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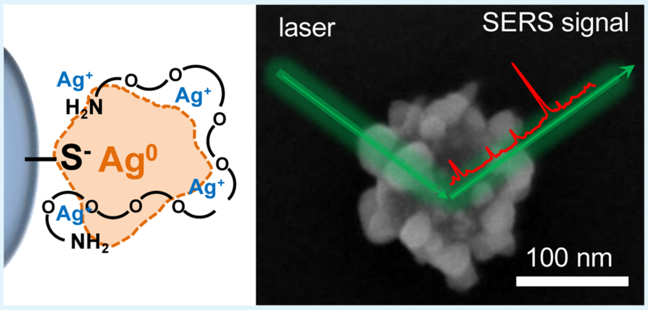
Polymer-Mediated Formation and Assembly of Silver Nanoparticles on Silica Nanospheres for Sensitive Surface-Enhanced Raman Scattering Detection

Homan Kang,[†] Joonhyuk Yim,[‡] Sinyoung Jeong,[§] Jin-Kyoung Yang,[‡] San Kyeong,[‡] Su-Ji Jeon,[∥] Jaehi Kim,[‡] Khee Dong Eom,[‡] Hyunmi Lee,[‡] Hye-In Kim,[∥] Dae Hong Jeong,[†,§] Jong-Ho Kim,*[,∥] and Yoon-Sik Lee*[,†,‡]

[†]Interdisciplinary Program in Nano-Science and Technology, Seoul National University, Seoul 151-747, Republic of Korea
[‡]School of Chemical and Biological Engineering, Seoul National University, Seoul 151-747, Republic of Korea
[§]Department of Chemistry Education, Seoul National University, Seoul 151-747, Republic of Korea
[∥]Department of Chemical Engineering, Hanyang University, Ansan 426-791, Republic of Korea

Supporting Information

ABSTRACT: To impart a desired optical property to metal nanoparticles (NPs) suitable for surface-enhanced Raman scattering (SERS) applications, it is crucial to assemble them in two or three dimensions in addition to controlling their size and shape. Herein, we report a new strategy for the synthesis and direct assembly of Ag NPs on silica nanospheres (AgNPs-SiNS) in the presence of poly(ethylene glycol) (PEG) derivatives such as PEG-OH, bis(amino)-PEGs (DA-PEGs), and *O*,*O*′-bis(2-aminopropyl)PEG (DAP-PEG). They exhibited different effects on the formation of Ag NPs with variable sizes (10−40 nm) and density on the silica surface. As the molecular weight (MW) of DA-PEGs increased, the number of Ag NPs on the silica surface increased. In addition, DAP-PEG (MW of 2000), which has a 2-aminopropyl moiety at both ends, promoted the most effective formation and assembly of uniform-sized Ag NPs on a silica surface, as compared to the other PEG derivatives with the same molecular weight. Finally, we demonstrated that AgNPs-SiNS bearing 4-fluorobenzenethiol on its surface induced the strong SERS signal at the single-particle level, indicating that each hybrid particle has internal hot spots. This shows the potential of AgNPs-SiNS for SERS-based sensitive detection of target molecules.



KEYWORDS: *silver nanoparticle assembly, amino-PEG-mediated reduction method, poly(ethylene glycol), surface-enhanced Raman scattering (SERS), single-particle detection*

1. INTRODUCTION

Metallic nanoparticles (NPs) have attracted great interest in various research areas, as they exhibit unique optical and catalytic properties and a large specific surface area.[1−3] Novel NPs, such as gold and silver NPs, show interesting plasmonic properties that can be tuned by controlling their size and shape.[4] These plasmonic NPs have been explored in various applications of the sensitive detection of biological molecules based on surface-enhanced Raman scattering (SERS) and localized surface plasmon resonance (LSPR),[5−14] and colorimetric sensing.[15,16] To instill specific chemical and physical properties in Au or Ag NPs for SERS application, it is crucial to assemble them in two or three dimensions[17−27] as well as to control their size and morphology. For signal amplification in SERS, the geometrical control of Ag and Au nanostructures is desirable for the creation of nanogap junctions between the particles where greater optical field enhancement can be induced.[18,28,29] In this way, SERS allows us to detect a target molecule with single-molecule sensitivity.[30−33]

Several approaches have been reported to create nanogap junctions or aggregates using Ag (or Au) NPs for molecular sensing applications.[32−35] According to the previous results, only a small portion of sites (0.0063% of all aggregated sites) in a metal NP array produced a strong SERS signal (>10^9 Raman enhancement factor),[36] indicating a heterogeneous distribution of the SERS signal. This heterogeneous signal could disturb quantitative and reproducible detection of target molecules. In this regard, finely controlled nanogap junctions and aggregates have been considered as novel SERS substrates, which can produce a strong Raman signal with high reproducibility.[32−34,37,38] It is important therefore to assemble Ag or Au

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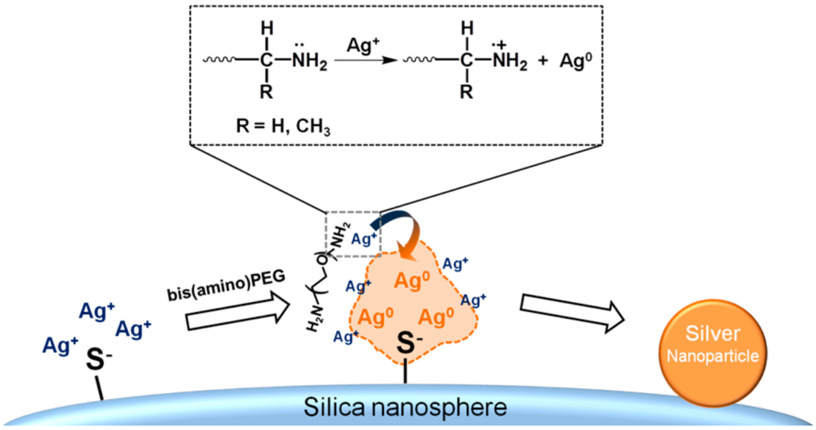


Figure 1. Schematic illustration for the fabrication of Ag NPs on silica nanospheres (AgNPs-SiNS).

NPs in a controllable and accessible manner to create reproducible nanogap junctions or aggregates. As yet, constructing reproducible and scalable SERS-active nanostructures remains challenging in the general application of SERS technology to ultrasensitive molecular detection.[36,39]

Various methods of synthesizing Ag or Au NPs have been reported such as solution-based reduction, ultrasonic assisted reduction, photoinduced reduction, and template-based reduction.[40−45] Among those, solution-based reduction, especially the polyol process using ethylene glycol as a reducing agent and a solvent, has been considered as a versatile chemical approach to fabricating metal NPs.[46,47] In the polyol process, poly(vinylpyrrolidone) (PVP) has been utilized as a surface passivation agent, preventing NPs from aggregation.[48] Poly(ethylene glycol) (PEG) has been widely used in biomedical applications because of its biocompatibility and, recently, in the synthesis of Ag NPs as a reducing and passivation agent.[49] Luo et al. reported the dependency of the molecular weight of PEG on the synthesis of Ag NPs,[50] while other research groups observed the temperature dependency of the PEG-based polyol process[51] and the conformational effect of PEG on the fabrication of Ag NPs.[52−54] However, high reaction temperatures of >80 °C were required to obtain the desired size of Ag NPs, but with a broader range of size distributions. Furthermore, there is no report yet that shows that the amino-PEG-based reduction process could be used in the synthesis and the assembly of Ag NPs on nanoparticle templates to create SERS-active nanogap junctions or aggregates. It would be worthwhile to examine whether the amino-PEG-based reduction method could be applicable to the synthesis and direct assembly of Ag NPs on nanoparticle templates under mild conditions to create hot spots that are active with respect to SERS.

Herein, we demonstrate a new approach to synthesizing and assembling Ag NPs on silica nanospheres, constructing SERS-active aggregate junctions in the presence of amino-PEG derivatives as reducing agents. The PEG-mediated reduction method allows the facile synthesis and assembly of Ag NPs with variable sizes and densities on silica nanospheres (SiNS) under very mild conditions (in ethylene glycol at 25 °C). We found that there are two important factors that influence the formation and assembly of Ag NPs on SiNS: (1) the conformation of the amino-PEGs in solution and (2) their reducing capability caused by their end-functional groups. Finally, SERS was measured on a single particle of AgNPs-SiNS prepared by various PEG derivatives, and the most intense SERS spectrum was obtained from the one prepared with *O*,*O*′-bis(2-aminopropyl)poly(ethylene glycol) (DAP-PEG) (MW of 2000). This new strategy for both the synthesis and direct assembly of NPs on template nanoparticles can facilitate the easy construction of various nanostructures for SERS.

2. EXPERIMENTAL METHODS

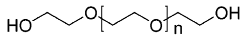
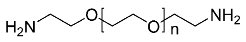
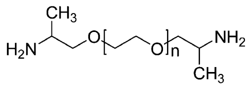
2.1. Materials. Poly(ethylene glycol) ($M_n \sim 2000$), poly(ethylene glycol) bis(amine) (DA-PEG; MW ∼ 2000, 3000, and 6000), tetraethylorthosilicate (TEOS, 98%), and 4-fluorobenzenethiol (4-FBT) were purchased from Aldrich (St. Louis, MO). Silver nitrate ($AgNO_3$, 99.9%), ethylene glycol (EG, 99%), and 3-mercaptopropyl trimethoxysilane (MPTS, 95%) were purchased from Sigma-Aldrich. *O*,*O*′-Bis(2-aminopropyl)poly(ethylene glycol) ($M_r \sim 2000$) was purchased from Fluka. Absolute ethanol (99.8%) was purchased from Carlo Erba (Milan, Italy). Ammonium hydroxide (NH_4OH, 27%) was purchased from Daejung Chemicals (Busan, Korea).

2.2. Preparation of MPTS-Treated SiNS. The fabrication of MPTS-coated SiNS was similar to that previously reported.[55] SiNS were prepared by sequentially adding 1.6 mL of TEOS and 3 mL of ammonium hydroxide to absolute ethanol (40 mL). After the mixture had been stirred at room temperature for 20 h, SiNS (120−150 nm) were obtained. The resulting silica colloids were washed with ethanol five times and then dispersed again in ethanol (5 mL). For the effective adsorption of silver ions on SiNS, thiol groups were introduced on the silica surface. After 100 mg of SiNS had dispersed in the ethanol, a 50 μL portion of MPTS and a 10 μL portion of ammonium hydroxide were added to the dispersion. The resulting mixture was then stirred at room temperature (25 °C) for 12 h, and the product was washed with ethanol five times to remove excess reagent.

2.3. Synthesis and Assembly of Ag NPs on Silica Nanospheres (AgNPs-SiNS) Using the PEG-Mediated Reduction Method. To synthesize and assemble Ag NPs on a silica surface, a 1 mg portion of MPTS-treated SiNS was added to the ethylene glycol medium (the final concentration of silica was 1 mg/mL). The silver nitrate and PEG derivatives were then added to the SiNS dispersion. The concentration of silver nitrate ($AgNO_3$) and PEG derivatives was adjusted to 6 mM, and the mixture was then shaken at room temperature (25 °C) for 1 h. The resulting AgNPs-SiNS were washed with ethanol five times to remove residual reagents for the measurement of UV−visible spectra. The resulting Ag NPs assembled on the silica surface were characterized by a UV−visible absorption spectrometer and an energy filtering transmission electron microscope (EF-TEM).

2.4. SERS Measurement on a Single Particle of AgNPs-SiNS. After the supernatant had been removed from the AgNPs-SiNS dispersion using centrifugation, a 1 mL portion of Raman label compound solution (2 mM 4-FBT in ethanol) was added to the AgNPs-SiNS dispersion. The resulting mixture was then dispersed by gentle sonication and shaken at room temperature for 1 h. The excess

Table 1. Structures of PEG Derivatives and Their pH Values in Ethylene Glycol Solutions

	Structure	Molecular weight	Number of repeating unit	pH
Poly(ethylene glycol) (PEG)		2000	~43	7.5
Polyethylene glycol bis(amine) (DA-PEG)		2000	~42	9.7
		3000	~63	9.9
		6000	~129	9.4
O,O'-bis(2-aminopropyl) polyethylene glycol (DAP-PEG)		2000	~41	9.8

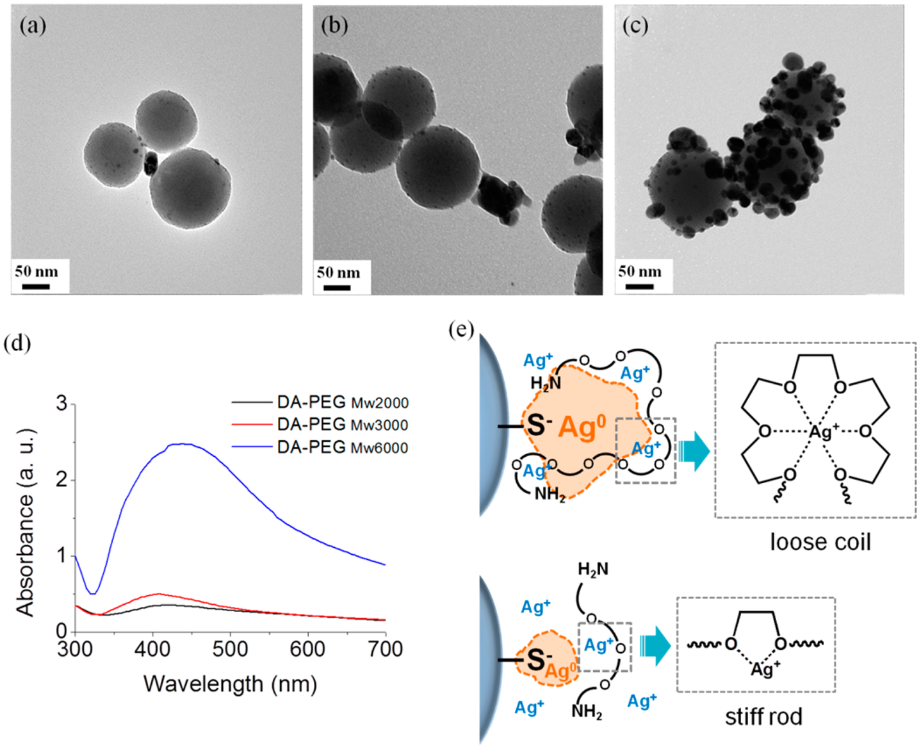


Figure 2. Effect of chain length of PEG derivatives in fabricating Ag NPs on silica surface. TEM images of Ag NPs on silica nanospheres (AgNPs-SiNS) fabricated using three different types of DA-PEG: (a) DA-PEG (MW of 2000), (b) DA-PEG (MW of 3000), and (c) DA-PEG (MW of 6000). (d) UV−vis spectra of the AgNPs-SiNS fabricated with DA-PEG (MW of 2000) (black), DA-PEG (MW of 3000) (red), and DA-PEG (MW of 6000) (blue). (e) Illustration of interactions between DA-PEG (MW of 2000) (top) or DA-PEG (MW of 6000) (bottom) and Ag^+ ion on a silica surface.

4-FBT was removed by centrifugation, and the AgNPs-SiNS bearing 4-FBT were redispersed in ethanol. Then, 1 mg of PVP (MW of 40000) was added to the AgNPs-SiNS dispersion. After being gently shaken for 1 h, AgNPs-SiNS were washed with ethanol five times. Then, the diluted AgNPs-SiNS dispersion (0.1 mg/mL in ethanol) was dropped on the patterned slide glass. Single-particle SERS was measured by point-by-point mapping with a 1 μm step size. All mapping experiments were conducted using a 100× objective lens (NA 0.90) with an acquisition time of 1 s. Raman spectra were obtained in a range between 350 and 1400 cm^{-1} using a 532 nm laser excitation of 1.6 mW. After the Raman measurement, the same area of Raman mapping was observed using field emission-scanning electron microscopy (SEM) to ensure that only single particles were observed.

2.5. Instruments. UV−vis absorption spectra were recorded with a UV−visible absorption spectrometer (Mecasys Co. Ltd., Optizen 2120 UV). TEM images were obtained using an EF-TEM (Carl Zeiss, LIBRA 120). The micro-Raman system (JY-Horiba, LabRam300) was used for the SERS experiments. SERS signals were collected with an optical lens (Olympus, BX41) in scattering light at a 180° direction. SEM images were obtained using FE-SEM (JSM-6701F, JEOL, Tokyo, Japan) to confirm single-particle states of AgNPs-SiNS.

3. RESULTS AND DISCUSSION

A graphic scheme of the synthesis and assembly of Ag NPs on silica nanospheres (AgNPs-SiNS) is shown in Figure 1. Silica nanospheres (SiNS) were prepared using the Stöber method,[56] and the surface of SiNS was functionalized with a thiol group for an effective assembly of Ag NPs on their surface. In our proposed mechnism, Ag^+ ions are reduced by amino-PEGs through the transfer of a single electron from the amino groups of bis(amino)-PEGs and then Ag^0 atoms are nucleated to form

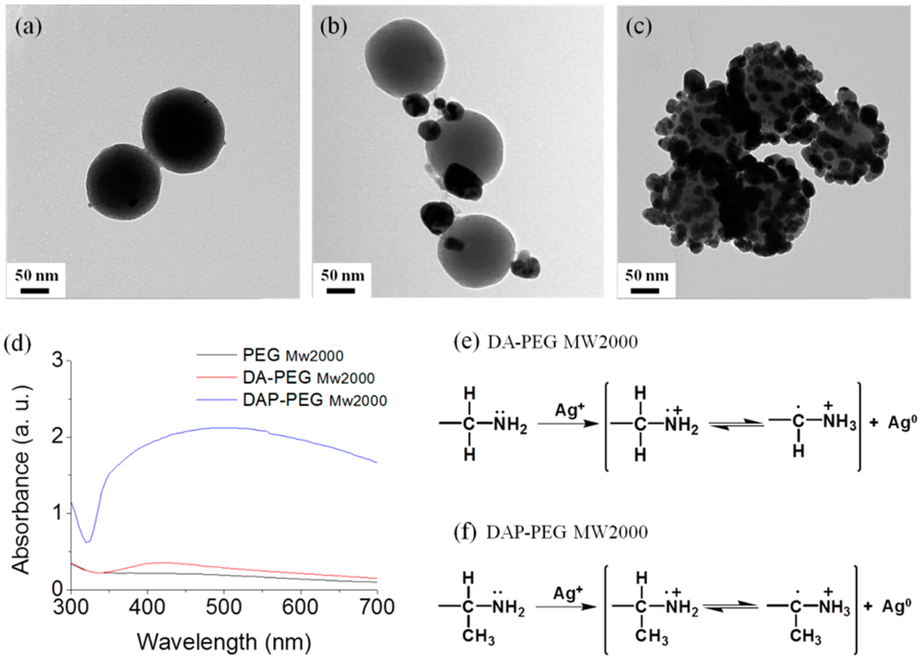


Figure 3. Effects of the end-functional group of PEG derivatives in fabrication of Ag NPs on a silica surface. TEM image of Ag NPs on silica nanospheres (AgNPs-SiNS) fabricated using three different PEG derivatives: (a) PEG (MW of 2000), (b) DA-PEG (MW of 2000), and (c) DAP-PEG (MW of 2000). (d) UV−vis spectra of the AgNPs-SiNS fabricated with PEG (MW of 2000) (black), DA-PEG (MW of 2000) (red), and DAP-PEG (MW of 2000) (blue). (e and f) Proposed mechanism for the reduction of Ag^+ ions by (e) DA-PEG (MW of 2000) and (f) DAP-PEG (MW of 2000).

AgNPs by an amino-PEG-mediated reduction process. To verify the mechanism of amino-PEG-induced formation of AgNPs-SiNP, several types of PEG derivatives with different molecular weights and end-functional groups were explored as reducing and passivation agents. Table 1 shows the molecular structures of three PEG derivatives and the pH values of the dissolving solution. PEG2000 (MW of 2000) bearing hydroxyl groups at both ends has a neutral pH value in solution, and DA-PEGs and DAP-PEG2000 have higher pH values (9.4−9.9) because of the amino groups, the basicity of which is stronger than that of hydroxyl groups. It should be noted that DAP-PEG2000 has methyl groups next to the amino groups at both ends, which is different from the case for DA-PEGs. The different chemical properties of the end-functional groups in the PEG derivatives could influence the reduction process of Ag^+ ions and the formation of Ag NPs on SiNS. In the case of DA-PEG, there are no differences in pH as the molecular weight varies from 2000 to 6000, suggesting that their molecular weights are a dominant factor in the reduction process. First, we investigated the effect of PEG chain length on the synthesis of AgNPs-SiNS. DA-PEGs with three different molecular weights (2000, 3000, and 6000) were added during the reaction at room temperature (25 °C). As shown in the TEM images in Figure 2a, very few Ag NPs were formed on the silica surface in the presence of DA-PEG2000. For DA-PEG3000 (Figure 2b), a few Ag NPs formed on the silica surface, but they were nonuniform. As DA-PEG6000 was added, a significantly increased number of Ag NPs on the silica surface were observed, with their size becoming more uniform. In the absence of DA-PEGs, no Ag NPs were formed under the same conditions (Figure S1 of the Supporting Information). These results suggest that the higher molecular weight of DA-PEG6000 is more effective in the synthesis and assembly of Ag NPs on a silica surface. The solubility of DA-PEG6000 in ethylene glycol was nevertheless limited.

Next, the plasmonic absorption of each particle was measured as shown in Figure 2d. AgNPs-SiNS prepared with DA-PEG6000 showed strong plasmonic absorption at 450 nm, indicating the formation of Ag NPs.[57,58] However, weak plasmon peaks were observed for DA-PEG2000 and -3000. The red-shift was observed in the spectrum for DA-PEG6000, demonstrating the formation of aggregated structures of Ag NPs on the silica surface (Figure 2c). The efficient formation and assembly of Ag NPs on SiNS by DA-PEG6000 at room temperature can be attributed to the increased local concentration of Ag ions induced by a large number of coordination sites on oxygen atoms and a loose coil conformation caused by its high molecular weight. The conformation of the polymer chain can be determined by various physicochemical conditions, such as concentration, temperature, chain length, terminal functional groups, and solvents.[54,59] The conformation of PEG molecules in solution tends to change from a stiff rod to a loose coil as their molecular weight increases (Figure 2e).[53] This loose PEG chain can stabilize Ag^+ ions and might increase their local concentration on the silica surface, enhancing the reducing rate and the effective nucleation at room temperature.[60,61] In addition, a loose coil conformation of PEG could be beneficial for the synthesis of a uniform size of NPs.[62]

We also explored the effect of end-functional groups such as hydroxyl, amino, and aminopropyl groups in the PEG derivatives with the same molecular weight (MW of 2000) on the synthesis of AgNPs-SiNS. Panels a−c of Figure 3 show the TEM images of AgNPs-SiNS synthesized in the presence of PEG2000, DA-PEG2000, and DAP-PEG2000, respectively. As shown in panels a and b of Figure 3, few Ag NPs were formed on the silica surface for PEG2000 and DA-PEG2000, and no Ag

NPs were observed even in the solution. These results indicate that the reducing capabilities of two PEG derivatives are not sufficiently strong to initiate the nucleation at room temperature regardless of the types of end-functional groups. However, DAP-PEG2000 remarkably accelerated the formation of Ag NPs on the silica surface, although its reducing capability is almost the same as that of DA-PEG2000 (Figure 3c). Ag NPs were coated more densely and uniformly on the silica surface, resulting in the creation of numerous nanogap junctions. As the concentration of DAP-PEG2000 increased, larger Ag NPs were formed densely on the silica surface (Figure S2 of the Supporting Information). In addition, the efficient formation of Ag NPs on SiNS in the presence of DAP-PEG2000 was confirmed by UV−vis spectroscopy. The strong plasmonic absorption peak appeared at the maximal wavelength of 500 nm for DAP-PEG2000, but very weak peaks appeared at 420 nm for PEG2000 and DA-PEG2000. Compared to the plasmon absorption peak for DA-PEG6000 (Figure 2c), the one for DAP-PEG2000 had shifted to the longer wavelength, indicating the formation of larger Ag NPs.[57,58]

The only difference between DA-PEG2000 and DAP-PEG2000 is that DAP-PEG2000 has an extra methyl group next to the amino group at both ends while DA-PEG2000 has no methyl group. According to the proposed mechanism for the synthesis of AgNPs on the silica surface, Ag$^+$ ions are reduced by the amino group of bis(amino)-PEGs via single-electron transfer, which results in the creation of a radical carbocation in the polymers. In case of DAP-PEG2000, the resulting carbocation can be more stabilized by the extra methyl group at its ends than that of DA-PEG2000, which leads to the more facile reduction of Ag$^+$ ions in the presence of DAP-PEG2000 (Figure 3e,f). This result clearly suggests that the size and density of Ag NPs introduced on the silica surface can be controlled by the chemical property of the end-functional group of PEG derivatives.

We analyzed the size and number of Ag NPs on SiNS quantitatively as shown in Table 2. The number of Ag NPs synthesized on the silica surface was increased from 3 to 19 per silica as the molecular weight of DA-PEG polymers increased (2000 to 6000), which corresponds to the TEM images in Figure 2a−c. The average size of Ag NPs increases from 13 to 24.9 nm with the increase in their molecular weight. For DAP-PEG2000, the number and average size of Ag NPs on the silica surface were 21.9 per silica and 27.8 nm, respectively, which were greater than the values for DA-PEG6000 with a higher molecular weight. We conclude that DAP-PEG2000 is a very effective polymer for the formation and assembly of Ag NPs on SiNS. Figure 4 shows a size distribution of Ag NPs formed on SiNS. Ag NPs fabricated by DAP-PEG2000 on SiNS showed a narrower size distribution with a relatively large diameter.

Table 2. Effects of PEG Derivatives on the Size Distributions of Ag NPs and Their Surface Coverage on Silica Nanospheres (SiNS)

	molecular weight	no. of Ag NPs on a single silica nanosphere[a]	average size[a] (nm)	standard deviation
PEG	2000	0.8	8.8	4.8
DA-PEG	2000	3	13	14.3
	3000	14.4	16.9	19.8
	6000	19.1	24.9	13.2
DAP-PEG	2000	21.9	27.8	7.3

[a] Average values of Ag NPs formed on a single silica nanosphere counted from 10 silica nanospheres.

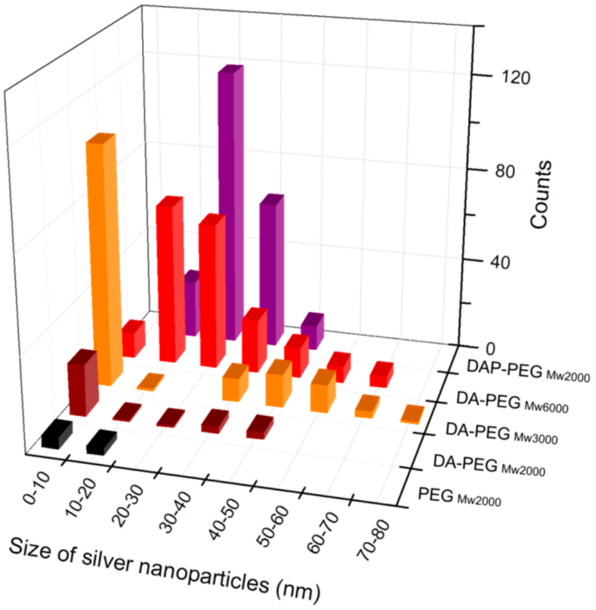


Figure 4. Effect of PEG derivatives on the size distributions of Ag NPs and their surface coverage on silica nanospheres.

Finally, SERS activity was investigated on a single particle of AgNPs-SiNS synthesized by the amino-PEG-mediated reduction process as shown in Figure 5. A simple thiol compound, 4-FBT, was added to the dispersion of each AgNPs-SiNS, and the resulting particles were diluted and dropped on a patterned slide glass, allowing us to easily distinguish the SERS-measured particles using SEM images. Then, we measured the SERS signal from a single particle of AgNPs-SiNS. After the SERS signals had been mapped with a 1 μm step size using a 532 nm laser line, the resulting mapping images were then overlaid with the corresponding SEM images. Figure 5 shows the overlaid images of SERS intensity mappings with their corresponding SEM images and the SERS spectra obtained from single particles for three different AgNPs-SiNSs prepared with DA-PEG2000, DA-PEG3000, and DAP-PEG2000. In the case of AgNPs-SiNS synthesized using DA-PEG2000 or -3000, SERS signals were barely detected at the single-particle level (Figure 5a,b). However, the AgNPs-SiNS prepared by DAP-PEG2000 can produce very strong SERS signals of 4-FBT even at the single-particle level (Figure 5c), indicating that each AgNPs-SiNP has hot spots created by numerous nanogap junctions of Ag NPs on silica surface, not by aggregation of the hybrid particles. The numerous nanogap junctions between Ag NP aggregates on the silica surface induce a large electromagnetic enhancement.[37] The result of SERS measurements from a single particle also corresponds to the structures of AgNPs-SiNP prepared with different types of PEG derivatives. This result clearly suggests that it is possible to control the formation and direct assembly of Ag NPs on SiNS, creating nanogap junctions for sensitive SERS, by varying the chemical and physical properties of PEGs. This amino-PEG-mediated reduction method for the synthesis and assembly of Ag NPs on silica templates allows the easy fabrication of hybrid

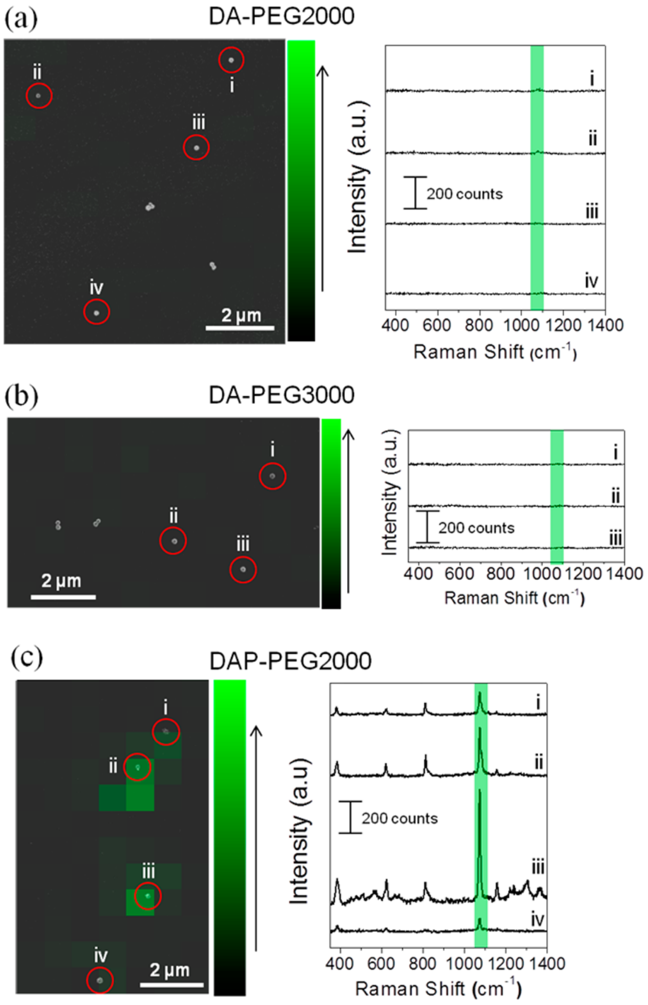


Figure 5. SERS measurement from a single particle of AgNPs-SiNP. (a) Overlaid image (left) between the SERS mapping of single AgNPs-SiNP and its corresponding SEM image and SERS spectra (right) obtained from a single particle with DA-PEG (MW of 2000), (b) DA-PEG (MW of 3000), and (c) DAP-PEG (MW of 2000). The SERS intensity mapping based on the peak of 4-FBT at 1075 cm^{-1} was measured on a single AgNPs-SiNS and overlaid with its corresponding SEM image. SERS mapping was conducted using a 532 nm laser excitation with a power of 1.6 mW and an acquisition time of 1 s.

nanomaterials and nanostructures for various applications, including SERS.

4. CONCLUSION

PEG-mediated synthesis and assembly of Ag NPs on SiNS were performed. It was found that the molecular weights and end-functional groups of PEG derivatives were crucial in the formation and assembly of Ag NPs on a silica surface. The size and density of Ag NPs on SiNS can be controlled by changing the molecular weights and the end-functional groups of PEG derivatives. The DAP-PEG2000 bearing the aminopropyl group at both ends was found to be the most effective mediator for synthesizing uniform and larger sizes of Ag NPs and for assembling them densely on a silica surface. Our results show the potential of nanostructures (AgNPs-SiNS) fabricated by the amino-PEG-mediated reduction process for sensitive SERS detection of target molecules.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

TEM images of Ag nanoparticles on silica nanospheres (AgNPs-SiNS) fabricated under various reaction conditions. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: kjh75@hanyang.ac.kr. Phone: +82-31-400-5275. Fax: +82-31-419-7203.
*E-mail: yslee@snu.ac.kr.

Author Contributions

H.K. and J.Y. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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