Effect of sodium dodecyl sulfate on solution behavior of thermoresponsive polymers and their mixtures

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Abstract: The process of thermal aggregation in water of thermoresponsive (co)polymers poly(N-isopropylacrylamide) PNIPAM, poly{[di(ethylene glycol) monomethyl ether methacrylate]-co-[oligo(ethylene glycol) monomethyl ether methacrylate]} P(D-co-O$_{300}$), the bioconjugate of P(D-co-O$_{300}$) with the peptide metenkephalin (Met$_{Dns}$) and their mixtures was investigated. The effect of the SDS (sodium dodecyl sulfate) addition on the behavior of thermoresponsive chains was evaluated by UV-Vis (ultraviolet-visible spectroscopy) and DLS (dynamic light scattering) methods. It was found that the presence of SDS influences the polymer transition temperature. It also reduces the size of the aggregates, which explains the higher transmittance value of the solution above phase transition.

Keywords: thermoresponsive polymers, polymer mixtures, SDS, aggregation, PNIPAM, OEGMA.

Wpływ dodecylosiarczanu sodu na zachowanie termoczułych polimerów i ich mieszanin w roztworze

Streszczenie: Zbadano proces termicznej agregacji w wodzie termoczułych (ko)polimerów PNIPAM [poli(N-izopropyloakryloamidu)], P(D-co-O$_{300}$) [poli(metakrylanu eteru monometylowego glikolu dietylenowego-co-metakrylanu eteru monometylowego glikolu oligoetylenowego)], koniugatu P(D-co-O$_{300}$) z peptydem metenkefaliną (Met$_{Dns}$) oraz ich mieszanin. Metodami UV-Vis (spektroskopia w ultrafiolecie i świetle widzialnym) i DLS (dynamiczne rozpraszanie światła) oceniono wpływ dodatku dodecylosiarczanu sodu (SDS) na zachowanie termoczułych łańcuchów. Stwierdzono, że obecność SDS wpływa na temperaturę przejścia polimerów. Powoduje także zmniejszenie rozmiaru agregatów, co wyjaśnia większą wartość transmitancji roztworu powyżej przejścia.

Słowa kluczowe: polimery termoczułe, mieszaniny polimerów, SDS, agregacja, PNIPAM, OEGMA.

Thermoresponsive polymers are a group of polymers that reacts on the changes in temperature by changing their properties. In dilute water solutions thermoresponsive polymers change fast and reversible from a hydro- philic to hydrophobic leading under proper conditions to formation of particles called mesoglobules.

Over past decades thermoresponsive polymers gain interest in many different fields of science and nanotechnology. One of the most promising field of application of thermoresponsive polymers is nanomedicine. To be applied in this field materials must meet a number of conditions like sizes, shapes, and surface properties. One of the main applications of thermoresponsive polymers are nanocarriers

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of biologically active substances [1–4]. This makes the size of polymer particles a question of great importance.

Studies on thermoresponsive polymers were expanded by investigation of solutions containing polymer mixtures [5–9]. Ieong *et al.* [5] described behavior of mixtures of poly(*N*-vinyl piperidone) of different molar masses. They have also studied mixtures of polymers from poly[oligo(ethylene glycol) monomethyl ether methacrylate] (OEGMA) family:poly(diethyleneglycidyl methacrylate) PDEGMA (M_n = 11 400 g/mol), P(OEGMA$_{475}$-DEGMA) (M_n = 20 500 g/mol) and POEGMA$_{300}$ (M_n = 20 100 g/mol). Mixtures of closely related polymers like poly(*N*-isopropylacrylamide) and poly(*N*-isopropylmetacrylamide) were studied by Djokpé and Vogt [6] and by Starovoytova *et al.* [7]. Lately we have shown that structures formed in mixed systems of thermoresponsive polymers depend on heating protocol [8], especially on the rate of temperature increase.

For a given polymer the size of mesoglobules is influenced by polymer molar mass, solution concentration and the heating rate. The size can be also controlled by the presence of salt or surface active agents in polymer solution.

The polymer-surfactant interactions are determined by the type of surfactant's hydrophilic "head" and the length of the hydrophobic "tail" [9]. In the solution, the hydrophobic "tails" of the surfactant interact with the hydrophobic fragments of the polymer chain. This limits the interchain association and the contact of the polymer with water. At the same time, the hydrophilic portion of the surfactant enlarges the solvation sphere around the polymer. This leads to an increase of the temperature at which phase separation takes place. The strength of this effect depends on the length of the hydrophobic "tail" of the surfactant as was demonstrated for PNIPAM transition temperature in the presence of fatty acid sodium salts (from capronic to myristic acid) [10, 11].

The structures formed in thermoresponsive polymer/surfactant solutions are shown in Fig. 1. Above the T_{CP} (the cloud point of the polymer), the surfactant may stabilize the mesoglobules only if the number of surfactant molecules remains in a such ratio to the amount of polymer (s/p) that the surfactant can surround the nascent mesoglobules. When s/p increased at the critical aggregation concentration (CAC),
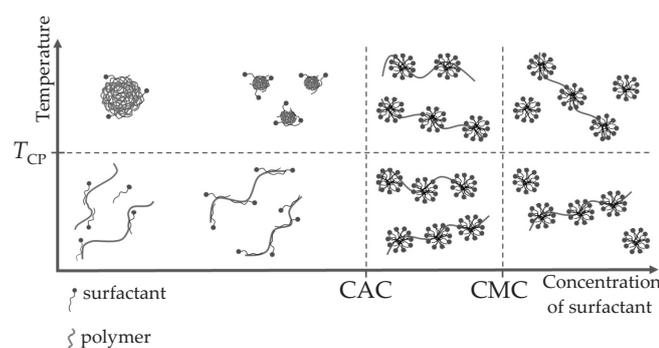
Fig. 1. Aggregation in thermoresponsive polymer/surfactant solutions; CAC – critical concentration of aggregation, CMC – critical concentration of micellization

mesoglobules disintegrate into single polymer chains, on which micelles of surfactant are formed [12].

Studies of PNIPAM-surfactant interactions were conducted by Loh *et al.* [9] to compare CMC (critical concentration of micellization) and CAC for sodium dodecyl sulfate (SDS) and others surfactants: hexadecyltrimethylammonium bromide (CTAB), dodecylammonium chloride (DAC), dodecyltrimethylammonium bromide (DTAB). Influence of counter ion on interactions between various thermoresponsive polymers network and surfactants were described by Lynch *et al.* [13]. Thermally induced aggregation in presence of SDS and CTAB was studied for thermoresponsive poly(glycidol-*co*-ethyl glycidyl carbamate) (M_n = 800 000 g/mol) [14]. Mesoglobules of poly(2-isopropyl-2-oxazoline) in the presence of SDS were described by Toncheva *et al.* [15].

The studies concerning the behavior of PNIPAM in the presence of surfactant are also discussed in [16–19]. Lee and Cabane [12] evidenced that mesoglobules of PNIPAM are stabilized by the surfactant when s/p is equal to 0.1–0.4. Weda *et al.* [19] obtained mesoglobules of PNIPAM in s/p range 0.5 to 5.5 and observed the decrease of their hydrodynamic radius with increasing concentration of SDS.

In this work the influence of SDS on temperature behavior of PNIPAM, poly{[di(ethylene glycol) monomethyl ether methacrylate]-*co*-[oligo(ethylene glycol) monomethyl ether methacrylate]} [P(D-*co*-O$_{300}$)] and the conjugate of the last with metenkephalin [P(D-*co*-O$_{300}$)-Met$_{Dns}$] were performed. T_{CP} values and the changes of hydrodynamic diameters of particles will be reported for systems containing two polymers P(D-*co*-O$_{300}$)/PNIPAM and P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM. The aggregation of studied macromolecules in water and in water/SDS solutions was followed by UV-Vis (ultraviolet-visible spectroscopy) and DLS (dynamic light scattering) methods.

EXPERIMENTAL PART

Materials

N-isopropylacrylamide (NIPAM, ≥ 99 %), copper(I) bromide, methyl 2-bromopropionate and sodium dodecyl sulfate (SDS, 98 %) were purchased from Sigma-Aldrich. Tris(2-dimethylaminoethyl)amine (Me$_6$TREN) was purchased from Alfa Aesar.

Synthesis of PNIPAM

1.4697 g (0.01298 mol) of NIPAM monomer, 0.0046 g (0.00002 mol) of the ligand – Me$_6$TREN, 0.0029 g (0.00002 mol) of catalyst – copper(I) bromide and 4.5 cm^3 of solvent mixture methanol/water (2/1, v/v) were placed in reactor. The contents of the reactor were degassed in three cycles of freeze-vacuum-thawing. Afterwards the reactor was purged with argon and 0.00293 cm^3 (0.00002 mol) of the initiator ethyl 2-bromo-2-methylpropanoate (EtBiB) was added to the frozen mixture. The po-

lymerization was carried out for 3 hours at room temperature. The reaction was terminated by blowing the contents of the reactor with air. The obtained polymer was purified by dialysis (Spectra/Por® 6 dialysis tubing, MWCO 6000–8000 Da) in a mixture of water/acetone (1/1, v/v) and dried. Acquired polymer has molar mass M_n = 112 000 g/mol and M_w/M_n = 1.09.

Poly{[di(ethylene glycol) monomethyl ether methacrylate]-*co*-[oligo(ethylene glycol) monomethyl ether methacrylate]} (M_n = 114 000 g/mol, M_w/M_n = 1.39) and its bioconjugate with metenkephalin (M_n = 104 500 g/mol, M_w/M_n = 1.16) were synthesized by controlled radical polymerization. The synthesis was similar to those described in [20].

The water used to obtain the polymer solutions was purified using a commercial ion exchange system (Hydrolab, Poland).

Methods of testing

The cloud points (T_{CP}) of polymers were determined on a Jasco V-530 UV–Vis spectrophotometer with a cuvette thermostated by a Medson MTC-P1 Peltier thermocontroller. The transmittances of the 0.2 g/dm³ solutions were monitored at λ = 550 nm as a function of temperature. The cloud points refer to the points of 10 % drop in transmittance.

Dynamic light scattering (DLS) measurements were performed on a Brookhaven BI-200 goniometer with vertically polarized incident light of wavelength λ = 632.8 nm supplied by a He-Ne laser operating at 35 mW and equipped with a Brookhaven BI-9000 AT digital autocorrelator. The scattered light was measured for aqueous (co)polymer solutions at concentrations of 0.2 g/dm³ at an angle of 90°. The autocorrelation functions were analyzed using the constrained regularized CONTIN method. The apparent hydrodynamic diameter (D_h^{90}) was obtained from the Stokes-Einstein equation. The dispersity of particle sizes was given as $\mu_2/\bar{\Gamma}^2$, where $\bar{\Gamma}$ is the average relaxation rate and μ_2 is its second moment. T_{CP} was determined as a point in half of D_h^{90} *vs.* temperature curve.

RESULTS AND DISCUSSION

Response to temperature of single polymer solutions in water and water/SDS

The aggregation of thermoresponsive polymer in solutions containing only one type of polymer was compared for the chains dissolved in pure water and in water with addition of SDS. All solutions were studied at 0.2 g/dm³ concentration of polymer. Surfactant to polymer weight ratio (s/p) was set to 0.2.

Temperature behavior of PNIPAM

First comprehensive studies on PNIPAM appeared in 1968 [21] and were continued later [22–26].

Our UV-Vis studies (Fig. 2a) of PNIPAM in pure water solution at concentration of 0.2 g/dm³ indicate its T_{CP} at 33.3 °C. It is close to literature data for this polymer [22]. Transmittance of this solution decreased by almost 70 %. No hysteresis was visible in heating/cooling cycle.

Transmittance of PNIPAM solution in the presence of SDS (Fig. 2b) revealed the shift of polymer phase transition to higher temperatures by around 1 °C to 34.6 °C. The significant difference was however the level of optical transmittance of this solution above phase transition. Here the decrease of only 25 % is observed. Similar results were obtained in other studies [27].

The difference in transmittance in both cases is visible by naked eye. Above transition temperature PNIPAM in pure water give milky dispersion whereas in water/SDS it was opalescent.

Thermally induced aggregation during slow heating of PNIPAM solution at concentration of 0.2 g/dm³ is shown in Fig. 3a in pure water and Fig. 3c in water/SDS. Based on these dependences T_{CP} was determined to 33.7 °C in pure water solution and 34.9 °C in water/SDS. Difference in T_{CP} is 1 °C, as in UV-Vis studies. Transitions in both solutions were sharp. Mesoglobules reached maximal size above 40 °C.
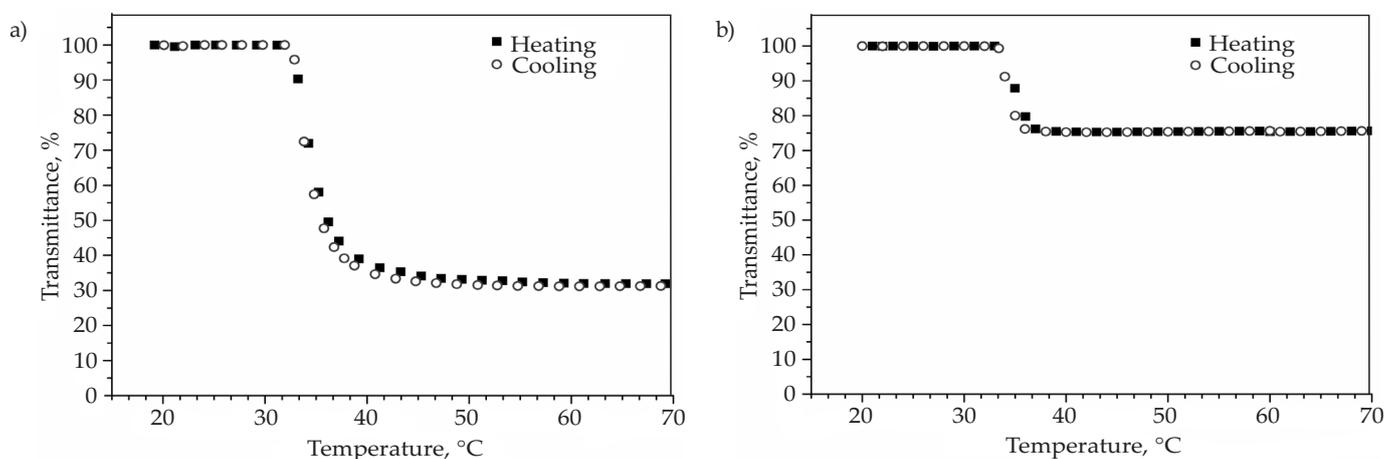

Fig. 2. Transmittance *vs.* temperature of PNIPAM a) in water solution, b) in water/SDS solution s/p = 0.2; polymer concentration 0.2 g/dm³, heating/cooling speed 1 °C/min
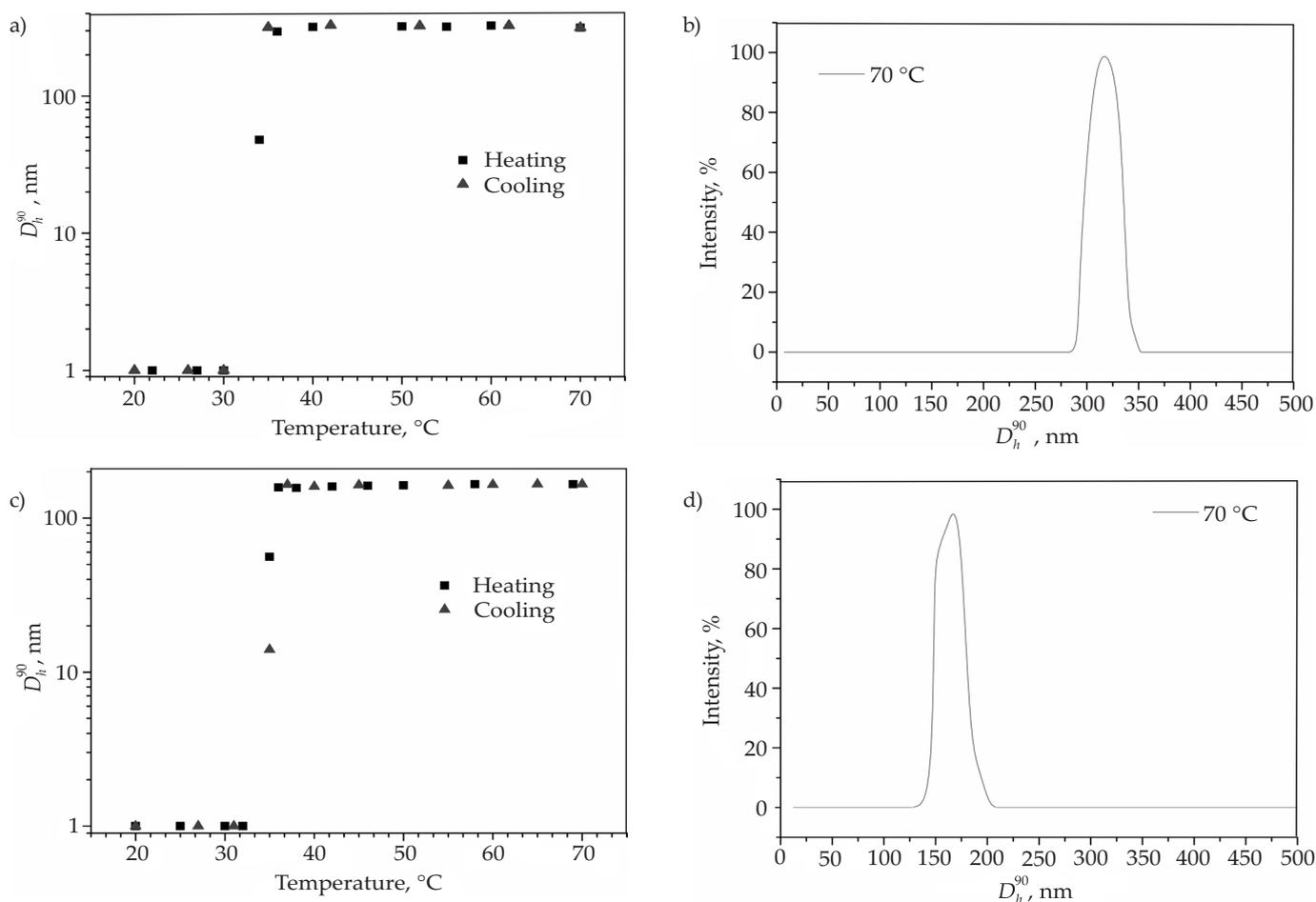
Fig. 3. a) D_h^{90} of PNIPAM in water as a function of temperature, b) size distribution of particles at 70 °C in water, c) D_h^{90} of PNIPAM in water/SDS s/p = 0.2 as a function of temperature, d) size distribution of particles at 70 °C in water/SDS; total polymer concentration 0.2 g/dm³
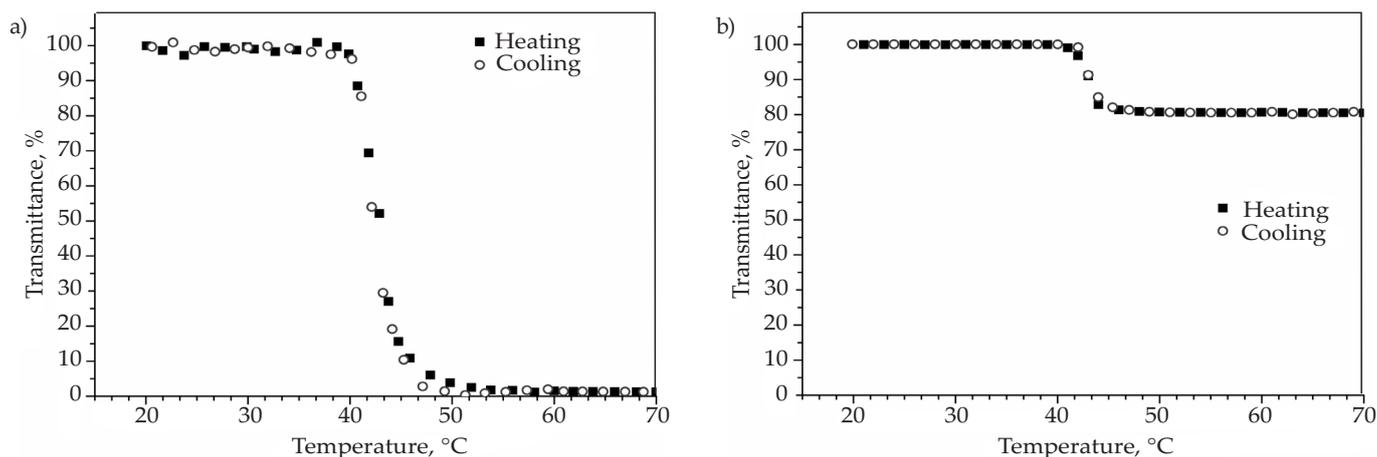

Fig. 4. Transmittance *vs*. temperature of P(D-*co*-O$_{300}$): a) in water solution, b) in water/SDS solution s/p = 0.2; polymer concentration 0.2 g/dm³, heating/cooling speed 1 °C/min

Presence of SDS caused the decrease of mesoglobules sizes by around 50 % from 320 nm in pure water to 165 nm in water/surfactant (Fig. 3b, 3d) and influenced the size distributions of particles (*PDI*). In both cases the distributions were monomodal but *PDI* decreased from 0.035 in water to 0.013 in water/SDS (Figs. 3b, 3d).

Temperature behavior of P(D-*co*-O$_{300}$)

Thermal behavior of different thermoresponsive OEGMA polymers was subject of many papers [28–34]. Here research concerns P(D-*co*-O$_{300}$) of M_n = 114 000 g/mol, (M_w/M_n = 1.39), 68 mol % D and 32 mol % O$_{300}$. The T_{CP}
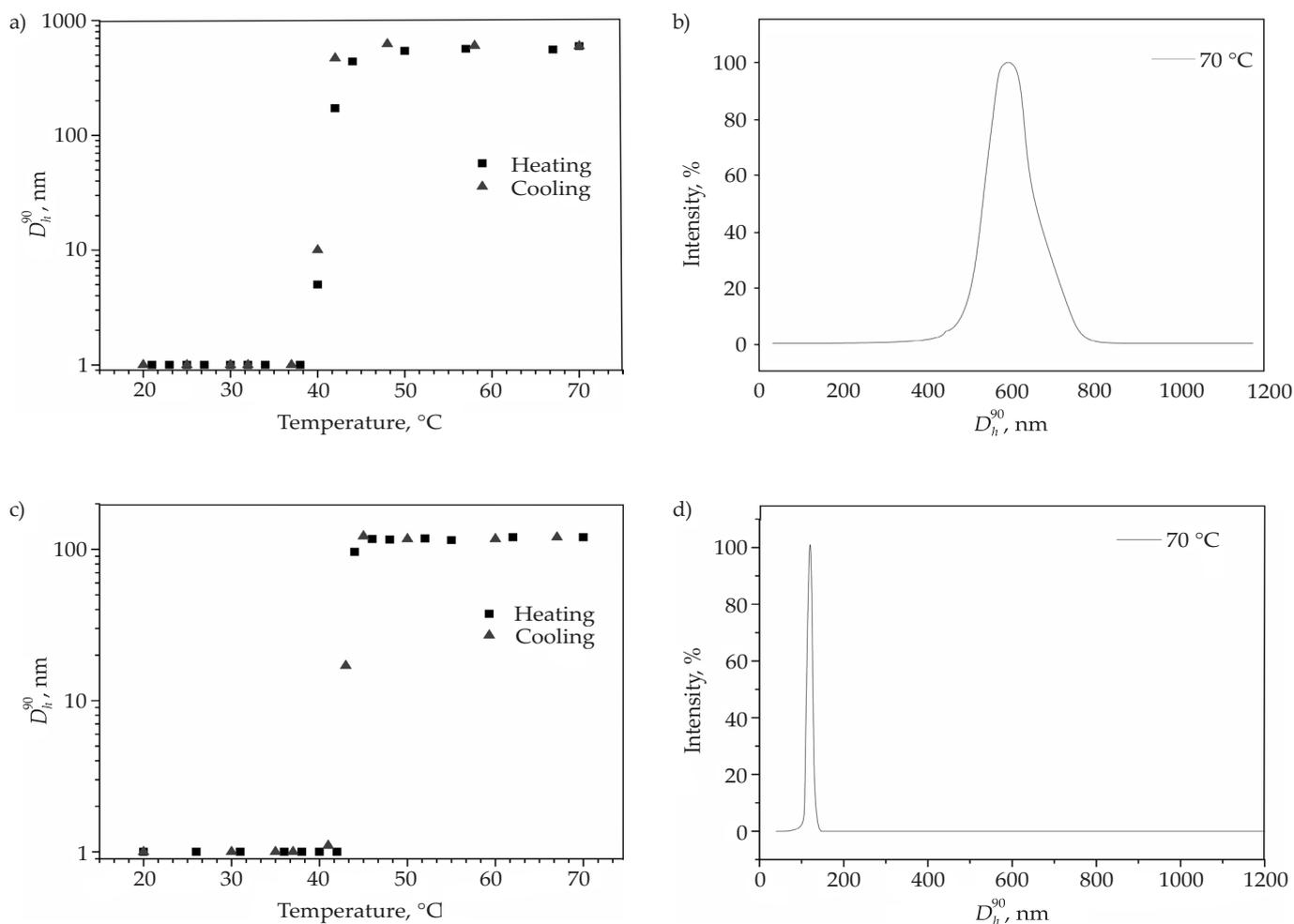
Fig. 5. a) D_h^{90} of P(D-*co*-O$_{300}$) in water as a function of temperature, b) size distribution of particles at 70 °C in water, c) D_h^{90} of P(D-*co*-O$_{300}$) in water/SDS s/p = 0.2 as a function of temperature, d) size distribution of particles at 70 °C in water/SDS; total polymer concentration 0.2 g/dm^3

established from transmittance changes during heating was 41.2 °C in pure water (Fig. 4a). The decline of the transmittance was wider than for PNIPAM. The transmittance failed to 0 %. The presence of the surfactant in P(D-*co*-O$_{300}$) solution caused a shift in the transition temperature of 1 °C towards higher temperatures (Fig. 4b) and led to the transmittance drop above T_{CP} to 80 % only. This increase in transparency in case of water/SDS solution can be correlated with particles sizes formed there by polymer, what will be explained later. The graphs do not show hysteresis in the heating and cooling cycle.

DLS studies revealed changes in particle sizes for both solutions, in water and in water/SDS, during slow heating and cooling process (Fig. 5). Plots do not show hysteresis. The transition temperature of P(D-*co*-O$_{300}$) determined from the DLS was 40.9 °C in pure water. Value of T_{CP} increased to 43.1 °C in the presence of SDS.

In water aggregates of P(D-*co*-O$_{300}$) reached a size of around 600 nm, at 70 °C, *PDI* = 0.3 (Fig. 5b). The presence of SDS in solution greatly influenced the copolymer aggregation process leading to diameter decrease to 120 nm, *PDI* = 0.19 (Fig. 5d).

Temperature behavior of P(D-*co*-O$_{300}$)-Met$_{Dns}$

Similar behavior as for PNIPAM and P(D-*co*-O$_{300}$) was observed for thermoresponsive bioconjugate of P(D-*co*-O$_{300}$) with peptide metenkephalin [P(D-*co*-O$_{300}$)-Met$_{Dns}$]. Metenkephalin was equipped with dansyl and conjugated to polymer chain by tyrosine moiety to leave the *N*-end of the peptide free. Structure of this conjugate is shown in Formula (I).

Based on transmittance *vs.* temperature curves T_{CP} of bioconjugates was determined to 39.5 °C (Fig. 6a). T_{CP} increased in the presence of SDS to 40.6 °C (Fig. 6b).

While in pure water transmittance above phase transition dropped to 0 %, it reached only around 90 % in the presence of SDS (Fig. 6b). This value, higher than that for unconjugated P(D-*co*-O$_{300}$) indicates the influence of peptide moiety on the aggregation of chains in the presence of surfactant.

The T_{CP} of P(D-*co*-O$_{300}$)-Met$_{Dns}$ determined from DLS measurements was 39.7 °C in pure water (Fig. 7a) and at 42.2 °C in water/SDS (Fig. 7c).

In pure water diameters of aggregates formed above T_{CP} were around 475 nm (*PDI* = 0.22). SDS addition sig-

Formula (I)
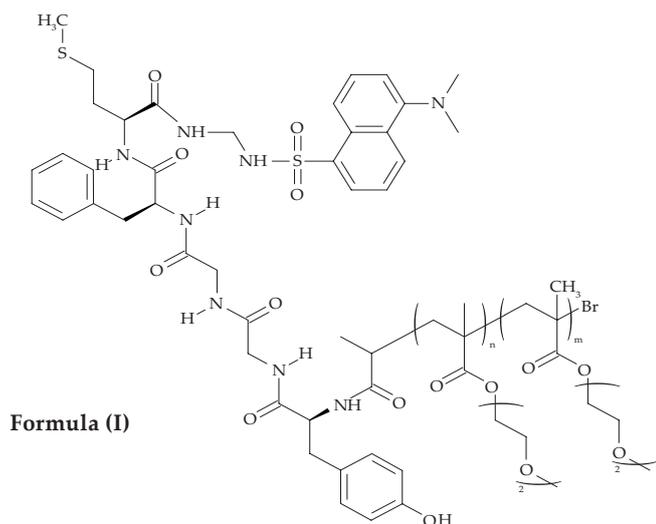
nificantly affected the aggregation of thermoresponsive chains. The aggregates became much smaller (75 nm), and the particle size distributions narrower (*PDI* = 0.011) compared to the aggregates formed in pure water. Addition of SDS caused around 400 nm reduction in size.

Temperature behavior of mixed polymer systems in water and water/SDS

Studies were conducted for binary polymers systems, P(D-*co*-O$_{300}$)/PNIPAM and P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM with mass ratio of 50/50. Polymers were dissolved in pure water and in water/SDS solution. Total concentration of polymers was 0.2 g/dm^3 and surfactant to polymer ratio (s/p) was equal to 0.2 in all cases.

Temperature behavior of P(D-*co*-O$_{300}$)/PNIPAM mixture

The changes in the transmittance of mixed P(D-*co*-O$_{300}$)/PNIPAM system in water and in water/SDS
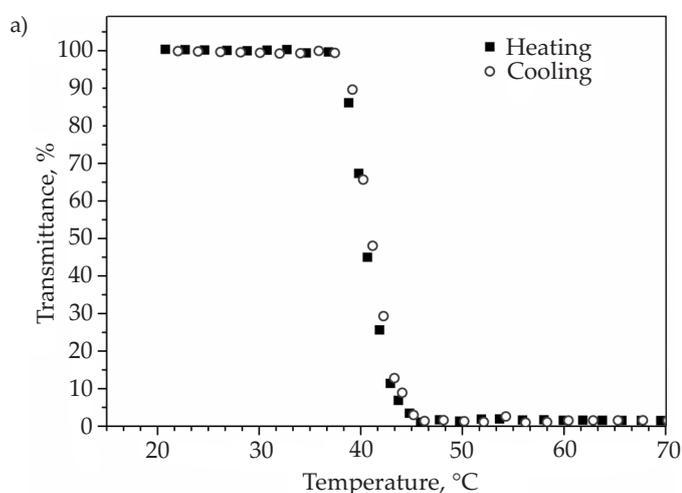
are shown in Figs. 8a and 8b respectively. In both cases two transitions attributed to the phase transitions of individual polymers can be distinguished.

In pure water, the transition at 35.7 °C can be related to aggregation of PNIPAM. The second transition which occurs at 41.1 °C is assigned to the phase transition of P(D-*co*-O$_{300}$). This transition is much wider, its width is *ca*. 5 °C.

In water/SDS, two transitions reflecting the transitions of individual components of P(D-*co*-O$_{300}$)/PNIPAM mixture (Fig. 8b) can be distinguished. The T_{CP} of PNIPAM occurs at 33.7 °C, while the transition of P(D-*co*-O$_{300}$) is also much wider and occurs at a temperature of 41.8 °C.

It should be noticed that final transmittance in case of P(D-*co*-O$_{300}$)/PNIPAM in water dropped to about 45 %. The minimum transmittance of the solution containing SDS is about 60 %, indicating creation of smaller aggregates in this case.

The UV-Vis data are confirmed by DLS measurements. Fig. 9a depicts changes in hydrodynamic diameters of structures formed during slow heating of P(D-*co*-O$_{300}$)/PNIPAM in pure water. Two transitions in 35.2 °C associated with PNIPAM and mild in 40.9 °C associated with P(D-*co*-O$_{300}$) can be seen.

In the presence of SDS (Fig. 9c) only one transition is clearly visible at 35.6 °C. There is a slight increase in the size of the mesoglobules in the range of 40–45 °C. Sizes of mesoglobules decreased from 310 nm in pure water to 250 nm in water/SDS solution (Figs. 9b, 9d). However size dispersity of particles grows from 0.025 to 0.06.

Temperature behavior of P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM mixture

Similar studies as described above were carried out for a mixed system of P(D-*co*-O$_{300}$)-Met$_{Dns}$ and PNIPAM. In the transmittance plot, the transitions observed in water are significantly less sharp than for P(D-*co*-O$_{300}$)/PNIPAM
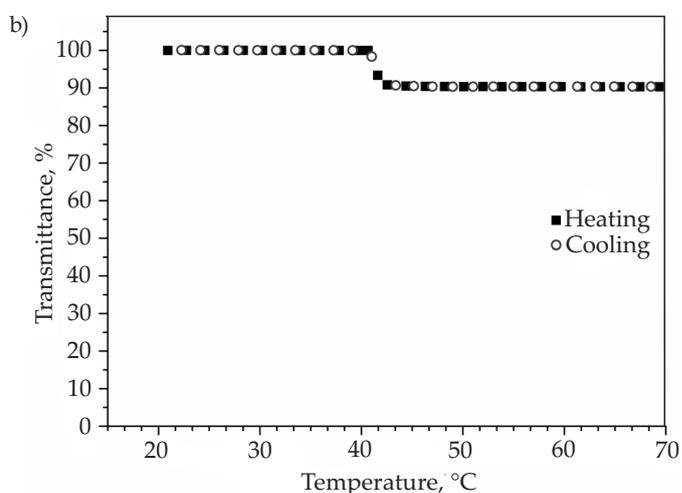
Fig. 6. Transmittance *vs*. temperature of P(D-*co*-O$_{300}$)-Met$_{Dns}$: a) in water solution, b) in water/SDS solution s/p = 0.2; polymer concentration 0.2 g/dm^3, heating/cooling speed 1 °C/min

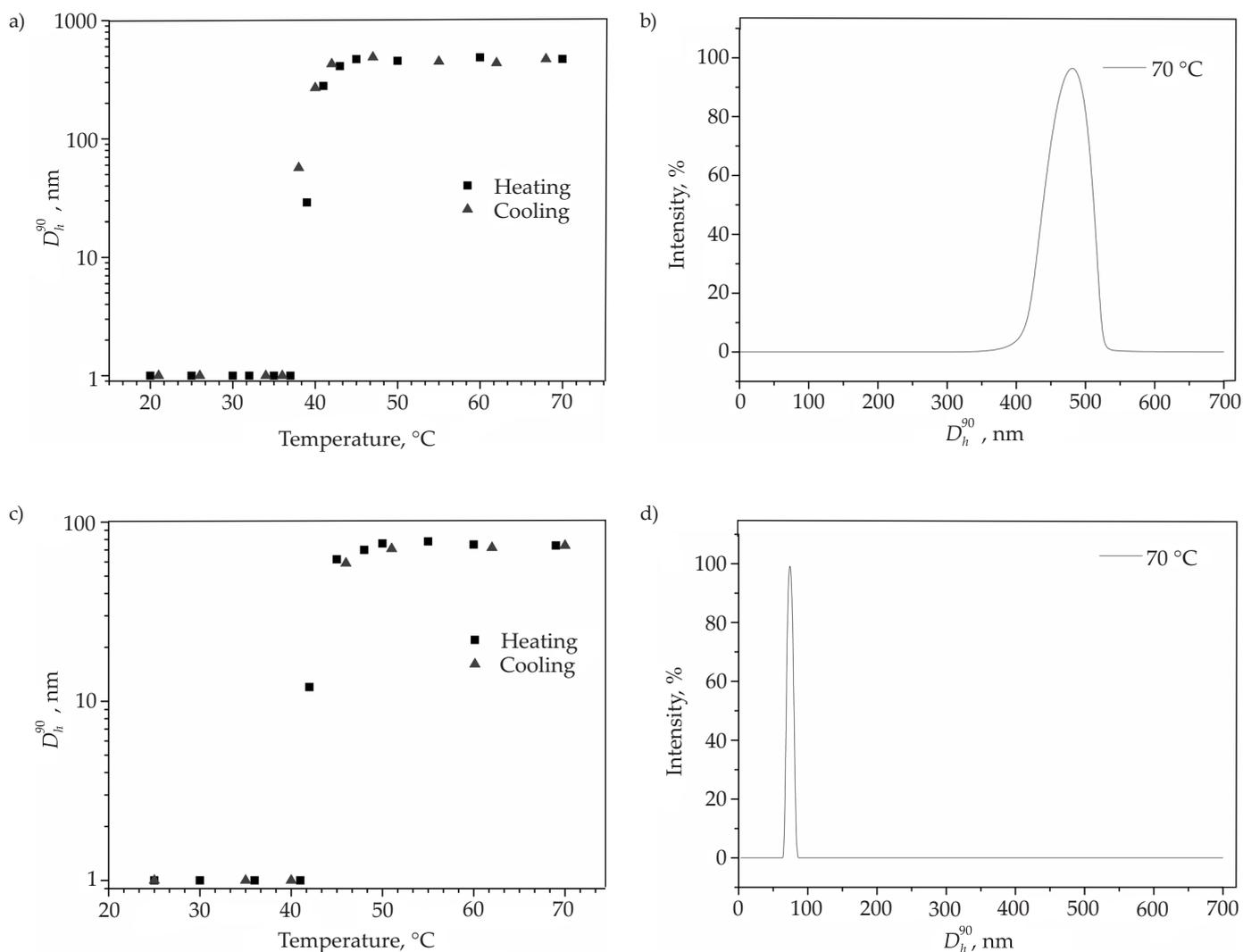**Fig. 7. a)** D_h^{90} **of P(D-*co*-O$_{300}$)-Met$_{Dns}$ in water as a function of temperature, b) size distribution of particles at 70 °C in water, c)** D_h^{90} **of P(D-*co*-O$_{300}$)-Met$_{Dns}$ in water/SDS s/p = 0.2 as a function of temperature, d) size distribution of particles at 70 °C in water/SDS; total polymer concentration 0.2 g/dm^3**
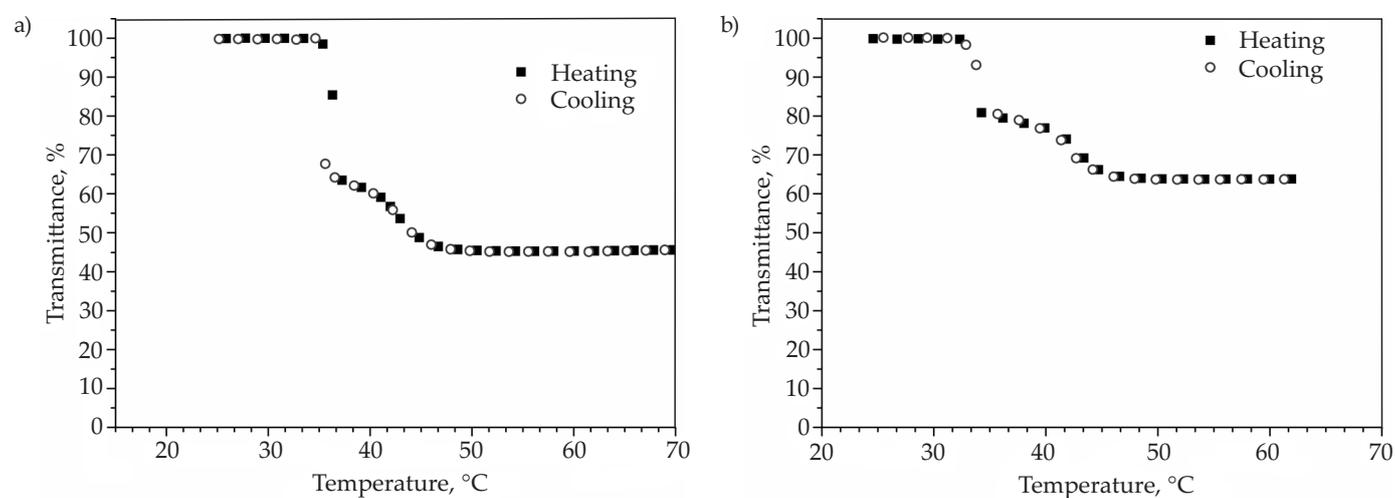

Fig. 8. Transmittance *vs*. temperature of P(D-*co*-O$_{300}$)/PNIPAM 50/50: a) in water solution, b) in water/SDS solution s/p = 0.2; polymer concentration 0.2 g/dm^3, heating/cooling speed 1 °C/min
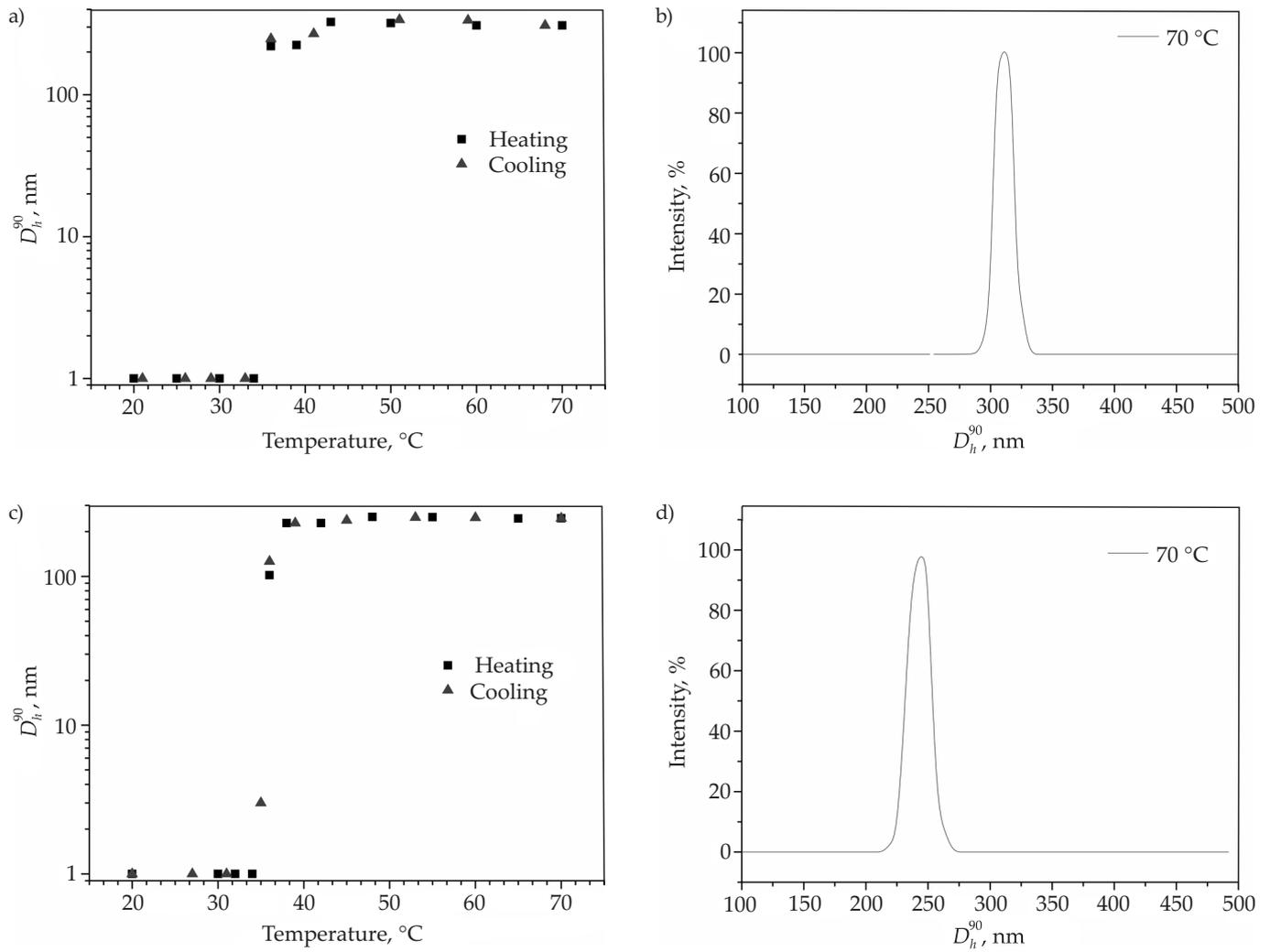
Fig. 9. a) D_h^{90} of P(D-*co*-O$_{300}$)/PNIPAM 50/50 as a function of temperature in water, b) size distribution of particles at 70 °C in water, c) D_h^{90} of P(D-*co*-O$_{300}$)/PNIPAM 50/50 as a function of temperature in water/SDS s/p = 0.2, d) size distribution of particles at 70 °C in water/SDS; total polymer concentration 0.2 g/dm³

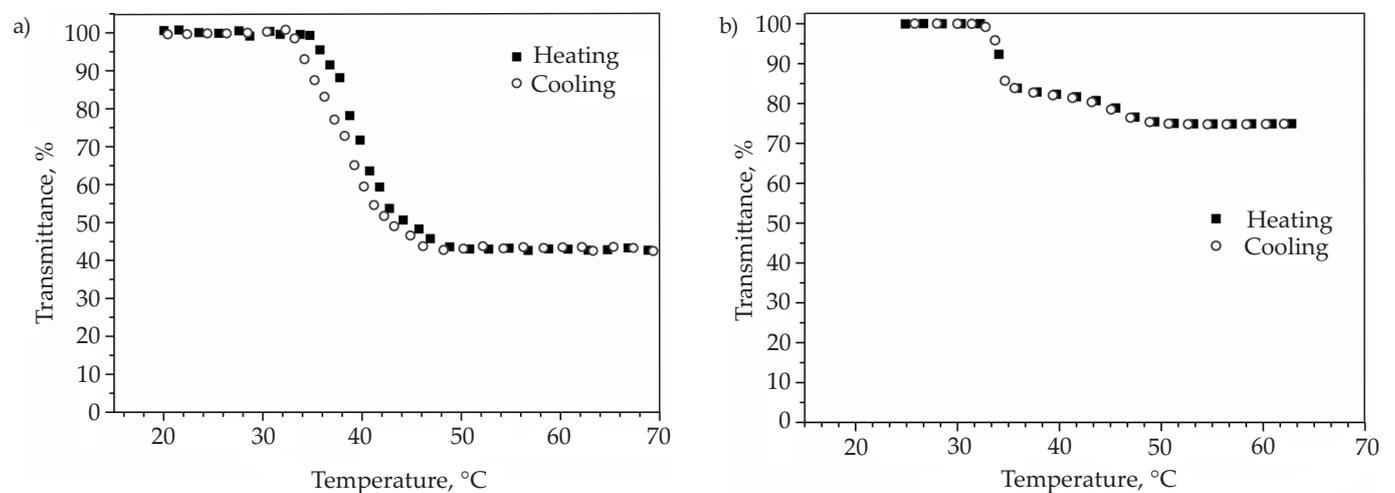Fig. 10. Transmittance *vs.* temperature of P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM 50/50: a) in water solution, b) in water/SDS s/p = 0.2 solution; total polymer concentration 0.2 g/dm³, heating/cooling speed 1 °C/min
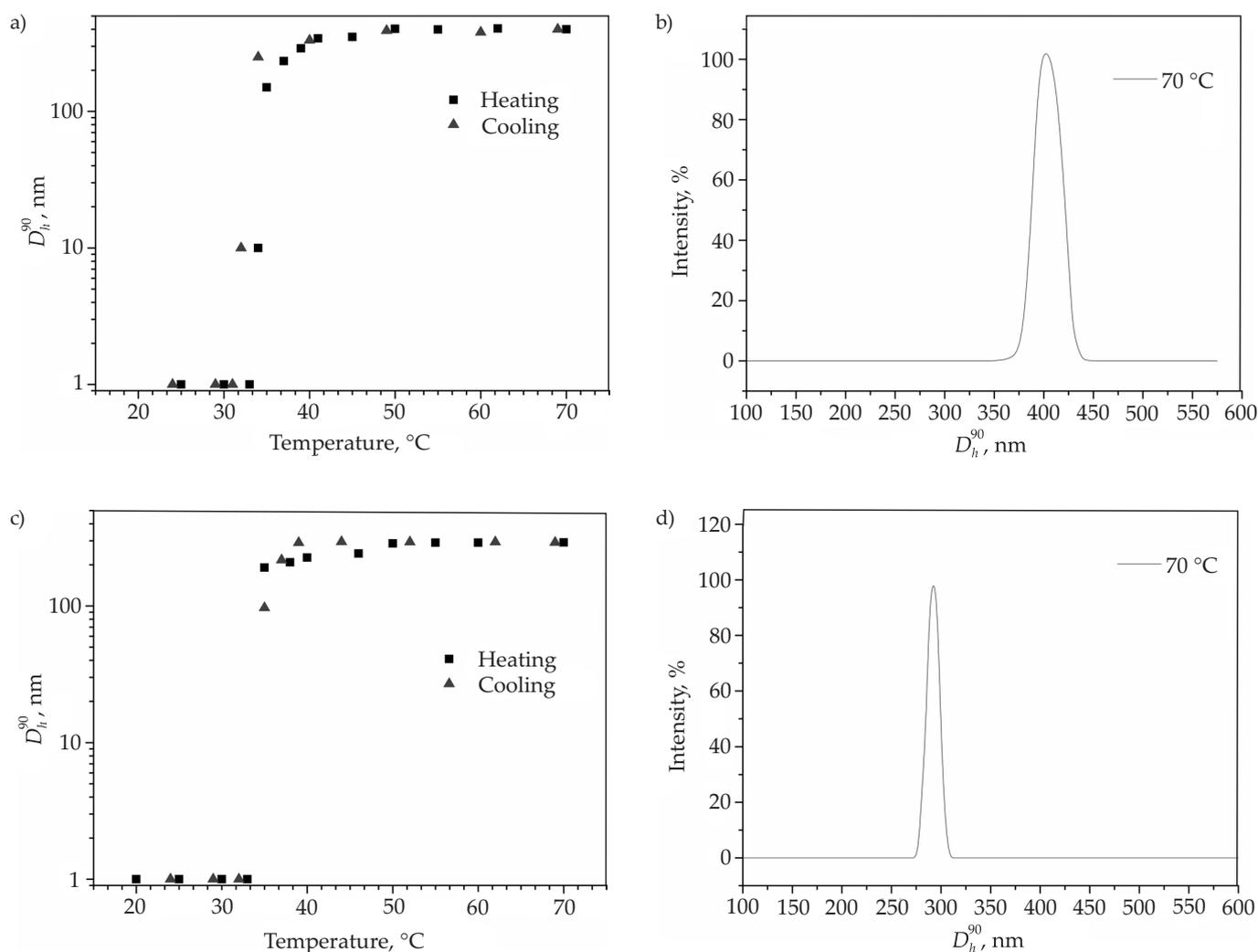
Fig. 11. a) D_h^{90} **of P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM 50/50 in water as a function of temperature, b) size distribution of particles at 70 °C in water, c)** D_h^{90} **of P(D*co*O$_{300}$)-Met$_{Dns}$/PNIPAM 50/50 in water/SDS, s/p = 0.2 as a function of temperature, d) size distribution of particles at 70 °C in water/SDS; total polymer concentration 0.2 g/dm^3**

(Fig. 10a). T_{CP} of PNIPAM can be found at 37.5 °C while for bioconjugate at 40.0 °C. The final transmittance drops to only *ca.* 40 %.

SDS greatly influences the aggregation of polymer and bioconjugate in P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM mixture. Two transitions: at 34.3 °C corresponding to PNIPAM and at 44.8 °C corresponding to P(D-*co*-O$_{300}$)-Met$_{Dns}$ are seen in transmittance curve (Fig. 10b). The second transmission associated with the bioconjugate is wide, it takes place in the range of 4–5 °C. The total decrease in the transmittance of this mixture in water/SDS is much smaller than in pure water. It reaches *ca.* 75 %.

D_h^{90} dependence of P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM (Fig. 11a) in water *vs.* temperature evidences 34.8 °C as T_{CP} of PNIPAM. The transition of bioconjugate is *ca.* 40 °C. Final diameter of particles at 70 °C was around 400 nm with *PDI* = 0.021 (Fig. 11b).

D_h^{90} *vs.* temperature and the size distribution of particles formed by P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM in the presence of SDS are shown in Figs. 11c and 11d. In Fig. 11c a clear transition associated with PNIPAM aggregation can be distinguished at 35.0 °C while the second one, associated with the bioconjugate (45.7 °C), is poorly marked.

The presence of SDS causes a significant reduction in the diameter of P(D-*co*-O$_{300}$)-Met$_{Dns}$/PNIPAM mesoglobules to approx. 270 nm, *PDI* also decreased to 0.01.

CONCLUSIONS

To compare the influence of SDS in solution on thermal aggregation of thermoresponsive polymers T_{CP} values measured by UV-Vis and particle sizes obtained by DLS for PNIPAM, P(D-*co*-O$_{300}$), P(D-*co*-O$_{300}$)-Met$_{Dns}$ in water and in water/SDS are presented in Table 1.

In each experiment, the SDS addition caused a slight shift in the transition temperatures of the thermoresponsive polymers towards higher temperatures.

T a b l e 1. Transition temperatures and sizes of nanoparticles for single polymer systems ($C = 0.2$ g/dm^3)

System	Solvent	T_{CP}, °C UV-Vis	T_{CP}, °C DLS	D_h^{90} nm
PNIPAM	Water	33.3	33.7	320
	Water/SDS	34.6	34.9	165
P(D-co-O$_{300}$)	Water	41.2	40.9	600
	Water/SDS	42.3	43.1	120
P(D-co-O$_{300}$)-Met$_{Dns}$	Water	39.5	39.7	475
	Water/SDS	41.6	42.2	74

T a b l e 2. Transition temperatures and sizes of particles for studied polymer mixtures ($C = 0.2$ g/dm^3)

System	Solvent	T_{CP1}, °C UV-Vis	T_{CP2}, °C UV-Vis	T_{CP1}, °C DLS	T_{CP2}, °C DLS	D_h^{90} nm
P(D-co-O$_{300}$)/PNIPAM 50/50	Water	35.7	41.1	35.2	40.9	310
	Water/SDS	33.7	41.8	35.6	40–45	250
P(D-co-O$_{300}$)-Met$_{Dns}$/PNIPAM 50/50	Water	37.5	41.7	34.8	≈ 40	400
	Water/SDS	34.3	44.8	35.0	45.7	290

The presence of SDS led also to significant reduction in the diameters of mesoglobules compared to those formed in pure water. This may also be evidenced by the distinctly higher transmittance of the samples containing SDS above the transition temperature.

For mixed P(D-co-O$_{300}$)/PNIPAM and P(D-co-O$_{300}$)-Met$_{Dns}$/PNIPAM systems T_{CP}s and sizes of aggregates in water and in water/SDS are presented in Table 2.

At slow heating of solution containing two thermoresponsive species the transitions related to both types of macromolecules are observed. The influence of SDS on thermoresponsive chains in mixed systems is similar to this observed for solutions with only one polymer.

Above phase transitions temperatures of both polymers, only one population of particles was present. This fact and stepwise aggregation visible in UV-Vis and DLS studies imply that particles formed exhibit core-shell structure, similar as was previously reported for poly(2-izopropyl-2-oxazoline)/poly(N-isopropylacrylamide) mixtures [8].

The presence of hydrophobic peptide moiety in polymer structure influences the interaction between polymer chains and surfactant molecules in solution leading to larger aggregates.

The transmittance curves clearly show the differences between P(D-co-O$_{300}$)-Met$_{Dns}$/PNIPAM in water and water/SDS. SDS leads to decrease in interaction between two types of polymer chains. This resulted in the appearance of two distinct transitions in DLS and UV-Vis curves.

REFERENCES

[1] Wei H., Cheng S.X., Zhang X.Z. *et al.*: *Progress in Polymer Science* **2009**, *34*, 893.
https://doi.org/10.1016/j.progpolymsci.2009.05.002

[2] Schmaljohann D.: *Advanced Drug Delivery Reviews* **2006**, *58*, 1655.
https://doi.org/10.1016/j.addr.2006.09.020

[3] Dworak A., Lipowska D., Szweda D. *et al.*: *Nanoscale* **2015**, *7*, 16 823.
https://doi.org/10.1039/C5NR04448K

[4] Ottenbrite R.M., Sung W.K.: "Polymeric drugs and drug delivery systems", CRC Press, 2019.

[5] Ieong N.S., Hasan M., Phillips D.J. *et al.*: *Polymer Chemistry* **2012**, *3*, 794.
https://doi.org/10.1039/C2PY00604A

[6] Djokpé E., Vogt W.: *Macromolecular Chemistry and Physics* **2001**, *202*, 750.
https://doi.org/10.1002/1521-3935(20010301)202:5<750::AID-MACP750>3.0.CO;2-8

[7] Starovoytova L., Spěváček J., Ilavský M.: *Polymer* **2005**, *46*, 677.
https://doi.org/10.1016/j.polymer.2004.11.089

[8] Trzebicka B., Haladjova E., Otulakowski L. *et al.*: *Polymer* **2015**, *68*, 65.
https://doi.org/10.1016/j.polymer.2015.04.085

[9] Loh W., Teixeira L.A.C., Lee L.T.: *The Journal of Physical Chemistry B* **2004**, *108*, 3196.
https://doi.org/10.1021/jp037190v

[10] Schild H.G., Tirrell D.A.: *Langmuir* **1991**, *7*, 665.
https://doi.org/10.1021/la00052a013

[11] Eeckman F., Amighi K., Moës A.J.: *International Journal of Pharmaceutics* **2001**, *222*, 259.
https://doi.org/10.1016/S0378-5173(01)00716-5

[12] Lee L.T., Cabane B.: *Macromolecules* **1997**, *30*, 6559.
https://doi.org/10.1021/ma9704469

[13] Lynch I., Sjostrom J., Piculell L.: *The Journal of Physical Chemistry B* **2005**, *109*, 4252.
https://doi.org/10.1021/jp045280+

[14] Trzebicka B., Weda P., Utrata-Wesołek A. *et al.*: *Journal of Polymer Science Part A Polymer Chemistry* **2010**, *48*, 4074. https://doi.org/10.1002/pola.24193

[15] Toncheva N., Tsvetanov Ch., Rangelov S. *et al.*: *Polymer* **2013**, *54*, 5166.
https://doi.org/10.1016/j.polymer.2013.07.042

[16] Umapathi R., Reddy P.M., Rani A. *et al.*: *Physical Chemistry Chemical Physics* **2018**, *20*, 9717.
https://doi.org/10.1039/c7cp08172c

[17] Fanova A., Sindelka K., Uchman M. *et al.*: *Macromolecules* **2018**, *51*, 7295.
https://doi.org/10.1021/acs.macromol.8b01161

[18] Konak C., Hruby M.: *Macromolecular Rapid Communications* **2006**, *27*, 877.
https://doi.org/10.1002/marc.200600065

[19] Weda P., Trzebicka B., Dworak A. *et al.*: *Polymer* **2008**, *49*, 1467.
https://doi.org/10.1016/j.polymer.2008.01.059

[20] Szweda R., Trzebicka B., Dworak A. *et al.*: *Biomacromolecules* **2016**, *17*, 2691.
https://doi.org/10.1021/acs.biomac.6b00725

[21] Heskins M., Guillet J.E.: *Journal of Macromolecular Science: Part A – Chemistry* **1968**, *2*, 1441.
https://doi.org/10.1080/10601326808051910

[22] Schild H.G.: *Progress in Polymer Science* **1992**, *17*, 163.
https://doi.org/10.1016/0079-6700(92)90023-R

[23] Meng H., Hu J.: *Journal of Intelligent Material Systems and Structures* **2010**, *21*, 859.
https://doi.org/10.1177/1045389X10369718

[24] Klouda L.: *European Journal of Pharmaceutics and Biopharmaceutics* **2015**, *97*, 338.
https://doi.org/10.1016/j.ejpb.2015.05.017

[25] Mazzotta E., Tavano L., Muzzalupo R.: *Pharmaceutics* **2018**, *10* (*3*), 150.
https://doi.org/10.3390/pharmaceutics10030150

[26] Kojima H.: *Polymer Journal* **2018**, *50* (*6*), 411.
https://doi.org/10.1038/s41428-018-0035-9

[27] Kunugi S., Yamazaki Y., Takano K. *et al.*: *Langmuir* **1999**, *15*, 4056.
https://doi.org/10.1021/la981184m

[28] Neugebauer D.: *Polymer International* **2007**, *56*, 1469.
https://doi.org/10.1002/pi.2342

[29] Akdemir Ö., Badi N., Pfeifer S. *et al.*: *ACS Symposium Series* **2009**, *1023*, 189.
https://doi.org/10.1021/bk-2009-1023.ch013

[30] Badi N., Lutz J.F.: *Journal of Controlled Release* **2009**, *140*, 224.
https://doi.org/10.1016/j.jconrel.2009.04.012

[31] Trzebicka B., Szweda D., Rangelov S. *et al. Journal of Polymer Science Part A: Polymer Chemistry* **2012**, *51*, 614.
http://dx.doi.org/10.1002/pola.26410

[32] Hu Z., Cai T., Chi C.: *Soft Matter* **2010**, *6*, 2115.
https://doi.org/10.1039/B921150K

[33] Lutz J.F.: *Advanced Materials* **2011**, *23*, 2237.
https://doi.org/10.1002/adma.201100597

[34] Lutz J.F., Akdemir Ö., Hoth A.: *Journal of the American Chemical Society* **2006**, *128*, 13046.
https://doi.org/10.1021/ja065324n