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*Research Article*

# Tuning Mechanical Properties of Polymeric Hydrogels Using Orthogonally Functionalized Crosslinkers

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A unique orthogonal crosslinker-induced hydrogel, whose mechanical strength can be tunable by the crosslinker topology upon thermal treatment, is described herein. The crosslinker containing cationic moieties and crosslinkable styrenyl groups was employed for the preparation of orthogonally crosslinked hydrogels having ionic and covalent characteristics. The manipulation of the orthogonal crosslinkers topology and the ionic bond strength between cationic and anionic moieties facilitated the control of the mechanical properties. Short-term temporal modulation of hydrogel moduli, a key factor of the substrates for cell development, was demonstrated and could provide dynamic microenvironment for biological process. In addition, on-demand control of the elastic properties of the hydrogels by application of a thermal stimulus provides new avenues to regulate cell growth. Furthermore, the orthogonality of the crosslinkers allowed molecular functionalization of a wide range of molecules of interest to the hydrogels by thiol-ene Michael addition (nucleophilic addition of sulfhydryl and carbon-carbon double bonds) in a friendly manner as demonstrated in our work.

## 1. Introduction

The development of functionalized synthetic hydrogels draws great interest for the applications in drug delivery and tissue engineering [1–4]. The applications of the hydrogels require mechanical tunability, and more significantly, the ability to introduce chemically active moieties for molecular functionalization. In particular, mechanically tunable hydrogels have attracted significant attention due to their control on cell growth behavior in culture media. In previous work, ionic crosslinked mechanically tunable hydrogels were prepared through polyampholyte and polyion complexes of oppositely charged electrolytes with double network feature [5, 6]. Trivalent iron ($Fe^{3+}$) coordination with carboxylic moieties ($COO^-$) along poly(acrylic acid) generated switchable hydrogels upon light irradiation [7]. Ionically and covalently crosslinked alginate and poly(acrylamide) produced highly stretchable and tough hydrogels by mixing two types of crosslinked polymers [8, 9]. The ionic bonds provided high stretch through zipping and unzipping reversible crosslinks while covalent crosslinks bridged the cracks upon stretching. Unfortunately, traditional strategies of hydrogel preparation cannot achieve the transformation from ionic form to covalent crosslinks containing hydrogels in one-pot synthesis. In addition, routine double network gels had network heterogeneities and crosslinking clusters such as PAMPS/PAAm hydrogel, ultimately reducing the mechanical strength [10, 11]. In most cases, mechanical strength of the hydrogels was controlled by polymer and crosslinker concentration. The challenges necessitate expanding current synthetic approaches that can transform soft hydrogels to mechanically robust hydrated network upon external stimuli.

In the category of cell-compatible hydrogels, a variety of techniques have been implemented to facilitate such material preparation. Bioorthogonal chemistry, which specifically proceeds for a given region in physiological conditions, has been adapted to generate cell-benign hydrogels for detecting

and probing biological functions. DeForest and Anseth created cytocompatible clickable hydrogels through spatially and temporally controlled crosslinks and pendant modification from click-functionalized macromolecular precursors [12]. Truong and coworkers designed double network hydrogels via simultaneously orthogonal reactions of nucleophilic thiol-yne and Diels-Alder additions for cell encapsulation [13]. Furthermore, azide-akyne click cycloaddition and Michael-thiol addition were employed to fabricate copolymer hydrogel with photopatternability containing orthogonally functionalizable chemical building blocks accessible for secondary reaction [14]. However, the preparation of bioactive hydrogels requires multiple-step synthesis of clickable strain promoted azide and cycloalkyne motifs. As demonstrated in previous work, mesenchymal stem cells can sense hydrogel mechanical properties and transduce the signals from the substrates to lineage specification [15]. Furthermore, the engineered elasticity of the hydrogels was capable of preferentially directing specific human cell growth [16–20]. In addition, the resulting hydrogels are not subject to delicate manipulation of elasticity for cell growth. There is a need to develop mechanically programmable hydrogels with orthogonal functionalization.

Inspired by bioorthogonal chemistry for bioactive hydrogel synthesis and inorganic crosslinkers for ionic hydrogel preparation, we sought to harness orthogonally organic crosslinkers to prepare mechanically transformable hydrogels based on its unique structures containing ionic crosslinks and crosslinkable covalent motifs. These hydrogels offer a myriad of advantages of mechanical manipulation and quantitative incorporation of bioactive moieties by directly chemical handles of crosslinkers. The new organic crosslinker design is a route to produce double crosslinked polymeric network. The hydrogels are easy in handling during preparation compared to traditional double network hydrogels. In addition, the hydrogel is mechanically manipulatable from ionically crosslinked hydrogels to polymeric network having ionic and covalent features.

Herein, we demonstrated how the mechanical properties of the synthesized hydrogels are tuned through our orthogonally organic crosslinker approach. The presence of cationic moieties and crosslinkable double bonds in the crosslinkers enables us to prepare ionic hydrogels and thus convert them to double network hydrogels upon external triggers. Temporal modulation of hydrogel moduli was demonstrated and could provide dynamic microenvironments for biological process. The orthogonal crosslinkers provide the chemical handles for functionalization by exploiting the pendant double bonds. This design allows the construction of mechanically tunable hydrogels and direct incorporation of bioactive molecules.

## 2. Experimental

### 2.1. Materials.
All chemicals and reagents were purchased from Sigma-Aldrich (St. Louis, MO) except as noted. 2-Acrylamido-2-methylpropanesulfonic acid (AMPS), acrylic acid (AA), sodium styrene sulfonate (Na-SS), sodium hydroxide, anhydrous ethanol (99.5%), methanol (99%), 2-

mercaptoethanol (BME), hexane, vinylbenzyl chloride (VBC) (90%) N,N,N′,N′-tetramethylethylenediamine (TEMED), N,N,N′,N′-tetramethyl-1,6-hexanediamine (TMHDA), N,N,N′,N″,N″-pentamethyldiethylenetriamine (PMDETA), Leuco Crystal Violet (LCV), and 2,2′-azobis(2-methylpropionamidine) dihydrochloride (V50) were used as received.

### 2.2. Analyses.
$^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectroscopy was performed on Varian INOVA 400 FT-NMR using DMSO-d6 as solvent and the residue peak at 2.50 ppm as an internal reference.

### 2.3. Rheological Studies.
The rheological properties of hydrogels were measured using a HAAKE MARS III rheometer (Thermo Scientific Inc.). The disc-shaped samples in ~1 mL were subject to rheological measurements at 25°C using parallel-plate geometry (P35 Ti L) with a gap of 0.5 mm. Oscillatory frequency sweep was performed from 0.1 to 100 rad s$^{-1}$ with a shear strain of 1% in the linear strain range. Oscillation time-dependent experiments were performed at a fixed frequency of 1 Hz and controlled stress of 10.0 Pa to obtain storage modulus of $G'$ and loss modulus of $G''$ as a function of time.

### 2.4. Synthesis of Orthogonally Crosslinked Na-AMPS Hydrogels.
All hydrogels were carried out in a similar fashion in glass vials. A typical polymerization is as follows: a stirring mixture of Na-AMPS (1.15 g, 5 mmol) and V50 (2.7 mg, 0.312 mmol) was bubbled with argon for 30 min and immersed in a preheated oil bath of 50°C until the solution reached high viscosity. The reaction solution was cooled to room temperature and diluted with DI water (1 mL). The prepared suspension solution of TMVBC (0.15 g, 0.36 mmol) and Na-AMPS (0.16 g, 0.72 mmol) in ethanol (1 mL) was dropwise added to the diluted solution under vigorous stirring. Thus, the ionic crosslinked hydrogel was formed. The mixture was cured in oven at 80°C for 12 h to produce orthogonally crosslinked hydrogel.

### 2.5. Directly TMVBC Crosslinked Sample Preparation.
A stirring mixture of Na-AMPS (1.15 g, 5 mmol), TMVBC (0.15 g, 0.36 mmol), and V50 (2.7 mg, 0.312 mmol) was bubbled with argon for 30 min and cured in oven at 80°C for 12 h to produce the hydrogel.

## 3. Results and Discussion

The general synthetic procedure of the mechanically tunable hydrogels involved the preparation of anionic linear polymers followed by addition of orthogonal crosslinkers as illustrated in Scheme 1. The anionic linear polymers were readily obtained by conventional radical polymerization of anionic monomers in the presence of water soluble initiator of 2,2′-azobis(2-methylpropionamidine) dihydrochloride (V50). The orthogonal crosslinkers containing polymerizable styrenyl groups and cationic moieties enabled the sequential preparation of ionically and covalently crosslinked hydrogels under thermal or UV conditions. One
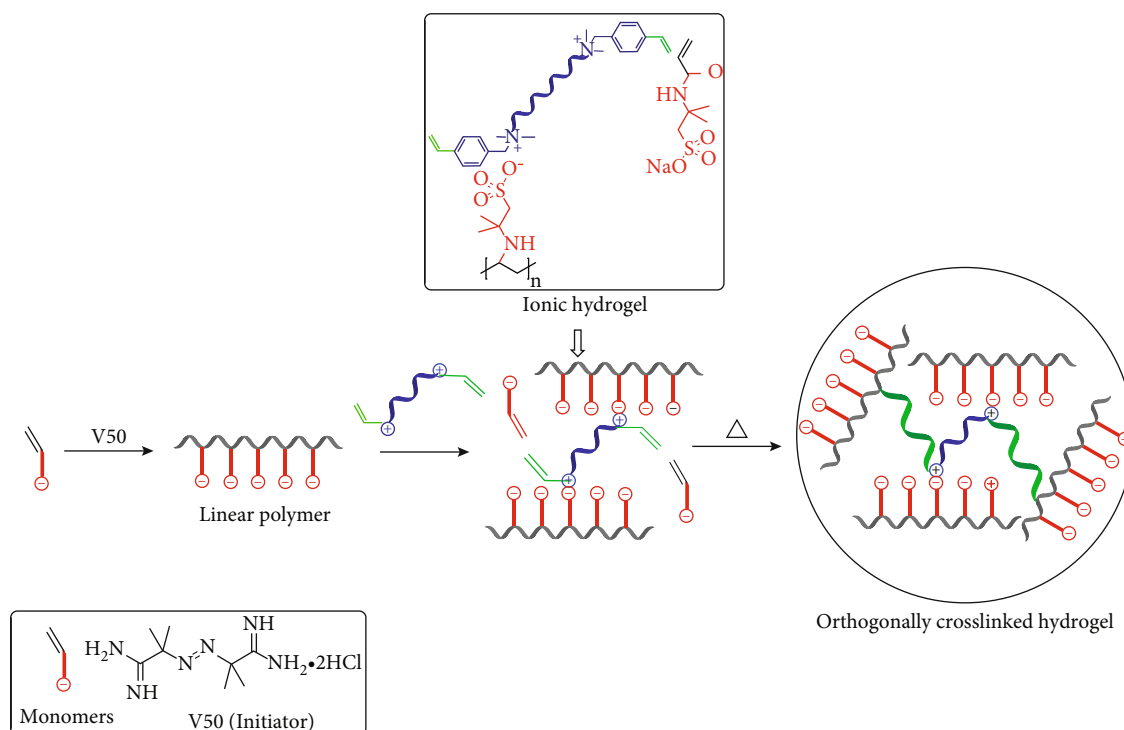
SCHEME 1: Synthetic scheme of orthogonal crosslinkers bearing ionic moieties and styrenyl groups based heating induced hydrogels.

benefit of this approach is that the prepared hydrogels were mechanically tunable by adjusting the topology of the crosslinkers. In addition, the mechanical integrity of our hydrogels was monomer-directed by adjusting the ionic strength between cationic moieties tethered to orthogonal crosslinkers and anionic motifs in the anionic polymers.
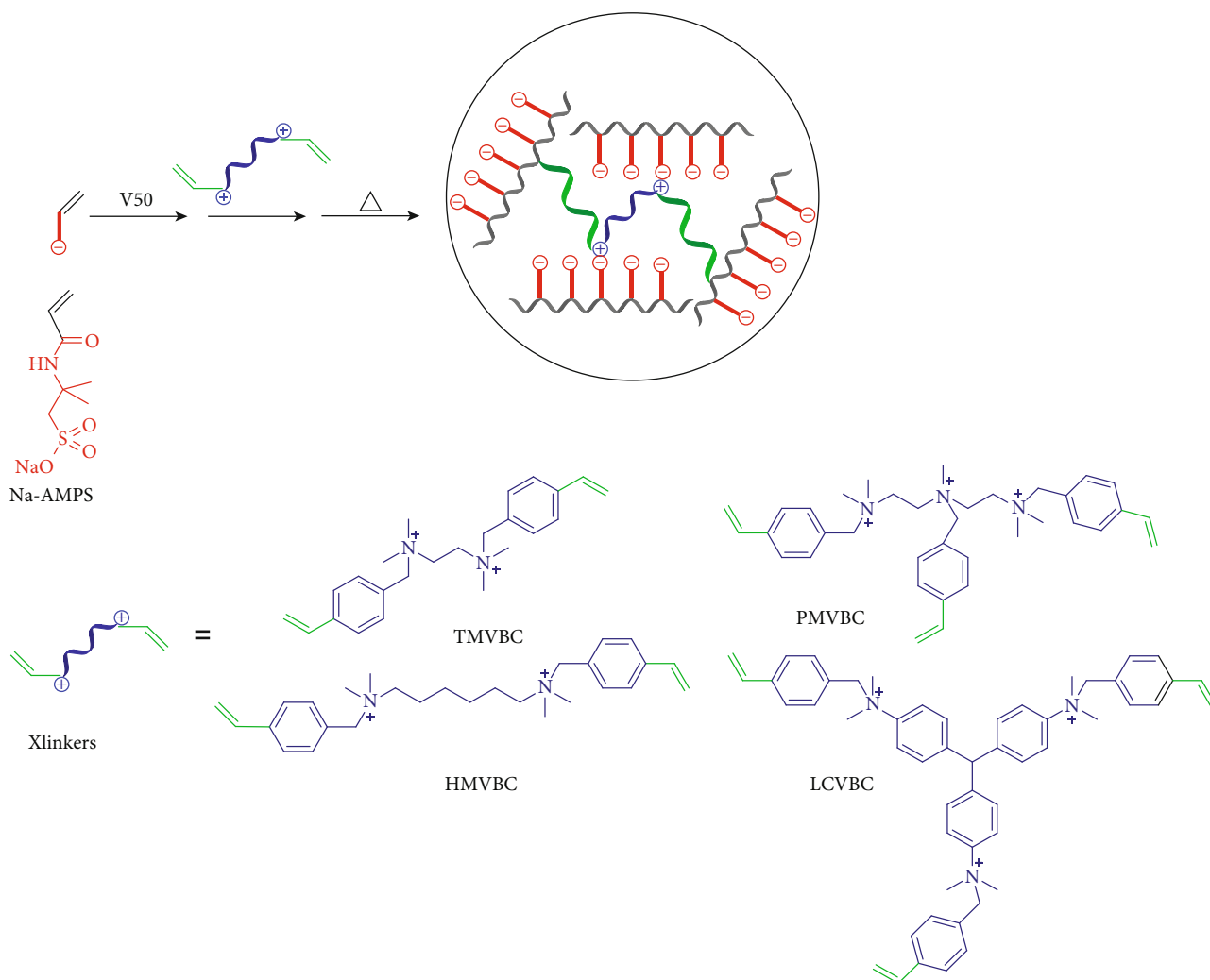
The selection of orthogonal crosslinkers ensured the successful implementation of physically and chemically crosslinked hydrogel synthesis. Tertiary amines with multiple functionalizable moieties were applied to our hydrogel synthesis since the reaction of styrenyl halide with tertiary amines would generate heterofunctional crosslinkers, which can be used to synthesize orthogonal hydrogels. Thiol-ene Michael addition chemistry can be employed to construct a wide range of molecules of interest containing hydrogels under environmentally benign conditions [21]. Direct introduction of thiol-containing molecules of interest by thiolene chemistry to the crosslinkers having styrenyl and acrylate moieties allowed the functionalization of the hydrogels at the molecular level. These approaches provided a wide range of straight modification having different functionalities inside the hydrogels (vide infra) through thiol-ene functionalizable chemistry on orthogonal crosslinkers.

To demonstrate our concept of mechanically tunable hydrogel preparation by orthogonal crosslinkers, orthogonal crosslinkers bearing cationic moieties and polymerizable styrenyl groups were designed and prepared from commercially available starting synthons as shown in Scheme 2. Reaction of vinylbenzyl chloride (VBC) with tertiary amines in methanol gave a family of water soluble vinylbenzyl chloride quarternary ammonium salt as white solids in excellent yield as evidenced by $^1$H and $^{13}$C NMR spectra (Figure S1,

supporting information). The product was readily purified by precipitation from hexane and suitable for our hydrogel synthesis. The topology manipulation of orthogonal crosslinkers would govern the mechanical integrity of the polymeric hydrogels.

On the basis of the previous results, polyion complexes formed soft stretchable to highly tough hydrogels by tuning the bonding strength of ionic linear polymers and counter ionic monomers [22]. The ionic bonds acting as the energy dissipation along with covalent network generated highly tough hydrogels. Given the chemical structure of our orthogonal crosslinkers, we can envision that the quarternary ammonium cation can be applied as the ionically physical crosslinker for soft hydrogel preparation while the styrenyl moieties can be utilized as the chemically covalent crosslinker under thermal treatment. In this fashion, mechanically manipulatable polymeric hydrogels governed by orthogonal crosslinkers could be obtained via temperature induced crosslinking from the orthogonally functionalized crosslinkers. These Na-AMPS anionic monomer-based hydrogels in this work were accessed to examine the feasibility of our concept using orthogonal crosslinker of TMVBC as the ionic and covalent crosslinks.

The time sweep profiles of storage moduli $G'$ and loss moduli $G''$ were showed in Figure 1. We found that direct addition of TMVBC crosslinker to the polymerized Na-APMS aqueous solution led to heterogeneous precipitation due to the fast formation of strong intramolecular ionic crosslinking between cationic moieties in crosslinker and anionic groups in PAMPS polymer (sample 1). The precipitation is akin to the production of the inhomogeneous poly(-acrylic acid) (PAA) hydrogels though the addition of

Scheme 2: Mechanical manipulation of the hydrogels by topology changes of the orthogonal crosslinkers.

trivalent cations ($Fe^{3+}$) to PAA aqueous solution [7]. The formation of the heterogeneous PAA hydrogels were due to the fast reaction rate of ferric ions $Fe^{3+}$ with carboxyl groups (-COO⁻). However, the introduction of citric acid chelated ferric ions to PAA solution generated the transparent hydrogels because the ferric ions were gradually released from the citric acid and ferric complexes. In a similar manner, in our study, the introduction of the prepared TMVBC and Na-AMPS suspension complexes to PAMPS aqueous solution generated homogeneously transparent soft ionic hydrogels via cationic orthogonal crosslinker TMVBC (see Figure S2 for LCVBC crosslinker-based gels, and the synthetic parameters was described in Table S1). Followed by vigorous mixing of the crosslinker and anionic polymer, treatment of physically crosslinked hydrogels in oven at 80°C produced mechanically enhanced chemically crosslinked opaque hydrogel from the styrenyl moieties (PH-CH=CH₂), which are crosslinkable under thermal conditions [23, 24]. The physical color change from transparency and opaqueness is due to the hydrophobic phase separation from hydrophilic Na-AMPS matrix. This phenomenon is similar to the hydrophobic moieties

containing hydrogels [25]. The mechanical strength of the transformable hydrogels was tuned by TMVBC crosslinker concentration in the hydrogels after ionic crosslinking. For example, sample 2 with 7 mol% crosslinker was semisoft upon vial inversion while hydrogel 3 having 14 mol% TMVBC was mechanically robust as indicated in Figure 1. The increase in crosslinker concentration during hydrogel synthesis significantly enhanced the mechanical integrity, which is consistent with previous study [26]. Increased crosslinking density evidently contributed to the mechanically reinforced hydrogels.

We posit that thermally induced covalent crosslinking approach would significantly increase the mechanical strength of the thermally sensitive ionic crosslinked hydrogels. As demonstrated in Figure 1, the ionic crosslinked hydrogel was quite flexible and soft while thermally enhanced chemically crosslinked hydrogel was rather strong and did not flow upon vial inversion. The storage moduli, $G'$ and loss moduli, $G''$, were measured as a function of time at a fixed frequency of 1 Hz. The storage modulus of covalently crosslinked sample 2 (53 Pa) is approximately one order of magnitude higher than that of ionic crosslinked hydrogel
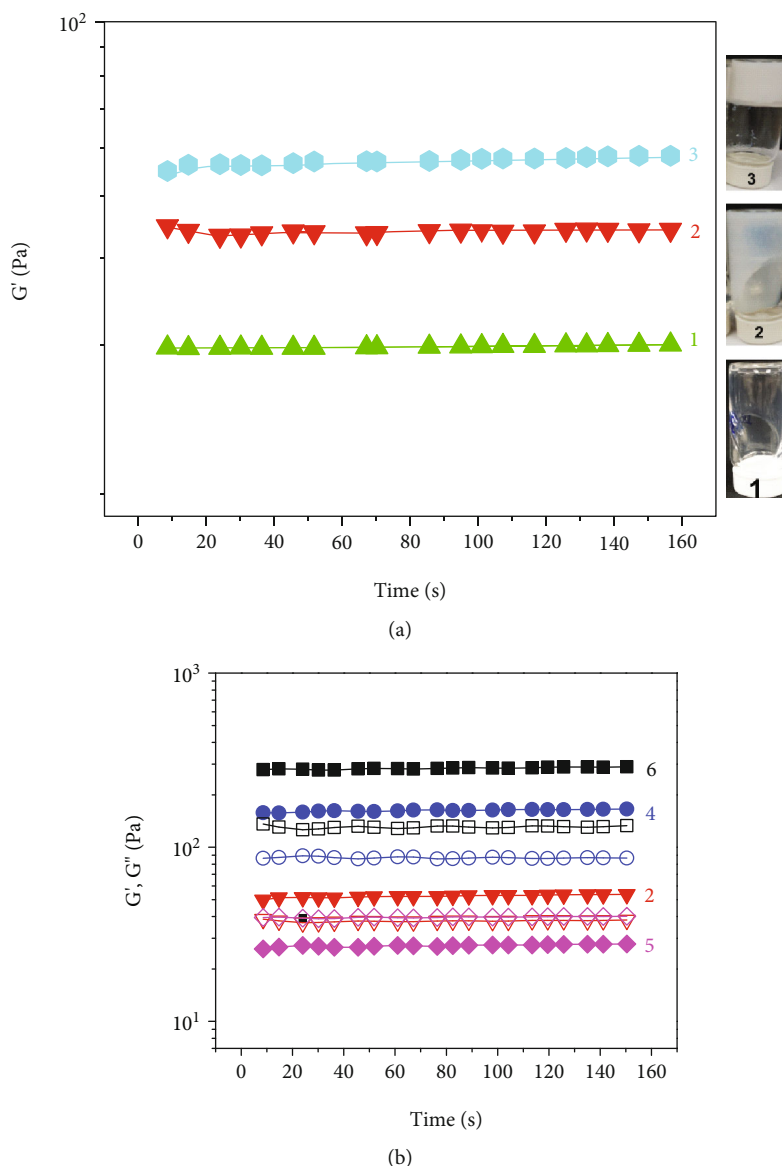
(a)



(b)

FIGURE 1: Time sweep profiles of storage moduli $G'$ (filled symbols) and loss moduli $G''$ (open symbols) of hydrogels based on different crosslinkers at 25°C under sweep frequency of 1 Hz. (a) TMVBC crosslinker-based hydrogels: 1: directly crosslinked hydrogel and 2, 3: double crosslinked sample. (b) 4: LCVBC sample, 5: HMVBC sample, and 6: PMVBC sample.

(5 Pa), indicating the formation of permanently covalent bonds among the polymer chains in the hydrogels. This result is well in agreement with cellulose reinforced gelatin double network hydrogels, whose storage modulus was approximately ten times higher than gelatin [27]. In sample 2, storage modulus of 53 Pa was greater than loss modulus of 38 Pa, showing solid-like behavior, while the directly crosslinked hydrogel had lower storage modulus than loss modulus, having liquid-like character. This also confirmed the generation of chemically crosslinked network in the sample 2 after thermal exposure. As the crosslinker concentration increased, the sample 3 with 14 mol% TMVBC crosslinker had improved mechanical strength ($G'$, 130 Pa) relative to 2 containing 7 mol% TMVBC ($G'$, 53 Pa). More interestingly, orthogonally crosslinked sample 2 displayed more than two times elastic modulus (53 Pa) compared to directly

crosslinked sample of 1 (22 Pa) having the same chemical composition, revealing the formation of superior microstructure network. Compared to the mechanical brittleness of conventional AMPS-based hydrogels crosslinked with $N,N'$-methylenebis(acrylamide) (MBA), the orthogonal crosslinker generated hydrogels were more flexible due to the introduction of ionic moieties. The enhancement of mechanical strength could be ascribed to the double crosslinked network by the locally covalently crosslinked interactions of polymer chains and ionic physical entanglement. The soft hydrogels could be applied as the matrix for preferential lineage of specific human cells as demonstrated in previous study [28].

The mechanical properties of the orthogonally crosslinked hydrogels were examined under the same crosslinker concentration. The mechanical strength of the samples
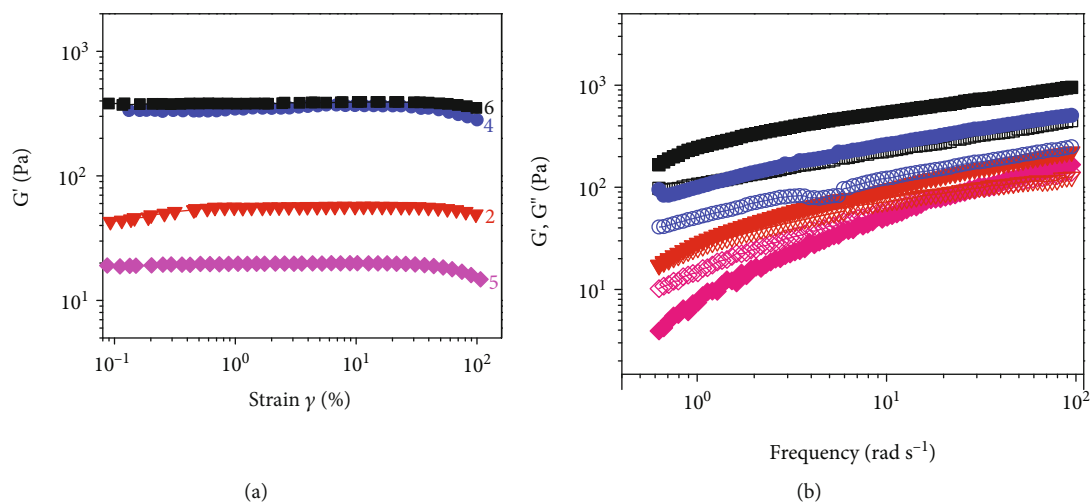
(a)

(b)

FIGURE 2: Rheological data of the hydrogels. (a) Strain amplitude sweeps ($\gamma = 0.1 - 100\%$). (b) Frequency sweeps ($\omega = 0.1 - 100 \, \text{rad} \, \text{s}^{-1}$) of the samples.
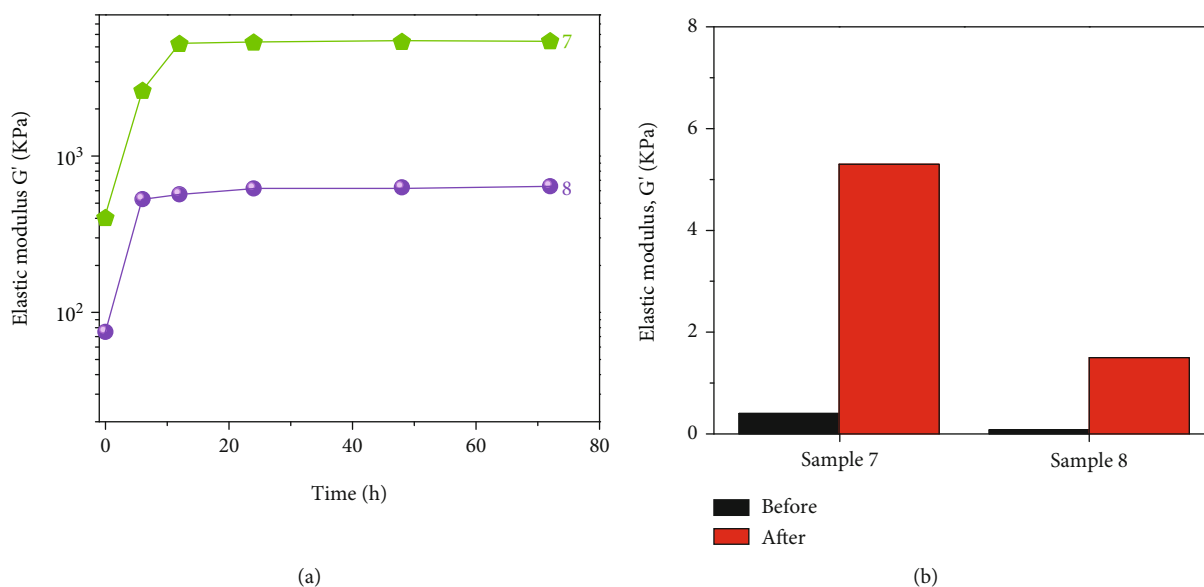


(a)

(b)

FIGURE 3: Dynamic shear elastic moduli $G'$ of (a) as-prepared direct crosslinked hydrogels of 7 and 8 as a function of time upon standing in water at 37°C. (b) On-demand control of hydrogel elasticity after treating the samples at 60°C for 6 h.

highly depends upon the crosslinker topology as indicated by the storage moduli in Figure 1(b) at the time scale of our measurements. As shown in Figure 1(b), the hydrogel generated with extended backbone crosslinker had lower storage modulus in comparison with the sample prepared with shorter bridge between the crosslinkable moieties. For example, linear HMVBC (having six carbons between crosslinkable sites) crosslinked sample showed storage modulus of 27 Pa while the storage modulus of TMVBC (having two carbon bridge-)-based hydrogel was 53 Pa (sample 5). Orthogonal HMVBC crosslinked hydrogel had liquid-like behavior as implied by the greater loss modulus of 39 Pa than storage modulus of 27 Pa. However, the branched LCVBC (sample 4)-based hydrogel with rigid backbone showed lower storage modulus than PMVBC crosslinked sample (sample 6),

probably due to lower density of covalent crosslinks. More interestingly, the covalently crosslinked sample bearing PMVBC crosslinker showed one order of magnitude higher elastic modulus of 288 Pa compared to the sample crosslinked with HMVBC having elastic modulus of 27 Pa, highlighting the significance of the topology of the crosslinker backbone to the mechanical integrity of the hydrogels.

As shown in Figure 2(a), strain amplitude sweeps of the covalently crosslinked hydrogels demonstrated an elastic solid-like behavior within the linear viscoelastic regime of 30–70%, depending upon crosslinker topology. The storage moduli of the hydrogels were weakly dependent on the sweep frequency and decreased over the critical regimes, indicating a collapse of the gel state and the presence of ionic crosslinks within the hydrogels. In stark contrast to
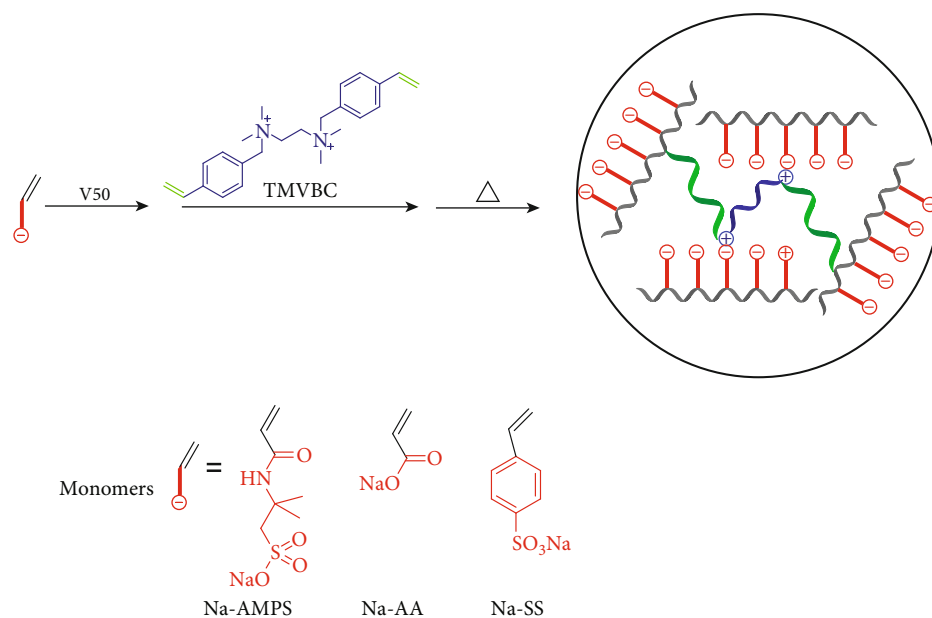
SCHEME 3: Monomers' effect on hydrogel mechanical integrity using orthogonal crosslinker of TMVBC.
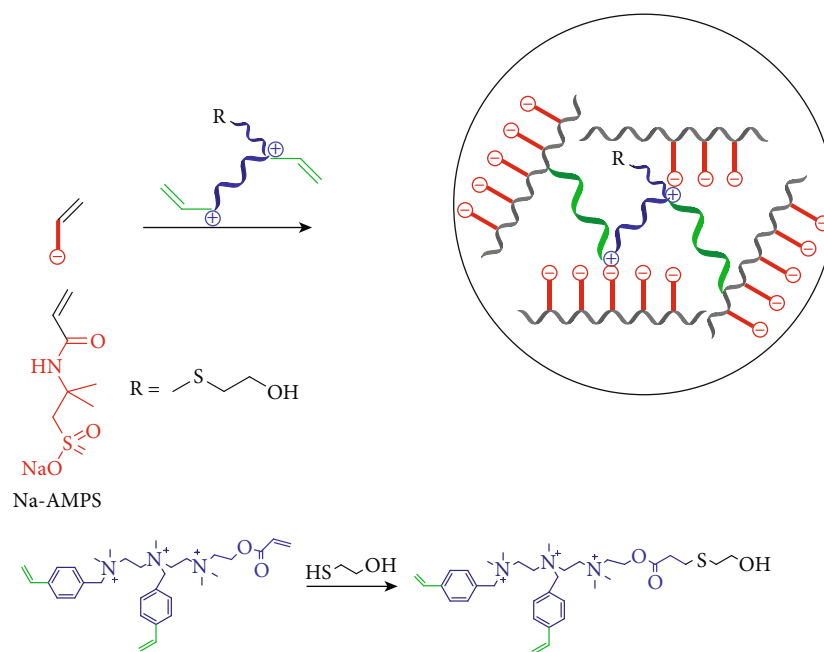


SCHEME 4: Direct functionalization of the hydrogels by heteroorthogonal crosslinker approach using selectively thiol-ene chemistry, 2-mercaptoethanol attached to the crosslinker.

covalently crosslinked networks, the hydrogels showed frequency-independent behavior due to the absence of energy dissipation pathway [29]. Furthermore, the rheological properties of the synthesized hydrogels were further studied as a function of angular frequency. As indicated in Figure 2(b), the elastic behavior ($G' > G''$) of the solid-like hydrogels was prevalent over the entire frequency range. For example, the storage modulus of TMVBC hydrogel was greater than loss modulus. The extended backbone

HMVBC hydrogel had radically different response to sweep frequency. At frequency lower than 23 rad s$^{-1}$, the hydrogel displayed liquid-like feature while the sample exhibited solid-like behavior above the crossover as revealed by Figure 2(b). These observations confirmed that mechanical properties of the orthogonally crosslinked hydrogels can be obtained by adjusting the topology of the crosslinkers. One benefit of this approach is that the prepared hydrogels were mechanically tunable.

The time-dependent shear elastic moduli, a metric of hydrogel stiffness, were monitored as a critical factor in the design of extracellular matrix [30]. The hydrogels in this work prepared at room temperature had short-term temporal modulation behavior under physiological conditions. The elasticity of the hydrogels gradually increased with time over days as shown in Figure 3(a) due to the formation of in situ covalent crosslinks from residual styrenyl moieties. The increase in the orthogonal crosslinker concentration increases hydrogel stiffness as in situ covalent linkages increased. Traditional evaluation of cell growth constrained to timescales of cell life cycle. However, short-term observations of growth dynamics offered valuable insights to correlate long-term dynamics of cell development [31]. In previous research, temporal mechanical modulation of the hydrogels over weeks was achieved by orthogonal sulfonium monomers containing hydrogels.

As a complimentary study, herein, we obtained short-term temporally controlled hydrogel stiffness over days. Furthermore, on-demand control of the hydrogel stiffness was achieved by an on-demand stimulus of heating. The hydrogels synthesized at room temperature were soft and transparent while the samples turned to opaque in water bath of 37°C, which was demonstrated by modulus increase as shown in Figure 3(b). The hydrogels consisting of 14 (sample 8) and 21 (sample 7) mol % TMVBC relative to Na-AMPS monomers had shear elastic moduli of 1.6, and 5.3 KPa, respectively. In stark contrast to previous work, most hydrogels had constant mechanical strength after preparation. Apparently, the elasticity of the hydrogels can be tuned by orthogonal crosslinker concentration upon thermal treatment. This synthetic hydrogels are ideal candidates to mimic extracellular matrix for short-term cell culture given its temporal mechanical properties.

To further broaden the scope of orthogonal strategy, this general approach was applied to various monomers system using TMVBC orthogonal crosslinker as shown in Scheme 3. The mechanical strength of the hydrogels could be tuned through the ionic interactions between cationic moieties and anionic sites. The addition of Na-AA monomer to our synthetic system dramatically reduced the storage modulus of 27 Pa compared to Na-AMPS hydrogel of 53 Pa under similar conditions. The reduction was ascribed to the weakly ionic interactions within the hydrogel given the chemical similarity of Na-AA and Na-AMPS. In addition, the interaction of anionic sodium styrene sulfonate (Na-SS) with cationic quaternary ammonium TMVBC crosslinker would form strong bonding between cationic moieties and anionic groups. We can anticipate that the replacement of Na-AMPS with Na-SS would significantly increase the mechanical strength of the hydrogel. As demonstrated in our work, Na-SS-containing sample 6 had approximately two orders of magnitude of elastic modulus (1800 Pa) in comparison with sample 7 of 27 Pa as shown in Figure S3. Apparently, the strong bonding between anionic styrene sulfonate and quaternary ammonium provided the enhanced mechanical strength via ionic crosslinking. The result is consistent with the experimental data of ionic crosslinked cationic PMPTC and anionic monomer Na-SS hydrogels, whose Young's modulus was greater than PMPTC and NaAMPS-based hydrogel [8, 9]. By tuning the ionic interactions within the hydrogels, we could generate the hydrogels with a broad range of elastic moduli in comparison with the gels controlled by crosslinker and monomer concentrations.

Direct functionalization approach is a convenient yet powerful method for the modification of the hydrogels to encapsulate bioactive molecules. The orthogonality of the crosslinker also enabled the encapsulation of molecules of interest in the hydrogels. In particular, the introduction of acrylate to the crosslinker readily realized the incorporation of bioactive molecules via environmentally benign Michael addition under physiological conditions. More explicitly, commercially available 2-mercaptoethanol as a test vehicle was applied to functionalize the hydrogels, as shown in Scheme 4, and the $^1$H NMR spectra of the crosslinkers are shown in Figure S4. The nucleophilic conjugation reaction was carried out under aqueous conditions at room temperature [32, 33]. As demonstrated in $^1$H NMR, the successful conjugation of BME was validated by corresponding characteristic peaks. This experiment demonstrated that the hydrogel functionality could be obtained by attachment of molecules of interest to our hydrogels in a temporal fashion. Compared to orthogonally functionalized hydrogels [16–19], the application of orthogonal crosslinkers during hydrogel synthesis facilitates the introduction of hydrophobic molecules to the hydrogels due to the presence of the ionic moieties, which would significantly increase the solubility of hydrophobic motifs.

## 4. Conclusion

In conclusion, bifunctional crosslinker-induced thermally enhanced hydrogel has been described. The mechanical strength of the hydrogels can be self-reinforced by thermal crosslinking due to the presence of thermal crosslinkable moieties in the bifunctional crosslinker, applicable to the preparation of ionically and covalently crosslinked hydrogels. Upon thermal treatment, the soft ionic hydrogel was transformed to a permanent, covalently crosslinked polymeric hydrogel network with ionic characteristics. The mechanical strength of double crosslinked hydrogels was higher than directly crosslinked hydrogel due to its double crosslinked feature. The mechanical property of the transformable polymeric network was tunable by manipulating the ionic bond strength and crosslinker concentration as demonstrated in this work. Owing to the crosslinker sensitivity to heat, light, and radicals, the hydrogels are trigger-responsive materials, which are promising to construct smart hydrogels with the aid of bifunctional crosslinker. Thus, the concept in this study might provide an avenue to build new stimulus responsive polymeric hydrogels.

## Data Availability

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

## Authors' Contributions

Bin Liu and Zhaoyan Hou contributed equally to this work.

## Acknowledgments

## Supplementary Materials

Associated Content. Supporting Information. Detailed characterization data of the hydrogel is provided including crosslinker and hydrogel synthesis and their characterizations. (*Supplementary Materials*)

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