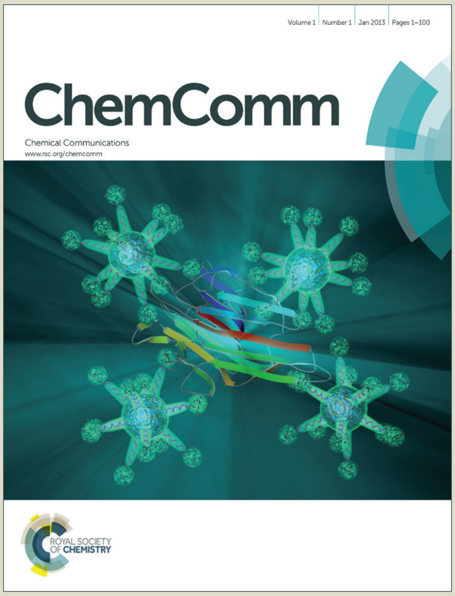
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Chemical Communications

COMMUNICATION

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Robust Platforms for Creating Organic-Inorganic Nanocomposite Microspheres: Decorating Polymer Microspheres Containing Mussel-Inspired Adhesion Layers with Inorganic Nanoparticles

H. Satoh,[a] Y. Saito[a] and H. Yabu[a,b*]

We describe a method for creating robust and stable core-shell polymer microspheres decorated with inorganic (IO) nanoparticles (NPs) by self-organization process and heterocoagulation with using a mussel-inspired polymer adhesive layer between the IO NPs and the microspheres.

Polymer microspheres decorated with functional inorganic (IO) nanoparticles (NPs) have received significant attention because of their potential applications in photonics, electronics, and biotechnology[1-4]. Functional IO NPs possess unique optical, electrical, mechanical, and chemical properties derived from their high surface-to-volume ratios and quantum effects[5-7]. Polymer microspheres may be excellent substrates for NPs because of their high surface-to-volume ratios and their ability to disperse readily in various solvents[8-10]. The surface decoration of functional IO NPs, such as those composed of magnetic, noble metal, and semiconductor materials, has produced composite particles that have demonstrated great potential for use in many applications, from photovoltaics to cancer therapies[11,12].Electrostatic interactions between oppositely charged IO NPs and polymer microspheres, known as heterocoagulation, are generally used to decorate polymer microspheres with IO NPs[13]. Many types of composite microspheres, including organic-organic, IO-organic, and IO-IO microspheres, have been developed based on heterocoagulation because it is a simple, facile fabrication method[3,14,15]. However, one disadvantage of heterocoagulation is its poor stability to environmental changes in the dispersion media, such as the solvent polarity, temperature, and salt concentration[16]. For example, the structures of heterocoagulated composite microspheres are easily damaged by high salt concentrations because of the electrostatic shielding of surface charges, both of IO NPs and microspheres[17]. To use heterocoagulated composite microspheres for practical applications, including under biological conditions where salt concentrations are usually high enough to remove IO NPs from the surface of microspheres, robust composite microspheres must be fabricated.

We have developed a simple method, known as self-organized precipitation (SORP), for preparing polymer microspheres[18]. The method involves evaporating a good solvent from a polymer solution containing a poor solvent. Microspheres have been prepared by SORP from a variety of materials, including conductive polymers, engineering plastics, biodegradable polymers, polymer blends, and block copolymers[19]. Furthermore, various kinds of composite microspheres containing phase-separated structures consisting of polymer-stabilized IO nanoparticles and polymers have also been fabricated[20,21]. We have also reported that the surface charges of microspheres can be controlled by end-functionalized polymers, and composite microspheres containing Au nanoparticles can be formed by heterocoagulation[22].Recently, it has been reported that the catechol group, which is found in the adhesive proteins of mussels, shows excellent adhesion properties for many materials, including noble metals, metal oxides, and other ceramics[23-26]. Catechol groups have also been used as anchoring moieties to fix polymers to the surface of NPs in order to disperse them in organic solvents[27,28]. An advantage of the catechol group over other adhesive moieties, such as thiols and silanes, is that the adhesion does not depend on the substrate. We have also reported that amphiphilic copolymers containing mussel-inspired adhesive moieties show excellent adhesion properties on IO substrates under harsh conditions such as low pHs[29]. Here, we describe a novel method for creating robust, stable polymer microspheres decorated with IO NPs by using a mussel-inspired polymer as an adhesive layer between the IO NPs and the microspheres. The core-shell polymer microspheres composed of PS cores and mussel-inspired adhesive polymer shells were prepared by SORP. Au, Fe_2O_3, and Al_2O_3 IO NPs adhered to the surface of the microspheres. We also investigated the stability of composite microspheres especially for high salt conditions, which decreased electrostatic interactions.

Mussel-inspired adhesive copolymers were synthesized according to literature methods[29]. The detail synthetic routes were shown in ESI, S-1. The compositions, molecular weights, and polydispersities of the synthesized copolymers are listed in Table 1. Tetrahydrofuran (THF) was purchased from Wako Chemical Industry, Co. Ltd., Japan. Polystyrene (PS; 44 kg/mol) and hydroxyl-terminated PS (PS-OH; 7 kg/mol) were purchased from Polymer Source Inc., Canada. An aqueous dispersion of citrate-reduced Au NPs (average diameter (D_{ave}) = 20 nm, ζ-potential = -40 mV) was purchased from Sigma-Aldrich, USA. An aqueous dispersion of positively charged Au NPs (D_{ave} = 25 nm, ζ-potential = +12 mV), modified with 2-aminoethanethiol hydrochloride, was synthesized according to a literature procedure[30] (ESI, S-2). Fe_2O_3 NPs (D_{ave} = 87 nm, ζ-potential = +10 mV) and Al_2O_3 NPs (D_{ave} = 128 nm, ζ-potential = +42 mV) were purchased from Aldrich.

Table 1. Synthesized copolymers of *N*-dodecyl acrylamide (DAA) and *N*-(3,4-Dihydroxyphenthyl)methacrylamide (DMA)

	DAA:DMA	Mn(Kg/mol)	Mw/Mn
Polymer 1	2:1	9.9	2.3
Polymer 2	4:1	12.0	2.5
Polymer 3	8:1	10.2	2.4
Polymer 4	12:1	14.1	2.4

Table 2. Prepared composite microspheres

	Shell	Core	D_h (nm)	ζ-potential (mV)
MS-1	Polymer 1	PS	336±121	-42.8
MS-2	Polymer 2	PS	756±342	-45.9
MS-3	Polymer 3	PS	215±64	-34.1
MS-4	Polymer 4	PS	343±170	-38.2
MS-5	PS-OH	PS	957±492	-44.1

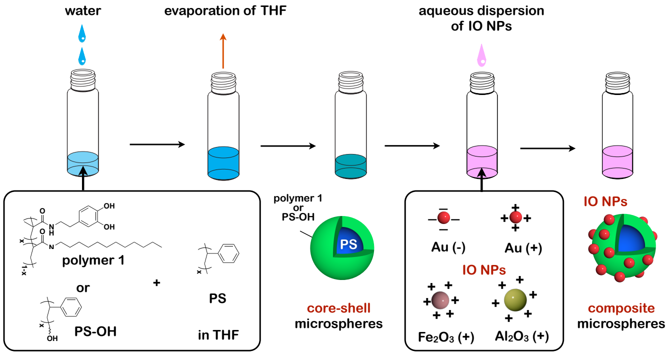


Figure 1. Schematic illustration of the preparation of core-shell microspheres and composite microspheres.

Figure 1 shows a schematic illustration of the preparation of core-shell microspheres (MS-1-5) and composite microspheres. Core-shell microspheres were prepared by SORP[31]. The composition of each microsphere is shown in Table 2. THF solutions of PS and other polymers were used to prepare 1.0 mg/mL THF solutions. Water (1 mL) was added slowly to each 1.0 mg/mL THF solution (0.5 mL) and the THF was evaporated for 2 days. After complete evaporation of THF, an aqueous dispersion of particles was obtained. It has been reported that core-shell type phase separation was formed during precipitation of two distinct polymers whose hydrophobicities are much different[22]. Since the polymers are precipitated as microspheres in water, more hydrophilic polymer forms shells of microspheres, the other forms core. Since the particles prepared from synthesized copolymers and PS form core-shell structures and negatively charged surfaces, PS-OH should be located on the surface of the particles with mixing with more hydrophobic PS. The hydrodynamic diameters (D_h) of the particles were measured by dynamic light scattering (DLS; Zetasizer Nano, ZS-1, Malvern, Inc., UK) after removal of free NPs by ultracentrifugation. The structural analysis was performed by scanning electron microscopy and transmission electron microscopy (ESI, S-3). Positively charged Au NPs (200 μL) were added to an aqueous dispersion of microspheres (100 μL) and incubated for 1 h at 25 °C in the water bath. UV-Vis spectra of the mixture were obtained by using a UV-Vis-NIR spectrometer (V-670, Jasco, Japan) after dilution with membrane-filtered water (300 μL). To evaluate effects of the addition of salt, 2 M KCl aq. (300 μL) was added to the mixture. UV-Vis spectra of the dispersions containing salt were also obtained. Surface structures of composite microspheres before and after the addition of salt were observed by SEM. Fe_2O_3 NPs or Al_2O_3 NPs (0.5 wt %) were dispersed in membrane-filtered water. After overnight incubation, large precipitates were removed. The dispersion (50 μL) and the MS-2 aqueous dispersion (100 μL) were mixed and stirred with a vortex mixer overnight. The composite microspheres were collected by centrifugation (2000 rpm, 15 min, 5 °C). The surface structures of the composite microspheres were also observed by FE-SEM. To examine the magnetic alignment of Fe_2O_3 NPs and MS-1 composite microspheres, the aqueous dispersion of composite microspheres (10 μL) was dropped onto a glass slide and a glass cover slip was placed over it. The alignment of the microspheres was observed by using an optical microscope (VHX-600, Keyence, Japan) with a neodymium magnet placed near the sample specimen.

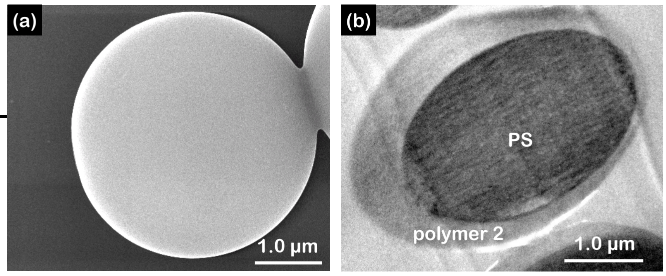


Figure 2. Typical SEM and cross-sectional TEM image of a core-shell microsphere (MS-2).

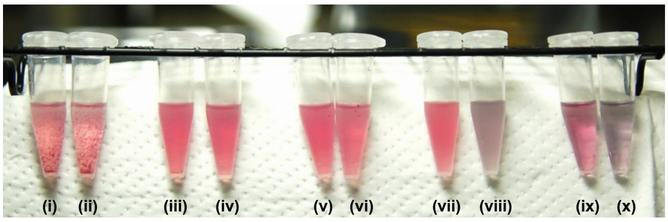


Figure 3. Photograph of composite microsphere dispersions of MS-1 (i), MS-2 (iii), MS-3 (v), MS-4 (vii), and MS-5 (ix) as-mixed Au NPs, and MS-1 (ii), MS-2 (iv), MS-3 (vi), MS-4 (viii), and MS-5 (x) after the addition of 2 M KCl solution.

Typical SEM and cross-sectional TEM images of MS-2 are shown in Figures 2 (a) and (b), respectively. Spherical particles were obtained with a core-shell structure consisting of a PS core, which had a higher electron density than polymer 2, and a polymer 2 shell. The structures of the other microspheres were also observed by TEM (ESI, S-4). The hydrodynamic diameters (D_h) and ζ-potentials of microspheres are listed in Table 2. Submicron- to micron-sized microspheres were prepared, and their ζ-potentials were negative. These results indicate that hydrophilic moieties including catechol and hydroxyl groups located at surfaces of microspheres. It was noteworthy MS-1 and MS-2 have larger negative values of surface ζ-potentials than MS-3 and MS-4, whose content of catechol groups less than MS-1 and MS-2. These results suggest that positively charged IO NPs were suitable for forming composite microspheres by heterocoagulation. The negatively charged Au NPs with citrate-stabilized surfaces did not adhere to the surface of the negatively charged microspheres (ESI, S-5). Since electrostatic interaction attracted core-shell polymer particles and inorganic nanoparticles from far field, however, only direct chemical interaction is allowed for catechol-gold interaction. Thus, the nanoparticles should be accumulated by electrostatic interaction, and then, catechol moieties stabilize further. When negatively charged gold nanoparticles mixed with negatively charged core-shell polymer particles, electrostatic repulsion avoided adhesion of nanoparticles.

To form composites of microspheres and Au NPs, a dispersion of positively charged Au NPs stabilized with aminoethanethiol hydrochloride were added to the dispersion of each microsphere. Figure 3 shows dispersions of MS-1 to MS-5 composite microspheres before and after the addition of 2 M KCl. To examine the stability of composite microspheres, 2 M KCl, which is a sufficiently high salt concentration to coagulate any IO NPs used in this experiment, was added to the dispersion of composite microspheres[32]. MS-1, which had a polymer 1 shell that contained the highest amount of catechol moieties, easily aggregated after Au NPs were added to the dispersion (Figure 3 (i)), and the aggregated particles were not changed by the addition of 2 M KCl (Figure 3 (ii)). Because of their excellent adhesion properties, the large number of catechol groups on the surface of the microspheres resulted in each Au NP being strongly attached to many microspheres, and the catechol groups acted as cross-linkers between microspheres and Au NPs. As a result, the microspheres and Au NPs aggregated three-dimensionally (ESI, S-6). This highlights the strong adhesive properties of catechol moieties. In contrast, other microspheres were still dispersed in water after the addition of Au NPs (Figures 3 (iii), (v), (vii), and (ix)). Furthermore, the color of the MS-2 and MS-3 composite microsphere dispersions did not change after the addition of 2 M KCl (Figures 3 (iv) and (vi)), whereas those of MS-4 and MS-5 microspheres changed from red to purple (Figures 3 (viii) and (x)). To reveal the nanoscale mechanism of these colorimetric changes, the absorption spectra in the visible light region and surface structures of the MS-2 and MS-5 composite microspheres before and after the addition of 2 M KCl were observed. At high salt concentrations, colloidal particles can be salted out because the shielding of the electric double layers formed on the surface of the colloidal particles reduces the Debye length. In the MS-5 and Au NP composite microspheres, the MS-5 microsphere and the Au NP were only bound together by electrostatic interactions. Figures 4 (a) and (d) show the absorption spectra of MS-2 and MS-5 composite microspheres before and after the addition of 2 M KCl, respectively. Before the addition of 2 M KCl, there were obvious absorption peaks around $\lambda = 530$ nm arising from the plasmonic absorption band of the Au NPs adhered to the MS-2 or MS-5 microspheres (black solid lines). After the addition of 2 M KCl solution, the plasmonic absorption peak of the MS-5 composite microspheres was substantially red-shifted, although that of the MS-2 microspheres was unchanged (black dashed lines). These results indicate that the Au NPs were aggregated in the MS-5 microspheres[33]. Figure 4 (b) and 4 (c) show the SEM images of the MS-2 composite microspheres before and after addition of the 2 M KCl solution, respectively. Au NPs adhered to the surface of the MS-2 microspheres and were homogeneously distributed. However, the Au NPs aggregated on the surface of MS-5 microspheres after addition of the 2 M KCl solution (Figure 4 (f)) compared with before the addition of the 2 M KCl solution (Figure 4 (e)). Furthermore, Au NPs removed from the surface of MS-5 microspheres were also observed as aggregates on the substrate (inset image in Figure 4 (f)). These results show that MS-2 microspheres, which had mussel-inspired adhesion polymers as the shell, have stable adhesion properties for Au NPs at high salt concentrations.

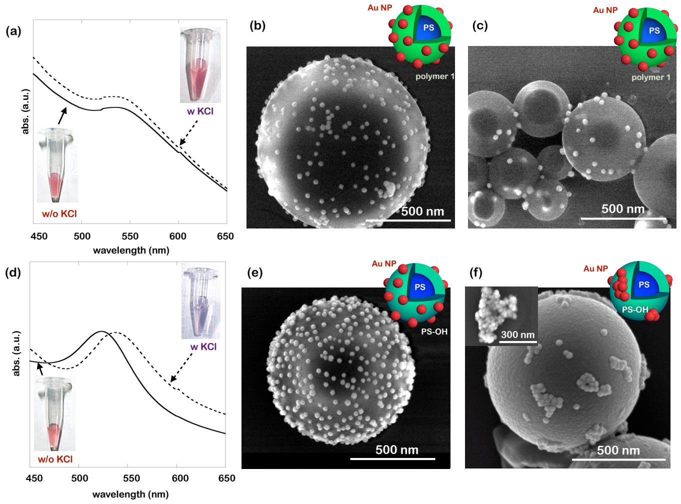


Figure 4. Absorption spectra of dispersions of composite microspheres composed of MS-2 (a) and MS-5 (d) before and after the addition of 2 M KCl solution. SEM images of composite microspheres of MS-2 (b), (c), and MS-5 (e), (f) before (b), (e) and after (c), (f) the addition of 2 M KCl solution.

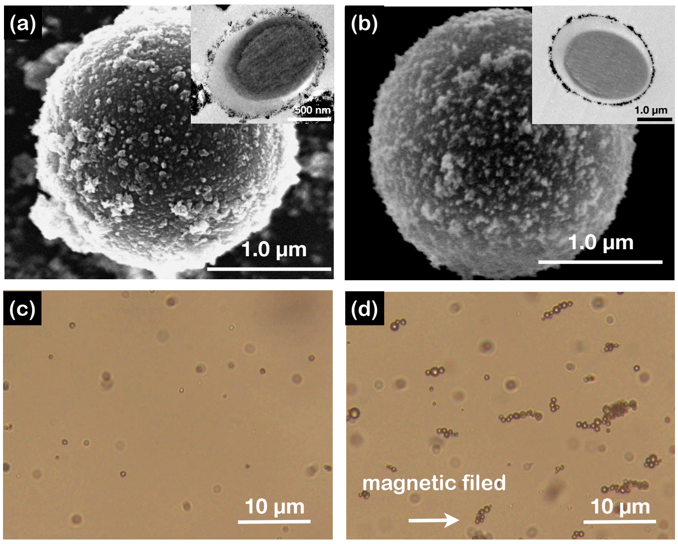


Figure 5. SEM (a), (b) and cross-sectional TEM (insets) images of MS-2 and Al_2O_3 (a) and MS-2 and Fe_2O_3 (b) composite microspheres. Optical microscope images of an aqueous dispersion of MS-2 and Fe_2O_3 composite microspheres as cast (c) and under an applied magnetic field (d).

When a high concentration salt solution was added to the dispersion of the composite microspheres, the shielding of the electric double layers weakened the electrostatic interactions between MS-5 microspheres and Au NPs. As a result, the Au NPs were detached from the surface of the MS-5 microspheres, and aggregated on their surface or the substrate. In contrast, MS-2 microspheres had a negative surface charge and the adhesion properties of the catechol moieties. Catechol moieties strongly adhere to Au surfaces[34]. When the salt solution was added, the electric double layers of the MS-2 composite particles were also weakened; however, the catechol moieties were still anchored to the Au NPs on the surface of the MS-2 microspheres. To prove the adoptability of catechol-containing polymer particles for other particles, we made composite particles with $Al_2O_3$and Fe_2O_3 NPs. SEM images of the MS-2 and Al_2O_3 NP microspheres and the MS-2 and Fe_2O_3 NP microspheres are shown in Figures 5 (a) and (b), respectively. Both types of NP successfully adhered to the MS-2 surfaces and formed composite microspheres. Inset images show cross-sectional TEM images of these composite microspheres. In both cases, the MS-2 and the adhered NP core-shell structures were clearly visible. Furthermore, when the dispersion of MS-2 and Fe_2O_3 NP microspheres were placed under a magnetic field, the composite microspheres aligned along the magnetic field without the removal of the Fe_2O_3 NPs (Figures 5 (c) and (d))[35]. These results show that the core-shell microspheres containing a suitable amount of catechol moieties can act as a platform for the preparation of organic-IO composite microspheres with various functional IO NPs.

Conclusions

We have prepared core-shell polymer microspheres composed of PS cores and mussel-inspired adhesive polymer shells by SORP. Au, Fe_2O_3, and Al_2O_3 NPs adhered to the surface of the microspheres. The composite microspheres showed high stability under high salt concentrations or in magnetic fields. These results indicate that composite microspheres composed of mussel-inspired adhesion layers are promising candidates for preparing a platform for stable functional nanocomposite particles. This strategy will pave the way for the fabrication of a new class of drug carriers in drug delivery systems, bioimaging agents, metamaterials with three-dimensional nanoarchitectures, and dispersable sensors based on the plasmonic absorption of noble metals through the incorporation of functional IO and metal NPs on microspheres[36-39].

Notes and references

[a] Institute of Multidisciplinary Research for Advanced Materials (IMRAM), Tohoku University, 2-1-1, Katahira, Aoba-Ku, Sendai 980-8577, Japan
[b] Precursory Research for Embryonic Science and Technology (PRESTO), Japan Science and Technology Agency (JST), Saitama, Kawaguchi 332-0014, Japan

Electronic Supplementary Information (ESI) available: Whole suppoting information included. See DOI: 10.1039/c000000x/

1. S. Srivastava, J. L. Schaefer, Z. Yang, Z. Tu, and L. A. Archer, Adv. Mater., 2013, 26, 201–234.
2. S. Mühlig, A. Cunningham, J. Dintinger, M. Farhat, S. B. Hasan, T. Scharf, T. Bürgi, F. Lederer, and C. Rockstuhl, Sci. Rep., 2013, 3.
3. C. S. Wagner, S. Shehata, K. Henzler, J. Yuan, and A. Wittemann, Journal of Colloid And Interface Science, 2011, 355, 115–123.
4. H.-B. Yao, Y. Guan, L.-B. Mao, Y. Wang, X.-H. Wang, D.-Q. Tao, and S.-H. Yu, J. Mater. Chem., 2012.
5. X. M. Qian and S. M. Nie, Chem. Soc. Rev., 2008, 37, 912.
6. M. Brust, J. Fink, D. Bethell, and D. J. Schiffrin, J Chem Soc, 1995.
7. A. R. Studart, Adv. Mater. Weinheim, 2012, 24, 5024–5044.
8. M. E. Pekdemir, D. Ertürkan, H. Külah, I. H. Boyacı, C. Ozgen, and U. Tamer, Analyst, 2012, 137, 4834–4840.
9. T. Ozel, S. Nizamoglu, M. A. Sefunc, O. Samarskaya, I. O. Ozel, E. Mutlugun, V. Lesnyak, N. Gaponik, A. Eychmuller, S. V. Gaponenko, and H. V. Demir, ACS Nano, 2011, 5, 1328–1334.
10. B. Su, C. Zhang, S. Chen, X. Zhang, L. Chen, Y. Wu, Y. Nie, X. Kan, Y. Song, and L. Jiang, Adv. Mater., 2014, in press.
11. V. E. Ferry, J. N. Munday, and H. A. Atwater, Adv. Mater., 2010, 22, 4794–4808.
12. L. C. Kennedy, L. R. Bickford, N. A. Lewinski, A. J. Coughlin, Y. Hu, E. S. Day, J. L. West, and R. A. Drezek, Small, 2010, 7, 169–183.
13. G. Li, X. Yang, and J. Wang, Colloids and Surfaces A: Physicochemical and Engineering Aspects, 2008, 322, 192–198.
14. J.-H. Lee, M. A. Mahmoud, V. Sitterle, J. Sitterle, and J. C. Meredith, J. Am. Chem. Soc., 2009, 131, 5048–5049.
15. B. Zhao and M. M. Collinson, Chem. Mater., 2010, 22, 4312–4319.
16. E. Tombácz, Á. Dobos, M. Szekeres, H. D. Narres, E. Klumpp, and I. Dékány, Colloid Polym Sci, 2000, 278, 337–345.
17. R. D. Nelson, *"Dispersing powders in liquids"*, 2012. Ed. J. C. Williams, T. Allen, Elsevier
18. H. Yabu, T. Higuchi, K. Ijiro, and M. Shimomura, Chaos, 2005, 15, 047505.
19. H. Yabu, Polym. J., 2013, 45(3), 261-268.
20. H. Yabu, K. Koike, K. Motoyoshi, T. Higuchi, and M. Shimomura, Macromol. Rapid Commun., 2010, 31, 1267–1271.
21. H. Yabu, M.-A. Kanahara, M. Shimomura, T. Arita, K. Harano, E. Nakamura, T. Higuchi, and H. Jinnai, ACS Appl. Mater. Interfaces, 2013, 5(8), 3262-3266.
22. M. Kanahara, M. Shimomura, and H. Yabu, Soft Matter, 2014, 10, 275–280.
23. H. Lee, B. P. Lee, and P. B. Messersmith, Nature, 2007, 448, 338–341.
24. J. L. Dalsin and P. B. Messersmith, Materials Today, 2005, 8(9), 38-46.
25. H. Lee, S. M. Dellatore, W. M. Miller, and P. B. Messersmith, Science, 2007, 318, 426–430.
26. B. H. Kim, D. H. Lee, J. Y. Kim, D. O. Shin, H. Y. Jeong, S. Hong, J. M. Yun, C. M. Koo, H. Lee, and S. O. Kim, Adv. Mater., 2011, 23, 5618–5622.
27. K. C. L. Black, Z. Liu, and P. B. Messersmith, Chem. Mater., 2011, 23, 1130–1135.
28. Q. Ye, F. Zhou, and W. Liu, Chem. Soc. Rev., 2011, 40, 4244.
29. Y. Saito, T. Kawano, M. Shimomura, and H. Yabu, Macromol. Rapid Commun., 2013, 34, 630–634.
30. M. Kanahara, M. Shimomura, and H. Yabu, Macromol. Mater. Eng., 2013, 299, 478–484.
31. T. Higuchi, A. Tajima, H. Yabu, and M. Shimomura, Soft Matter, 2008, 4, 1302-1305.
32. F. Ito, K. Makino, H. Ohshima, H. Terada, and S. Omi, Colloids and Surfaces A: Physicochemical and Engineering Aspects, 2004, 233, 171–179.
33. S. Link and M. A. El-Sayed, J. Phys. Chem. B, 1999, 103, 4212–4217.
34. X. Fan, L. Lin, J. L. Dalsin, and P. B. Messersmith, J. Am. Chem. Soc., 2005, 127, 15843–15847.
35. D. Nagao, M. Sugimoto, A. Okada, H. Ishii, M. Konno, A. Imhof, and A. van Blaaderen, Langmuir, 2012, 28, 6546–6550.
36. J. H. Mun, Y. H. Chang, D. O. Shin, J. M. Yoon, D. S. Choi, K.-M. Lee, J. Y. Kim, S. K. Cha, J. Y. Lee, J.-R. Jeong, Y.-H. Kim, S. O. Kim, Nano Lett., 2013, 13(11), 5720-5726.
37. D. O. Shin, J. H. Mun, G-T. Hwang, J. M. Yoon, J. Y. Kim, J. M. Yun, Y.-B. Yang, Y. Oh, J. Y. Lee, J. Shin, K. J. Lee, S. Park, J. U. Kim, S. O. Kim, ACS Nano, 2013, 7(10), 8899-8907.
38. D. O. Shin, D. H. Lee, H.-S. Moon, S.-J. Jeong, J. Y. Kim, J. H. Mun, H. Cho, S. Park, S. O. Kim, Adv. Func. Mater., 2011, 21(2), 250-254.
39. H. Yabu, T. Higuchi, H. Jinnai, Soft Matter, 2014, 10(17), 2919-2931.