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Synthesis and characterization of novel thermo- and salt-sensitive amphoteric terpolymers based on acrylamide derivatives

A novel linear amphoteric terpolymers based on neutral monomer — N-isopropylacrylamide (NIPAM), anionic monomer — 2-acrylamido-2-methyl-1-propanesulfonic acid sodium salt (AMPS), and cationic monomer — (3-acrylamidopropyl) trimethylammonium chloride (APTAC) were synthesized by free-radical polymerization in aqueous solution and characterized by methods of ¹H NMR and FTIR spectroscopy, TGA, GPC, Dynamic light scattering (DLS) and zeta-potential. The thermal and salt sensitivity of amphoteric ternary polymers of various compositions, particularly, [NIPAM]:[AMPS]:[APTAC] = 90:2.5:7.5; 90:5:5; 90:7.5:2.5 mol.% were studied in aqueous and aqueous-salt solutions in the temperature range from 25 to 60 °C and at the NaCl ionic strength μ interval from 10⁻³ to 1M. It was found that due to hydrophobic/hydrophilic balance, the temperature dependent conformational and phase change of macromolecular chains becomes sensitive to salt addition and allows the fine-tuning of the phase transition. In aqueous and aqueous-salt solutions, the average hydrodynamic size of amphoteric terpolymers is varied from 8 to 300 nm exhibiting bimodal distribution at room temperature. The number average (M_n) and weight average (M_w) molecular weights, polydispersity index (PDI), and zeta-potentials of amphoteric terpolymers in aqueous solutions were determined.

Keywords: amphoteric terpolymers, thermal response, salt sensitivity, phase transition temperature, hydrophobic/hydrophilic balance, core-shell structure.

Introduction

Numerous non-ionic thermally responsive homopolymers phase separate from their aqueous solutions upon heating [1]. Such macromolecules are amphiphilic, i.e. they consist of hydrophilic and hydrophobic fragments. Formation of hydrogen bonds between the hydrophilic polar groups of the polymer chain and water molecules contributes favorably to the free energy of mixing in cold water. Strength of the hydrogen bonds decreases upon heating. When the temperature of a solution is raised above the phase separation temperature, the hydrophobic backbone and/or other nonpolar groups of the polymer tend to associate. This causes intra- and intermolecular aggregation leading to a collapse of the individual polymer chains (microphase separation) and precipitation of the polymer (macrophase separation) within narrow temperature range. Poly(N-isopropylacrylamide) (PNIPAM) is the most extensively studied thermally responsive homopolymer [1–3]. PNIPAM exhibits a well-defined lower critical solution temperature (LCST) in water around 32 °C that is a critical temperature, below which all polymer-solvent compositions are miscible [4].

Basic solution properties of thermoresponsive polymers can be chemically altered. Additional highly polar or ionic groups enhance the overall solubility of these polymers in water. Thus, there are numerous examples of the poly(ethylene oxide) (PEO) usage to induce colloidal stability of the aggregates formed above

LCST [5]. This steric stabilization by nonionic hydrophilic polymers results in core-shell architectures and is typically independent of the ionic strength, assuming that the added low-molar-mass salt does not drastically change the thermodynamic quality of the aqueous solvent. Hydrophilization of the thermoresponsive polymers with ionic comonomers typically results to stable spherical particles with charged surface. However, copolymerization of PNIPAM with a weak acid may also disfavor chain expansion: the complexes between methacrylic acid and NIPAM at certain pH are able to undergo an intramolecular conformational transition from a coil state to a more compact folded state without considerable loss of the chain solubility [6].

Copolymerization of PNIPAM with two oppositely charged comonomers (terpolymer) brings up further complexity to the balance of various interactions in solution. On the other hand, a combination of several external stimuli within one macromolecule leads to the formation of multi-responsive NIPAM-based polyampholytes [7-9] that are used as smart sensors [7], drug delivery [8], and metal ion recognition systems [9].

Polyampholytes in general and quenched (strongly charged) polyampholytes in particular are macromolecules, which properties drastically change in response to various stimuli, e.g. temperature, salt, co-solvent, light, etc. [10-12]. Inclusion of thermoresponsive N-isopropylacrylamide (NIPAM) [13, 14] and N-(tert-butyl)methacrylamide [15] monomers into macromolecular chains leads to the targeted modification of conformational and macroscopic phase separation behavior of amphoteric macromolecules upon heating.

Thermally and pH responsive linear and crosslinked polyampholytes based on N-acryloyl-N-ethyl piperazine and maleic acid have recently been prepared by means of the free-radical solution polymerization [16]. The adsorption capacity of the reported hydrogels was investigated using a Congo red as a model dye varied in the range of 8.37-11.45 mg/g that corresponds to an absorption efficiency of 68-93 %. The synthesis of alternating charge-neutral polyampholytes was described via the reversible addition-fragmentation chain transfer (RAFT) statistical copolymerization of cationic styrenic and anionic N-substituted maleimide monomers [17]. The thermoresponsive behavior of the obtained charge-neutral polyampholytes was demonstrated in water and water-alcohol (methanol, ethanol and 2-propanol) mixtures.

In this paper, we report synthesis and characterization of a novel charge-balanced and charge-imbalanced amphoteric terpolymers derived from N-isopropylacrylamide (NIPAM), 2-acrylamido-2-methyl-1-propanesulfonic acid sodium salt (AMPS) and (3-acrylamidopropyl) trimethylammonium chloride (APTAC). The behavior of these ternary polyampholytes has been studied in aqueous and aqueous-salt solutions to evaluate the conformational and phase transitions upon changing of temperature and salt addition. Understanding the physico-chemical properties of the new linear NIPAM-based polyampholytes is an important criterion in the development of targeted drug delivery models.

Experimental

Materials

Monomers — N-isopropylacrylamide (NIPAM, 97 % purity), 2-acrylamido-2-methylpropanesulfonic acid sodium salt (AMPS, 50 wt.%) and (3-acrylamidopropyl) trimethylammonium chloride (APTAC, 75 wt.% in water), ammonium persulfate (APS, 98 % purity), sodium metabisulfite (SMBS, 97 % purity), sodium chloride, dialysis tubing cellulose membrane were purchased from Sigma-Aldrich Chemical Co., and used without further purification.

Methods

FTIR spectra of NIPAM-APTAC-AMPS terpolymers were recorded on a Cary 660 FTIR (Agilent, USA). ^1H NMR spectra in D_2O were registered on an impulse Fourier NMR spectrometer JNN-ECA 400 MHz (Jeol, Japan). Ultraviolet-visible (UV-Vis) spectra were collected using a Specord 210 plus, Germany. Dynamic light scattering (DLS) and zeta-potential measurements were implemented with the help of a Zetasizer Nano ZS 90 (Malvern, UK), equipped with a 633 nm laser source. Thermogravimetric analysis (TGA) was performed applying a LabSys Evo (Setaram, France).

Synthesis of polyampholyte terpolymers based on NIPAM-APTAC-AMPS

Polyampholyte terpolymers were synthesized via conventional redox initiated free radical (co)polymerization at 60 °C for 4 h. Briefly, the desired composition of the monomers was dissolved in de-ionized water at room temperature in a 50 mL beaker under constant stirring. After that the solution of monomers was filtered through a 5-micron syringe filter and purged with argon gas for 15-20 min to remove the dissolved oxygen. The solution then was carefully transferred to a screw cap vial and the dry APS and SMBS powders were added. The vial was immersed in a water bath with periodical shaking of the mixture. Later, the vial was removed from the water bath and cooled at room temperature. Obtained polymer solutions were dialyzed against distilled water for 72 h and then freeze-dried. Synthetic protocol of NIPAM-APTAC-AMPS

terpolymers is given in Table 1. It is seen that the yield of the terpolymers is high and varied from 80 to 93 wt.%.

Table 1

Synthetic protocol of NIPAM-APTAC-AMPS terpolymers

Initial monomer feed, mol. %			NIPAM, g	APTAC, g	AMPS, g	H ₂ O, mL	APS, mg	SMBS, mg	Yield, wt. %
NIPAM	APTAC	AMPS							
90	5	5	2	0.135	0.225	21.8	22	37	89.3
90	7.5	2.5	2	0.406	0.225				80
90	2.5	7.5	2	0.135	0.675				93

Determination of phase transition temperature of NIPAM-APTAC-AMPS terpolymers

The phase transition temperatures of NIPAM-APTAC-AMPS terpolymers in aqueous and aqueous-salt solutions (at the NaCl ionic strength $\mu = 0.001; 0.005; 0.01; 0.05; 0.1; 0.5$ and 1M) were determined by monitoring the change in the solution transmittance upon varying temperature. Aqueous and aqueous-salt solutions of NIPAM-APTAC-AMPS terpolymers are transparent at room temperature, i.e. when temperature is lower than LCST. When the temperature is above LCST, the solution appears as milky white and the transmittance decreases because the NIPAM-APTAC-AMPS terpolymers dehydrate and become more hydrophobic and thus less soluble in water. The phase transition experiments were carried out at $\lambda = 700\text{ nm}$ with the concentration of NIPAM-APTAC-AMPS terpolymers $0.1\text{ wt.}\%$, at the heating rate $0.5\text{ }^\circ\text{C}\cdot\text{min}^{-1}$ and in the temperature range $25\text{--}60\text{ }^\circ\text{C}$.

Results and Discussion

Synthesis and characterization of NIPAM-APTAC-AMPS terpolymers

Linear terpolymers of various compositions [NIPAM]:[APTAC]:[AMPS] = $90:5:5$; $90:7.5:2.5$; $90:2.5:7.5\text{ mol.}\%$, were synthesized via conventional redox initiated free radical polymerization (Fig. 1). The resulted terpolymer samples have randomly distributed charged units along the macromolecular chain [12].

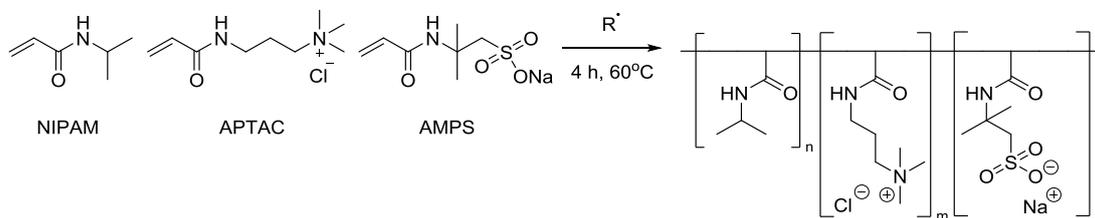


Figure 1. Schematic representation of free-radical polymerization of NIPAM, APTAC and AMPS monomers

The composition of the obtained terpolymers was established by ^1H NMR spectroscopy (Fig. 2).

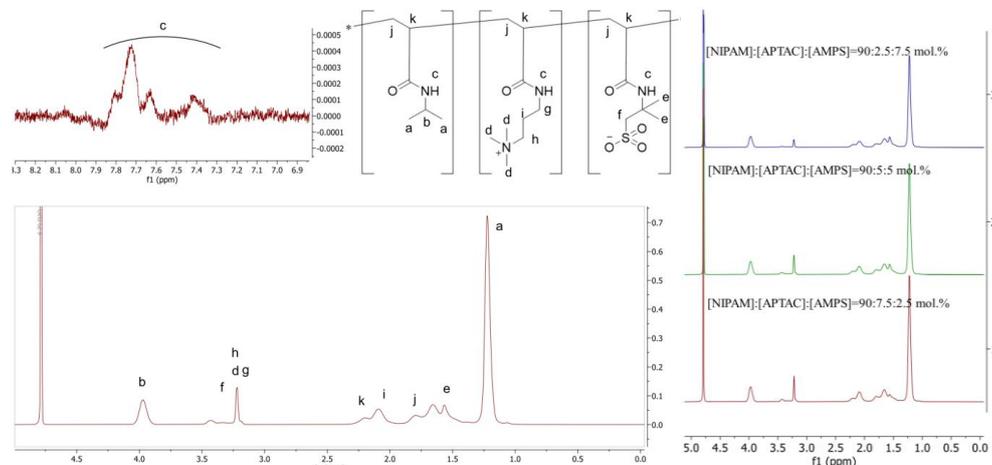


Figure 2. NMR spectra of NIPAM-APTAC-AMPS terpolymers and identification of proton signals

The resonance bands observed at 1.8 and 2.2 ppm were attributed to the protons of methylene and methine groups of the main chain of the terpolymers, respectively. Nevertheless, these peaks overlapped with the peaks of methyl and methylene protons of AMPS and APTAC. The resonance bands at 3.2–3.4 ppm were assigned to suspended protons of methyl and methylene groups in AMPS and APTAC. Since these signals were superimposed each other, the exact compositions of the NIPAM-APTAC-AMPS terpolymers could not be determined from the ^1H NMR spectra. Despite this, it can be assumed that the amount of APTAC and AMPS in terpolymers will be in good agreement with the initial monomer mixture, since the reactivity of all monomers is similar and close to one [12]. Taking into account all above reasons, it can be argued that the final composition of terpolymers possesses charge-balanced and charge-imbalanced structures. For instance, the amphoteric terpolymer $[\text{NIPAM}]:[\text{APTAC}]:[\text{AMPS}] = 90:5:5$ mol.% composed of the equal number of positively (APTAC) and negatively (AMPS) charged monomers refers to a charge-balanced polyampholyte, while the terpolymers $[\text{NIPAM}]:[\text{APTAC}]:[\text{AMPS}] = 90:7.5:2.5$ mol.% and $[\text{NIPAM}]:[\text{APTAC}]:[\text{AMPS}] = 90:2.5:7.5$ mol.% containing an excess of positively (APTAC) or negatively (AMPS) charged monomers belong to charge-imbalanced polyampholytes.

FTIR spectra of NIPAM-APTAC-AMPS terpolymers

Figure 3 illustrates FTIR spectra of the terpolymers. The wide absorption band in the region of $3200\text{--}3500\text{ cm}^{-1}$ corresponds to the secondary and tertiary amine groups, the absorption bands in the region of $2800\text{--}3000\text{ cm}^{-1}$ correspond to the asymmetric and symmetric vibrations of the CH groups. The absorption bands at 1650 and 1530 cm^{-1} belong to the vibrations of the N-substituted groups, i.e. to Amide I and Amide II, respectively. The absorption band at 1450 cm^{-1} is characteristic of bending vibrations of CH groups. The absorption band in the region of 1040 cm^{-1} corresponds to fluctuations of the S=O groups contained in the AMPS fragments.

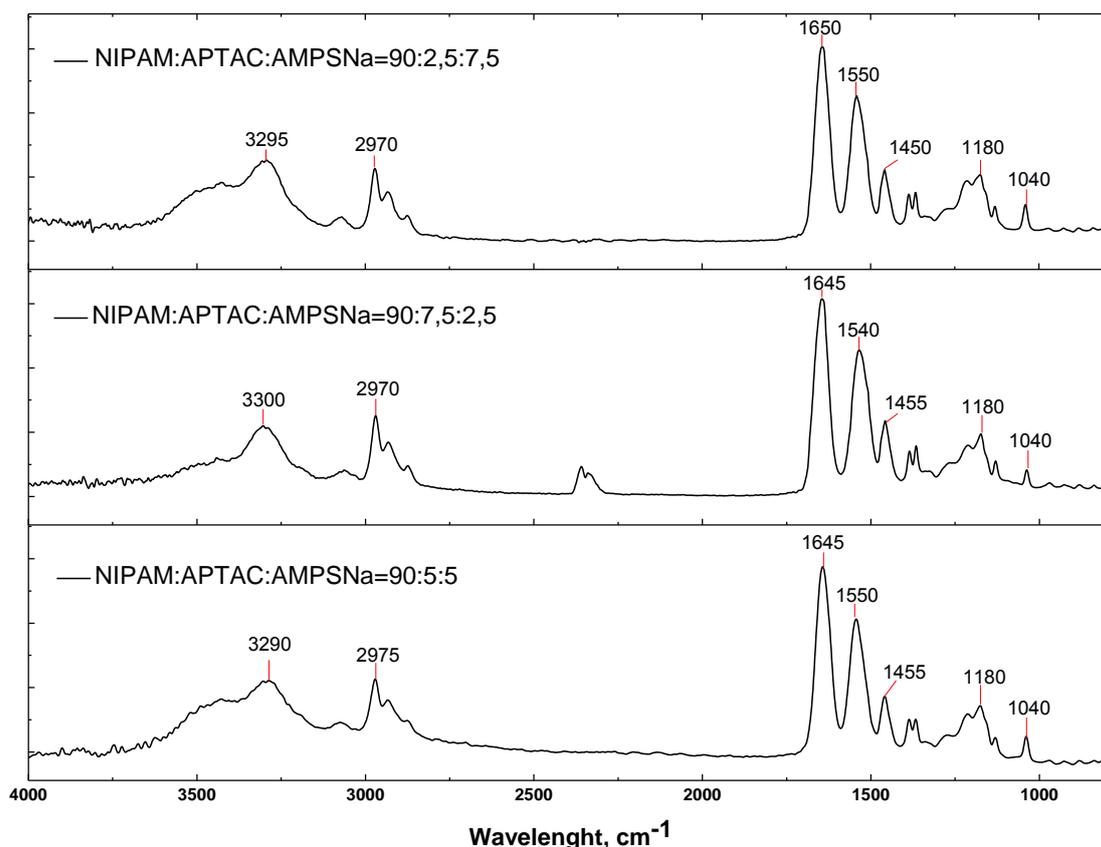
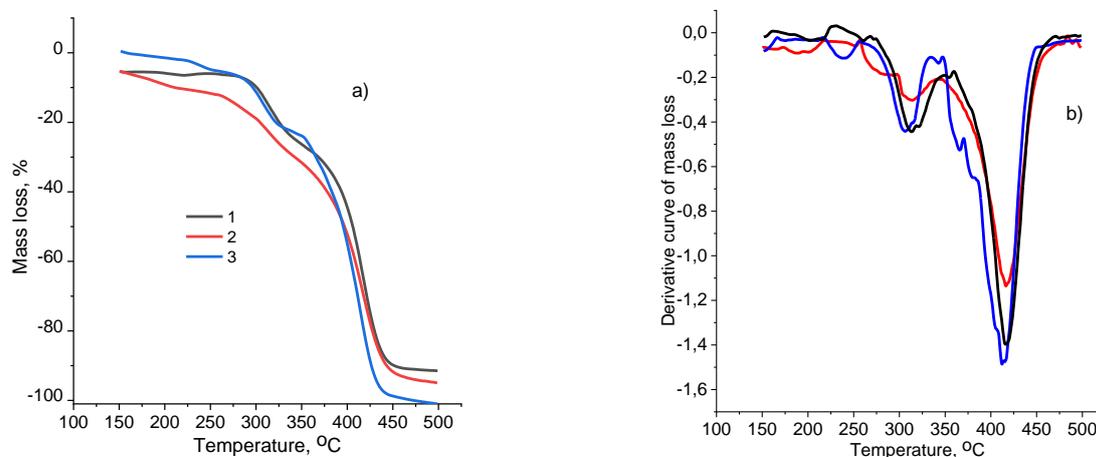


Figure 3. FTIR spectra of NIPAM-APTAC-AMPS terpolymers

TGA and DTA data of NIPAM-APTAC-AMPS terpolymers

Figure 4 shows the results of TGA and DTA. Dry terpolymers demonstrate a weight loss of approximately 5 % between room temperature and $150\text{ }^{\circ}\text{C}$. However, this additional weight loss is hard to assign to water loss alone, as the TGA and DTA data do not indicate a clear jump in this temperature range. In our

opinion, the weight loss up to approximately 200 °C may be a result of evaporation of residual water and beginning of the copolymers decomposition. The complete thermal decomposition of NIPAM-APTAC-AMPS terpolymers takes place in the temperature range from 413 to 417 °C.



Curve 1 — 90:5:5; curve 2 — 90:7.5:2.5; curve 3 — 90:2.5:7.5 mol.%

Figure 4. TGA thermograms (a) and differential curves (b) of copolymers NIPAM-APTAC-AMPS

The weight average molecular weight M_w , the number average molecular weight M_n , and the polydispersity index (PDI) of the NIPAM-APTAC-AMPS terpolymers

Table 2 represents the values of M_w , M_n and PDI for NIPAM-APTAC-AMPS terpolymers measured by gel-permeation chromatography in aqueous solution.

Table 2

The values of M_w , M_n and PDI for NIPAM-APTAC-AMPS terpolymers

Composition, mol. %			$M_w \times 10^{-5}$, Da	$M_n \times 10^{-4}$, Da	PDI = M_w/M_n
NIPAM	APTAC	AMPS			
90	5	5	1.4	4.6	≈ 3.0
90	7.5	2.5	0.5	3.1	≈ 1.6
90	2.5	7.5	2.5	6.4	≈ 4.0

The M_w of terpolymers is in the range of $(0.5-2.5) \cdot 10^5$ Dalton, the M_n is $(3.1-6.4) \cdot 10^4$ Dalton. The PDI of terpolymers is between 1.6 and 4.0. The broad molecular weight distribution of terpolymers is probably due to the use of free-radical polymerization method, which does not allow precise control of the molecular weights of polymers.

Zeta-potentials (ζ) of NIPAM-APTAC-AMPS amphoteric terpolymers in aqueous solutions at 25 °C

Zeta potentials of charge-balanced and charge-imbalanced NIPAM-APTAC-AMPS terpolymers in aqueous solution were measured as a function of polymer concentration (data is not shown). The terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% with the excess of positively charged APTAC monomer independently on the polymer concentration (0.01–0.1 wt.%) has $\zeta = +7 \pm 1$ mV. In contrast, the amphoteric terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.% with the excess of negatively charged AMPS monomer slightly depends on concentration (0.01–0.1 wt.%) and has $\zeta = -16 \pm 3$ mV. It can be expected that in the ideal case, when the amount of positive and negative charges in [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% is equal and compensates each other, the total charge of macromolecular chain is electroneutral, the value of ζ should be around zero. However, in our case, the ζ value of the charge-balanced amphoteric terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:5:5 deviates from zero and is slightly positive independently on polymer concentration (0.01–0.1 wt.%). Its value equals $+2 \pm 1$ mV probably due to a tiny excess of the positively charged APTAC monomer. Thus, the fact that we have synthesized the charge-balanced and charge-imbalanced amphoteric terpolymers is obvious.

The average hydrodynamic size and the phase transition temperature of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% in pure water and salt solutions

The average hydrodynamic size (R_h) and the phase transition temperature ($T_{p.t.t.}$) of charge-balanced amphoteric terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% in deionized (DI) water and in NaCl solutions ($\mu = 0.001; 0.005; 0.01; 0.05; 0.1; 0.5; 1\text{ M NaCl}$) are presented in Figures 5 and 6.

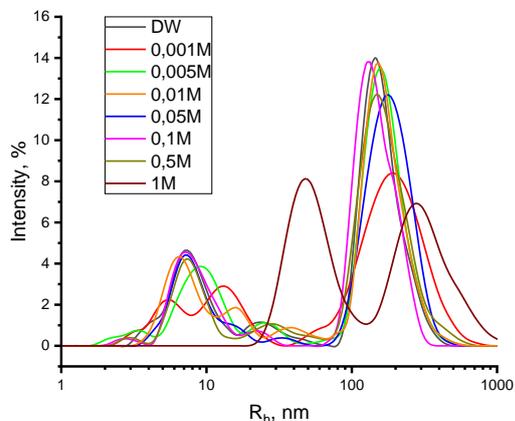


Figure 5. The effect of the μ on the average hydrodynamic size of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% at 25 °C

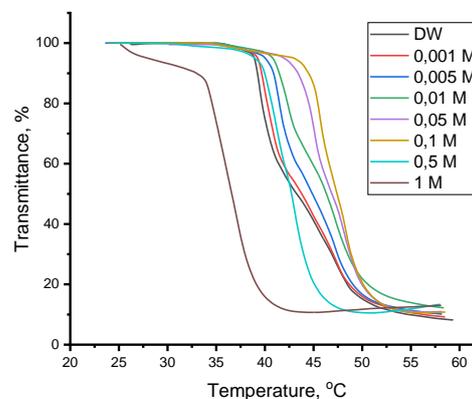


Figure 6. Temperature dependent phase behavior of terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% at various μ

Figure 5 illustrates presence of two types of particles in solutions. Average peak value of R_h of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% equals to 7.4 and 150 nm in pure water. Evidently that 7.4 nm represents individual macromolecules, whereas 150 nm corresponds to multimolecular aggregates. The relative contribution of the aggregates in the intensity distributions is large due to their high mass, though they are minor by their number. The individual chains of amphoteric terpolymer in deionized water may be imagined as well swollen coils since water is a good solvent for PNIPAM at room temperature. However, $R_h=7.4$ nm is not big enough for such a molecule. One should remember that the oppositely charged repeating units of the chain are attracted to each other and can form ion pairs similar to intrapolyelectrolyte complexes in pure water. Their low-molar-mass counterions become free, leave to the bulk water and this way increase the total entropy of the system. Addition of low-molar-mass salt makes this entropic effect less pronounced: added salt breaks the intramolecular ionic pairs and chains become effectively more charged with increasing the ionic strength, though the number of charges along each chain remains constant. Coulomb interactions of ion pairs act on longer distances than H-bonds between PNIPAM and water and create polar regions of bound water within each coil, which enhance total stability of the copolymer against phase separation upon heating.

The model presented above is fully supported by experiments. The phase transition temperature ($T_{p.t.t.}$) of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% in DI water equals to 38.7 °C (see Table 3) and bigger than $T_{p.t.t.}$ of poly(NIPAM) itself (that is 32 °C) [4]. When the ionic strength (μ) increases, the ion pairs between AMPS and APTAC break apart, copolymer becomes effectively more charged and $T_{p.t.t.}$ shifts to the higher values. At μ above 0.1 M, all ionic pairs are not only broken but added salt screens all the charges of copolymer and original thermal behavior of pure poly(NIPAM) is recovered.

Two phenomena should be discussed separately: 1) Aggregates formed by the copolymer above the phase transition temperature ($T_{p.t.t.}$) are stable against further precipitation; 2) Transmittance vs. temperature curves show a shoulder above $T_{p.t.t.}$ at μ below 0.1 M. Formation of neutral colloiddally stable multimolecular aggregates by poly(NIPAM) has been well-documented and mechanisms responsible for their stability have been suggested [1, 5]. Existence of hydrated ion pairs from AMPS and APTAC within coils additionally contribute to the stability of particles above $T_{p.t.t.}$. Naturally, when aggregates are formed and dehydrate upon further heating, charged units cannot stay inside the organic surrounding, and they migrate to the surface of the aggregates, which is observed as a shoulder in the transmittance curves (Figure 6).

The conformational change of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% in pure water upon heating is schematically shown in Figure 7. Dehydration of NIPAM fragments and intensification of hydrophobic

interactions with increasing of temperature lead to the formation of a high-density hydrophobic NIPAM “core” surrounded by low-density hydrophilic “shell”. The latter consists of AMPS and APTAC monomers that preserve the whole macromolecules in water and protect them from precipitation.

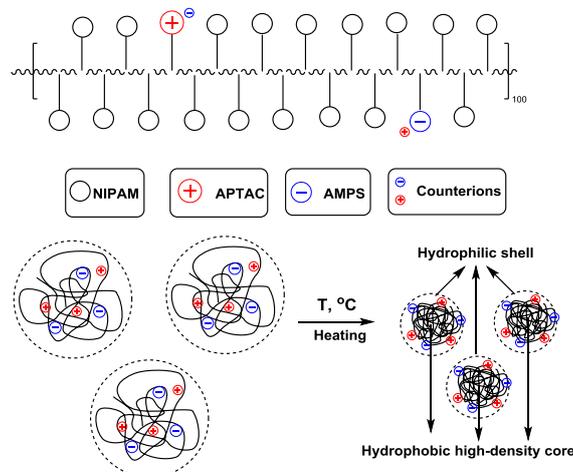


Figure 7. Schematic representation of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% terpolymer in DI water upon heating

At the interval of the $\mu = 0.001\text{-}0.1\text{M}$ NaCl, the mean R_h values are equal to 7 ± 1 nm and 175 ± 25 nm. However, the value of $T_{p.t.t.}$ gradually increases from 39.88 °C in DI water to 46.08 °C in 0.1M NaCl upon heating (Table 3).

Table 3

The effect of the ionic strength (μ) on the phase transition temperature of [NIPAM]:[APTAC]:[AMPS]=90:5:5 mol.%

μ , mol·L ⁻¹ (NaCl)	DI water	0.001	0.005	0.01	0.05	0.1	0.5	1.0
$T_{p.t.t.}$, °C	39.88	40.29	41.93	41.96	45.5	46.08	42.96	36.84

These results can be explained as follows. Upon heating the swollen in DI water macromolecular chains of amphoteric terpolymer due to strengthening of the hydrophobic interactions are supposed to transform to high-density hydrophobic “core” consisting of mostly NIPAM monomers. At the same time, an increase in the ionic strength adjusted by NaCl that strengthens the compactization of the NIPAM chains, but weakens the electrostatic attraction between positively and negatively charged monomers. As a result, the hydrophilic edge (or a low-density hydrophilic “shell”) consisting of AMPS and APTAC monomers is formed on the surface of compact macromolecules and preserves the polymer particles from precipitation (Fig. 8).

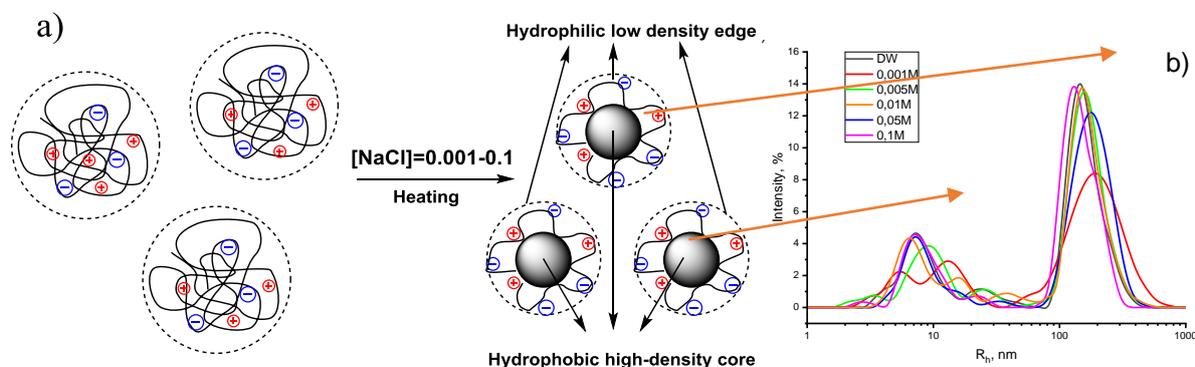


Figure 8. Schematic representation of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% macromolecules at the interval of $\mu = 0.001\text{-}0.1\text{M}$ NaCl upon heating (a) DLS data at $\mu = 0.001\text{-}0.1\text{M}$ NaCl (b)

However, in 1M NaCl solution the R_h maxima are shifted to 50 and 300 nm, respectively. Apparently, the macromolecular coils are aggregated at high μ . This statement is confirmed by the effect of temperature on the phase behavior of terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% in dependence of μ as represented in Figure 9. At the interval of μ between 0.5 and 1M NaCl the $T_{p.t.t.}$ decreases from 39.5 °C to 33.2 °C (see Table 3). The reversal or backward change of the $T_{p.t.t.}$ in 0.5 and 1M NaCl solutions is probably due to aggregation of small particles to bigger one as demonstrated in Figure 9 and confirmed by DLS data. However, in 0.5 and 1M NaCl solutions the precipitation of aggregated macromolecular particles does not occur because the hydrophilic “shell” on the surface of such aggregates preserves them from precipitation.

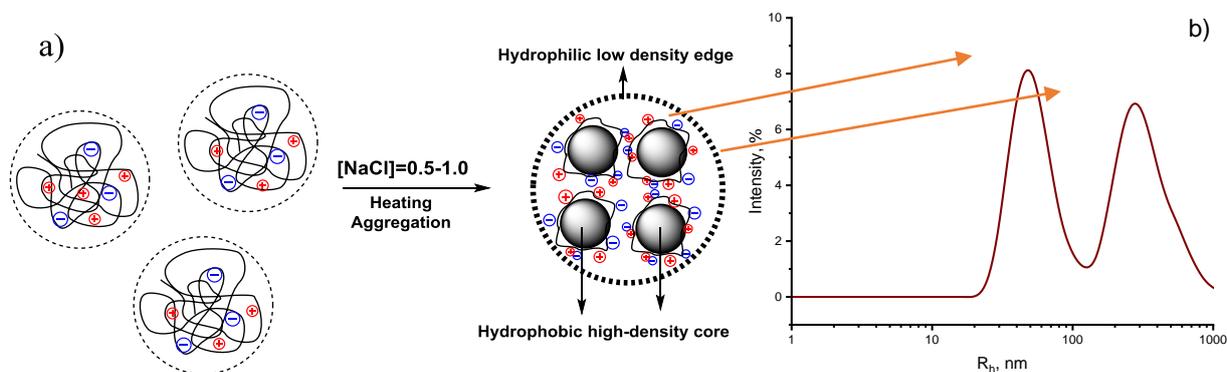


Figure 9. Schematic representation of macromolecular size of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% at the ionic strength 0.5 and 1M NaCl upon heating (a) and DLS data in 1M NaCl (b)

Thus, as follows from the obtained results, the macromolecular chains of [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.% in DI water collapse upon heating due to the dehydration of NIPAM chains and enhancement of hydrophobic interactions. At the interval of $\mu = 0.001-0.1$ M NaCl macromolecular chains gradually shrink upon heating but preserve the solubility in spite of the turbidity. At high ionic strength $\mu = 0.5-1$ M NaCl the formation of bigger aggregates is observed.

The average hydrodynamic size and phase transition temperature of [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.% in aqueous and aqueous-salt solutions

Figure 10 represents the average hydrodynamic size of amphoteric terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.% in DI water and in NaCl solutions ($\mu = 0.001; 0.005; 0.01; 0.05; 0.1;$ and 0.5M). In 1M NaCl the terpolymer was insoluble. The average hydrodynamic radius of macromolecules R_h at $\mu = 0.001; 0.005; 0.01; 0.05; 0.1$ M NaCl is about 20-35 nm, but in 0.5M NaCl solution two obvious peaks are observed with R_h equal to 20 and 200 nm.

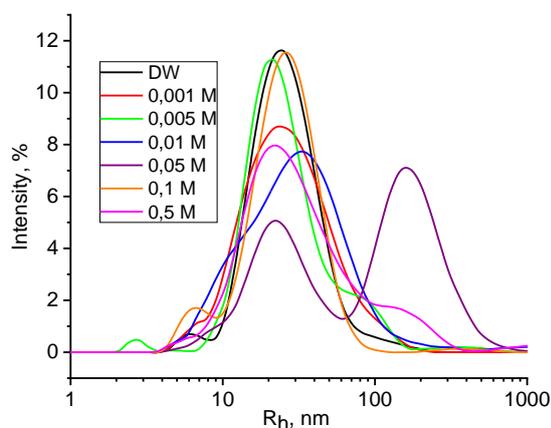


Figure 10. Effect of the μ on the average hydrodynamic size of [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.% at 25 °C

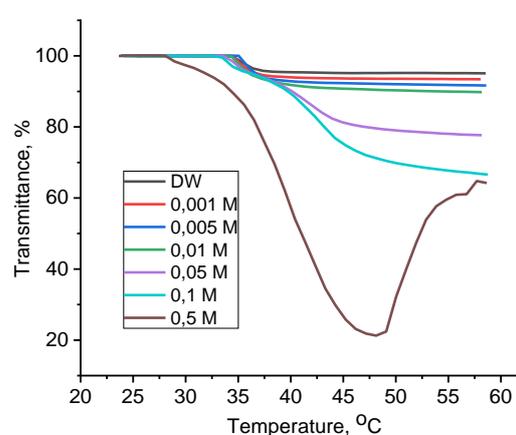


Figure 11. Temperature dependent phase behavior of terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.% at different μ

The effect of temperature on the phase behavior of terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.% in DI water and at $\mu = 0.001\text{--}0.5\text{M}$ NaCl is demonstrated in Table 4 and Figure 11.

Table 4

The effect of the ionic strength (μ) on the phase transition temperature of [NIPAM]:[APTAC]:[AMPS]=90:2.5:7.5 mol.%

μ , mol·L ⁻¹ (NaCl)	DI water	0.001	0.005	0.01	0.05	0.1	0.5	1.0
$T_{p.t.t.}$, °C	35.45	35.38	35.98	35.33	34.41	34.48	39.42	insoluble

At the interval of μ between 0.001 and 0.05M NaCl the $T_{p.t.t.}$ is slightly shifted to lower or higher temperatures. In this range a gradual increase of the turbidity is observed. Increasing of the μ up to 0.5M NaCl leads to early phase separation of the polymer at 28 °C. At $\mu = 0.5\text{ M}$ NaCl there are fractures on the turbidity curves and the transparency decreases in the range of 40–47.5 °C. Further heating of polymer solution at $T > 47.5\text{ °C}$ causes the precipitation of polymer chains due to the salting-out effect, which leads to a significant increase in transparency.

The average hydrodynamic size and phase transition temperature of [NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% in aqueous and aqueous-salt solutions

In case of [NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% terpolymer, the average hydrodynamic size of macromolecules changes insignificantly as a function of the ionic strength (Fig. 12). The average size of R_h lies in the regions of 6–8 nm and 150–300 nm.

The effect of temperature on the $T_{p.t.t.}$ of the terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% at different ionic strength of the solution is shown in Table 5 and Figure 13.

Table 5

The effect of the ionic strength (μ) on the phase transition temperature of [NIPAM]:[APTAC]:[AMPS]=90:7.5:2.5 mol.%

μ , mol·L ⁻¹ (NaCl)	DI water	0.001	0.005	0.01	0.05	0.1	0.5	1.0
$T_{p.t.t.}$, °C	38.98	37.16	38.35	38.85	42.33	43.2	37.21	37.51

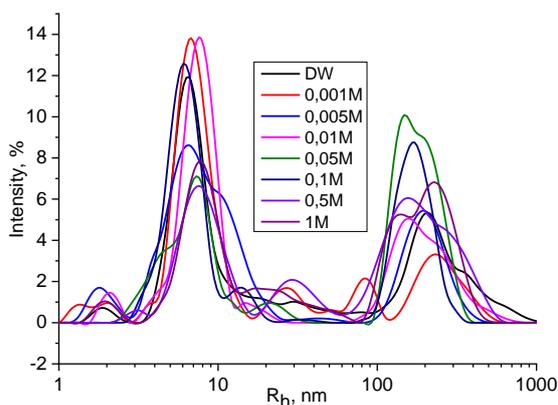


Figure 12. Effect of the ionic strength of the solution on the average hydrodynamic size of [NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% at 25 °C

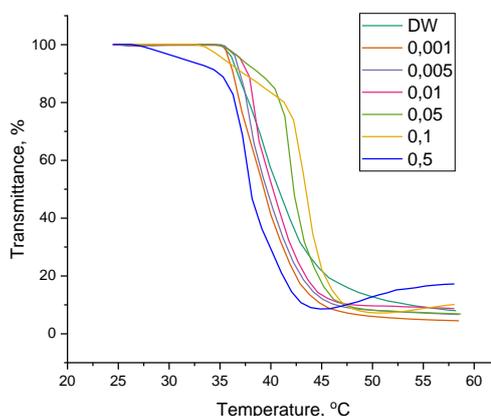


Figure 13. Temperature dependent phase behavior of [NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% at different μ

Increasing of the μ in the range of 0.001–0.1M gradually shifts the $T_{p.t.t.}$ to higher temperatures. This is probably due to the screening of positively charged APTAC fragments by NaCl counterions. However, at a higher ionic strength $\mu = 0.5\text{--}1.0\text{M}$ NaCl the $T_{p.t.t.}$ shifts backward, e.g. to lower temperatures. Apparently, at a high NaCl concentration, the polyelectrolyte effect caused by the excess of positive charges is completely suppressed, and the macromolecular chain becomes close to neutral and more hydrophobic. An increase in temperature enhances the hydrophobic interactions and aggregation of macromolecular chains. Thus, in aqueous-salt solutions the behavior of charge balanced amphoteric terpolymer

([NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.%) differs from the properties of unbalanced polyampholytes ([NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% and [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.%). A small excess of positive or negative charges in terpolymers leads to the predominance of polyelectrolyte effect. Expanded in pure water polyelectrolyte chains shrink in salt solution due to the screened electrostatic repulsion between uniformly charged monomers (polyelectrolyte effect). Compact structure of charge-balanced quenched polyampholyte unfolds in salt solution due to screening of the electrostatic attraction between oppositely charged monomers (the antipolyelectrolyte effect).

Conclusions

The structure of new amphoteric terpolymers NIPAM-AMPS-APTAC, synthesized by free-radical polymerization of neutral (NIPAM), anionic (AMPS), and cationic (APTAC) monomers was identified by ^1H NMR and FTIR spectroscopy. In aqueous and aqueous-salt solutions, the dynamic light scattering (DLS) data show a bimodal distribution of the average hydrodynamic size of amphoteric macromolecules. Zeta-potential measurements confirm the formation of charge-balanced and charge-imbalanced amphoteric terpolymers. In aqueous and aqueous-salt solutions the amphoteric terpolymers based on NIPAM-AMPS-APTAC demonstrate the temperature-responsive behavior upon heating. The temperature and salt-induced phase transition of amphoteric terpolymers is associated with the hydrophobic-hydrophilic balance and the formation of high-density of hydrophobic “core” surrounded by low-density hydrophilic “shell”. In case of charge-balanced amphoteric terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:5:5 mol.%, the phase transition temperature increases and passes through the maximum at $\mu = 0.1\text{M}$ NaCl. A similar phenomenon is observed for the charge-imbalanced terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:7.5:2.5 mol.% with the excess of cationic monomer (APTAC). The temperature-dependent phase transition of charge-imbalanced terpolymer [NIPAM]:[APTAC]:[AMPS] = 90:2.5:7.5 mol.% with the excess of anionic monomer (AMPS) exhibits complicated behavior at high ionic strength up to phase separation. The phase transition temperature of amphoteric terpolymers can be finely tuned to the desired one by adding the salt. The combination of different stimuli within one macromolecular chain can open up a wide space of sensing applications, in particular as a drug delivery system.

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Акриламид туындыларының негізінде алынған жаңа термо- және тұзға сезімтал амфотерлік терполимерлерді синтездеу және зерттеу

Бейтарап мономер N-изопропилакриламид (НИПАМ), аниондық мономер — 2-акриламидо-2-метил-1-пропансульфон қышқылының натрий тұзы (АМПС) және (3-акриламидопропил) триметиламмоний хлориді (АПТАХ) негізіндегі жаңа жоғары зарядталған полиамфолиттер сулы ерітіндіде бос радикалды полимерлену жолымен синтезделді және ¹H ЯМР және ИК-Фурье спектроскопиясымен, ТГА, ГӨХ, ДЛС және дзета-потенциал әдістерімен сипатталды. Өртүрлі құрамдағы үштік амфотерлі полимерлер, атап айтқанда [НИПАМ]:[АМПС]:[АПТАХ] = 90:2.5:7.5; 90:5:5; 90:7.5:2.5 мол.%, температураның 25 пен 60 °C аралығында және ерітіндінің иондық күшінің 10⁻³ пен 1M NaCl аралығында зерттелді. Гидрофобты/гидрофильді тепе-теңдіктің арқасында макромолекулалық тізбектердің температураға байланысты конформациялық және фазалық өзгерісі тұз қосылыстарына сезімтал болып, фазалық ауысулардың жақсы реттелуіне мүмкіндік беретіні анықталды. Су мен тұзды-су ерітінділеріде амфотерлі терполимерлердің орташа гидродинамикалық өлшемдері бөлме температурасында бимодальды таралуды көрсете отырып, 8-ден 300 нм-ге дейін өзгереді. Амфотерлі терполимерлердің сандық орташа (M_n) және салмақтық орташа (M_w) молекулалық салмақтары, полидисперстілік индексі (ПДИ) және дзета потенциалдары су ерітіндісінде анықталды.

Кілт сөздер: күшті зарядталған амфотерлі терполимерлер, термосезімталдық, тұзғасезімталдық, конформациялық және фазалық ауысу, гидрофобты/гидрофильді тепе-теңдік, ядро-қабықша құрылымы.

А.Е. Аязбаева, А.В. Шахворостов, Т.М. Сейлханов, В.О. Асеев, С.Е. Құдайбергенов

Синтез и исследование новых термо- и солечувствительных амфотерных терполимеров на основе производных акриламида

Новые сильнозаряженные линейные полиамфолиты на основе нейтрального мономера — N-изопропилакриламида (НИПАМ), анионного мономера — натриевой соли 2-акриламидо-2-метил-1-пропансульфоновой кислоты (АМПС) и катионного мономера — (3-акриламидопропил) триметиламмоний хлорида (АПТАХ) синтезированы свободнорадикальной полимеризацией в водном растворе и охарактеризованы методами ¹H ЯМР и ИК-Фурье спектроскопии, ТГА, ГПХ, ДЛС и дзета-потенциала. Термо- и солечувствительность амфотерных тройных полимеров различных составов, в частности, [НИПАМ]:[АМПС]:[АПТАХ] = 90:2.5:7.5; 90:5:5; 90:7.5:2.5 мол.%, изучена в диапазоне температур от 25 до 60 °C и в интервале ионной силы раствора от 10⁻³ до 1M NaCl. Найдено, что благодаря гидрофобно-гидрофильному балансу, конформационные и фазовые изменения макромолекулярных цепей в зависимости от температуры становятся чувствительными к добавкам соли и позволяют тонко регулировать фазовые переходы. В воде и водно-солевом растворе среднегидродинамические размеры амфотерных терполимеров изменяются в пределах от 8 до 300 нм, проявляя бимодальное распределение при комнатной температуре. Определены среднечисленные (M_n) и средневесовые (M_w) молекулярные массы, индекс полидисперсности (ИПД) и дзета-потенциалы амфотерных терполимеров в водном растворе.

Ключевые слова: сильнозаряженные амфотерные терполимеры, термочувствительность, солечувствительность, конформационный и фазовый переходы, гидрофобно/гидрофильный баланс, структура «ядро–оболочка».

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