Regular Article

Thermoresponsive nanoparticle agglomeration/aggregation in salt solutions: Dependence on graft density

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Graphical abstract

Article info

Article history:
Received 5 May 2017
Revised 11 July 2017
Accepted 15 July 2017
Available online 17 July 2017

Keywords:
Graft density
Thermoresponsive agglomeration
Nanoparticle stability

Abstract

Gold nanoparticles with a graft density of 0.09, 0.30 and 0.40 chains/nm² of poly(N-isopropylacrylamide) were reproducibly synthesized by varying the ratio of disulfide terminated poly(N-isopropylacrylamide) to gold nanoparticle. The polymer coated nanoparticles were stable at room temperature in 50 mM NaCl, yet agglomerated at 37 °C. Previous studies have observed conflicting results as to the reversibility of this agglomeration. Particle agglomeration with three different graft densities was studied in 50 mM NaCl by measurements of their localized surface plasmon resonance and hydrodynamic diameter, and imaging with electron microscopy. Agglomerates with a polymer graft density of 0.30 and 0.40 chains/nm² could be dispersed with sonication, while particles with a graft density of 0.09 chains/nm² irreversibly aggregated. The graft density dependence on whether agglomeration or aggregation occurred is due to changes in collapsed polymer steric effects. Localized surface plasmon resonance measurements of agglomerates were discordant with hydrodynamic diameter measurements in determining agglomeration reversibility, which shed light on reasons previous reports yielded different interpretations on the reversibility of this agglomeration.
1. Introduction

Poly (N-isopropylacrylamide) (PNIPAM) is one of the most studied thermoresponsive polymers, in part because its lower critical solution temperature (LCST) is \( \sim 32^\circ C \) enabling its use for many potential biological studies [1,2]. In water below the LCST, the polymer swells forming energetically favorable hydrogen bonds between the acrylamide group and water. Above the LCST, the polymer spontaneously desolvates to form inter- and intra-chain hydrogen bonds leading to contraction from a coil to a globule, increasing its hydrophobicity. Decreasing the separation distance between polymer grafting sites leads to steric hindrance in the polymer chains. The steric hindrance is observed as an increase in chain height; in other words, the graft density (chain/nm\(^2\)) determines the chain height in solution [3,4]. Fig. 1 illustrates the increase in chain height with increasing grafting density. For thermoresponsive polymers the graft density determines not only the extended (<LCST), but also the collapsed (>LCST) polymer thickness [5–7]. When the polymer collapses, at low graft densities, it will stretch along the surface to entangle with nearby chains [8]. With increasing graft density, the collapsed polymer thickness increases [9].

Repulsive forces prevent nanoparticles from clustering and include electrostatic and steric forces. An insufficient repulsive force between particles enables van der Waals forces to dominate, and causes particle clustering, yielding agglomerates or aggregates [10]. For this work, the IUPAC definition is used to distinguish agglomeration from aggregation [11]. An agglomerate is defined as dispersed particles that are held together by weak physical interactions. Agglomeration is a reversible process. An aggregate is comprised of strongly interacting particles and leads to irreversible changes in particle morphology.

Steric stabilizers prevent the clustering of nanoparticles due to a required force to compress the polymer layer during nanoparticles collision. The osmotic pressure required for brush compression is directly related to the graft density of a sterically stabilizing polymer [12]. A graft density dependent aggregation of PNIPAM nanoparticles in water has been reported by Du et al. who observed nanoparticles with a high graft density of PNIPAM heated above the LCST, contracted reversibly, while nanoparticles with a low graft density of PNIPAM aggregated in water, the only solvent used in this particular study [12]. However, gold nanoparticles (AuNPs) coated with PNIPAM (AuNP-PNIPAM) are stable above their LCST in water, but flocculate above their LCST in salt solutions [16–19]. Salt dehydration of PNIPAM has been shown to depress the LCST of the polymer [13,14], and dehydrate the polymer beyond what is observed with a temperature change alone [13,14]. The reversibility of this flocculation in salt has not been fully investigated, with no study conducted using more than a single graft density. An irreversible change in particle morphology caused from aggregation, affects particles’ surface area, reactivity and alters their biodistribution and cellular uptake [20–22].

The three most prominent means of studying nanoparticle agglomeration are: (1) monitoring the localized surface plasmon resonance (LSPR), (2) dynamic light scattering (DLS), and (3) imaging samples with electron microscopy. Each of these techniques have inherent measurement biases that can affect the results [23]. The LSPR peak position is sensitive to the nanoparticle size, shape, composition, changes in local refractive index, and the separation distance between particles [24–27]. As particle separation distance between adjacent particles decreases to less than five times the radius of the particle, coupling of their plasmon modes causes a redshift in the LSPR peak position [28]. This shift in extinction peak position is commonly used to determine agglomeration of plasmonic nanoparticles [29,30]. DLS measures scattered light intensity fluctuations of particles in solution undergoing Brownian motion [31]. DLS is biased toward detecting larger particles and impurities in polydisperse samples due to scattering intensity increasing to the sixth power relative to particle diameter (\(1 \propto d^6\)) [32]. Increases in the hydrodynamic diameter of particles is indicative of agglomeration [33]. Transmission electron microscopy (TEM) has been used to study nanoparticle agglomeration and aggregation structures [29,34] and has been used in studies describing thermal agglomeration of nanoparticles [35]. A benefit of TEM analysis for studying nanoparticle agglomeration is the ability to visualize heterogeneous structures, as both DLS and LSPR are ensemble measurements, with biases towards measuring large agglomerates or decreasing separation distance between particles.

Most studies describing the agglomeration and aggregation of AuNP-PNIPAM above the LCST in salt solutions used a single graft density, which is typically not reported. Thiol terminated PNIPAM is known to adsorb to gold surfaces with increasing graft density over 11 h, given a sufficient polymer solution concentration [36]. The length of time allowed for thiol terminated PNIPAM to adsorb to the AuNPs is variable and not always reported. So, it is possible different agglomeration and aggregation results obtained from previous studies are caused by different polymer thicknesses related to the polymer graft density. Additionally, reversible AuNP-PNIPAM agglomeration has been observed when measuring the LSPR peak position, while irreversible increases in \(D_h\) have been observed when studying the agglomeration and aggregation with DLS [16,17,19,37]. In part, the contradictory results of many previous studies can be explained by the choice of measurement techniques and/or graft density.
In this work, the agglomeration and aggregation of PNIPAM-coated nanoparticles in salt solutions was studied with different graft densities. It is likely these variations in collapsed polymer thickness, due to different polymer graft densities, affect whether agglomerates or aggregates are formed. Van der Waals forces are dominant at small particle separation distances and prevent particle separation. For this study, three different techniques were used to study AuNP-PNIPAM agglomeration in a salt solution, using three different graft densities. We find that whether agglomeration or aggregation in a salt solution occurs is dependent upon the polymer graft density. Additionally, monitoring LSPR peak position presented evidence of agglomeration, while increases in hydrodynamic diameter persisted over the conditions studied. Our data suggest aggregates form due to a thin collapsed polymer thickness enabling van der Waals forces to become prominent. So, it is possible different agglomeration and aggregation results are caused by different polymer thicknesses related to the polymer graft density.

2. Experimental section

2.1. Reagents

Tetrachloroauric (III) acid trihydrate ACS grade was purchased from Acros Organics. Lipoic acid terminated neutral PNIPAM 13 kDa (n ~ 110) as determined by NMR was a gift from Guorong Sun at Texas A&M University and used as received. An 1H NMR spectrum of the polymer is shown in Fig. S1. Trisodium citrate, potassium chloride and sodium chloride (99.5%) were purchased from Sigma-Aldrich. HPLC-grade water from Fisher was used for all experiments. Solutions used for DLS studies were filtered using a 0.2 µm PES syringe filter from GE Healthcare before nanoparticle dilution.

2.2. AuNP synthesis

All glassware was cleaned using aqua regia and thoroughly washed before use. Gold nanoparticles were synthesized using the Turkevich method as previously described [38]. A total of 300 mL of aqueous tetrachloroauric (III) acid trihydrate (0.5 mg/mL) was brought to a boil with magnetic stirring and 30 mL of a 300 mL of aqueous tetrachloroauric (III) acid trihydrate (0.5 mg/mL) was added dropwise, until a final concentration of the disulfide was achieved. The solutions were left sealed for 24 h with stirring. Residual particles were removed by centrifuging the solutions at 10,000 rpm for 10 min, the particles were removed from heat and cooled to room temperature, the solutions were agitated by pipetting and the extinction of AuNPs and AuNP-PNIPAM was independently repeated three times for each graft density studied. The LSPR of the modified AuNPs redshifted to 528 ± 1 nm, 529 ± 1, and 529 ± 1 nm for AuNP-Low, AuNP-Medium, and AuNP-High, respectively, as shown in Table 1 and Fig. 2A.

2.3. PNIPAM modification of AuNPs

Gold nanoparticle solutions were purged with nitrogen for 30 min., after which the lipoic acid-terminated PNIPAM solution was added drop wise, until a final concentration of the disulphide PNIPAM in the nanoparticle solution was 100, 10 or 1 µM, hereafter referred to as AuNP-High, AuNP-Medium or AuNP-Low, respectively. The solutions were left sealed for 24 h with stirring. Residual polymer was removed by centrifuging the solutions at 10 °C, removing the supernatant, and suspending the particles in water three times. PNIPAM modification of the same initial stock of gold particles was repeated at the same polymer concentration on different days to test the reproducibility in obtaining the same graft density and the agglomeration results.

2.4. AuNP-PNIPAM characterization

Particle concentration assuming spherical concentration was determined by atomic absorbance using a GBC 932 Plus from GBC Scientific Equipment. Transmission electron microscope (TEM) images of AuNPs were taken using a JEOL-1011 and ImageJ was used to size the AuNPs. The extinction of AuNPs and AuNP-PNIPAM was measured with 1 nm increments using a Nanodrop 2000c. The zeta potentials and intensity-weighted hydrodynamic diameter (Dh), or z-average, of the particles was determined using a 90 plus particle sizer from Brookhaven. The source had a λ of 658 nm and the scattering angle was set to 90°. The zeta potential was measured in a 1 mM KCl solution. Unless otherwise stated, dynamic light scattering (DLS) measurements were performed at 23 ± 0.1 °C. Particle stability was studied in water and in a 50 mM salt solution after a 10 min equilibration at 37 °C. Thermo-gravimetric analysis (TGA) experiments were performed using a Q50 from TA Instruments using a 10 °C/min ramp to 500 °C using samples lyophilized in water. The graft density (δ) was determined based on a previously reported method (Eq. (1)) [39]. In Eq. (1), NPNIPAM is the number of polymer ligands lost during heating from 300 to 425 °C, SAuNP is the surface area of a spherical nanoparticle, Na is Avogadro’s number, MAu is the mass at the end of the TGA which is attributed to gold, VAuNP is the volume of a spherical nanoparticle, VAl is the volume of a gold atom (1.7 × 10⁻²⁹ m³), and MWAu is the molecular weight of gold. The particle size determined by atomic absorbance using a GBC 932 Plus from GBC Scientific Equipment.

\[
\delta = \frac{N_{PNIPAM}}{S_{AuNP} \times \frac{M_{Au}}{M_{Au}}} \quad (1)
\]

2.5. AuNP-PNIPAM agglomeration studies

AuNP-PNIPAM nanoparticles were diluted to 1.08 ± 0.07 nM in water or 50 mM NaCl and incubated at 37 °C for up to 6 h. The 50 mM NaCl concentration was chosen as a previous study reported sedimentation affected DLS results when AuNP-PNIPAM were heated in higher salt concentrations [16]. After heating, all samples were sonicated for 10 s, following which the extinction and hydrodynamic diameters of aliquots were measured. Then, the solutions were placed at room temperature (~23 °C) to relax the contracted polymer. After 150 min of relaxation at room temperature, the solutions were agitated by pipetting and the extinction and hydrodynamic diameters of the aliquots were measured in 50 mM NaCl. The change in Dh and in LSPR peak position was recorded with respect to their initial positions in 50 mM NaCl. Samples in 50 mM NaCl which had undergone a 2 h heat treatment or remained at room temperature were drop-cast on TEM grids. The average area of AuNPs heated and unheated was determined using ImageJ. Only particles with an area above 67 nm² were included in the analysis. This 67 nm² threshold was chosen because the smallest measured nanoparticle would have this area, assuming circular geometry. Particulate with an area below this threshold is believed to be due to salt.

3. Results and discussion

3.1. AuNP-PNIPAM characterization

Spherical AuNPs with a diameter of 20.5 ± 6.5 nm were synthesized with an initial LSPR of 525 nm. The polydispersity index (PDI) for the synthesized particles was 0.103, which is lower than other reported syntheses [40]. Fig. S2 displays a representative TEM image and the corresponding size histogram. Modification of these particles with PNIPAM was independently repeated three times for each graft density studied. The LSPR of the modified AuNPs redshifted to 528 ± 1 nm, 529 ± 1, and 529 ± 1 nm for AuNP-Low, AuNP-Medium, and AuNP-High, respectively, as shown in Table 1 and Fig. 2A. This redshift is due to an increase in refractive index.
from essentially water to a carbonaceous polymer. A similar red-shift was observed by Zhang et al. in which their AuNPs shifted from 525 to 529 nm after PNIPAM modification [17]. The PDI of the particles increased upon PNIPAM modification from 0.103 to 0.22. This increase in PDI is likely due to dispersity in the polymer, as the PDI increased similarly for all graft densities The \( D_h \) of the AuNPs increased from 31.3 ± 0.3 nm to 55.6 ± 4.6, 56.0 ± 0.8, or 53.7 ± 0.8 nm for AuNP-Low, AuNP-Medium, and AuNP-High, respectively, displayed in Fig. 2B. Size analysis by TEM measures the nanoparticle metal core, while DLS measures the core and polymer coating. There was no significant difference in \( D_h \) between the grafting conditions studied; all had essentially the same LSPR peak. The similarity in \( D_h \) is not wholly unexpected, as on spherical surfaces the polymer density distribution is less sensitive to increasing graft densities relative to that of flat surfaces [41]. There is an increasing volume the polymer can occupy with increasing distance from the spherical surface.

The zeta potential, or the electrokinetic potential, of the particles increased with increasing graft density, reaching \( \sim 0 \) mV at the highest polymer concentration used. The zeta potentials were \(-17.2 \pm 2.1, -2.1 \pm 0.4, \) and \( 0.3 \pm 0.3 \) mV for AuNP-Low, AuNP-Medium, and AuNP-High, respectively. The increase in zeta potential with increasing graft density is expected, as the citrate is displaced by the anchor group from the polymer chain. The neutralization in zeta potential confirms an increase in polymer coverage and a change in forces that stabilize the particles. At a low polymer graft density and negative zeta potential, particles are stabilized with a combination of steric and electrostatic forces. During polymer collapse in water, residual citrate ions on AuNP-Low electrostatically stabilize the particles against agglomeration, which is screened in high ionic strength solutions. As the polymer saturates the particle surface, all citrate ions are displaced and the particles are stabilized by steric forces.

Increasing the concentration of PNIPAM, while keeping the AuNP concentration the same, led to an increase in mass loss percentage from 300-425 °C as measured by TGA, corresponding to the loss of PNIPAM (Fig. 2C). Eq. (1) was used to calculate the graft density. The determined graft densities were 0.40, 0.30, and 0.09 chains/nm² for AuNP-High, AuNP-Medium, and AuNP-Low, respectively. Increasing the PNIPAM concentration to 500 \( \mu M \) yielded no observable increase in mass loss compared to 100 \( \mu M \), indicating saturation of the AuNP surface is reached at 0.40 chains/nm². This graft density is lower than previous studies with AuNPs modified with a thiol terminated PNIPAM (0.9 chains/nm²) [16] because a lipoic acid terminated polymer (bidentate disulfide anchor) was used rather than a monodentate thiol anchor [42].

The \( D_h \) of the AuNP-PNIPAM decreased and increased reversibly in water following a 30 min application of heat at 37 °C (>LCST). The particles returned to their initial \( D_h \) after sonication, as is shown in Fig. S3. All particles were stable in the salt solution prior to heating as there was no shift in LSPR, the \( D_h \) was the same as in water, and TEM images displayed primary particles as seen in Fig. 3A and B and Table 1. However, when heated in a 50 mM NaCl solution agglomeration onset occurred at \( >30 \) °C as seen in Fig. 4.

### Table 1

Characterization of AuNPs.

<table>
<thead>
<tr>
<th>Particle name</th>
<th>LSPR position (nm)</th>
<th>Mass% Loss (%)</th>
<th>( \delta ) (chains/nm²)</th>
<th>( D_h ) water 23 °C (nm)</th>
<th>PDI water 23 °C</th>
<th>Zeta potential (mV)</th>
<th>( D_h ) water 37 °C (nm)</th>
<th>( D_h ) 50 mM NaCl 23 °C (nm)</th>
<th>( D_h ) 50 mM NaCl 37 °C (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AuNP</td>
<td>525</td>
<td>NA</td>
<td>NA</td>
<td>31.3 ± 0.3</td>
<td>0.103 ± 0.011</td>
<td>NM</td>
<td>NM</td>
<td>NM</td>
<td>NM</td>
</tr>
<tr>
<td>AuNP-Low</td>
<td>528 ± 1</td>
<td>2.6 ± 0.1</td>
<td>0.09 ± 0.01</td>
<td>55.6 ± 4.6</td>
<td>0.226 ± 0.018</td>
<td>-17.2 ± 2.1</td>
<td>38.6 ± 3.2</td>
<td>54.7 ± 6.0</td>
<td>179.5 ± 28.6</td>
</tr>
<tr>
<td>AuNP-Medium</td>
<td>529 ± 1</td>
<td>8.7 ± 0.8</td>
<td>0.30 ± 0.03</td>
<td>56.0 ± 0.8</td>
<td>0.222 ± 0.025</td>
<td>-2.1 ± 0.4</td>
<td>42.9 ± 1.0</td>
<td>56.3 ± 0.9</td>
<td>192.6 ± 2.9</td>
</tr>
<tr>
<td>AuNP-High</td>
<td>529 ± 1</td>
<td>11.3 ± 0.4</td>
<td>0.40 ± 0.03</td>
<td>53.7 ± 0.8</td>
<td>0.229 ± 0.026</td>
<td>0.3 ± 0.3</td>
<td>41.4 ± 1.3</td>
<td>52.4 ± 1.8</td>
<td>187.4 ± 41.5</td>
</tr>
</tbody>
</table>

n = 3 experimental replicates for all except AuNP, in which n = 1. Error bars represent ±1 s.d. NA represents not applicable, and NM represents not measured. For DLS measurements, samples were equilibrated 10 min at the specified temperature before measurements were made.
3.2. AuNP-PNIPAM agglomeration as a function of graft density and heating time

Agglomerates/aggregates formation was dependent upon the PNIPAM graft density and the length of time the solution was maintained at 37°C. AuNP-Low irreversibly aggregated despite sonication and the 150 min relaxation period. Both the LSPR peak position and $D_h$ remained significantly different relative to the initial positions for all heating times ($p < 0.05$). The LSPR peak position redshifted with increasing heating times, up to 107 nm after a 6 h heat treatment in 50 mM NaCl as seen in Fig. 5. This increasing redshift with increasing heating times occurs due to further contraction of the polymer layer, decreasing the particle separation distance, which couples the plasmon modes. After 150 min at room temperature, the LSPR peak position remained redshifted 78 nm. A slight redshift in LSPR peak position of 2–5 nm during collapse of polymer is expected, because the increase in polymer density changes the refractive index [43]. A further redshift is due to
decreasing separation distance between particles, with a 57 nm redshift reported for 15 nm AuNP agglomerated using 8 nm DNA spacers [44]. Interestingly, the D_h had no appreciable change after the relaxation period. This constant D_h while the LSPR peak position blueshifts is interpreted as agglomerated particles separating during chain rehydration causing an increased separation distance between particles. The representative TEM image of heated AuNP-Low revealed heterogeneous clusters AuNPs surrounded by primary AuNPs with an increase in average particle area and variance as seen in Fig. 3D and Table 2. It is worth noting that several of these clusters contain nanoparticle cores adjacent to one another; this is suggestive of attractive particle-particle interactions. Increasing the polymer graft density lead to less substantial decreases in D_h and LSPR peak position after sonication. The increase in D_h and LSPR peak position for AuNP-Medium was between AuNP-Low and AuNP-High. The D_h for AuNP-High after 30 min of heat treatment and sonication was significantly different, (p < 0.05). The increase in D_h for AuNP-High remained significant after the 150 min relaxation period for heating times greater than 30 min. Chain-chain interactions between particles may persist over the relaxation period that was studied. The LSPR peak position for AuNP-High after heating for 6 h and sonication was redshifted 3 nm. This LSPR peak position returned to its initial value during the 150 min relaxation at room temperature. For AuNP-High, the separation distance between AuNP surfaces is sufficient to no longer induce coupling of the plasmon modes, as the LSPR peak position returns to its initial position. LSPR monitoring is insensitive to chain entanglements far from the particle surface that are observable with DLS. The TEM images of AuNP-High heated for 120 min revealed only primary particles, with no increase in particle area as seen in Fig. 3C and Table 2, suggestive of polymer entanglements that are not seen with TEM.

Saturation of the AuNPs was reached at a graft density of 0.40 chains/nm², indicating the footprint of the disulfide head is ~2.5 nm². A 20 nm diameter AuNP with a graft density of 0.09 chains/nm² would leave ~78% of the AuNP surface area without ligand head groups. This has the repercussion of allowing PNIPAM to collapse against the particle surface, reducing polymer thickness, and allowing van der Waals forces to become pertinent.

To shed light on the cause for graft density-dependent reversibility, a soft sphere model is used to calculate the total potential energy (E_tot) between sterically-stabilized particles [45]. The straightforward soft sphere model has been used to study the agglomeration of AuNPs stabilized with various molecular weights of poly(oxypropylene)diadime [46]; however more complex models predicting AuNP agglomeration exist [47]. In the soft sphere model, the E_tot is the sum of the steric (E_s) and van der Waals forces (E_vdw), as shown in Eq. (2). A negative E_tot value indicates attraction between particles. The van der Waals force of attraction (Eq. (3)) arises due to the high polarizability of the gold cores, while the steric repulsion (Eq. (4)) is due to the polymer coating on the particles. Electrostatic stabilization is neglected as citrate stabilized AuNPs agglomerate in 50 mM NaCl; the Debye length in 50 mM NaCl is 1.36 nm. In Eqs. (3) and (4), C is the center-to-center distance between particles, A is the Hamaker constant (1.95 eV for Au particles) [48], d is the diameter, I is the brush thickness, σ_A is the diameter of the area occupied by the disulfide on the particle (~1.6 nm). Graft density determines extended and collapsed polymer thickness. As seen in Fig. 6, an attractive van der Waals minimum develops with decreasing polymer thickness. The brush thickness was varied from 12 to 3.5 nm as the hydrodynamic radius of the AuNP increases 12 nm upon polymer modification, which contracts to 3.5 nm with polymer collapse at 37°C in water. The AuNP-Low still have a significant zeta potential, ~17 mV, stabilizing the particles during thermal collapse in water.

![Fig. 6. Variation in E_vdw with decreasing C at various polymer thicknesses from 12 nm (black) to 3.5 nm (green). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)](Image)

\[
E_{\text{tot}} = E_s + E_{\text{vdW}}
\]

\[
E_{\text{vdW}} = -\frac{A}{12} \left( \frac{d^2}{C^2} - \frac{d^2}{C^2} + 2 \ln \left( \frac{C^2 - d^2}{C^2} \right) \right)
\]

\[
E_s = \frac{500d^2}{(C-d)^2} k_B T e^{-\frac{(C-d)}{\sigma_A}}
\]

Particles with a high polymer graft density have a thick collapsed polymer layer that prevents van der Waals forces from becoming applicable during polymer collapse in salt solutions. With decreasing graft density, the collapsed polymer thickness decreases, giving rise to attractive van der Waals force between particles. Short separation distances between particles leads to a van der Waals force between particles leading to agglomeration. With smaller separation distances between particles the attractive force increases causing aggregation. The TEM images of the AuNP-Low agglomerates show groupings of overlapping particles, which in addition to the dramatic increase in LSPR peak position, suggests AuNP-Low surfaces are brought in close proximity (<10 nm) while AuNP-High are not.

### 4. Conclusions

Before AuNP-PNIPAM can be applied to an environment, a predictable response both above and below the LCST must be known. Clustering of nanoparticles changes the nanoparticles’ surface area, toxicity, and biodistribution. In salt solutions above the LCST of the polymer, AuNP-PNIPAM with a low graft density aggregate irreversibly. Agglomerates of AuNP-PNIPAM with a graft density of 0.40 chains/nm² can be dispersed with sonication however an increase in D_h is observed for graft densities studied in this work. The graft density dependent agglomeration and aggregation results seek to relate the importance of collapsed ligand structure on nanoparticle stability, and guide future design of AuNP-PNIPAM.
to be used in salt solutions. Additionally, when characterizing the agglomeration and aggregation of plasmonic nanoparticles, DLS and LSPR monitor different phenomenon which yield complementary information.

Acknowledgment

We would like to thank Guorong Sun for synthesis and characterization of the polymer used, and Tengjiao Wang for the HR-TEM characterization of the polymer.

Author contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Funding sources

Arkansas Biosciences Institute.

Appendix A. Supplementary material

The as synthesized AuNP TEM and corresponding histogram, AuNP-PNIPAM, hydrodynamic radius reversibility in water. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jcis.2017.07.044.

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