

# Insights in the Thermal Volume Transition of Poly(2-oxazoline) Hydrogels

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Polymers with a lower or an upper critical solution temperature (LCST or UCST) can precipitate in a very narrow temperature range. Cross-linking of such polymers and adding them to suited solvent results in smart gels that are capable of greatly changing their dimensions with changing temperature. This transition occurs very often in a broad temperature range, which limits the applicability of smart materials. To shed some light into the design of thermo-responsive hydrogels with a narrow phase transition, poly(2-ethyl-2-oxazoline) (PEtOx), poly(2-isopropyl-2-oxazoline), and statistical copolymers of 2-butyl-2-oxazoline and 2-ethyl-2-oxazoline, respectively, are synthesized and the concentration-dependent cloud point temperatures ( $T_{cp}$ ) of the free polymers in aqueous media are determined in relation to the thermo-responsive swelling behavior of the respective hydrogels. A narrow thermal transition of the hydrogels can only be achieved when the  $T_{cp}$  of the free polymers in water is independent on the concentration. Aqueous salt solutions can render even PEtOx into a concentration independent LCST polymer. However, this salt effect does not work for hydrogels.

changes of 800%.<sup>[19]</sup> Especially, water-swollen polymer networks—hydrogels—that undergo a temperature triggered phase transition in aqueous solution are of great interest, for example, for medical applications or microfluidic devices.<sup>[20]</sup> One class of such polymers are the lower critical solution temperature (LCST) polymers, which are fully soluble in water at low temperatures and phase-separate upon heating.<sup>[21]</sup> This phase separation is indicated by a visible precipitation appearing at the cloud point temperature ( $T_{cp}$ ). The polymer volume transition at LCST can be understood as a transition from an expanded coil-like state to a collapsed state.<sup>[22–24]</sup> LCST polymers with a very narrow molecular weight distribution or a high molecular weight of more than 20.000 g mol<sup>-1</sup> undergo this phase transition within a temperature range of 1 to 2 K.

Such a narrow phase transition is usually not found for water-swollen polymer

networks that are composed of cross-linked LCST polymers, which limits the application of these interesting thermo-switching materials. Only a few thermo-responsive hydrogels with a narrow phase transition have been described so far, such as Poly(N-isopropylacrylamide) (PNiPAM),<sup>[25,26]</sup> cellulose-ether hydrogels,<sup>[27]</sup> and polyacrylamide in acetone-water mixtures.<sup>[28]</sup>


In general, highly swollen hydrogels composed of LCST polymers shrink much stronger with increasing temperature than hydrogels composed of polymers without an LCST. The strongest change of the degree of swelling occurs near the LCST of the polymer. This is the switching point, which defines the switchable dimensions and/or porosities of the hydrogel. After reaching the LCST, the polymer network still contains water, depending on the degree of cross-linking. The specific shrinkage near the LCST can be characterized by the swelling-deswelling rate  $dS/dT$ .

Hydrogels with narrow transitions have in common that they are composed of LCST polymers that are lowly cross-linked. Further, these LCST polymers show no concentration-dependency on the cloud point temperature ( $T_{cp}$ ) in solution. Based on this, the broadness of the swelling-deswelling phase transition might be explainable as follows: In cross-linked macromolecules the molecular weight between cross-links ( $M_c$ ) is the responsible for the properties of the polymers. Thus, the cross-linked LCST polymers rather act as low molecular weight polymers, which have LCST phase transitions that are strongly dependent on molecular weight distribution and the nature of the end groups.<sup>[29]</sup> Since the molecular weight distribution in cross-linked systems

## 1. Introduction

Smart or responsive polymeric materials react to external stimuli, such as temperatures ranging from room or body temperature<sup>[1,2]</sup> up to 350 °C,<sup>[3,4]</sup> chemicals or chemical vapors,<sup>[5]</sup> radiation<sup>[6]</sup> or mechanical stress,<sup>[7,8]</sup> by changing at least one of their properties, such as shape,<sup>[9,10]</sup> conductivity,<sup>[11]</sup> stiffness,<sup>[12,13]</sup> or optical properties.<sup>[14]</sup> Besides reacting to signals, smart polymers can also memorize environmental changes<sup>[15]</sup> or selectively react changing signal such as to the speed of heating.<sup>[16,17]</sup> While bulk materials, such as shape memory polymers, can reversibly switch up to the 15-fold of their initial length,<sup>[18]</sup> swollen polymer networks, referred to as gels, can reversibly undergo volume

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is often broad, this also results in a broad phase transition. If  $M_c$  is very high, the phase transition is less dependent on the dispersity, enabling a narrower phase transition as well. Further, if an LCST polymer has a concentration dependence on  $T_{cp}$ , the respective hydrogel does not show a discrete transition either.  $T_{cp}$  at a certain concentration can be translated into a degree of swelling of the cross-linked polymer at a respective temperature. Thus, the swelling is continuous and does not abruptly change with temperature. Altogether, only hydrogels composed of lowly cross-linked LCST polymers with a concentration independent  $T_{cp}$ -curve should be able to perform a narrow thermo-induced phase transition.

The present manuscript investigates this phenomenon on the example of hydrogels composed of different lowly cross-linked LCST poly(2-oxazoline)s in water and salt solutions.

## 2. Experimental Section

### 2.1. Materials

The chemicals and solvents were obtained from various suppliers and used as received.

Merck: Acetone (laboratory grade). VWR Chemicals: sodium chloride (NaCl). Acros Organics: ammonium sulfate (AS), valeronitrile, calcium hydride ( $\text{CaH}_2$ ), methyl tosylate (99%), 2-ethyl-2-oxazoline (EtOx) (99%). Alfa Aesar: guanidine hydrochloride (GHCl), zinc acetate dihydrate (98%), isobutyronitrile (99%). Fisher Scientific: ethanolamine (99+%), acetonitrile. Sigma Aldrich: dicumyl peroxide (DCP) (98%), triallyl isocyanurate (TAIC) (98%), and poly(2-ethyl-2-oxazoline) (PEtOx) with a molecular weight  $M_w$  labeled as  $500 \text{ kg mol}^{-1}$ . The number average molecular weight  $M_n$  was determined to  $122 \text{ kg mol}^{-1}$  with a polydispersity  $\mathcal{D}$  of 2.9 using size exclusion chromatography (SEC) as described in a previous work.<sup>[30]</sup>

### 2.2. Monomer Synthesis

EtOx was distilled twice from  $\text{CaH}_2$  under reduced pressure and argon atmosphere. Acetonitrile was dried with a solvent drying system from MBRAUN of type SPS-800 via activated aluminum oxide column under argon atmosphere. All these chemicals were stored in an argon atmosphere and over molecular sieves (4 Å) at  $-20^\circ\text{C}$ . All other chemicals were of analytical grade or purer and used without further purification if not noted otherwise. Methyl tosylate was distilled under reduced pressure. The syntheses of 2-iso-propyl-2-oxazoline (iPropOx) from isobutyronitrile and 2-butyl-2-oxazoline (ButOx) from valeronitrile were carried out according to literature.<sup>[31–33]</sup> The reaction times were 72 h for ButOx and 48 h for iPropOx.

### 2.3. Polymer Synthesis

For polymerization methyl tosylate (1 eq) and 5 mL of the respective monomer(s) were dissolved in 15 mL of dry acetonitrile under an argon atmosphere. The mixture was stirred in closed vessels at  $80^\circ\text{C}$  for 72 h. The product was precipitated in 150 mL

**Table 1.** Average molecular weight  $M_n$  and dispersity  $\mathcal{D}$  of Poly(2-iso-propyl-2-oxazoline) (PiPropOx).

Polymer	$M_{n,SEC} [\text{kg mol}^{-1}]$	$\mathcal{D}_{SEC} [-]$
PiPropOx	18.6	1.9
	17.7	1.9

**Table 2.** Average molecular weight  $M_n$ , dispersity  $\mathcal{D}$ , and composition of the synthesized P(EtOx-stat-ButOx) copolymers.

Polymer	$M_{n,SEC} [\text{kg mol}^{-1}]$	$\mathcal{D}_{SEC} [-]$	ButOx <sub>NMR</sub> [mol%]
P(EtOx-stat-ButOx)	23.6	2.8	15
	26.6	2.7	25
	25.2	3.0	43

cold diethyl ether ( $\text{Et}_2\text{O}$ ). The precipitant was separated from the  $\text{Et}_2\text{O}$  phase by centrifugation (5000 rpm, 5 min). After decantation of the  $\text{Et}_2\text{O}$  phase, the polymer was re-dissolved in chloroform and precipitated in ether again. The procedure was repeated three times. The resulting polymer was dialyzed against methanol for 6 h using conditioned benzoylated cellulose membranes (ZelluTrans, Roth,  $1000 \text{ g mol}^{-1}$  molecular weight cutoff). The methanol was removed using a rotary evaporator apparatus to obtain a white powder and the yield of the polymer products are  $\approx 50\text{--}70\%$ . The composition of the polymers was calculated from the  $^1\text{H NMR}$  spectrum in deuterated chloroform ( $\text{CDCl}_3$ ). The molecular weight distribution was calculated via SEC in  $N,N$ -dimethylformamide (DMF) using polystyrene standards for calibration.

### 2.4. Polymer Characterization

SEC was performed on a Viscotek GPCMax equipped with a refractive index detector (tempered to  $55^\circ\text{C}$ ) using a Tosoh TSKgel GMHHR-M (5.0  $\mu\text{m}$  pores,  $2\times + 1\times$  precolumn) column set to determine the molecular weight  $M_n$  and the dispersity  $\mathcal{D}$  of the synthesized polymers. Saline DMF + LiBr, 20 mmol, was used as eluent at  $60^\circ\text{C}$  at a flow rate of  $0.70 \text{ mL min}^{-1}$ . Calibration was performed with poly(styrene) standards (from Viscotek).

$^1\text{H NMR}$  spectra were recorded in  $\text{CDCl}_3$  using a Nanobay AVANCE-III HD-400 spectrometer with a 5 mm BBFOsmart probe from Bruker BioSpin GmbH operating at 400 MHz and a DD2-500 spectrometer with 5 mm triple resonance H(C,X) probe from Agilent Technologies operating at 500 MHz to determine the composition of the different copolymers. The  $^1\text{H NMR}$  spectra are displayed in Figures S7–S9, Supporting Information.

The results are displayed in Tables 1 and 2.

### 2.5. Network Synthesis

The different polymers were radically crosslinked with a combination of DCP (radical starter) and TAIC (crosslinker) as described elsewhere.<sup>[30,34]</sup> The crosslinking was controlled by varying the amount of DCP added to the polymer, while keeping the DCP:TAIC ratio of 1:8 constant. The amounts used in the experiments are summarized in Table 3.

**Table 3.** Mass of radical starter DCP  $m_{\text{DCP}}$  and crosslinker TAIC  $m_{\text{TAIC}}$  used to crosslink 10 g of the different polymers and the resulting  $N_{\text{rep}}$ .

Polymer	$m_{\text{DCP}}$ [g]	$m_{\text{TAIC}}$ [g]	$N_{\text{rep}}$ [-]
PEtOx	0.008	0.061	341
	0.010	0.079	318
	0.015	0.119	279
	0.020	0.164	238
	0.039	0.315	168
PiPropOx	0.049	0.395	140
	0.061	0.490	570
P(EtOx-stat-ButOx)	0.060	0.478	165
	0.061	0.485	175
	0.060	0.482	550

DCP and TAIC were dissolved in 30 mL acetone before 10 g of powdered polymer were added and stirred until a high viscous liquid formed. Subsequently, the acetone was completely removed by tempering in an oven at 80 °C for at least 24 h. The remaining mixture of polymer, DCP and TAIC was compression molded to sheets with the dimensions 50 mm × 30 mm × 1 mm (length, width, thickness) and cured for 30 min under exclusion of air in a heating press using a force of 35 kN and a temperature of 160 °C.

## 2.6. Network Characterization

The number of repeating units between crosslinks  $N_{\text{rep}}$  of the differently composed polymer-networks was calculated from the Young's modulus determined by a dynamic thermomechanical analyzer (DMA2980). The respective Young's modulus versus temperature curves are shown in Figures S1–S3, Supporting Information.

The  $N_{\text{rep}}$ s were calculated according to Flory's theory of viscoelasticity<sup>[35]</sup> in Equation (1) as the quotient of the netchain molecular weight  $M_c$  of the hydrogel and the molecular weight of the repeating unit  $M_{\text{rep}}$ , which can be expressed as

$$N_{\text{rep}} = \frac{2(1 + \vartheta) \cdot \rho(T) \cdot R \cdot T \cdot g^{\frac{1}{3}}}{E(T) \cdot M_{\text{rep}}} \quad (1)$$

where  $R$  is the universal gas constant (8.314 J mol<sup>-1</sup> K<sup>-1</sup>),  $\rho(T)$  the density,  $g$  the gel content,  $T$  the absolute temperature and  $E(T)$  the equilibrium storage modulus. The equilibrium moduli were taken from the respective DMA measurements at 160 °C. The thermal expansion coefficient was measured with a thermomechanical analyzer (TMA2940) and used for calculating the density  $\rho(T)$  to 1.01 g cm<sup>-3</sup> at 160 °C. The respective gel contents  $g$  were determined by extracting the respective network with deionized water and calculated as the ratio of the dry masses after and before the extraction. The gel contents  $g$  of the PiPropOx- and P(EtOx-stat-ButOx)-networks are displayed in Table S1, Supporting Information, while  $g$  of the PEtOx-networks can be taken from Ref. [36]. The Poisson ratio  $\nu$  is assumed as 0.4 as published in various papers.<sup>[37–39]</sup>

## 2.7. Measurement of the Degree of Swelling

The differently crosslinked hydrogels were swollen in water and water/salt mixtures of varying concentrations. After extraction of the sol content with water, the weight  $m_{\text{dry}}$  of the dried samples was determined. The samples were swollen for at least 48 h in the respective solvent at temperatures ranging between –10 and 95 °C using a Lauda Eco Silver Thermostat. The equilibrium weight of the swollen samples  $m_{\text{swollen}}(T)$  was measured at the respective temperature after removal of excess water from the samples. The swelling temperature was decreased stepwise from 95 to up to –10 °C, depending on the used solvent, and increased again stepwise to 95 °C.

The gravimetric degree of swelling  $S(T)$  is calculated as stated in Equation (2).

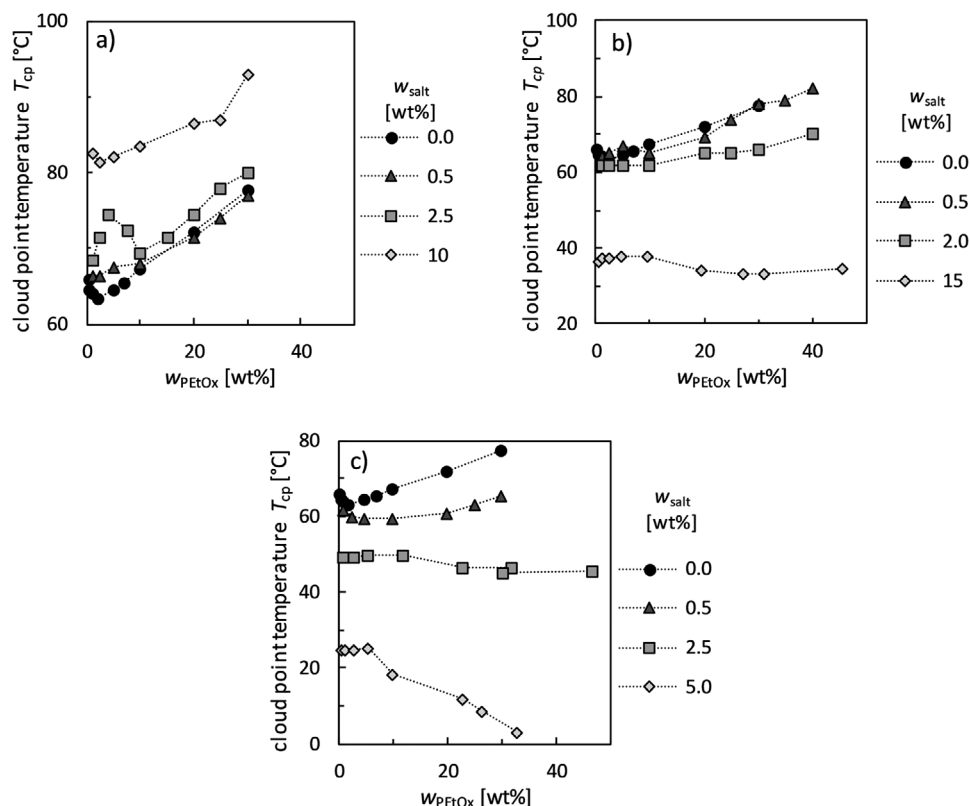
$$S(T) = \frac{m_{\text{swollen}}(T)}{m_{\text{dry}}} \quad (2)$$

## 2.8. Cloud Point Temperature $T_{\text{cp}}$

The polymers were dissolved in the chosen solvent at different concentrations and stored at 6 °C until the polymer was completely dissolved. This takes up to 2 weeks at high polymer concentrations, since the liquid becomes highly viscous. The aqueous polymer solutions were then transferred into a quartz-glass cuvette and placed into a photometer (Specord S 600 from Analytik Jena). The transmission was measured at a wavelength of 500 nm. The cuvette was heated using a peltier element with a heating rate of 30 K h<sup>-1</sup>. The temperature at which the transmission reached 50% was considered to be the cloud point temperature. The respective transmission-temperature curves are shown in Figures S4–S6, Supporting Information.

## 3. Results and Discussion

We propose that the discrete switching of LCST hydrogels depends on the concentration-dependent  $T_{\text{cp}}$  of the free polymer in aqueous solutions and on a narrowly distributed netchain molecular weight  $M_c$ . In this work, the number of repeating units between crosslinks  $N_{\text{rep}}$ , which is expressed as the quotient of the netchain molecular weight  $M_c$  of the hydrogel and the molecular weight of the repeating unit  $M_{\text{rep}}$  is used to describe and compare the differently structured hydrogels. In contrast to the poly(2-oxazoline) networks cross-linked by the end groups,<sup>[40,41]</sup> we chose to cross-link these polymers via their side groups. Previously reported PEtOx hydrogels cross-linked this way show a nearly linear decrease of swelling in water with increasing temperature over a very wide temperature range.<sup>[36]</sup> Given the concept above, the transition of PEtOx hydrogels should be more discrete in an environment, where the free PEtOx shows no concentration dependency on  $T_{\text{cp}}$ . The LCST behavior of PEtOx in aqueous salt environments has been performed for selected low polymer concentrations and these studies revealed that the LCST of PEtOx shifts to lower temperatures.<sup>[42–46]</sup> The  $T_{\text{cp}}$  versus concentration curve of PEtOx was only determined in lowly concentrated aqueous sodium chloride (NaCl) solutions, which resulted



**Figure 1.**  $T_{cp}$ -curves of PEtOx with an  $M_w$  of  $122 \text{ kg mol}^{-1}$  in water solutions with a) GHCl, b) NaCl, and c) AS at different salt concentrations. The data points from the experiments without salt were taken from Ref. [36].

in a shift of the curve to lower temperatures without changing the shape of the curve.<sup>[47]</sup> In order to find an environment that might also reduce concentration dependency of the curve, we investigated the cloud point temperatures of PEtOx with an average molecular weight  $M_w$  of  $122 \text{ kg mol}^{-1}$  in different highly concentrated aqueous salt solutions. The salts were chosen according to their classification in the Hofmeister series.<sup>[48]</sup> Kosmotropes are well-hydrated ions that cause a salting-out effect by destabilizing the hydrogen bonds between water and the polar groups of the polymer. This increases the cost of hydration and enhances hydrophobic interactions and thus, results in a decrease of the  $T_{cp}$ s and solubility with increasing salt concentration.<sup>[49–51]</sup> Chaotropes on the other hand are poorly hydrated ions, which increase  $T_{cp}$  and the solubility. GHCl was chosen as a chaotrope, NaCl as a weak kosmotropic salt and AS as a strong kosmotrope.

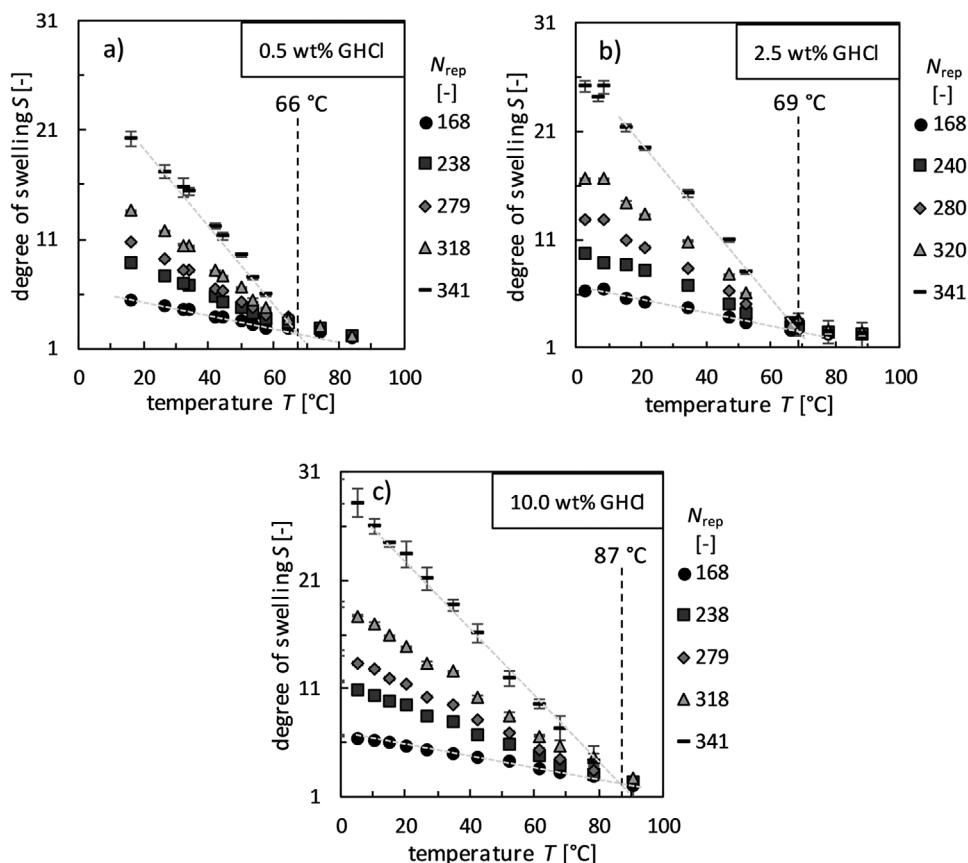
As seen in **Figure 1**, PEtOx greatly reacts to salts in the surrounding aqueous environment. The LCST of PEtOx in water is  $64 \text{ °C}$  at a PEtOx concentration of  $2 \text{ wt\%}$ . Higher polymer concentrations result in increased  $T_{cp}$ s. When adding the chaotropic salt GHCl to water (Figure 1a), the LCST increases. This effect gets more pronounced with higher salt concentrations. Interestingly, the aqueous solution of the  $2.5 \text{ wt\%}$  GHCl affords an atypical  $T_{cp}$ -curve, changing the type 1 LCST PEtOx to a type 3 LCST polymer. The latter polymers are known to show a maximum and a minimum of the  $T_{cp}$  versus concentration curve. Further increasing the salt concentration seems to diminish this effect. Al-

together, the  $T_{cp}$  of PEtOx strongly increases with higher polymer concentrations for all GHCl concentrations.

When adding the weakly kosmotropic salt NaCl (Figure 1b), the transition temperatures shift as well, but in this case to overall lower  $T_{cp}$ s. The polymer concentration dependence of PEtOx on  $T_{cp}$  becomes less pronounced with higher salt concentrations and nearly diminishes at  $15 \text{ wt\%}$  NaCl. The  $T_{cp}$  is even slightly decreasing by  $3\text{--}4 \text{ K}$  at higher polymer concentrations.

The kosmotropic salt AS also results in lowered  $T_{cp}$ s (Figure 1c). Interestingly, here the  $T_{cp}$ s of PEtOx become nearly independent on the concentration at an AS concentration of only  $2.5 \text{ wt\%}$ . Further increasing the AS concentration to  $5 \text{ wt\%}$  is not only decreasing the cloud points of PEtOx, but also renders the slope of the  $T_{cp}$  versus concentration curve negative. A possible explanation for this behavior is that the lower critical solution concentration (LCSC), the concentration at which the LCST occurs, is shifted to higher values due to the kosmotropic salts. The LCSC shifts from  $\approx 2 \text{ wt\%}$  PEtOx in pure water to  $\approx 30 \text{ wt\%}$  PEtOx at an AS concentration of  $2.5 \text{ wt\%}$ . The LCSC at  $5 \text{ wt\%}$  AS is supposedly at a higher concentration. It seems reasonable to assume that the concentration-dependence of LCST polymers in aqueous solution is diminished by salts, because they form a corona (diffusion layer) around the polymer coil, which hinders intermolecular interactions and, thus, precipitation.

Thus, all three salt solutions afford changed  $T_{cp}$ s and the two kosmotropic salts NaCl and AS at certain concentrations render PEtOx a concentration-independent LCST polymer.



**Figure 2.** Swelling curves of PEOx-networks swollen in water with GHCl-concentrations of a) 0.5 wt% (0.05 M), b) 2.5 wt% (0.27 M), and c) 10.0 wt% (1.16 M), respectively.

This should make the resulting hydrogels thermo-responsive with narrow phase transitions. The temperature-dependent swelling-deswelling of PEOx hydrogels in different media is discussed in the following. During the swelling experiments, no differences between degrees of swelling were measured during the heating or cooling cycle, even at highest salt concentration. This means the hydrogels were at the equilibrium during testing.

First, the swelling of PEOx hydrogels in aqueous GHCl is examined. To this end, solutions with salt concentrations of 0.5, 2.5, and 10 wt%, respectively, were prepared and PEOx networks with different degrees of cross-linking were swollen in these solutions.

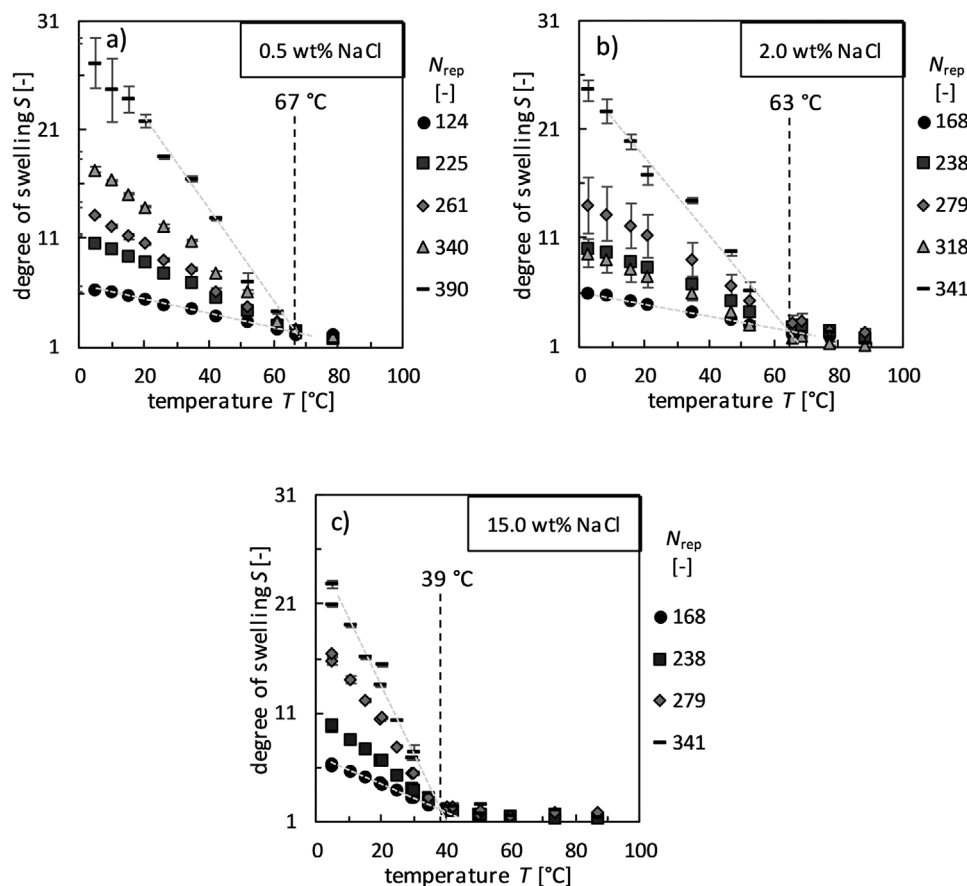
All swelling curves seen in **Figure 2** converge at a break point temperature  $T_{BP}$  similar to the one reported for PEOx in pure water.<sup>[36]</sup> The chaotropic salt GHCl has two effects on the swelling behavior of the PEOx hydrogels. On the one hand, the degree of swelling  $S$  increases for every degree of crosslinking and temperature. On the other hand,  $T_{BP}$  of the networks also increases toward higher values. Both is in accordance with the behavior of PEOx shown in Figure 1 and reported in the literature.<sup>[49–51]</sup>  $T_{BP}$  increased from 60 to  $\approx 90$  °C at a concentration of 10 wt% GHCl. The overall shape of the swelling curve did not change. This was expected, since the  $T_{cp}$ -curves of PEOx show the same concentration dependence at all GHCl concentrations.

In contrast to aqueous GHCl, a solution of NaCl in water renders PEOx into a concentration independent LCST polymer.

The results of the PEOx hydrogels swollen in differently concentrated aqueous NaCl solutions at different temperatures are shown in **Figure 3**. Instead of increasing  $S$ , like it was the case for GHCl,  $S$  decreases with increasing NaCl concentration for every degree of crosslinking and temperature.  $T_{BP}$  is also decreased from  $\approx 67$  °C for 0.5 wt% NaCl to 42 °C for 15 wt% NaCl. The change of swelling is linear over the whole temperature range in all cases. Thus, the salt does not afford a more discrete thermal switching, as would be expected from the  $T_{cp}$ -curve in Figure 1b at the highest NaCl concentration. However, the swelling-deswelling rate  $dS/dT$  slightly increases with rising NaCl concentration, most notably for the hydrogel with the lowest  $N_{rep}$ .

As seen in **Figure 4**, the kosmotropic AS, which has a strong effect on the concentration-dependence of  $T_{cp}$ , also lowers  $S$  and  $T_{BP}$  in the PEOx hydrogels with increasing concentration. The temperature-induced swelling is still linear at 0.5 and 5 wt%. In contrast, the swelling-deswelling curve in 2.5 wt% aqueous AS solution is diverging from the linear slope to a somewhat sigmoidal shape, indicating that the  $T_{cp}$ -dependence of PEOx on the concentration in this medium (Figure 1) is influencing the swelling deswelling/curve. However, the effect cannot be interpreted as discrete switching of the thermo-responsive hydrogel.

Altogether, aqueous salts particularly those with kosmotropic character are capable of influencing the concentration-dependence of  $T_{cp}$  of PEOx. Optimal salt concentrations of



**Figure 3.** Swelling curves of PEOx-networks swollen in water with NaCl-concentrations of a) 0.5 wt% (0.09 M), b) 2 wt% (0.35 M), and c) 15.0 wt% (3.02 M), respectively.

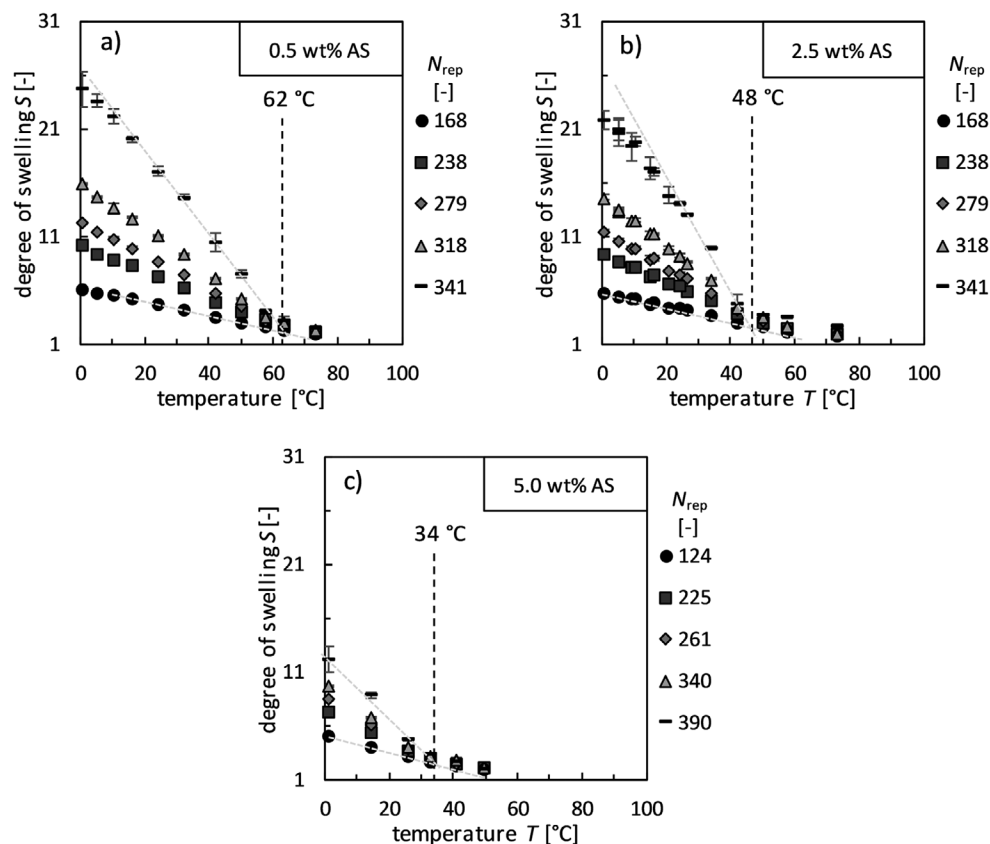
NaCl and AS have the potential to render PEOx a concentration-independent LCST polymer similar to PNiPAM in water. The PEOx hydrogels, however, only react to the aqueous salt solutions by changing their break point temperature, but still show a broad nearly linear shrinking with higher temperatures and not the expected more discrete, sigmoidal-like switching curve of PNiPAM hydrogels. Only a 2.5 wt% aqueous AS solution affords a weak effect that indicates a slight influence of the salt. One reason for the weak influence of the salts on the volume transition of PEOx hydrogels could be that the salting-out effect does not work within hydrogels, because it might need more free space to form an effective diffusion layer on the surface of the polymers. Another reason could be that the here used cross-linking strategy renders  $M_c$  very broad and, thus, the transition as well. In order to investigate this, poly(2-oxazoline)s without concentration dependence on  $T_{cp}$  were cross-linked applying the strategy above.

Poly(2-iso-propyl-2-oxazoline) (PiPropOx), which is similar to PNiPAM, was synthesized in molecular weights of  $\approx 18$  kg mol $^{-1}$ . The  $T_{cp}$  versus concentration curve in water shows the same behavior as PNiPAM (Figure 5a). Radically cross-linking this polymer with 0.4 wt% DCP and 3.2 wt% TAIC results in a polymer network that is hardly swellable in water. This is due to the crystalline character of the material, which is preserved even in swollen state.<sup>[52,53]</sup>

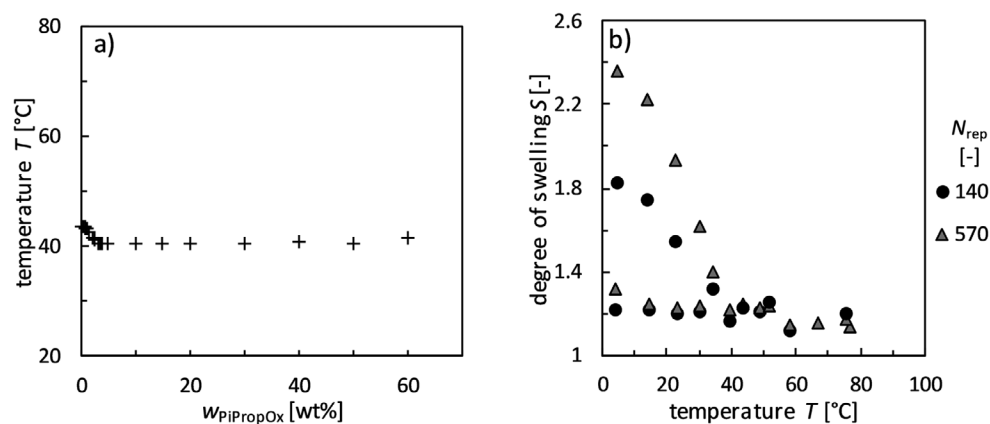
As found for the other hydrogels, the swelling curves of all differently cross-linked PiPropOx hydrogels converge at a temperature ( $T_{BP}$ ), which corresponds to the LCST of the respective PiPropOx in water (Figure 5a). In contrast to the swelling curves of PEOx in aqueous salt solutions, lowly cross-linked PiPropOx shows a somewhat sigmoidal shape, indicating a more discrete thermal switching of the PiPropOx hydrogels near LCST. However, the crystalline character of the hydrogels prevents larger changes in swelling.

In order to create stronger swellable thermo-responsive hydrogels, amorphous statistical copolymers prepared with EtOx and ButOx in different compositions with molecular weights of 23 to 27 kg mol $^{-1}$  were synthesized and cross-linked as described above. The  $T_{cp}$  versus temperature curves of the free polymers shown in Figure 6a indicate a near concentration-independence on  $T_{cp}$ . The temperature-dependent swelling curves of the cross-linked polymers shown in Figure 6b all have a sigmoidal shape.

Particularly, the hydrogel with 43 mol% BuOx shows a strong shrinkage from  $S = 3$  to  $S = 1.57$  in a narrow temperature range of 5 K near the LCST of the linear polymer. This is close to the shrinkage found for a PNiPAM hydrogel and shows that the cross-linking strategy is generally suited to synthesize thermo-sensitive hydrogels with narrow phase transitions.



**Figure 4.** Swelling curves of PETox-networks swollen in water with AS-concentrations of a) 0.5 wt% (0.04 M), b) 2.5 wt% (0.15 M), and c) 5 wt% (0.40 M), respectively.

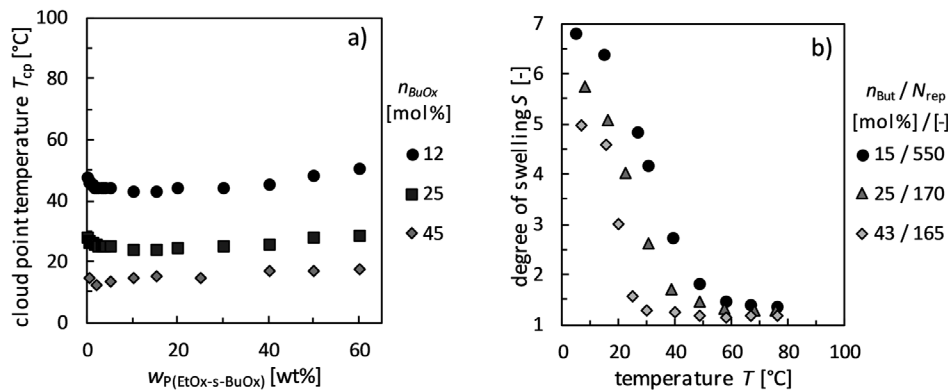


**Figure 5.** a) Cloud point curve of PiPropOx with a  $M_n$  of  $18 \text{ kg mol}^{-1}$ . The data points from the experiments were taken from Ref. [29] b) Swelling curves of PiPropOx-networks in water.

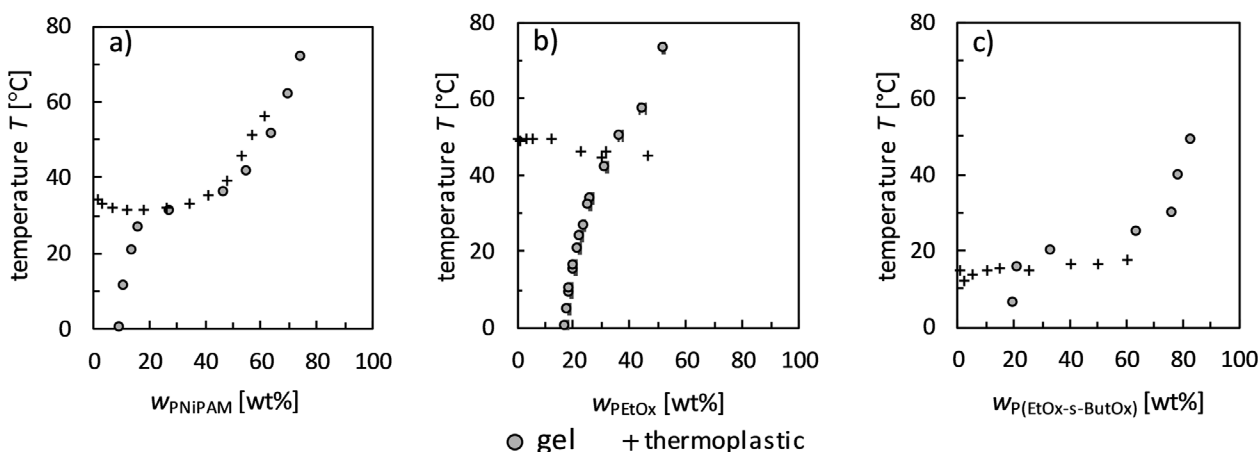
## 4. Conclusions

As shown in the present manuscript, salts of kosmotropic character are suited to diminish the concentration-dependence of  $T_{cp}$  of an LCST polymer (PETox) in water resulting in  $T_{cp}$ -curves similar to PNiPAM. It was expected that this affords for a PETox hydrogel in the respective salt solution a PNiPAM hydrogel like thermally induced volume transition (Figure 7a).

Unfortunately, the salt solutions do not lead to a narrow phase transition of thermo-sensitive hydrogels prepared from PETox, as seen by the swelling curve not following the  $T_{cp}$ -curve (Figure 7b). The concentration-dependence of LCST polymers in aqueous solution is diminished by kosmotropic salts in suited concentrations, which is an observation not yet reported and may be of potential future use. We assume the salts ions form a corona (diffusion layer) around the polymer coil, which hinders



**Figure 6.** a) Cloud point curve of P(EtOx-stat-ButOx) with a similar  $M_n$ . The data points from the experiments were taken from Ref. [29] b) Swelling curves of P(EtOx-stat-ButOx)-networks in water.



**Figure 7.** Comparison of the swelling curves and the cloud point curves of a) thermoplastic<sup>[54]</sup> and lowly cross-linked<sup>[55]</sup> PNiPAM, b) thermoplastic and lowly cross-linked ( $N_{rep} = 168$ ) PEtOx in a solution with 2.5 wt% AS, c) thermoplastic (45 mol% ButOx)<sup>[29]</sup> and lowly cross-linked P(EtOx-stat-ButOx) (43 mol% ButOx,  $N_{rep} = 165$ ).

intermolecular interactions and, thus, precipitation. This would not work in a hydrogel, because the cross-linked polymers do not provide enough free volume for such a corona.

The narrow transition of hydrogels prepared by cross-linking of concentration independent LCST polymers using the same cross-linking strategy shows that this argumentation is valid (Figure 7c). Interestingly, the salts still enable the same shift of  $T_{BP}$  in the hydrogel as it affords a shift in LCST of the free polymer in aqueous salt solution. Altogether, the present study shows that it is mandatory for near discrete switching of thermo-responsive hydrogels to lowly cross-link high molecular weight LCST polymers that have no concentration dependence on  $T_{cp}$ .

## Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

Research data are not shared.

## Keywords

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