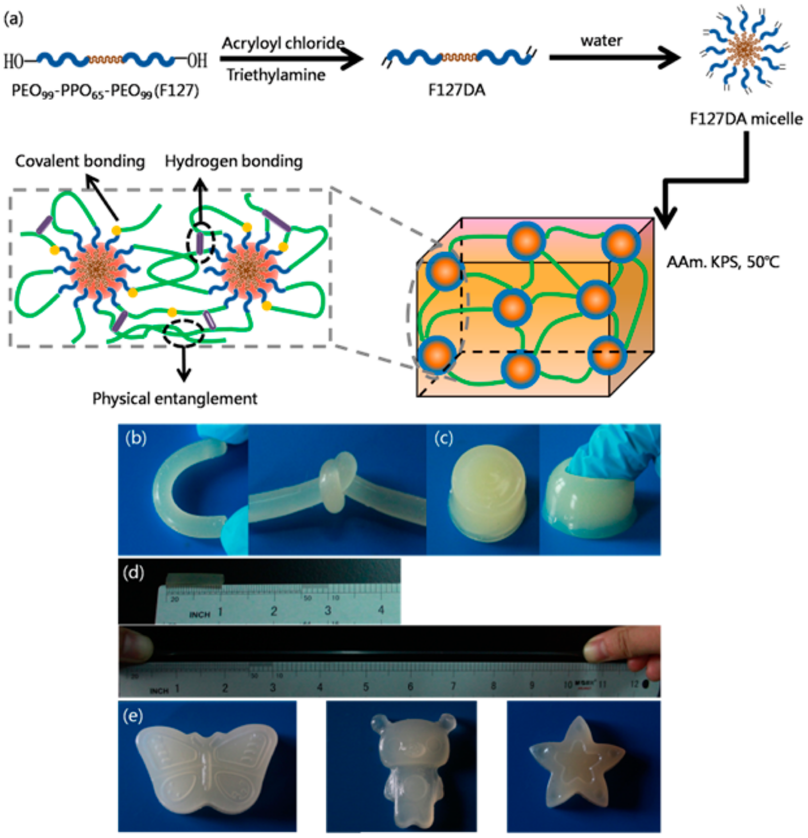


Figure 1. (a) Schematic illustration of the synthesis of $PEO_{99}-PPO_{65}-PEO_{99}$ diacrylate (F127DA) and the hydrogels with the micelles as macro-cross-linkers. (b−e) The hydrogels could withstand (b) bending, knotting, (c) compression, and (d) ultrastretching, and (e) could be synthesized in free-shaped molds with accurate replication of the details.

cross-linkers. No chemical cross-linking agents were used. The NM gels showed high tensile and compressive properties, and showed recoverability upon cyclic compressive tests without irreversible damage.

The F127 diacrylate (F127DA) was synthesized by acrylation of the end hydroxyl groups of F127 with acrylol chloride with the presence of triethylamine, as confirmed by ^{1}H NMR (Figure S1) and FTIR (Figure S2) data. The acrylation degree of F127DA was more than 90%. The acrylation of the end hydroxy groups did not change the solubility and hydrophilicity of the PEO blocks. The obtained F127DA chains self-assembled in aqueous solution in a manner identical to the F127 chains according to dynamic light scattering measurements (Table S1). These micelles were used as macro-cross-linkers for the radical polymerization of bubbled acrylamide monomers initiated by potassium persulfate at 50 °C for 12 h in a water bath, yielding hydrogels without using any small molecule cross-linkers. The concentrations of AAm (C_{AAm}) and F127DA (C_{F127DA}) were 5 mol/L and 6×10^{-3} mol/L, respectively, unless otherwise specified. For the PAAm hydrogel as a reference, the C_{AAm} and MBAA concentration (C_{MBAA}) were 5 mol/L and 6×10^{-3} mol/L, respectively.

Hydrogels with F127DA micelles as cross-linkers appeared soft, resilient, and tough. It could be bent, knotted, compressed, or stretched by more than 10 times and recover to its initial state after unloading (Figure 1d). This one-pot synthesis could take place in free-shaped molds, yielding hydrogels with accurate replication of the details (Figure 1e). The terminal vinyl groups are critical for the formation and properties of the hydrogels. Gelation did not occur when F127 replaced F127DA in parallel experiments.

The F127 copolymer is known for its lower critical solution temperature (LCST), above which the hydrophobic interactions of the PPO blocks increases. As the F127DA micelle solution (6×10^{-3} mol/L) was heated from room temperature (about 20 °C) to 55 °C, the hydrated micelle diameter decreased from about 320 to 180 nm according to DLS measurements (Figure S3). In order to probe the response of the NM hydrogels to temperature, dynamic mechanical tests were conducted by using a rheometer at 1 Hz and a deformation amplitude (γ_0) of 0.5% strain to ensure that the oscillatory deformation is within the linear regime (Figure 2a). As the hydrogel was heated from 25 to 50 °C, a transition was observed for G', G'', and tan δ from 30 to 38 °C (Figure 2b−d), which is consistent with the response temperature range for the F127 micelles.[20] In contrast, the chemically cross-linked PAAm gels showed no response to temperature change (Figure 2b−d). This thermoresponsive behavior indicates the viscoelasticity of these NM hydrogels, probably attributed to the physical association and the soft nature of F127DA micelle cross-linkers.

The mechanical tests were performed by using as-prepared samples. Compressive tests of these NM gels at a crosshead speed of 10% strain per min showed extraordinary strength and toughness. The hydrogels did not fracture at 98% compressive strain ($\varepsilon_c = 0.98$; Figure 3a) and recovered to the initial shape immediately upon unloading. As the C_{AAm} was increased from 2 to 6 mol/L, the compressive stress at 98% strain ($\sigma_{c,0.98}$) was increased from 28 to 75.5 MPa, the compressive Young's

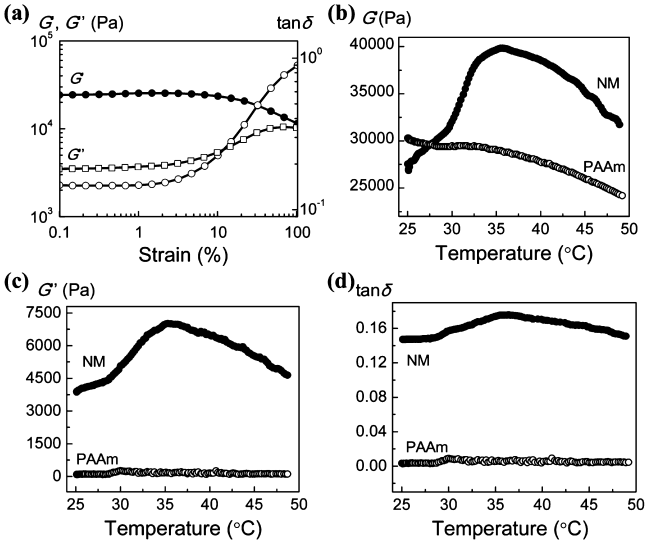


Figure 2. Evolution of G' and G'' and tan δ of the nanomicelle and PAAm hydrogels during heating from 25 to 50 °C with a frequency ω = 1 Hz, and a deformation amplitude γ_0 = 0.005.

modulus was increased from about 50 to 260 kPa (Figure 3b), and the deformation toughness, as defined by the area under the compressive stress−strain curve, was increased from about 0.6 to 2.34 MJ/m^3 (Figure 3c). The increased modulus, strength and toughness indicate the formation of dense networks, which is confirmed by the lower swelling ratio with higher C_{AAm} (Figure S4a). With a higher C_{AAm}, the PAAm chains were also longer as the C_{F127DA} was constant, which may establish more entanglements and thus a dense and strong network.

Consecutive cyclic compressive loading−unloading tests on the NM gels without waiting with 90% strain (ε_c = 0.90) resulted in completely overlapping hysteresis loops (Figure 3d). In contrast, the loading−unloading loops of the PAAm hydrogel decayed rapidly and fractured upon the fourth loading (Figure 3d). Figure 3e further plots the variation of the compressive stress over time upon cyclic loading−unloading tests, which demonstrates the immediate recovery of the NM gels after unloading with negligible decay for four consecutive loadings. These results indicate an excellent fatigue resistance of these NM hydrogels.

It is noted that the PAAm hydrogels cross-linked with MBAA showed higher modulus and stress at 90% strain than NM gels in the first run, although the C_{F127DA} and C_{MBAA} were the same (6×10^{-3} mol/L). This could be attributed to the denser network of PAAm hydrogels, as indicated by the lower swelling ratio than the NM gel (Figure S4b). However, the covalent PAAm network is prone to fracture upon cyclic loadings, leading to rapid decreases in the stress and fracture (Figure 3d,e).

These hydrogels are ultrastretchable upon uniaxial tensile tests at a crosshead speed of 80 mm min^{-1}. The NM gel with 2 mol/L AAm concentration showed a tensile fracture strain of about 3000% (Figure 4a), in comparison to the 319% fracture strain of the PAAm hydrogel (Figure 4a, inset). With the increasing C_{AAm}, the fracture strain gradually decreased to about 2000%, while the fracture stress was increased to 276 kPa (Figure 4b). With a relatively low C_{AAm}, the ultrastrechability may root from the sparse entanglements of the PAAm chains. The gels are relatively weak. As mentioned previously, the increased C_{AAm} may result in increases in the chain length and entanglements. More energies are needed to deform and fracture the NM gels. The fracture energy showed a linear dependence on the C_{AAm} (Figure 4b).

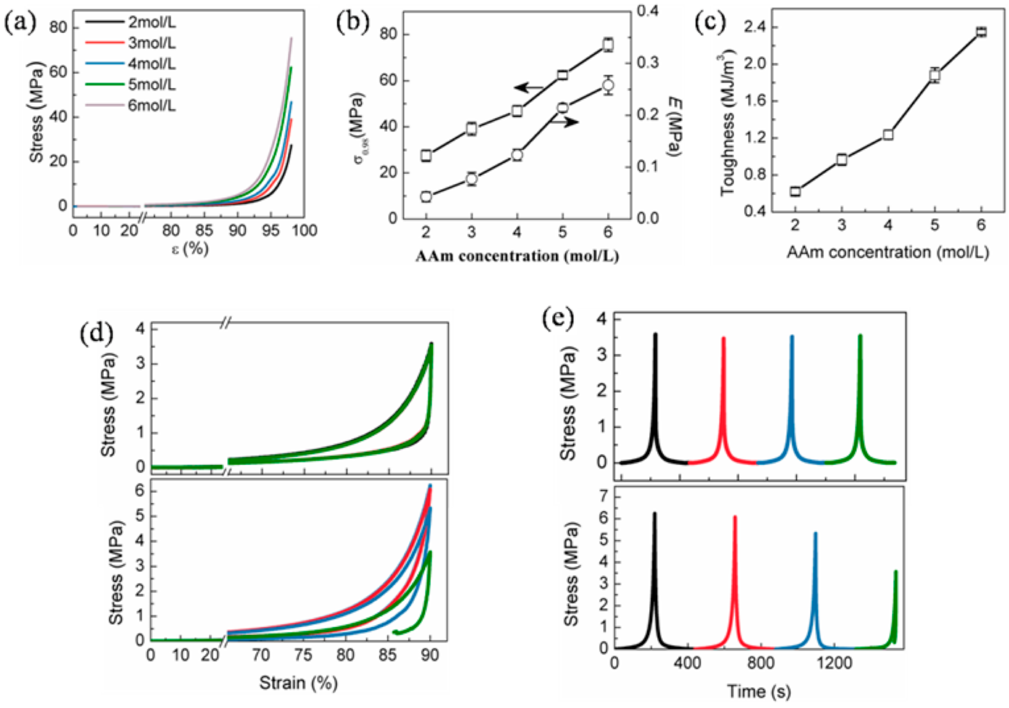


Figure 3. (a) Compressive stress−strain curves of the nanomicelle hydrogels with different AAm concentrations (C_{AAm}). The dependence of (b) the stress at 98% strain and Young's modulus and (c) compressive toughness on C_{AAm}. (d) Cyclic compressive stress−stain and (e) stress−time curves at 90% strain.

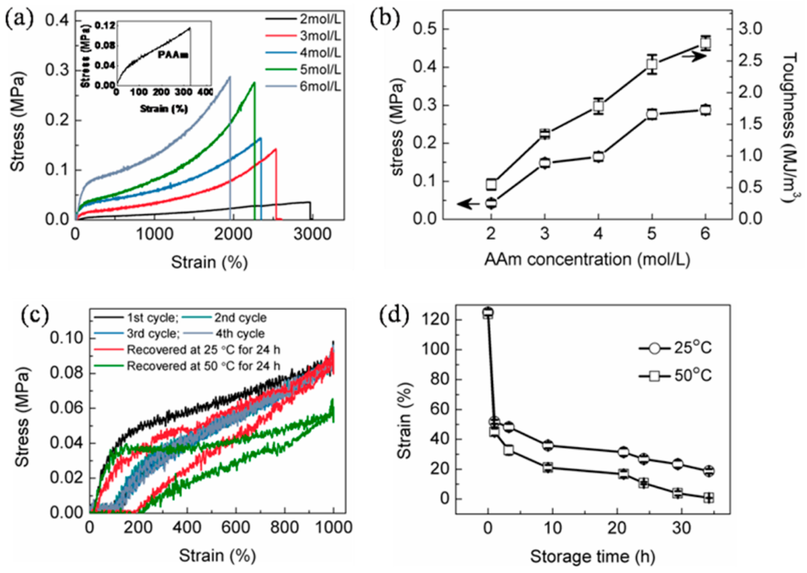


Figure 4. (a) Tensile stress−strain curves of hydrogels with different C_{AAm} values, (b) the dependence of tensile stress and fracture toughness on C_{AAm}, and (c) cyclic tensile curves of a NM hydrogel at 1000% strain for four cycles and after subsequent recovery at 25 and 50 °C for 24 h. (d) The decay of residual strain of tensile tested samples over time at different temperatures.

Cyclic tensile loading−unloading tests at a crosshead speed of 80 mm min^{-1} were conducted to reveal the energy dissipation mechanism of these NM hydrogels. The first loading−unloading cycle exhibited a hysteresis, which became negligible for the following runs (Figure 4c). This hysteresis loop suggests an energy dissipation during uniaxial stretching, presumably due to the deformation and dislocation of the F127DA micelles under stress. Residual strain was observed after unloading. This 120% residual strain could spontaneously but partly recover at 25 °C for about 30 h, leaving an unrecoverable residual strain of about 20% (Figure 4d). At an elevated temperature (e.g., 50 °C), the recovery was accelerated to eliminate the residual strain (Figure 4d).

Subsequent tensile tests were conducted to examine the recovery extent of the cross-linked structures. After recovery at 25 °C, the hydrogels showed a lower modulus than the as-prepared sample during loading to 1000% strain (Figure 4c). Subsequent unloading curve was below those for the as-prepared gel, with a residual strain of 180%. In contrast, the treatment at 50 °C led to a complete shape recovery, but the recovered hydrogel exhibited a typical yielding behavior with lower modulus and weak strain hardening, leaving a residual strain of 200% upon susbequent loading−unloading tests (Figure 4c). These results indicate that the nanomicelle cross-linkers may dislocate upon ultrastretching without decomposition, accompanied by slippage of PAAm chains. The ultrastretching may reduce chain entanglements, which could not be re-established at room temperature, leading to a reduction in modulus. At elevated temperatures, the polymer relaxation is accelerated, leading to full recovery of the strain. However, the micelle size decreased at elevated temperatures, which may cause irreversible changes in the hydrogel structures. As a result, the strength and modulus of the NM gels were reduced.

These nanomicelle cross-linked hydrogels behaved differently from the chemically cross-linked hydrogels and the nanocomposite hydrogels based on physical adsorption[19] or covalent bonding[7] of polymer chains onto inorganic nanoparticles. The soft assemblies of F127DA chains may allow for chain slippage and disentanglements under loading so as to exhibit ultrastretchability. Thus, the cleavage of covalent chains is avoided. As a result, the ultrastretched chains and network could recover upon unloading, leaving small residual strain (Figure 4c) with respect to the ultrahigh strain. Such residual strain is recoverable at low temperatures. On the other hand, the micelle-cross-linked polymer network withstands high compressions and recovers to the original dimension without losing its toughness upon cyclic loadings. The complete overlapping of the loading−unloading curves (Figure 3d) indicates an unprecedented fatigue resistance. It is reasonable that the neither the network or the micelle macro-cross-linkers have been damaged. The hysteresis energy dissipation may root from the deformation and relative motion of the F127DA micelles linked by PAAm chains.

In summary, novel super tough, ultrastretchable, and thermoresponsive hydrogels have been successfully synthesized by using Pluronic F127 diacrylate micelles as macro-cross-linkers. The thermoresponsiveness of the F127 micelles imparts viscoelasticity of these nanomicelle hydrogels with a transition from 30 to 38 °C. The hydrogels showed extraordinary compressive toughness and fatigue resistance against cyclic loadings. Moreover, these hydrogels could be stretched up to 3000%, or a fracture energy up to 2.34 MJ/m^3. The ultrahigh strains could be recovered with low residual strains upon unloading. The flexible dislocation of the macro-cross-linkers along with the chain slippage may account for the ultrastretchability and toughness of these NM hydrogels.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Materials, synthesis of Pluronic F127 diacrylate (F127DA), PAAm gels, NM gels, characterization for ^1H NMR spectra, FTIR, DLS analysis, rheological experiments, swelling tests, compression and cyclic compression tests of hydrogels, and tensile and cyclic tensile tests of hydrogels. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: fujun@nimte.ac.cn.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was funded by the Natural Science Foundation of China (51103172, 212101064), the Hundred Talents Program of the Chinese Academy of Sciences (J.F.), the Zhejiang Natural Science Foundation of China (LR13B040001), the Zhejiang Nonprofit Technology Applied Research Program (2013C33190), and the Program for Ningbo Innovative Research Team (2012B82019).

REFERENCES

(1) Zhao, X. *Soft Matter* **2014**, *10* (5), 672−687.

(2) Gong, J. P. *Soft Matter* **2010**, *6* (12), 2583−2590.

(3) Hu, J.; Hiwatashi, K.; Kurokawa, T.; Liang, S. M.; Wu, Z. L.; Gong, J. P. *Macromolecules* **2011**, *44* (19), 7775−7781.

(4) Sun, J.-Y.; Zhao, X.; Illeperuma, W. R. K.; Chaudhuri, O.; Oh, K. H.; Mooney, D. J.; Vlassak, J. J.; Suo, Z. *Nature* **2012**, *489* (7414), 133−136.

(5) Chen, Q.; Zhu, L.; Zhao, C.; Wang, Q.; Zheng, J. *Adv. Mater.* **2013**, *25* (30), 4171−6.

(6) Carlsson, L.; Rose, S.; Hourdet, D.; Marcellan, A. *Soft Matter* **2010**, *6* (15), 3619−3631.

(7) Wang, Q.; Hou, R. X.; Cheng, Y. J.; Fu, J. *Soft Matter* **2012**, *8* (22), 6048−6056.

(8) Yang, J.; Wang, X.-P.; Xie, X.-M. *Soft Matter* **2012**, *8* (4), 1058−1063.

(9) Haraguchi, K.; Takehisa, T. *Adv. Mater.* **2002**, *14* (16), 1120−1124.

(10) Zhu, M.; Liu, Y.; Sun, B.; Zhang, W.; Liu, X.; Yu, H.; Zhang, Y.; Kuckling, D.; Adler, H.-J. P. *Macromol. Rapid Commun.* **2006**, *27* (13), 1023−1028.

(11) Miyazaki, S.; Endo, H.; Karino, T.; Haraguchi, K.; Shibayama, M. *Macromolecules* **2007**, *40* (12), 4287−4295.

(12) Liu, R.; Liang, S.; Tang, X.-Z.; Yan, D.; Li, X.; Yu, Z.-Z. *J. Mater. Chem.* **2012**, *22* (28), 14160−14167.

(13) Liu, J.; Chen, C.; He, C.; Zhao, J.; Yang, X.; Wang, H. *ACS Nano* **2012**, *6* (9), 8194−8202.

(14) Huang, T.; Xu, H. G.; Jiao, K. X.; Zhu, L. P.; Brown, H. R.; Wang, H. L. *Adv. Mater.* **2007**, *19* (12), 1622−1626.

(15) He, C.; Jiao, K.; Zhang, X.; Xiang, M.; Li, Z.; Wang, H. *Soft Matter* **2011**, *7*, 2943−2952.

(16) Tuncaboylu, D. C.; Sari, M.; Oppermann, W.; Okay, O. *Macromolecules* **2011**, *44* (12), 4997−5005.

(17) Baskan, T.; Tuncaboylu, D. C.; Okay, O. *Polymer* **2013**, *54* (12), 2979−2987.

(18) Sun, K.; Raghavan, S. R. *Langmuir* **2010**, *26* (11), 8015−8020.

(19) Wu, C.-J.; Gaharwar, A. K.; Chan, B. K.; Schmidt, G. *Macromolecules* **2011**, *44* (20), 8215−8224.

(20) Wanka, G.; Hoffmann, H.; Ulbricht, W. *Macromolecules* **1994**, *27* (15), 4145−4159.