Design of acrylamide-based thermoresponsive copolymer with potential capability for physical network formation in water: a molecular dynamics study

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Abstract
In this work, a new smart copolymer of poly(N-isopropylacrylamide)-b-polyacrylamide-b-poly(N-isopropylacrylamide) (PNIPAm-b-PAM-b-PNIPAm) was designed as an efficient thermo-sensitive polymer with a potential for formation a physical network structure above a certain temperature in water. To design the desired copolymer, molecular behaviors of the copolymer blocks were investigated in water at different blocks fractions and temperatures via atomistic simulation. The blocks were evaluated from the interactional aspects via estimating the electrostatic and van der Waals contributions of their interaction energies with the media to consider the amount of hydrophilicity variation of the blocks with temperature variation. To find the origin of changes in blocks hydrophilicity, the structure and orientation of interfacial water were determined via calculating coordination number and order parameters of the water molecules in the first and second hydration shell of the blocks. In this regard, a novel parameter based on water ordering and hydration level was presented. The PAM block in the copolymer with shorter PNIPAm blocks, particularly 8 mol% (percentage by mole) PNIPAm, enforced the thermoresponsive end blocks to behave like a water-soluble polymer above their lower critical solution temperature. In contrast, increasing the PNIPAm content to 32 mol% caused an interactive competition between the blocks. Finally, the copolymer with the PNIPAm/PAM = 0.19 was found as the most efficient copolymer composition for the mentioned goal via using the analysis of variance (ANOVA) of the calculated responses.

1. Introduction
Thermoresponsive copolymers are a popular type of smart polymers which can create spherical, cylindrical, gyroidal and lamellar morphologies in a solution via changing the temperature [1]. These copolymers have some portions in their structures, i.e., blocks, branches or segments, which modify the chain physicochemical properties with raising an external stimulant, such as temperature [2]. These thermally responsive portions are generally divided into two groups: those with the phase separation behavior upon heating (lower critical solution temperature; LCST) and those with the phase separation upon cooling (upper critical solution temperature; UCST) [3]. In fact, the temperature changes the portions physicochemical behaviors in a solvent media through the variation of their thermodynamic characteristics [4]. This behavioral variation is the basis of the use of thermally responsive copolymers in various applications, e.g., drug delivery [5], gene therapy [6], gelation [7] and enhanced oil recovery (EOR) [8]. The chemical and physical characteristics of the thermosensitive portions

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have the intense impacts on their thermal responsivity and the copolymer molecular behaviors in solutions, particularly in aqueous media [9–11]. Recently, Stoica et al [9] studied the effect of hydrophilic spacer, (CH$_2$)$_n$, on the coil-to-globule transition temperature ($T_c$) of poly(N-isopropylacrylamide) (PNIPAm) in water. According to their results, increasing the hydrophobicity level of the polymer via setting a hydrophobic spacer in its structure led to the reduction of the PNIPAm transition temperature. Lessard et al [10] investigated the impact of molecular weight on thermodynamic properties of poly(N, N-diethylacrylamide) (PDEA) in aqueous solution. Their results showed that the increment of chain length of PDEA caused the decrement of its LCST and the change of solution entropy. However, the LCST was constant after a critical molecular weight. In spite of various molecular architectures for thermal responsive copolymers, the block classification has attracted the attention of scientists to create proper self-assembly structures in aqueous solution due to its high efficiency [12, 13]. In the past decades, water-soluble polymers along with thermoreversible blocks have been used to create particular association structures in aqueous media [13]. Ding et al [14] evaluated the influence of poly($\gamma$-benzyl-L-glutamate)-b-poly(ethylene glycol) (PBLG-b-PEG) conformation change on its self-assembly behavior. The results indicated that reducing the fraction of rigid block in an AB diblock copolymer changed its micellar structure from helix to coil, and transformed the aggregates from rod-like to spherical shape. Wessels et al [15] measured the impact of branching level of amphiphilic block copolymers on their assembly in a solution. The results illustrated that the copolymer architecture, block sequence and composition affected the thermodynamic behavior of solutions and the association of amphiphilic copolymer chains. In another work, Brown et al [16] considered AB block copolymers with a gradient region located between the pure A and B block in which the region composition smoothly changes from B to A with the B side of the taper bonded to the A block. Their results showed that the designed copolymer structure led to changing the morphology to microphase-separated structures of inverse tapered block copolymers. In fact, the conformational behavior of a block copolymer in solution depends on the molecular feature of the blocks, i.e., the number of repeating units, fraction of the blocks, and on the interaction parameter between each block and media [17–19]. Also, the morphology of block copolymer in a solution can be controlled via changing the type of blocks and optimizing their lengths. Virtually, tuning the block copolymer structure would vary the size, composition and local properties of the micro- and nanoscale domains created by phase separation. Therefore, investigation of a block copolymer in a dilute solution from intermolecular interactional aspect in the hydration shell could make a correlation between its conformation and structure [19]. Moreover, the consideration of arrangement and structure of interfacial water in the hydration shell of copolymers in an aqueous solution can reveal the origin of the behavioral differences of thermo-responsive copolymers. Molecular dynamics (MD) simulation is a powerful method to study polymeric solutions from the molecular points of view [14, 15, 20]. Additionally, this method can give useful information relative to the dynamic and static properties of block copolymers in solutions [21–23].

Recently, modified polyacrylamide with the branched architecture has been used to enhance the solution viscosity in enhanced oil recovery (EOR) via preparation of an associative polymer solution [24]. In fact, a controlled micro-phase separation in the solution is required to raise the solution viscosity. The creation of a physical network structure (PhNS) [24] based on effective micro-phase separation leads to a significant change in solution rheological features. However, copolymers with the branched classification do not have adequate potential to form an efficient PhNS in low-concentration aqueous solutions with desirable properties. These copolymers lead to less expansion of the network structure in the solution. Thus, a copolymer with another structure is needed to create a more stable and expandable PhNS in the solution to significantly increase the solution viscosity, especially at much lower polymer concentrations. In this work, a triblock copolymer consists of a middle polyacrylamide (PAM) block and the same thermoresponsive end blocks of PNIPAm, was designed as a new polymeric additive (see figure S1(a) (Supporting Material) (available online at stacks.iop.org/MRX/9/095302/mmedia)). This copolymer chains would form a smart PhNS in water above LCST of the end blocks (according to figure S1(b)). Accordingly, to find an efficient fraction for the blocks, various molecular characteristics of the copolymer with different fractions of blocks were considered in water in a temperature range via MD simulation. The blocks behaviors from the interactional aspect were investigated to study their hydration level and hydrophilicity variations in water. Additionally, the role of water molecules orientation at the interface on the hydrophilicity variation of the blocks with increasing the temperature was also evaluated using a novel parameter based on the water ordering level. Finally, the proper fraction of the blocks with a potential capability for PhNS formation in water was obtained using a statistical method, the analysis of variance (ANOVA).
2. Model and simulation technique

In this work, the presented triblock copolymer consists of a PAM inner block and two PNIPAm end blocks, PNIPAm-\(b\)-PAM-\(b\)-PNIPAm. The Interactional, interfacial and conformational behaviors of the copolymer was studied at different blocks contents and temperatures in a dilute aqueous solution.

2.1. Simulation details

In this study, the simulations of dilute copolymer solutions were implemented using LAMMPS software package developed at the Sandia National Laboratories\[25\]. Despite the various force fields used to characterize acrylamide-based polymers in aqueous solutions, Polymer Consistent Force Field (PCFF) force field was applied for the simulations because of its accuracy and efficiency\[11, 18, 26–28\]. In the simulations, Nose–Hoover thermostat and Berendsen barostat were used to keep the temperature and the pressure constant, respectively. The coupling time of 1 ps was employed for temperature (\(\tau_T\)) and pressure (\(\tau_P\)). The velocity Verlet method with a time step of 1 fs was also applied as an integrator algorithm in all the simulations. Dispersive contribution to the non-bonded interactions was calculated via cut-off distance of 1.2 nm, and the long-range electrostatic contribution was also estimated using particle mesh Ewald (PME)\[29\]. In our previous work\[18\], the accuracy and efficiency of the PCFF force field and aforementioned simulation methodology were proved for the acrylamide-based copolymer in an aqueous solution via calculating the polymer physicochemical characteristics and their comparison with experimental results. In addition, the last forty percent of the main current simulations was used for data sampling and statistical analysis.

2.2. Model construction

In the beginning, the structures of NIPAm and AM monomers were built and then were geometrically optimized via GAMESS software package with internally stored B3LYP/6–31 G (\(d\), \(p\)) basis set\[30\]. Afterward, the optimized structure of the monomers was used to generate the triblock copolymer with the PAM inner block and two PNIPAm end blocks with the same length. As known, the PNIPAm and PAM tacticity have impacts on their physicochemical behaviors\[11\]. However, the process was controlled to achieve only the atactic stereochemistry because this type of tacticity is more accessible in polymerization process. In this work, three copolymer chains each one with 100 repeating units were constructed, in which the number of repeating units \(m\) in PNIPAm end blocks was 4, 8 and 16 units (see figure 1). The copolymer chain was designated as CPx in which \(x\) is the molar percentage of PNIPAm, e.g., CP8 \((m = 4)\), CP16 \((m = 8)\) and CP32 \((m = 16)\). Thereafter, the constructed copolymer chains were energetically optimized using the conjugate gradient (CG) algorithm to reach a minimum level of energies. The initial CPx/water (CPx/W) dilute solution model containing a single copolymer chain in water were created in a periodic boundary condition to implement the main MD simulation. In the models, there are no intermolecular interactions between the copolymer chain and its neighbor images due to large dimensions of the solutions boxes. Characteristics of the CPx copolymer chain and its primary concentration \(C\) in the solution box are listed in table 1.

Before starting the main simulation, the initial 3D models of CPx/W solution were optimized using the CG algorithm to minimize their energies. Then, the simulation boxes were exposed to a NVT simulation for
NPT simulation as follows. The radius of gyration autocorrelation function is used to investigate the effect of length of blocks on the interactional behaviors. This study was accomplished via simulation of the solution model in terms of the radius of gyration, \( R_g \). The \( R_g \) values are calculated as follows:

\[
R_g = \left( \frac{\sum_{i=1}^{N} M_i r_i^2}{\sum_{i=1}^{N} M_i} \right)^{1/2}
\]

where \( M_i \) is the atom mass and \( r_i \) is the distance from the atom mass to the center of mass (COM) of the polymer. The parameter of \( R_g \) is determined based on the weight average value of the radius of gyration of the \( CP_x/W \) model, a suffix of repeating units of the PNIPAm and PAM blocks in copolymer structure, respectively. The parameter of \( NP \) is the number of copolymer chains, and \( C_i \) is the copolymer concentration in the primary solution model.

The parameters of \( m \) and \( n \) are the number of repeating units of the PNIPAm and PAM blocks in copolymer structure, respectively. The calculated parameters are shown in Table 1.

### Table 1. Details of \( CP_x/W \) solution models.

| Model  | \( m \) | \( n \) | \( NP \) | \( C (g \text{ml}^{-1}) \) |
|--------|--------|--------|--------|------------------|
| \( CP8/W \) | 4     | 92     | 1      | 0.05             |
| \( CP16/W \) | 8     | 84     | 1      | 0.06             |
| \( CP32/W \) | 16    | 68     | 1      | 0.07             |

In our previous simulation work, the PNIPAm LCST of 302.6 K was obtained. The selected temperatures were below or above the PNIPAm LCST [31]. The PNIPAm LCST of 302.6 K was obtained in our previous simulation work [20], which has a good conformity with the experimental amount of 305 K [31].

### 3. Results and discussion

#### 3.1. Equilibration of solution model

To achieve an equilibrated \( CP_x/W \) model, a sufficient simulation time duration should be applied on the solution box. Accordingly, to ensure the adequacy of the implemented simulation time on the \( CP_x/W \) model, the radius of gyration autocorrelation function \( (C(t)) \) of each \( CP_x \) chain in its solution was calculated during the NPT simulation as follows [32]:

\[
C(t) = \frac{[R_g(t) - \langle R_g \rangle][R_g(0) - \langle R_g \rangle]}{\langle R_g^2 \rangle - \langle R_g \rangle^2}
\]

where \( R_g(t) \) and \( R_g(0) \) indicate the radius of gyration of the \( CP_x \) chain at any time \( t \) and the initial time, \( t = 0 \), respectively. The angular bracket, \( \langle \ldots \rangle \), represents an average over the simulation time. The parameter of \( R_g \) was determined based on the weight average of the \( CP_x \) chain atoms distances from the copolymer center of mass (COM) as follows [33]:

\[
R_g = \left( \frac{\sum_{i=1}^{N} M_i r_i^2}{\sum_{i=1}^{N} M_i} \right)^{1/2}
\]

where \( M \) and \( r \) indicate the atom mass and its distance from the COM of the \( CP \) chain, respectively. The subscript \( i \) is the atom number of the copolymer chain, from 1 to \( N \). The calculated \( C(t) \) for each \( CP_x \) chain in its solution model was exhibited in figure S2. As seen, the end of \( C(t)-t \) curves approached zero, indicating the sufficiency of the applied simulation time duration on the \( CP_x/W \) solutions. Factually, the obtained \( C(t) \) results confirmed that all the \( CP_x \) chains released from their initial conformational history at the end of NPT simulation. The parameters of \( m \) and \( n \) are the number of repeating units of the PNIPAm and PAM blocks in copolymer structure, respectively. The parameter of \( NP \) is the number of copolymer chains, and \( C_i \) is the copolymer concentration in the primary solution model.

#### 3.2. Intermolecular interaction behaviors

Intermolecular interactions in a polymer solution play a key role on molecular dynamic behaviors of the immersed polymer and influence the solution properties [34]. This issue has higher importance when a thermoresponsive copolymer dissolves in a solvent [35]. In fact, the temperature variation would influence significantly the non-bonded interactions between the polymer solute and media with changing the polymer chemical characteristics [36]. Therefore, investigation of the \( CP_x/W \) solutions from the intermolecular interactional point of view is necessary. This consideration can create a deep insight into the effects of PNIPAm and PAM blocks on the interactional behaviors between the blocks and the media with increasing the temperature. Moreover, this evaluation is very vital to design an efficient thermoresponsive triblock copolymer to create a particular 3D physical network structure in aqueous media as thickening agents [37] (see figure S1(b)). The presence of different blocks with diverse innate affects the copolymer chemical and physical features [38]. In fact, this matter is the base of micro-phase separation of copolymers in an aqueous copolymer solution [39]. In the present work, we studied the non-bonded interactions between the \( CP_x \) blocks and water media to investigate the effect of length of blocks on the interactional behaviors. This study was accomplished via...

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calculating the electrostatic (elc) and van der Waals (VdW) contributions of the interaction energy ($E_{\text{int}}$) between the blocks and water versus temperature and amount of $x$. The interaction energy of CP$_x$-W in each solution was calculated by the following equation [40].

$$E_{\text{int}} = E_i - (E_b + E_w)$$  \hspace{1cm} (3)

where, $E_i$, $E_b$, and $E_w$ represent the total potential energies of the solution, copolymer block and water, respectively. The obtained elc and vdw contributions of the interaction energies per repeating unit of the block (mer), i.e., $E_{\text{int-elc}}$ and $E_{\text{int-vdW}}$, for both PAM and PNIPAm blocks are shown in Figure 2.

As seen, the $E_{\text{int-elc}}$ is the dominant intermolecular interaction between the blocks and the water owing to high electronegativity of the elemental composition in the blocks, i.e., oxygen and nitrogen. The $E_{\text{int-vdW}}$ amounts were much lower than the $E_{\text{int-elc}}$ values, with an irregular trend. However, the presence of hydrophobic moiety of isopropyl in the NIPAm structure led to higher dispersive interactions than the PAM one (see Figures 2(b) and (d)). According to the figure, the connection of the PNIPAm and PAM blocks together affected the interactions between the blocks and water molecules competitively. The PAM block compatibility with the media was increased with raising the temperature, especially at the lower amount of $x$, e.g., $x = 8$ mol% (percentage by mole). This behavior is due to more negative amounts of the $E_{\text{int-elc}}$. For the CP32/W model ($x = 32$), increasing the temperature up to the PNIPAm coil-to-globule transition temperature ($T_{cg} = 302.6$ K) [20] enhanced the PAM compatibility, while further temperature increment decreased the affinity. In CP8 and CP16 copolymers, length of the inner block was much longer than that of the end blocks. Consequently, impact of the end blocks on the PAM block was slightly. In contrast, the inner block exhibited a predominant effect on the copolymer behaviors in water. However, increasing the length of end blocks lowered the dominant effect of the inner block and decreased the $E_{\text{int-elc}}$ amount to a smaller negative value when the temperature increased above $T_{cg}$.

At the lower amount of $x$, it seems that the PAM block improves the tendency of the end blocks to water with increasing the temperature, especially for the CP8/W solution. Increasing the $x$ amount in the copolymer structure, CP16, decreased the PAM predominant effect and changed significantly the intertional behaviors at the temperatures above $T_{cg}$. The intermolecular interactional behavior of the CP32 blocks was completely competitive; the PAM block tends to influence the PNIPAm interactional characteristics and vice versa. Factually, the interactional natures of the blocks and their mutual impacts changed the tendency of the blocks to the solvent molecules. Both the end and inner blocks exhibited a hydrophilic nature at the temperatures below the $T_{cg}$. On the contrary, increasing the temperature above the $T_{cg}$ decreased the hydrophilicity of PNIPAm significantly. In fact, these observed differences can be attributed to the presence of amide groups and the

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**Figure 2.** Electrostatic ($E_{\text{int-elc}}$) and van der Waals ($E_{\text{int-vdW}}$) contributions of the interaction energy per block repeating units between: (a, b) the PAM block and (c, d) the PNIPAm blocks and water molecules as a function of $T$ and the PNIPAm content ($x$).
respectively. As seen in can be attributed to water-soluble interactions and thermoresponsive behavior of the PAM and PNIPAm blocks, around a solute in which the solute and water molecules in polymer solution properties interactions between the polymer chain and media substantially. This issue leads to changing the solution where \( r_0 \) entropy penalty originated from the hydrophobic pendant moiety of isopropyl influencing the interactions between the blocks.

3.3. Water capturing and hydration level
The cluster of solvent molecules surrounding a polymer solute in a solution influences the intermolecular interactions between the polymer chain and media substantially. This issue leads to changing the solution properties [41]. Also, the ordered solvent molecules in the solvation shell causes many behavioral variations in polymer solution [11]. As a whole, the solvation or hydration shell in aqueous solutions is the interfacial region around a solute in which the solute and water molecules influenced each other strongly [42]. Hydration number or coordination number of water molecules around a solute is a criterion to measure the captured water molecules at the hydration layer [39]. In the present work, we calculated the coordination number of the water molecules around the amide groups of the CPx blocks \( (N_{A-W}) \) in their hydration shells. In addition, the affinity of the blocks to water molecules as well as the effect of interfacial water on the hydrophilicity level versus \( T \) and \( x \) were investigated [39]. In fact, rearrangement of the interfacial water molecules within the hydration shell would change the strength of non-bonded interactions between the blocks and the water molecules, particularly the electrostatic contribution [43]. Accordingly, the hydration shell of the PAM and PNIPAm blocks in the equilibrated solution was determined via calculating the radial distribution function (RDF) of water COM relative to the COM of the blocks amide, \( g_{A-W}(r) \) (see figure 3).

In the estimation process of the PAM and PNIPAm hydration shell, the CP16 copolymer chain was used at the temperature of 280 K. In fact, the \( T \) and \( x \) only influence the intensity of the RDF peaks, while these variables have no significant effects on the solvation radius [11, 39]. In order to obtain the \( N_{A-W} \) amounts for each block in the hydration shell, the following equation was used [11].

\[
N_{A-W} = 4\pi \rho \int_0^{r_0} g_{A-W}(r)r^2dr
\]  

where \( r_0 \) indicates the range of integration cut-off or the first solvation shell, which was selected according to figure 3, i.e., \( r_0 = 0.31 \) nm for PAM and 0.35 nm for PNIPAm. These values are in a good agreement with the amounts published elsewhere [39, 44]. The obtained \( N_{A-W} \) results for each block as a function of \( T \) and \( x \) are shown in figure 4. According to the figure, the \( N_{A-W} \) of PAM was increased with increasing the temperature, while the trend was changed for the copolymer chain with higher amount of \( x \) at the temperatures above the transition temperature of the PNIPAm. This means that the affinity of the inner block to the media was improved with increasing the temperature. Nonetheless, this behavior was changed for the copolymer with longer PNIPAm, i.e., CP16 and CP32, at the temperatures above their \( T_{g'} \) values. This observed behavior can be attributed to the effect of the PNIPAm on the conformation of the middle block of the copolymer in water. In conjunction with the end blocks, increasing the temperature above the transition point led to increasing the hydration level of the PNIPAm for the CP8 chain and vice versa for the CP16 one. In contrast, the influence of the inner block on the end block and their tendency to the media led to an irregular trend in hydration change of the CP32 blocks. In addition, the \( N_{A-W} \) variation for PAM block in all the copolymers was almost the same, while \( N_{A-W} \) values were shifted to lower amounts for the blocks with increasing their length. This different observation can be attributed to water-soluble interactions and thermoresponsive behavior of the PAM and PNIPAm blocks, respectively. As seen in figure 4, the \( N_{A-W} - T \) variation for both the PAM and PNIPAm blocks represents a similar trend to \( E_{int-elec} - T \) variations (figures 2(a) and (c)).

\[\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig3.png}
\caption{Radial distribution function (RDF) of the water COM relative to the COM of amide group, \( g_{A-W}(r) \), for the PAM and PNIPAm blocks of the CP16 at 280 K. Highlighted areas are the first hydration shell for the blocks.}
\end{figure}\]
This similar changes are due to increasing the hydration level, which leads to increasing the $E_{\text{int-elc}}$ values to more negative amounts, and subsequent enhancement of compatibility between the blocks and water molecules. Actually, the physicochemical characteristics of the similar and dissimilar blocks have a mutual influence on each other, which determines the hydration level for the CPx/W models.

### 3.4. Interfacial structure of water

Interfacial structure of water molecules and their spatial arrangement around a polymer solute in a solution lead to diverse behaviors. The existence of non-bonded interactions with different strengths between polymer and solvent causes different water interfacial structures [45]. Therefore, the determination of orientation of the interfacial water relative to the amide groups of the blocks in the hydration shell is necessary. For this purpose, order parameters, i.e., $\theta$ and $\phi$, as helpful criteria provide a deep insight into the origin of conformational changes in the blocks copolymers affected by the interfacial water [46]. The schematic representation of $\theta$ and $\phi$ parameters for a water molecule around the amide group are shown in figure 5.

The calculation process of $\theta$ and $\phi$ parameters was performed in the first hydration shell of the blocks. The distances equal or less than 0.31 nm around the COM of amide groups of PAM ($r < 0.31$ nm), and equal or less than 0.35 nm ($r < 0.35$) for the amide groups of PNIPAm were obtained. The water molecules surround each amide group of the blocks in this zone (first hydration shell) and strongly interact with the solute compared to the other space zones [42]. In fact, the stronger intermolecular interactions, such as hydrogen bonding, are created at the proper direction between the hydroxyl groups of the water molecules and the polymer solute in aqueous media [26]. This issue significantly influences the affinity between the solute and the aqueous media, especially for the solutions containing thermoresponsive polymers. Accordingly, this phenomenon indicates the complex behavior of the solute in the media. District of the first hydration shell of the amide groups of PAM and PNIPAm blocks were highlighted with the blue and pink colors in the $g_{A,W}(r)$-$r$ curves, respectively (see figure 3).

The probability distribution ($P$) based on the $\theta$ and $\phi$ parameter for the PAM and PNIPAm blocks of the CPx chains versus $T$ are illustrated in figures 6 and 7, respectively. Also, the width and the height of the $P$-Degree maximum peaks in figures 6 and 7 were calculated to quantify the broadness of the maximum peaks. The results for the PAM and PNIPAm blocks are summarized in tables S1 and S2, respectively. As seen in figures 6 and 7,
increasing the temperature enhanced the $P$ amount of the $\theta$ and $\phi$ parameters to some extent. The block with a more negative amount of $E_{\text{int-elc}}$ (figure 2) exhibits a narrower and more intensive peak in its $P$-degree curve (see tables S1 and S2).

As seen in tables S1 and S2, more sharp peaks with higher height and smaller width belong to the PNIPAm end blocks with thermoresponse innate as compared with the PAM inner block. This issue means that the water molecules were ordered significantly in the adjacent of the PNIPAm amide groups than the PAM amide groups. In fact, a large number of the interfacial water molecules in the first hydration shell got almost the same $\theta$ and $\phi$ values. In this regard, the steric hindrance of the copolymer affects the $\theta$ and $\phi$ values as well [18, 20]. In addition, this analysis assists to detect the variation of hydrophilicity level of the copolymer blocks with changing the temperature. For instance, the hydrophilicity of CP8 blocks was increased with increasing the temperature because of lowering the width of the maximum peaks and increasing their intensity (see tables S1 and S2). Increasing the PNIPAm length in the copolymer structure lowered the difference in tendency of the PAM and PNIPAm block to the solvent molecules (see figures 6(C) and 7(C)).

The arithmetic mean of the $P$ amounts of the peaks with the highest probability ($P_{\text{max}}$) for $\theta$ and $\phi$ parameters on the $P$-degree curve, $\langle P_{\theta/\phi}\rangle$, was calculated at each temperature using following equation:

$$
\langle P_{\theta/\phi}\rangle (T) = 1/2[ P_{\text{max}_{\theta}}(T) + P_{\text{max}_{\phi}}(T) ]
$$

(5)

The calculation process was carried out to quantitate the variation of interfacial structure of water molecules with temperature and, consequently, to find the origin of the changes in hydrophilicity of the blocks in the media. This parameter is important to characterize the thermoresponse polymer in aqueous media because it contains the information of interfacial properties, water ordering, structural and hydrophilicity variations of the polymer solute with increasing the temperature. Factually, $\langle P_{\theta/\phi}\rangle$ acts as an alternative parameter for the existing thermodynamic parameters, e.g., Gibbs free energy and entropy, to study the behavior of polymer dilute solutions. The latter parameters have high computational cost, even further than the main simulation runs. Nevertheless, the former parameter through calculating the order parameters of $\theta$ and $\phi$ of the interfacial water has a negligible computational cost. As we know, the $\theta$ and $\phi$ order parameters have not been used for the polymeric materials yet. The order parameters were only used for a charged C$_{60}$, which has a simple geometry [46]. Whereas, the calculation of order parameters is too difficult in polymer solutes.

In order to make the $\theta$ and $\phi$ parameters interpretable for polymers, the equation (5) was invented. In this equation, the maximum peak of $P$-Degree curve was set as a representative of the maximum ordering of interfacial water molecules around the polymer solute. Accordingly, the arithmetic average was performed on the calculated $\theta$ and $\phi$ parameters. It is worth mentioning that this mathematical process is correct because the mentioned parameters have the same dimension from the physics point of view (both are probability density function). The $\langle P_{\theta/\phi}\rangle$-$T$ curves are illustrated in figure 8. In addition, the quantitative amounts of $\langle P_{\theta/\phi}\rangle$ for all the simulation models were reported as a function of temperature (Table S3). As seen, the temperature enforced the water molecules to have a particular arrangement relative to the amides groups for the CP8 and CP16 copolymer chains. This rearrangement enhances the water ordering level around the blocks, leading to an increase in blocks hydrophilicity. Increasing the temperature above the LCST of the PNIPAm led to disordering of the conformation of interfacial water around the CP16. This issue decreases the hydrophilicity of the end blocks due to the reduction of their $\langle P_{\theta/\phi}\rangle$ values. As discussed earlier, an irregular behavior was observed for the blocks of the CP32 chain. This behavior can be attributed to drastic impacts of its inner and end blocks on each other and
to the affinity of the blocks to the media. According to figure 8, increasing the PNIPAm length caused the increment and decrement of the ordering of the interfacial water molecules around the PAM and PNIPAm blocks, respectively. This issue has a good conformity with the observed interactional behaviors (figure 2). In fact, changing the blocks length influences their steric hindrance and solubility in the media. The parameter of $\langle P_{\theta f} \rangle$ is an efficient parameter to measure the CPx-water interactional and interfacial characteristics and hydration level.

In addition, the $P$ value for the $\theta$ and $\phi$ order parameters in the second hydration shell of the blocks, i.e., $0.31 < r \leq 0.50$ nm for PAM and $0.35 < r \leq 0.55$ nm for PNIPAm, were calculated as well. The effect of water structure in the second hydration shell on the blocks behaviors was investigated.

Figures S3 and S4 illustrate the $P$-degree results of $\theta$ and $\phi$ parameters as a function of temperature in the second hydration shells of the PAM and PNIPAm blocks, respectively. According to the figures, the Gaussian-like curve with the uniform distribution was observed for the $P$-Degree variations of the copolymer blocks in the second hydration shell. This behavior can be attributed to little effects of the water molecules on the amide

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Figure 6. Probability distribution ($P$) in the form of (a) $\theta$ and (b) $\phi$ order parameter of interfacial water molecules at the first hydration shell around the PAM amide groups versus temperature for: (A) CP8, (B) CP16 and (C) CP32 in an equilibrated solution state.
groups in the second hydration shell. However, the similarity was decreased for the PAM block when the length of PNIPAm blocks was increased. This issue is due to the variation of interaction strength between water molecules and the amide groups. According to the results, water capturing and hydration level in the first solvation shell considerably influence the thermophysical properties of the blocks in the solution, and vary the interactions between the copolymer and water with changing the temperature.

### 3.5. Intramolecular characteristics of the copolymer blocks

Despite some studies done on the thermoresponsive copolymers in aqueous solutions, less attention has been paid to the impact of the temperature and volume fraction of the blocks on the copolymer intramolecular features. These characteristics would change the conformational behavior of the copolymer in the solution with changing the temperature \([47]\). Accordingly, the evaluation of intramolecular interactions \(E_{\text{intr}}(T)\) of the CPx copolymers in water can be helpful to unmask why the chain conformation varies with the temperature and the

![Figure 7. Probability distribution \(P\) based on calculated order parameters, (a) \(\theta\) and (b) \(\phi\), of the interfacial water molecules at the first hydration shell around the amide groups of the PNIPAm blocks for (A) CP8, (B) CP16 and (C) CP32 copolymers as a function of temperature in the equilibrated solution state.](image)
Figure 8. Arithmetic mean of the $P$ amounts, $\langle P_{\theta_f} \rangle$, for the peaks with the maximum probability ($P_{\text{max}}$) on the $P$-degree curves (figures 6 and 7) versus temperature for: (a) PAM and (b) PNIPAm blocks in the CP$x$ chains.

block fraction. Figure 9 illustrates the $E_{\text{intra}}$ amounts per block repeating units for the inner and end blocks of CP8, CP16, and CP32 copolymers. As seen, increasing the temperature enhanced the $E_{\text{intra}}$ value to higher negative amounts of the inner block, especially for the copolymers with shorter end blocks. Whereas, the variation of intramolecular interactions of the PAM block at the temperatures above the LCST of the PNIPAm showed a different trend, particularly for the longest PNIPAm blocks, i.e., $x = 32$ mol%.

In conjunction with the PNIPAm blocks, this behavior was descending for the CP8 and was ascending for the CP16 and CP32. For the copolymer with the shortest PNIPAm blocks, the PAM inner block exhibited a predominant behavior with a good solubility in the water molecules (see figure 2). Indeed, increasing the temperature reduced the blocks intramolecular interactions and the amounts of interaction energies. Nonetheless, increasing the length of the PNIPAm blocks led to an enhancement in chain entropy, which lowers the interactions between the blocks and the media. The increment of the $E_{\text{intra}}$ value of the PNIPAm blocks with temperature to more positive amounts lowers their compatibility with the media. According to the results, decreasing the PNIPAm length in the copolymer structure increases the block instability due to enhancing the intramolecular interactional barriers in the blocks. In fact, this phenomenon occurs due to the lack of PNIPAm ability to fold at the lower chain length. It was found that smaller PNIPAm chain has a rod-like conformation at lower chain length and does not have an ability for folding [20]. Furthermore, to study the influence of interactional and interfacial features of the blocks on their conformational and spatial properties, the radius of gyration and end-to-end distance ($\langle r_0 \rangle$) of the blocks were determined as the dimensional criteria. The calculated dimensional results are summarized in table 2. As seen in the table, the dimensions of the shorter blocks were not changed with increasing the temperature. Actually, the blocks represented an unexpected dimensional behavior with increasing the temperature. The observed behavior can be attributed to the folding ability of the blocks. In fact, the shorter PNIPAm blocks with $m = 4$ and 8 are so small to exhibit the dimensional variation with temperature enhancement. However, the largest PNIPAm block with $m = 16$ is able to change its
Figure 9. Intramolecular interactions ($E_{\text{intra}}$) per block repeating units versus $T$ for: (a) the PAM and (b) the PNIPAm end blocks.

Table 2. Dimensional parameters of the PAM and PNIPAm blocks of the CP$_x$ copolymer versus PNIPAm content, $x$, and temperature. The radius of gyration and end-to-end distance of the blocks are shown as $R_g$ and $\langle r_0 \rangle$, respectively.

| $T$ (K) | CP$_x$ | $R_g$ (Å) | $\langle r_0 \rangle$ (Å) |
|--------|-------|----------|-----------------|
|        |       | PAM      | PNIPAm         | PAM      | PNIPAm   |
| 280    | CP8   | 15.23 ± 0.03 | 4.33 ± 0.01 | 35.83 ± 0.04 | 6.01 ± 0.01 |
|        | CP16  | 16.84 ± 0.03 | 5.58 ± 0.01 | 28.73 ± 0.03 | 12.30 ± 0.02 |
|        | CP32  | 11.23 ± 0.02 | 8.46 ± 0.02 | 16.51 ± 0.03 | 17.37 ± 0.03 |
| 290    | CP8   | 15.34 ± 0.03 | 4.37 ± 0.01 | 36.28 ± 0.04 | 6.02 ± 0.01 |
|        | CP16  | 16.85 ± 0.03 | 5.63 ± 0.01 | 28.86 ± 0.03 | 12.16 ± 0.02 |
|        | CP32  | 11.03 ± 0.02 | 8.42 ± 0.02 | 16.11 ± 0.03 | 17.00 ± 0.03 |
| 300    | CP8   | 15.38 ± 0.03 | 4.42 ± 0.01 | 36.51 ± 0.04 | 5.98 ± 0.01 |
|        | CP16  | 16.87 ± 0.03 | 5.66 ± 0.01 | 28.69 ± 0.03 | 12.09 ± 0.02 |
|        | CP32  | 11.19 ± 0.02 | 8.41 ± 0.02 | 16.12 ± 0.03 | 16.54 ± 0.03 |
| 310    | CP8   | 15.42 ± 0.03 | 4.39 ± 0.01 | 36.64 ± 0.04 | 6.00 ± 0.01 |
|        | CP16  | 16.93 ± 0.03 | 5.58 ± 0.01 | 28.70 ± 0.03 | 12.08 ± 0.02 |
|        | CP32  | 11.06 ± 0.02 | 8.38 ± 0.02 | 16.81 ± 0.03 | 18.01 ± 0.03 |
| 320    | CP8   | 15.45 ± 0.03 | 4.42 ± 0.01 | 36.79 ± 0.04 | 5.97 ± 0.01 |
|        | CP16  | 16.94 ± 0.03 | 5.57 ± 0.01 | 29.13 ± 0.03 | 11.55 ± 0.02 |
|        | CP32  | 11.04 ± 0.02 | 8.21 ± 0.02 | 16.72 ± 0.03 | 18.06 ± 0.03 |
| 340    | CP8   | 15.47 ± 0.03 | 4.37 ± 0.01 | 36.90 ± 0.04 | 5.96 ± 0.01 |
|        | CP16  | 16.96 ± 0.03 | 5.50 ± 0.01 | 28.91 ± 0.03 | 11.52 ± 0.02 |
|        | CP32  | 11.09 ± 0.02 | 8.19 ± 0.02 | 16.79 ± 0.03 | 18.49 ± 0.03 |

* For the PNIPAm blocks, the values are based on an average on the values for the two blocks.
Table 3. The calculated responses versus PNIPAm percentage (x) in the copolymer structure.

| Response | x (mol%) |
|----------|----------|
|          | 8        | 16       | 32       |
| $\Delta E_{\text{int-ec}} \mid \text{PNAm}$ (kcal mol$^{-1}$, mer$^{-1}$) | -17.02   | -8.26    | 0.15     |
| $\Delta E_{\text{int-ec}} \mid \text{PNIPAms}$ (kcal mol$^{-1}$, mer$^{-1}$) | -19.24   | 17.94    | -5.99    |
| $\Delta N_{\text{AW-W}} \mid \text{PAM}$ (1/mer) | 0.15     | 0.10     | 0.01     |
| $\Delta N_{\text{AW-W}} \mid \text{PNIPAms}$ (1/mer) | 0.30     | -0.49    | 0.07     |
| $\Delta E_{\text{elc}} \mid \text{PAM}$ | 0.008    | 0.014    | 0.016    |
| $\Delta E_{\text{elc}} \mid \text{PNIPAms}$ | 0.051    | -0.003   | 0.007    |

conformation. Therefore, the PNIPAm blocks with the largest length, $m = 16$, would change easily their spatial dimensions according to their interactional behaviors (see figures 2 and 9).

The block with a negative $E_{\text{int-ec}}$ value (see figure 2) represents a good compatibility with the media and exhibits an expanded conformation in water. This issue is due to the stable intramolecular interactions with a more negative $E_{\text{int-ec}}$ amount in the block chain (figure 9). While the blocks with more positive amounts of the inter- and intramolecular interactions tend to have a collapse conformation in water to reduce their contact area with the solvent molecules. Regarding the middle block of the copolymers, the dimensional variation of the block was according to its chemical characteristics presented in table 2. In fact, the rearrangement in the special orientation of the interfacial water led to the change of intra- and intermolecular interactions between the solute and the solvent when the temperature varied.

3.6. Analysis of variance (ANOVA)
The calculated intermolecular interactional and interfacial characteristics should be considered simultaneously to choose the CPx copolymer with a proper length of the PNIPAm blocks. This investigation is very essential in order to find an efficient CPx to suggest as a useful thermo-associating copolymer to form a physical network in the aqueous media. In fact, the presented network structure (Figure S1b) needs the CPx chain consisted of a middle and end blocks with the water-compatible and thermoresponsive features, respectively. In the present work, the results of analysis of variance (ANOVA) performed by the Python programming language [48] were used to find the desirable CPx chain structure. The ANOVA provides the analysis of each calculated response in order to evaluate the statistical significance of physicochemical characteristics of the blocks [49]. In this study, the significance of the PNIPAm content, $x$, in the copolymer structure was examined to find its interaction on the responses. Firstly, a special parameter was defined to achieve the responses using the following equation.

$$\Delta \bar{Y} = \bar{Y}_2 - \bar{Y}_1$$

(6)

where symbol of $\bar{Y}$ represents the arithmetic average value of a physicochemical characteristic, which is related to the CPx blocks in the solution. The symbol of $\bar{Y}$ with subscript 1 and 2 is an average amount of the results before and after the transition zone, respectively. The temperature transition zone is the region beyond of which the remarkable changes are observed. In this study, the temperature transition zone of 310–320 K was detected on the $E_{\text{int-ec}} - T$ (figure 2) and $N_{\text{AW-W}} - T$ (figure 4) curves. It should be mentioned that the presence of the PNIPAm end blocks in the CPx structure enhanced the transition zone of the PNIPAm in comparison with their homo-polymer with transition zone of 300–310 K [20]. Accordingly, $\Delta E_{\text{int-ec}}, \Delta N_{\text{AW-W}}$ and $\Delta E_{\text{elc}}$ exhibit the behavioral changes of the PAM and PNIPAm blocks with varying the temperature. Moreover, the PNIPAm percentage in the CPx structure, $x$, was considered as a variable. The simulation results and responses versus $x$ are summarized in table 3.

The fitted models provided by the numerical coefficients [50] and related to the characteristics of the blocks were obtained from ANOVA analysis for all the responses (table 4). The coefficients in each equation (table 4) indicate the effect of the related term on that property. It should be mentioned that the positive and negative coefficients in the model have a synergistic and reducing effect on the responses, respectively. In order to find the best fraction of the end blocks in the copolymer structure to form an efficient physical network in water above the $T_{\text{cp}}$, an optimization process was performed on the fitted models (table 4).

The goal of optimization was to minimize $|\Delta E_{\text{int-ec}} \mid \text{PAM}|, |\Delta N_{\text{AW-W}} \mid \text{PNIPAms}|, |\Delta E_{\text{elc}} \mid \text{PAM}|$, and maximize $|\Delta E_{\text{int-ec}} \mid \text{PNIPAms}|, |\Delta N_{\text{AW-W}} \mid \text{PAM}|, |\Delta E_{\text{elc}} \mid \text{PNIPAms}|$, respectively. For self-assembly of the copolymer chains (shown in figure S1b), the copolymer should consist of an inner block with a good affinity to water molecules and two thermoresponsive end blocks with a suitable $T_{\text{cp}}$. In the optimization process, the desirability function approach (D) was used. This function is based on converting each response into a desirability amount, combining the individual properties into a composite function and then its optimization [51]. For more comprehensive evaluation of the variables and responses, the interaction plot was created (see figure 10). The
The simulation data indicated that the electrostatic interactions between the blocks and water molecules around the blocks amides groups in the hydration shells to captured water molecules around the blocks were measured via calculating the coordination number of the temperature. Whereas, this issue was competitive in higher amounts of thermoresponsive blocks to higher temperatures, i.e., 310 K. In the copolymers with lower x, particularly x = 8 mol%, the middle block, PAM, seems to enforce the end blocks to behave similarly, especially at the temperatures above the PNIPAm transition temperature. Whereas, this issue was competitive in higher amounts of x, i.e., x = 32 mol%. Moreover, the captured water molecules around the blocks were measured via calculating the coordination number of the water molecules around the blocks amides groups in the hydration shells to find the origin of variations in the behavior of the blocks. The simulation data indicated that the electrostatic interactions between the blocks and the media were altered with increasing the temperature through varying the hydration level, the main factor to change the hydrophilicity of the blocks. In addition, a novel parameter, \( P(\theta) \), was presented to study the role of interfacial structure of water on the blocks hydrophilicity and water ordering levels. This parameter is based on the order parameters of interfacial water in the first hydration shell, \( r \leq 0.31 \text{ nm} \) for the PAM block and \( r \leq 0.35 \text{ nm} \) for the PNIPAm one. The presented parameter contains the information of interfacial properties, water ordering, structural and hydrophilicity variations of the blocks with increasing the temperature. The simulation results showed that the blocks with a good compatibility with the media and lower intramolecular energy exhibit a higher amount of \( P(\theta) \) with the narrower, stronger and fewer numbers of peaks in the \( P\)-degree curve. Additionally, the same calculation process was also implemented in the second hydration shell of the blocks, 0.31 < \( r \leq 0.50 \) nm for the PAM and 0.35 < \( r \leq 0.55 \) nm for the PNIPAm block. In this case, the water molecules in the first hydration shell were the determinant molecules to change the blocks behaviors. The resultant data showed that the interactional and interfacial behaviors of the blocks influenced their dimensional properties. According to the ANOVA analysis as a suitable statistical method, CPx chains with \( x = 16 \text{ mol}\% \) (PNIPAm8-b-PAM84-b-PNIPAm8) seems to be a good candidate for formation of a physical network structure in water at the temperatures above the \( T_{CG} \) of the PNIPAm (Figure S1(b)). In this copolymer composition, PNIPAm/PAM = 0.19, the PAM showed a higher tendency to the media, while the affinity of the PNIPAm was decreased as the temperature was increased above \( T_{CG} \). It should be mentioned that investigation of copolymer chain composition from the interactional, conformational, and interfacial points of view with a good accuracy and efficiency is possible in the molecular scale via MD simulation. Enhancing the concentration of the

### Table 4. Linear model for the responses. The parameter of \( x \) is the PNIPAm percentage (in mol%) in the copolymer structure.

| Response | Linear model |
|----------|---------------|
| \( \Delta E_{elc - PNIPAm} \) (kcal/mol.mer) | \( -8.377-8.643 \times 8\% + 0.1167 \times 16\% + 8.5270 \times 32\% \) |
| \( \Delta E_{elc - PAM} \) (kcal/mol.mer) | \( -2.430-16.81 \times 8\% + 20.37 \times 16\% - 3.560 \times 32\% \) |
| \( \Delta N_{elc - PNIPAm} \) (1/mer) | \( 0.08867 + 0.06733 \times 8\% + 0.01133 \times 16\% - 0.07867 \times 32\% \) |
| \( \Delta N_{elc - PAM} \) (1/mer) | \( -0.04000 + 0.3400 \times 8\% - 0.4500 \times 16\% + 0.1100 \times 32\% \) |
| \( \Delta P_{elc - PNIPAm} \) | \( 0.01267-0.004667 \times 8\% + 0.001333 \times 16\% + 0.003333 \times 32\% \) |
| \( \Delta P_{elc - PAM} \) | \( 0.01833 + 0.03267 \times 8\% - 0.02133 \times 16\% - 0.01133 \times 32\% \) |

plot is used to recognize whether the variables have any interaction effect on the responses. In fact, the interaction plot helps us to interpret the interaction effects of the variables on the responses. Interactions occur when variables act together to impact the responses. Accordingly, all the variables are plotted together on the same figure to show their effects on the responses [52]. In this work, all the variables and responses, the optimum amounts of \( x \) (red line in the figure) with the desirability function of the optimization process (according to the equations presented in table 4) were shown in figure 10. According to figure 10, the PNIPAm content should be set at \( x = 16 \text{ mol}\% \) to reach an optimum copolymer composition with the desired properties for physical network formation at the temperatures above the \( T_{CG} \).

As seen in figure 10, the obtained composite desirability of 0.956 indicates the appropriate settings for getting the desirable results for all the responses [53] in table 3. Accordingly, the CPI6 seems to be an efficient thermoresponsive copolymer to form a physical network structure above \( T_{CG} \) (Figure S1(b)). Above this temperature, the tendency of the PNIPAm blocks to the media was decreased considerably.

### 4. Conclusions

In the present work, temperature dependency of a triblock copolymer including a middle hydrophilic block, i.e., PAM, and two thermoresponsive end blocks, PNIPAm, with different lengths was comprehensively studied via MD simulation. The simulation was carried out using PCFF force field to consider the solutions in a dilute regime. For this purpose, the contribution of the electrostatic and van der Waals interactions between the blocks and water versus temperature and blocks fraction was calculated. The simulation results showed that the connection of the middle and end blocks together affected the intra- and intermolecular interactional behaviors of the blocks in the media significantly. This issue shifted the transition temperature region for thermoresponsive blocks to higher temperatures, i.e., 310–320 K compared to their corresponding homopolymer, i.e., 300–310 K. In the copolymers with lower \( x \), particularly \( x = 8 \text{ mol}\% \), the middle block, PAM, seems to enforce the end blocks to behave similarly, especially at the temperatures above the PNIPAm transition temperature. Whereas, this issue was competitive in higher amounts of \( x \), i.e., \( x = 32 \text{ mol}\% \). Moreover, the captured water molecules around the blocks were measured via calculating the coordination number of the water molecules around the blocks amides groups in the hydration shells to find the origin of variations in the behavior of the blocks. The simulation data indicated that the electrostatic interactions between the blocks and the media were altered with increasing the temperature through varying the hydration level, the main factor to change the hydrophilicity of the blocks. In addition, a novel parameter, \( P(\theta) \), was presented to study the role of interfacial structure of water on the blocks hydrophilicity and water ordering levels. This parameter is based on the order parameters of interfacial water in the first hydration shell, \( r \leq 0.31 \text{ nm} \) for the PAM block and \( r \leq 0.35 \text{ nm} \) for the PNIPAm one. The presented parameter contains the information of interfacial properties, water ordering, structural and hydrophilicity variations of the blocks with increasing the temperature. The simulation results showed that the blocks with a good compatibility with the media and lower intramolecular energy exhibit a higher amount of \( P(\theta) \), with the narrower, stronger and fewer numbers of peaks in the \( P\)-degree curve. Additionally, the same calculation process was also implemented in the second hydration shell of the blocks, 0.31 < \( r \leq 0.50 \) nm for the PAM and 0.35 < \( r \leq 0.55 \) nm for the PNIPAm block. In this case, the water molecules in the first hydration shell were the determinant molecules to change the blocks behaviors. The resultant data showed that the interactional and interfacial behaviors of the blocks influenced their dimensional properties. According to the ANOVA analysis as a suitable statistical method, CPx chains with \( x = 16 \text{ mol}\% \) (PNIPAm8-b-PAM84-b-PNIPAm8) seems to be a good candidate for formation of a physical network structure in water at the temperatures above the \( T_{CG} \) of the PNIPAm (Figure S1(b)). In this copolymer composition, PNIPAm/PAM = 0.19, the PAM showed a higher tendency to the media, while the affinity of the PNIPAm was decreased as the temperature was increased above \( T_{CG} \). It should be mentioned that investigation of copolymer chain composition from the interactional, conformational, and interfacial points of view with a good accuracy and efficiency is possible in the molecular scale via MD simulation. Enhancing the concentration of the
copolymer chain near the threshold concentration ($C^*$) to observe the physical network formation leads to high computational cost which is not rational. To resolve this problem, we are improving a coarse-grained method to study the capability of the designed copolymer to form a physical network structure in our future work.

Figure 10. Interaction plot for the individual responses presented in table 3.
Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

Supporting material

The auxiliary information including supportive evidences were reported in Supporting Material (Tables S1–S3, figures S1–S4), to strengthen the claims presented in the main text.

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