

Self-Assembled Materials Hot Paper

International Edition: DOI: 10.1002/anie.201702572 German Edition: DOI: 10.1002/ange.201702572

## Double-Layered Plasmonic–Magnetic Vesicles by Self-Assembly of Janus Amphiphilic Gold–Iron(II,III) Oxide Nanoparticles

Jibin Song<sup>+</sup>, Binghui Wu<sup>+</sup>, Zijian Zhou, Guizhi Zhu, Yijing Liu, Zhen Yang, Lisen Lin, Guocan Yu, Fuwu Zhang, Guofeng Zhang, Hongwei Duan,\* Galen D. Stucky,\* and Xiaoyuan Chen\*

**Abstract:** Janus nanoparticles (JNPs) offer unique features, including the precisely controlled distribution of compositions, surface charges, dipole moments, modular and combined functionalities, which enable excellent applications that are unavailable to their symmetrical counterparts. Assemblies of NPs exhibit coupled optical, electronic and magnetic properties that are different from single NPs. Herein, we report a new class of double-layered plasmonic–magnetic vesicle assembled from Janus amphiphilic Au-Fe<sub>3</sub>O<sub>4</sub> NPs grafted with polymer brushes of different hydrophilicity on Au and Fe<sub>3</sub>O<sub>4</sub> surfaces separately. Like liposomes, the vesicle shell is composed of two layers of Au-Fe<sub>3</sub>O<sub>4</sub> NPs in opposite direction, and the orientation of Au or Fe<sub>3</sub>O<sub>4</sub> in the shell can be well controlled by exploiting the amphiphilic property of the two types of polymers.

anus nanoparticles (JNPs) are a special class of anisotropic NPs exhibiting biphasic geometry of core compositions or distinct surface modifications, as presented by de Gennes in his Nobel lecture in 1991.<sup>[1]</sup> JNPs with diverse potential applications in surface property control, self-assembly, optical and electronic devices, have gained increasing interests in the field of chemistry, physics, materials science, and biology.<sup>[2]</sup> Recently, a variety of JNPs have been developed including organic NPs (such as block copolymer micelles, dendrimers, and nanofibers), inorganic NPs (such as dumbbell-, acorn-, or

[*]	Dr. J. Song, <sup>[+]</sup> Dr. Z. Zhou, Dr. G. Zhu, Dr. Y. Liu, Z. Yang, Dr. L. Lin,
	Dr. G. Yu, Dr. F. Zhang, Dr. G. Zhang, Dr. X. Chen
	Laboratory of Molecular Imaging and Nanomedicine
	National Institute of Biomedical Imaging and
	Bioengineering, National Institutes of Health
	Bethesda, MD 20892 (USA)
	E-mail: shawn.chen@nih.gov
	Dr. B. Wu, <sup>[+]</sup> Dr. G. D. Stucky
	Department of Chemistry & Biochemistry, University of California
	Santa Barbara, CA 93106 (USA)
	and
	Collaborative Innovation Center of Chemistry for Energy Materials
	Xiamen University, Xiamen 361005 (China)
	E-mail: stucky@chem.ucsb.edu
	Dr. H. Duan
	School of Chemical and Biomedical Engineering, Nanyang Techno-
	logical University
	70 Nanyang Drive, Singapore 637457 (Singapore)
	E-mail: hduan@ntu.edu.sg
[+]	These authors contributed equally to this work.
	Supporting information and the ORCID identification number(s) for
-	

the author(s) of this article can be found under: https://doi.org/10.1002/anie.201702572. raspberry-like clusters), and hybrid NPs with bicompartmentgrafted small molecules, polymer brushes or surfactants.<sup>[3]</sup> More interestingly, Janus metal or inorganic NPs exhibit unique features, such as functional compositions, modular functionalities, precisely controlled distribution of surface grafted molecules, hydrophilicity and hydrophobicity, dipole moments, which offer diverse applications that are not available to their symmetrical counterparts.<sup>[3a,b,4]</sup>

Most recently, there has been a growing interest in the construction of nanometer-sized assemblies of inorganic NPs because of their unique and enhanced optical and electronic properties that originate from the interaction or coupling of individual NPs.<sup>[4b,5]</sup> As de Gennes pointed out, the Janus feature often leads surfactant-like structures for JNPs, exhibiting intriguing assembly behaviors and properties.<sup>[1,2]</sup> According to computer simulation results, JNPs can form complex structures unavailable to homo NPs.<sup>[6]</sup> Although a series of JNPs have been prepared or functionalized, their assembly behavior and mechanism have rarely been investigated.<sup>[7]</sup> Even the experimental works on the self-assembly of small JNPs (<20 nm in diameters) are scarcely reported. So far, research on the self-assembly of JNPs are mainly focused on mono-component NPs of biphasic geometry with distinct surface functionalities, such as JNPs with bicompartment small molecules or DNAs on two sides.<sup>[8]</sup> Limited reports are available on the preparation of JNPs with both biphasic core compositions and Janus distribution of surface coatings, and investigation of their self-assembly properties.

Herein, we report a new model of "bundled amphiphilic block copolymer brushes" for the self-assembly of Janus Au-Fe<sub>3</sub>O<sub>4</sub> NPs, coated with Janus amphiphilic distribution of hydrophilic and hydrophobic polymer brushes on Au and  $Fe_3O_4$  surface, respectively (in Figure 1 a,b). Janus Au-Fe\_3O\_4 NPs, containing amphiphilic distribution of hydrophilic and hydrophobic polymer grafts, were prepared by exploiting the different surface binding abilities of Au and Fe<sub>3</sub>O<sub>4</sub> to thiolated and phosphonated groups, resulting in so-called Janus amphiphilic particles. As an exemplary system, we used amphiphilic Janus Au-Fe<sub>3</sub>O<sub>4</sub> NPs, whose self-assembly allows exact control on positioning and direction of JNPs. We considered the JNPs as amphiphiles, resembling "A-B" diblock copolymer "bundled brushes", and used the assembling ability of block copolymers to organize in a kinetically and thermodynamically controlled nanostructures due to the Janus segregation of the constituent amphiphilic blocks. Interestingly, two kinds of double-layered plasmonic-magnetic vesicles, with Au or Fe<sub>3</sub>O<sub>4</sub> localized dominantly on the outer or interior surface of the vesicular shell, were formed by changing the



**Figure 1.** Schematic illustration of the Janus Au-Fe<sub>3</sub>O<sub>4</sub> NPs grafted with hydrophilic polyethylene glycol (PEG) on Au and hydrophobic polystyrene (PS) on Fe<sub>3</sub>O<sub>4</sub> (a), with PS on Au and PEG on Fe<sub>3</sub>O<sub>4</sub> (b), and with binary mixed PEG and PS (c), and the hierarchical self-assembly of the resulting three kinds of Janus amphiphilic nanoparticles into double-layered plasmonic–magnetic vesicle 1 (d) and 2 (e) and mono-layered vesicle 3 (f) in aqueous media.

amphiphilic property of the polymer bushes on the Au or  $Fe_3O_4$  surface (Figure 1 d,e). In the double-layered vesicles (DL-Ve), the Au and  $Fe_3O_4$  not only imparted their intriguing physical properties to the assembly but also led to enhanced physical properties (SERS, optical, photoacoustic and magnetic activities) compared with those in discrete units. We attribute this to the interaction and coupling of the individual JNPs. More importantly, the vesicles with enhanced optical and magnetic properties were served as dual functional probes for in vivo dual photoacoustic and magnetic resonance (MR) imaging with high resolution and accuracy.

The Janus bifunctional composite 6.5–6.0 nm Au-Fe<sub>3</sub>O<sub>4</sub> NPs, containing Au and Fe<sub>3</sub>O<sub>4</sub> NPs, respectively, were firstly synthesized by a microwave heating approach (Figures 2 and S1, see the Supporting Information for the synthetic procedure).<sup>[9]</sup> The plasmon absorption peak of Au NP at  $\approx$  533 nm in the Janus Au-Fe<sub>3</sub>O<sub>4</sub> NPs showed a 16 nm red-shift compared with the Au NP prior to coating Fe<sub>3</sub>O<sub>4</sub> NP at 517 nm. The red-shift was caused by the charge variation of the Au while conjugating with Fe<sub>3</sub>O<sub>4</sub>, confirming the successful preparation of the JNPs.<sup>[10]</sup> The lattice fringes of Au have a spacing of 0.240 nm which corresponds to the (111) interplanar distance of face centered cubic (fcc) Au; the



Figure 2. a) TEM images of the Janus Au-Fe $_3O_4$  NP. b) UV/Vis spectra of Au NP and Janus Au-Fe $_3O_4$  NP in chloroform.

Angew. Chem. Int. Ed. 2017, 56, 8110-8114

© 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

distance between two adjacent planes in Fe<sub>3</sub>O<sub>4</sub> is 0.484 nm, resulting from a group of (111) planes in the inverse spinel structured  $Fe_3O_4$ . The (111) interplanar distance in  $Fe_3O_4$  is almost twice of that in Au with a very small lattice mismatch (<1%), indicating that the Fe<sub>3</sub>O<sub>4</sub> NPs are epitaxially overgrown on Au NPs due to their lattice matching.<sup>[10,11]</sup> The presence of Au and Fe<sub>3</sub>O<sub>4</sub> surfaces facilitates the modification of different chemical functionalities.<sup>[12]</sup> Au and Fe<sub>3</sub>O<sub>4</sub> show good conjugating ability specifically with thiolated and phosphonated molecules, respectively. Thus, thiolated polyethylene glycol (PEG-SH) and polystyrene (PS-SH), and phosphonated PEG (PEG-P) and PS (PS-P), were synthesized, where PEG (MW = 2 kDa) and PS (MW = 26 kDa) (Figure S2) are hydrophilic and hydrophobic polymers, respectively (Schemes S1, S2, and the Supporting Information for the synthesis procedures). Two types of amphiphilic Janus Au-Fe<sub>3</sub>O<sub>4</sub> NPs, coated with bicompartment polymer brushes with opposite amphiphilic property on Au and Fe<sub>3</sub>O<sub>4</sub> surface were synthesized using ligand exchange method, respectively, as depicted in Figure 1 a,b. Specifically, the type 1 Janus NPs, with PEG coating on Au and PS coating on Fe<sub>3</sub>O<sub>4</sub> (Au@PEG-Fe<sub>3</sub>O<sub>4</sub>@PS) were prepared by adding a mixture of PEG-SH and PS-P to Au-Fe<sub>3</sub>O<sub>4</sub> NPs (Figure 1 a). The type 2 Janus NPs, with PS grafting on Au and PEG on Fe<sub>3</sub>O<sub>4</sub> (Au@PS-Fe<sub>3</sub>O<sub>4</sub>@PEG), were prepared by adding a mixture of PEG-P and PS-SH to JNPs (Figure 1c). The <sup>1</sup>H NMR results (Figure S3) and high weight fraction of the polymer brushes coated on Janus NPs (over 35%) (Figure S4) confirmed the successful preparation of the amphiphilic NP<sub>8</sub>. This strategy demonstrates a particularly effective procedure for chemically coating amphiphilic distinct polymers on Au and Fe<sub>3</sub>O<sub>4</sub> surfaces, to give tunable structural parameters (graft density, molecular weight, etc.) and well-controlled physicochemical properties.

Since the amphiphilic polymer brushes densely covered the surface of the JNPs, the obtained Au@PEG-Fe<sub>3</sub>O<sub>4</sub>@PS or Au@PS-Fe<sub>3</sub>O<sub>4</sub>@PEG looked like a "bundle" of conventional amphiphilic diblock copolymers. We expected that the amphiphilic JNPs would show excellent self-assembly property in aqueous solution, thus leading to directed selfassembly of the NPs of diverse morphologies. The selfassembly process was initiated by adding a mixture of tetrahydrofuran and water to a solution of amphiphilic JNPs in a mixed organic solvent of DMF and THF. The assembled nanostructures were purified by centrifugation to remove the free JNPs. We first investigated the self-assembly property of type 1 Au@PEG-Fe<sub>3</sub>O<sub>4</sub>@PS, where Au@PEG and Fe<sub>3</sub>O<sub>4</sub>@PS serve as the hydrophilic and hydrophobic blocks, respectively. Figure 3a and S5, S6 illustrates the Transmission Electron Microscopy (TEM) images of the resultant vesicles, revealing a hollow structure with different contrast between the shell and interior. More interestingly, we found that the vesicular shell was composed of two layers of Au-Fe<sub>3</sub>O<sub>4</sub> NPs with Au extended dominantly to the outside of the shell and Fe<sub>3</sub>O<sub>4</sub> localized mostly face to face inside the shell, named doublelayered vesicle 1 (DL-Ve 1) (Figure 1d and Figure 3a). From element mapping images of DL-Ve-1, Au elements were localized outside of DL-Ve 1 shell (Figure 3b).We measured the shell thickness of the disrupted vesicle, caused by the high





*Figure 3.* TEM, SEM images, and TEM-element mapping images of the DL-Ve 1 (a, b), DL-Ve 2 (c, d), and ML-Ve 3 (e, f).

vacuum pressure while obtaining SEM images, as  $\approx 28$  nm (Figure 3a), comparable with the total size of two JNPs. Furthermore, the type 2 Au@PS-Fe<sub>3</sub>O<sub>4</sub>@PEG NPs (Figure 1b) also formed uniform double-layered vesicle using the same method (Figures 3c, S6), named double-layered vesicle 2 **(DL-Ve 2)**. As displayed in Figure 3c, Fe elements were placed outside of DL-Ve 2 shell, confirming the Fe<sub>3</sub>O<sub>4</sub> NPs were localized mostly outside the vesicular shell, which is opposite to the DL-Ve 1. In TEM images, the DL-Ve 2 exhibited a lower contrast compared with DL-Ve 1, due to the surface of DL-Ve 2 was coated with Fe<sub>3</sub>O<sub>4</sub> NP with low electron density. For DL-Ve-2, Fe<sub>3</sub>O<sub>4</sub>@PEG served as the hydrophilic part, assisting the vesicle to disperse in water. The average size of the DL-Ve1 and 2 is approximately 110 and 115 nm, respectively (Figure S7).

The amphiphilic Janus distribution of the polymer brushes on the Au-Fe<sub>3</sub>O<sub>4</sub> NP surface determines the unique doublelayered nanostructure of the vesicles as well as the position of the Au and Fe<sub>3</sub>O<sub>4</sub> in the vesicular shell. As an example, we find that the Au@PS-Fe<sub>3</sub>O<sub>4</sub>@PEG NPs formed dimers to short chains (Figure S8) with Au face to face with increasing initial concentration of the JNP during self-assembly. The driving force for the orientation of the JNP is the hydrophobic-hydrophobic interaction of the attached PS on Au surface when add water into the organic solution of JNP. To further verify the assumptions, we prepared Au-Fe<sub>3</sub>O<sub>4</sub> NPs coated with mixed PEG and PS on both Au and Fe<sub>3</sub>O<sub>4</sub> surfaces (type 3: Au-Fe<sub>3</sub>O<sub>4</sub>@PEG/PS) as a control sample (Figure 1e). It was self-assembled into mono-layered vesicles, mono-layered vesicle 3 (ML-Ve 3), whereas Au and  $Fe_3O_4$ were randomly paralleled inside the vesicular shell, as shown in Figure 1 f, Figure 3e and Figure S6, S9. From element mapping image, Au and Fe elements were mixed together in the ML-Ve 3 shell (Figure 3 f). Furthermore, when the MW of PS was decreased to 15 kDa (Figure S2), the obtained Au@PEG-Fe<sub>3</sub>O<sub>4</sub>@PS (Figure S10) or Au@PS-Fe<sub>3</sub>O<sub>4</sub>@PEG formed micelles, not vesicles (Figure S11). The Au and Fe<sub>3</sub>O<sub>4</sub> were located at the outer interface of the micelles formed by the first and second NPs, respectively, since both of them coated with PEG as hydrophilic part. We ascribed this to the reduced volume of the hydrophobic part due to using PS of lower MW; micelles are a more stable morphology to minimize the overall free energy of the system.<sup>[13]</sup>

The surface plasmon resonance (SPR) of gold nanocrystals is extremely sensitive to interparticle distances.<sup>[14]</sup> In comparison with the SPR band of Au-Fe<sub>3</sub>O<sub>4</sub> NP in the visible region, the SPR band for both DL-Ve 1 and 2 was broadened and red-shifted to the near-infrared (NIR) region, owing to interparticle plasmonic coupling between the Au NPs in the vesicular shell. The DL-Ve 2 exhibited a greater red shift than that of the DL-Ve 1, because the Au NPs were directed faceto-face and had shorter interparticle distance in the DL-Ve 2. For the single vesicle, scattering spectra obtained using the dark-field imaging microscopy (Figure S12), revealed greater red shift for the DL-Ve 2 than that of DL-Ve 1, which is consistent with the absorption spectra of the samples in aqueous solution.

Surface-enhanced Raman scattering (SERS) of the Raman dye attached on gold nanocrystal surface can be enhanced by the interparticle plasmonic coupling between gold nanocrystals upon clustering.<sup>[14b,15]</sup> We introduced thiolated Rhodamine (RhB-SH, Scheme S3) on the Au surface through Au-S bond to test the Raman scattering enhancement of the double-layered vesicle. The SERS enhancement factor of the DL-Ve 2 is  $2.5 \times 10^7$ , which is higher than that of the DL-Ve 1 ( $3.8 \times 10^6$ ) and ML-Ve 3 ( $5.8 \times 10^5$ ). We attributed the better SERS activity of the A DL-Ve 2 compared to the activities of the other two vesicles (Figure 3b) to the more closely spaced two layers of Au NPs in the vesicular shell.

Owing to their strong photoacoustic (PA) property, gold nanocrystal assemblies that have a high optical absorption coefficient have been used as optical agents in the biomedical imaging field.<sup>[16]</sup> Figure 4c shows the PA images of the double-layered and mono-layered vesicles at the same optical density (OD) value at 750 nm when illuminated with 750 nm laser. The PA amplitude of DL-Ve 2 was 2.2 and 5 times higher than the PA amplitudes of DL-Ve 1 and ML-Ve 3, respectively, at the same OD<sub>785</sub> (Figure 4d), which is consistent with the results of SPR red-shift and SERS enhancement.

Magnetic resonance imaging (MRI) is a powerful, noninvasive widely applied in clinical diagnostics.<sup>[17]</sup> To improve resolution and quality of MR image, special endeavor has been made to improve the  $T_2$  contrast efficiency  $(r_2)$ .<sup>[17–18]</sup>



**Figure 4.** a) UV/Vis spectra, b) SERS spectra, c) photoacoustic (PA) images, d) PA amplitude, e)  $T_2$ -weighted MR images and f) corresponding  $r_2$  values of the DL-Ve 1 and 2, and ML-Ve 3 and Janus NPs.

Among them, introducing assemblies of magnetic nanoparticles is probably the most effective yet intriguing approach for enhancing the  $r_2$ , which increases with decreasing interparticle distance.<sup>[19]</sup> In our experiment, we found that the DL-Ve exhibited greatly enhanced  $r_2$  activity compared with that of single JNPs (Figure 4e,f). The  $r_2$  values of the DL-Ve 1 ( $405 \pm 12.4 \text{ mm}^{-1}\text{s}^{-1}$ ) and DL-Ve 2 ( $295 \pm 7.2 \text{ mm}^{-1}\text{s}^{-1}$ ) are about 7 and 5 times greater than that of single JNP ( $56 \pm$  $4.2 \text{ mm}^{-1}\text{s}^{-1}$ ), due to the strong magnetic dipole interaction of the Fe<sub>3</sub>O<sub>4</sub> NPs in the vesicular shell. We attribute the better  $r_2$ activity of the DL-Ve 1 compared to that of DL-Ve 2 and ML-Ve 3 ( $193 \pm 6.6 \text{ mm}^{-1}\text{s}^{-1}$ ) to two layers of Fe<sub>3</sub>O<sub>4</sub> positioned face-to-face with shorter interparticle distance in the vesicle shell of DL-Ve 1.

Since the vesicles showed strong optical absorption in the NIR region and enhanced magnetic properties, and are stable under physiological conditions (Figure S13) and safe for bioapplication (Figure S14), we employed the DL-Ve 2 as dual PA and MRI agents in order to determine the accumulation of vesicles in the tumor region after injecting the vesicle (200  $\mu$ L, 500  $\mu$ g Au-Fe<sub>3</sub>O<sub>4</sub>mL<sup>-1</sup>) in PBS intravenously. The continuous enhancement of the PA signals (Figure 5a) and intensities (Figure S15) over time in the tumor region confirmed the accumulation and distribution of the vesicle in the tumor. Using high resolution 3D PA images (Figure S16) of the tumor, we obtained extensive information about the tumor, such as position, size and morphology. Consistent with the PA imaging findings, as shown in the  $T_2$ weighted MR images (Figure 5b) and  $T_2$  contrast intensity (Figure S17), we observed an obvious darkening effect at the tumor site after the vesicles were administered, which is



**Figure 5.** In vivo a) photoacoustic images and b)  $T_2$ -weighted MR images of tumor before and after injection of the double-layered vesicle 2, the yellow circles indicate the tumor sites.

a beneficial consequence of the high  $r_2$  value of the vesicle. The dual PA and MR imaging with the double-layered vesicles are able to provide rich information of tumor and also guide the cancer therapy, such as photothermal and photodynamic treatment, showing advantages than singe gold nanorod and iron oxide nanoparticle (Figure S18). Taken together with the SERS activity and high tumor accumulation efficiency (Figure S19) of the double-layered vesicles, the results demonstrated the great potential of the vesicles, formed by the self-assembly of JNPs, as multifunctional contrast agents and probes for future biomedical applications.<sup>[20]</sup>

In summary, we prepared two kinds of amphiphilic Janus Au@PS-Fe<sub>3</sub>O<sub>4</sub>@PEG and Au@PEG-Fe<sub>3</sub>O<sub>4</sub>@PS NPs using a highly efficient, easy procedure. Due to the amphiphilic Janus distribution of the polymer grafts on the Janus Au-Fe<sub>3</sub>O<sub>4</sub> surface, double-layered plasmonic-magnetic vesicles were formed mimicking the nature of classical amphiphilic "bundled block polymers". The positions of the Au and Fe<sub>3</sub>O<sub>4</sub> in the vesicular shell could easily be reversed by changing the amphiphilic property of the polymer brushes coated on their surface. Benefitting from the interparticle plasmonic coupling of the Au NPs and magnetic diploe interaction of the Fe<sub>3</sub>O<sub>4</sub> localized in the doubled vesicular shell, the vesicles exhibited greatly enhanced optical and magnetic properties. They demonstrated the potential to be used as a dual optical and MR imaging agent in vivo. Given current advances in the synthesis of functional copolymers and inorganic nanoparticles, the proposed strategy may open up a new avenue for the controlled preparation of novel Janus colloidal building blocks with adjustable surface coating for the fabrication of new functional materials and devices.

## Acknowledgements

This work was supported by the Intramural Research Program of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Institutes of Health (NIH).

## **Conflict of interest**

The authors declare no conflict of interest.



**Keywords:** amphiphilic polymers · imaging · Janus nanoparticles · self-assembly · vesicles

How to cite: Angew. Chem. Int. Ed. 2017, 56, 8110–8114 Angew. Chem. 2017, 129, 8222–8226

- [1] P. G. de Gennes, Rev. Mod. Phys. 1992, 64, 645-648.
- [2] a) A. Walther, A. H. E. Müller, *Chem. Rev.* 2013, *113*, 5194–5261; b) B. Wang, B. Li, B. Zhao, C. Y. Li, *J. Am. Chem. Soc.* 2008, *130*, 11594–11595; c) L. C. Bradley, K. J. Stebe, D. Lee, *J. Am. Chem. Soc.* 2016, *138*, 11437–11440.
- [3] a) F. Liang, K. Shen, X. Qu, C. Zhang, Q. Wang, J. Li, J. Liu, Z. Yang, Angew. Chem. Int. Ed. 2011, 50, 2379–2382; Angew. Chem. 2011, 123, 2427–2430; b) F. Wurm, A. F. M. Kilbinger, Angew. Chem. Int. Ed. 2009, 48, 8412–8421; Angew. Chem. 2009, 121, 8564–8574; c) B. Wang, B. Li, B. Dong, B. Zhao, C. Y. Li, Macromolecules 2010, 43, 9234–9238; d) J.-K. Kim, E. Lee, Z. Huang, M. Lee, J. Am. Chem. Soc. 2006, 128, 14022–14023.
- [4] a) S. X. Xing, Y. H. Feng, Y. Y. Tay, T. Chen, J. Xu, M. Pan, J. T. He, H. H. Hng, Q. Y. Yan, H. Y. Chen, *J. Am. Chem. Soc.* 2010, *132*, 9537–9539; b) J. van Herrikhuyzen, G. Portale, J. C. Gielen, P. C. M. Christianen, N. A. J. M. Sommerdijk, S. C. J. Meskers, A. P. H. J. Schenning, *Chem. Commun.* 2008, 697–699.
- [5] a) S. Mallidi, T. Larson, J. Tam, P. P. Joshi, A. Karpiouk, K. Sokolov, S. Emelianov, *Nano Lett.* 2009, *9*, 2825–2831; b) N. J. Halas, S. Lal, W.-S. Chang, S. Link, P. Nordlander, *Chem. Rev.* 2011, *111*, 3913–3961; c) Z. H. Nie, D. Fava, E. Kumacheva, S. Zou, G. C. Walker, M. Rubinstein, *Nat. Mater.* 2007, *6*, 609–614; d) J. Hu, T. Wu, G. Zhang, S. Liu, *J. Am. Chem. Soc.* 2012, *134*, 7624–7627.
- [6] a) F. Sciortino, A. Giacometti, G. Pastore, *Phys. Rev. Lett.* 2009, 103, 237801; b) S. C. Glotzer, *Science* 2004, 306, 419–420; c) S. C. Glotzer, M. J. Solomon, *Nat. Mater.* 2007, 6, 557–562.
- [7] L. Hong, A. Cacciuto, E. Luijten, S. Granick, *Langmuir* 2008, 24, 621–625.

- [8] L. H. Tan, H. Xing, H. Chen, Y. Lu, J. Am. Chem. Soc. 2013, 135, 17675-17678.
- [9] B. Wu, S. Tang, M. Chen, N. Zheng, Chem. Commun. 2014, 50, 174–176.
- [10] H. Yu, M. Chen, P. M. Rice, S. X. Wang, R. L. White, S. Sun, *Nano Lett.* 2005, 5, 379–382.
- [11] B. Wu, H. Zhang, C. Chen, S. Lin, N. Zheng, Nano Res. 2009, 2, 975–983.
- [12] C. Xu, J. Xie, D. Ho, C. Wang, N. Kohler, E. G. Walsh, J. R. Morgan, Y. E. Chin, S. Sun, *Angew. Chem. Int. Ed.* **2008**, 47, 173–176; *Angew. Chem.* **2008**, 120, 179–182.
- [13] a) C. Yi, S. Zhang, K. T. Webb, Z. Nie, Acc. Chem. Res. 2017, 50, 12–21; b) R. Shenhar, T. B. Norsten, V. M. Rotello, Adv. Mater. 2005, 17, 657–669.
- [14] a) A. Klinkova, R. M. Choueiri, E. Kumacheva, *Chem. Soc. Rev.* **2014**, 43, 3976–3991; b) A. Kumar, S. Kim, J.-M. Nam, *J. Am. Chem. Soc.* **2016**, *138*, 14509–14525.
- [15] a) M. J. Banholzer, J. E. Millstone, L. Qin, C. A. Mirkin, *Chem. Soc. Rev.* 2008, *37*, 885–897; b) R. A. Alvarez-Puebla, L. M. Liz-Marzán, *Small* 2010, *6*, 604–610.
- [16] L. Nie, X. Chen, Chem. Soc. Rev. 2014, 43, 7132-7170.
- [17] D. Ling, N. Lee, T. Hyeon, Acc. Chem. Res. 2015, 48, 1276-1285.
- [18] N. Lee, T. Hyeon, Chem. Soc. Rev. 2012, 41, 2575-2589.
- [19] a) Y. Matsumoto, A. Jasanoff, *Magn. Reson. Imaging* 2008, 26, 994–998; b) D. Wang, B. Lin, T. Shen, J. Wu, C. Xia, B. Song, H. Ai, *Sci. Bull.* 2016, 61, 1023–1030.
- [20] L. Vigderman, E. R. Zubarev, *Adv. Drug Delivery Rev.* **2013**, *65*, 663–676.

Manuscript received: March 11, 2017

- Revised manuscript received: May 5, 2017
- Accepted manuscript online: May 30, 2017
- Version of record online: June 8, 2017