

Chemically Patterned Microspheres for Controlled Nanoparticle Assembly in the Construction of SERS Hot Spots

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One of the goals in surface enhanced Raman spectroscopy (SERS) is to fabricate SERS-active nanostructures that are reproducible, dependable, and sensitive, by controlling both the density and distribution of electromagnetic (em) “hot spots” (locations where the SERS enhancement is and the placement of the analyte molecules within these regions).^{1–4} A number of promising platforms for ultra-sensitive SERS have been proposed to meet this challenge including the construction of dimerlike nanoaggregates,^{1,2} nanowire bundles, and aligned rafts,^{3,4} or highly ordered periodic 2-D nanostructures composed of close-packed nanoparticles or metal films evaporated over template spheres.^{5,6} Although many of these technologies produce efficient SERS-active systems, the fabrication of systems where the location of the analyte-containing hot spots can be found easily, for example, by using optical microscopy, remains a challenge.

In this Communication we demonstrate a chemically driven SERS-active system that overcomes this challenge. Using a short linker molecule as a model analyte in conjunction with a novel microsphere (MS) patterning technique, nanoparticle (NP) hot spots can be found using routine optical microscopy and easily analyzed by both Raman and TEM, thus eliminating the need for mapping large areas to find SERS signals. Additionally, the NP aggregates are limited in size by the MSs so that by matching the laser probe diameter and MS (here $\sim 1 \mu\text{m}$ and $0.88 \mu\text{m}$, respectively) the analysis of individual NP clusters is possible. We describe how this self-assembly technique enables optical identification and structure–function assignment by spanning multiple length scales.

A masking process is used to pattern silica microsphere support surfaces with regions of two different chemical affinities; one of which selectively binds silver nanoparticles (Ag–NPs) so that they become localized at discrete spots on the surface of the MS. A subsequent NP crosslinking step with a bifunctional silver-binding linker draws the MSs together to form small Ag nanoparticle aggregates with a number of linkers located within the junctions. The micrometer size of the MSs allows the junctions to be located and imaged optically and restricts the number of Ag–NPs within each cluster by the geometric exclusion effect of the large MSs. We demonstrate the approach using two dithiol molecules and silver nanoparticles, but note that the method is generalizable to any bifunctional bridge molecule with affinity for noble metal surfaces. Ag was chosen because it produces the largest enhancement factor among the most tractable metal SERS candidates.^{7–9}

The five-step procedure (Figure 1a) for creating the SERS systems begins by forming a tightly packed assembly of contact surface-masked $\sim 880 \text{ nm}$ silica MSs through centrifugation. Next, the exposed (unmasked) surfaces silanols are functionalized with 2-[methoxy(polyethyleneoxy)propyl] trimethoxysilane (PEG-silane) (step 1) to provide a chemoresistive coating that covers all but the MS–MS contact regions. The MSs are then redispersed by

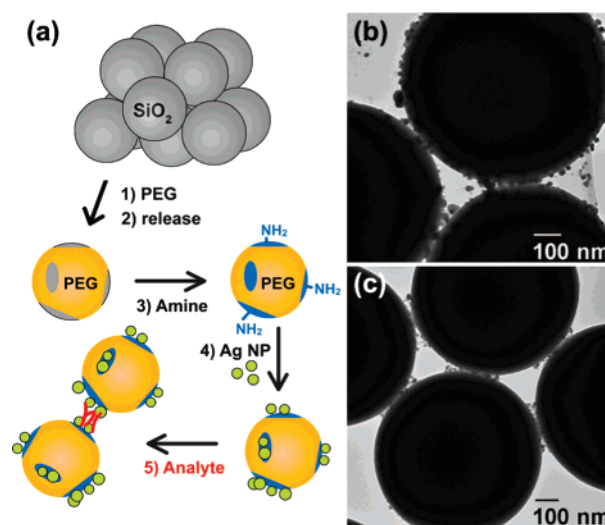


Figure 1. (a) Schematic of the five-step process for molecular-linker-controlled NP-patterned MS assembly: (1) Silica MSs are centrifuged to form a close-packed network. The exposed surface silanols are functionalized with PEG-silane. (2) The MSs are redispersed. (3) The remaining silanols are backfilled with aminosilane. (4) Ag–NPs bind selectively to the aminosilane-functionalized regions. (5) Linker molecules are added, leading to crosslinking. (b and c) TEM images of Ag–NP MSs, crosslinked by OPV: (b) unmasked MS functionalized with aminosilane and (c) contact masked MS patterned first with PEG-silane and then with aminosilane.

sonication (step 2) to expose the unfunctionalized portions of the silica surfaces. These regions are reacted with *N*-(6-aminohexyl) aminopropyltrimethoxysilane (step 3), and then Ag–NPs are added which bind selectively to the amines (step 4). The MSs are washed between steps using centrifugation. Linker molecules are added leading to crosslinking (step 5). A control experiment in which the PEG–silane contact masking step was eliminated showed Ag–NPs distributed uniformly across the surface (Figure 1b). By contrast, masked MS show distinct Ag–NP-covered regions (Figure 1c).

The molecules 1,4-benzenedithiol (BDT, 0.8 nm S–S distance) or thioacetyl-terminated oligo(phenylenevinylene) (OPV, $\sim 1.9 \text{ nm}$ S–S distance) were explored as model crosslinkers (step 5). In addition to their excellent Ag affinity these molecules have large Raman cross-section and generate intense signals, presumably as a result of resonance contributions alongside em enhancement.^{10,11} The size of the molecules enable small interparticle distances (i.e., $< 2 \text{ nm}$), leading to large em field concentration and thus high SERS enhancement.^{12–14}

Following the assembly process the material was deposited onto TEM grids for confocal Raman spectroscopy (514.5 nm excitation, 100 \times objective). Crosslinked MSs could be easily discerned from single MSs in the optical microscopic images (see Supporting

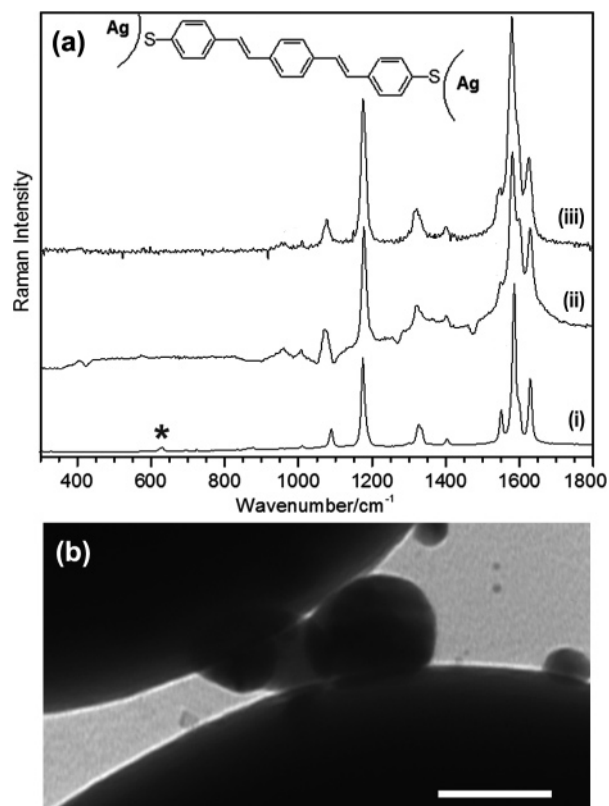


Figure 2. Correlated TEM and SERS spectra: (a) Micro-Raman spectrum of (i) neat solid OPV (acetyl protected); (ii) SERS spectrum of OPV/ethanol solution added to colloidal Ag-NPs (ethanol spectrum subtracted in the 300–1800 cm^{-1} region); (iii) SERS spectrum of OPV-crosslinked, masked MS/Ag-NPs presented in panel b. Thioacetyl (indicated with a *, 630 cm^{-1}) and SH (bending, 915 cm^{-1}) vibrations are absent in both of the SERS spectra (ii, iii), indicating Ag–S bonding. The inset shows the proposed structure of OPV-crosslinked Ag-NPs (only one OPV molecule is depicted for clarity). (b) TEM of OPV-linked NP-patterned MSs at the position where spectrum ii was collected. This junction contains a trimer. Scale bar is 25 nm.

Information). The spectra obtained from the junctions between MSs display the expected Raman scattering of the linking molecules (Figure 2a and Supporting Information). While an identical SERS spectrum was obtained from both assembled NP–MS junctions and solutions of the dithiol with colloidal Ag-NPs, acquisition of the colloidal-derived spectra required much longer integration times and higher laser powers for equivalent SERS intensity, implying a greater SERS enhancement factor for the MS-based junctions versus a solution ensemble of aggregates. We estimate the enhancement factor of the junctions to be $\sim 10^8$ to 10^9 , a factor $\sim 10^2$ to 10^3 greater than simply adding linker to Ag colloid solution⁸ (see Supporting Information). We believe this is because for a MS junction of interest to be formed, the linker analyte will automatically locate itself in the hot spot that it forms.

A detailed examination of the Raman spectra indicates that the linking molecules bridge the Ag–NP gap (Figure 2a). Vibrational modes of the terminal thiol or thioacetyl groups detectable in the ordinary Raman spectrum of the neat solid were absent in the SERS spectra and are consistent with deprotection of this functionality¹⁰ (Figure 2a and Supporting Information). Ag phenyl ring vibrations at 1077, 1581, and 1176 cm^{-1} and the ethylene stretch at 1626

cm^{-1} (assuming C_{2h} symmetry) are not significantly shifted or broadened with respect to their counterparts in the ordinary Raman spectrum (except for mode 1, see Supporting Information).¹⁵ This indicates OPV binding occurs through the end groups orienting the molecule perpendicular to the Ag surface. However, BDT shows broadening and thus appears to lie more parallel to the surface, consistent with previous reports.^{15,16} The absence of intermolecular disulfide bonds ($\nu(\text{S}–\text{S})$ 530 cm^{-1})¹⁵ in the SERS spectra indicates that the bridging molecules form at most a monolayer.

In summary, we describe a useful platform for constructing and analyzing SERS hot spots. We demonstrate this using short dithiol molecules to cross-link Ag–NP coated onto restricted areas of silica MS. By restricting the area of Ag deposition onto the silica MS and by using sufficiently large MSs, the location of the hot spots can be easily and reliably found using optical microscopy eliminating the need to “hunt” for regions of high SERS signals. As we have shown, the regions from which SERS measurements are collected can be easily probed and correlated using TEM to yield a detailed picture of the local enhancement region. We speculate that this chemically driven self-assembly strategy may facilitate analysis of plasmonic and other optically active nanostructures that depend sensitively on effects from nanomaterial size, shape, crystallinity, and interparticle geometry.

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Supporting Information Available: Details on the synthesis, additional spectra and EM images, enhancement factor estimation, and vibrational assignments for the thiol- and thioacetyl-terminated bifunctional linkers. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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