

Environmentally Responsive Surface-Enhanced Raman Scattering Substrates for High Sensitivity

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Surface-enhanced Raman scattering (SERS) has been of growing interest as a powerful tool to study vibrational information of molecules adsorbed on metallic nanoparticles (MNPs).^{1,2} Recently, environmentally responsive SERS substrates composed of a variety of inorganic-organic composites have been developed for highly sensitive chemical detection because of enhanced electromagnetic plasmonic coupling which occurs by different external stimuli.³ Specifically, hybrid plasmonic nanostructures composed of MNPs and thermoresponsive poly(*N*-isopropylacrylamide) (p(NIPAM)) brushes grown on gold substrates were prepared by surface-initiated atom-transfer radical polymerization of NIPAM, followed by immobilization of gold NPs exclusively at the end of p(NIPAM) chains *via* covalent bonding or non-covalent interaction, which are capable of thermally-induced electromagnetic coupling as advanced SERS substrates.^{3,4} However, there have been obstacles to strong ionic interaction between gold NPs and entire p(NIPAM) chains for ultrasensitive detection.

In this work, we first report the synthesis and characterization of a new class of thermoresponsive SERS substrates composed of branched GNPs (bGNPs) with sharp features and poly(NIPAM-co-allylammonium chloride) (p(NIPAM-co-AA)) chemically conjugated with 1,10-decanedithiol of the self-assembled monolayer (SAM) of the gold-patterned microarray chip (Figure 1).^{5,6} As organic-inorganic composites, these SERS substrates were formed by strong ionic interaction between negatively charged bGNPs and positively charged p(NIPAM-co-AA) tethered on the gold pattern. When rhodamine B isothiocyanate (RBITC) was introduced to bGNPs as Raman dye, thermally-triggered collapse and aggregation of p(NIPAM-co-AA) chains in aqueous solution above the lower critical solution temperature (LCST) produced a SERS signal higher than that seen below LCST, potentially due to the decreased distance between bGNPs or between bGNPs and the gold pattern.

To evaluate the thermoresponsive characteristics of the gold-patterned microarray chip, positively charged p(NIPAM-co-AA)s were synthesized by radical polymerization in *t*-butyl alcohol at 83 °C for 24 h in the presence of 4 mM diethyl phosphite and 2 mM 4,4'-azobis(4-cyanovaleic acid). Figure 2(a) shows detailed chemical schemes of (1) synthesis of p(NIPAM-co-AA) with terminal -COOH, (2)

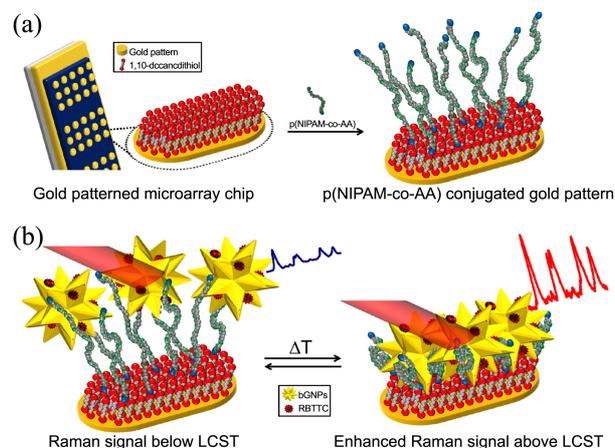


Figure 1. Schematics of (a, b) thermoresponsive SERS substrates composed of bGNPs and thermally responsive p(NIPAM-co-AA) chemically conjugated with 1,10-decanedithiol of the SAM of the gold-patterned microarray chip. Thermally-triggered collapse and aggregation of p(NIPAM-co-AA) chains in aqueous solution above LCST produces a SERS signal higher than that below LCST.

its maleimide functionalization by *N*-(2-aminoethyl) maleimide *via* AA protection with di-*tert*-butyl dicarbonate (Boc₂O) and activation with 1-ethyl-3-(3-dimethyl-aminopropyl) carbodiimide (EDC) and (3) grafting of p(NIPAM-co-AA) with maleimides to the 1,10-decanedithiol of the SAM of the gold pattern *via* AA deprotection with 6 mM hydrochloric acid and a maleimide-thiol coupling reaction in dimethyl sulfoxide. The ¹H nuclear magnetic resonance (NMR) spectra of p(NIPAM-co-AA) with a molecular weight of 30 kDa indicates the presence of both NIPAM (peak d, e) and AA (peak c) units (Figure 2(b)). Conjugation between maleimide and thiol has been reported to be efficient under mild reaction conditions, and the stable covalent linkage is maintained once it is formed. As shown in Figure 2(c), due to its LCST behavior and charge density, two different p(NIPAM-co-AA)s showed sharp transitions at 34 °C and 43 °C when the feed molar ratios of NIPAM and AA were 5:1 and 3:1, respectively.

Finally, in order to prepare thermoresponsive SERS substrates with bGNPs, they were prepared in HEPES buffer, and they had an average size of 20 nm and 2-6 arms, as characterized by transmission electron microscopy (TEM)

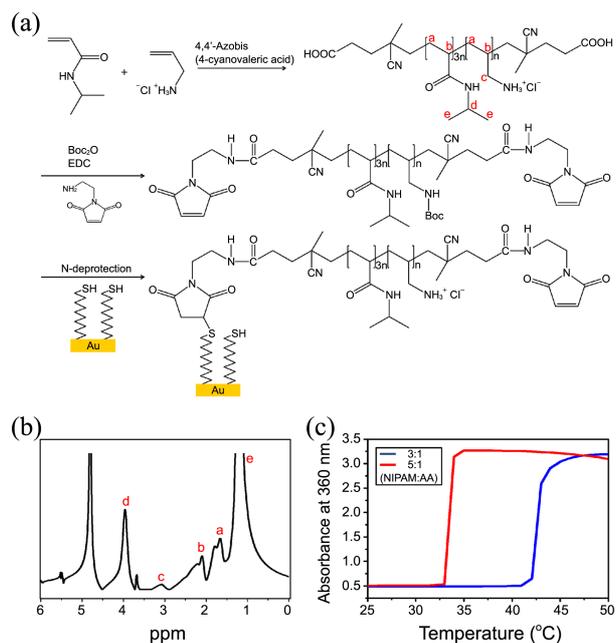


Figure 2. (a) Detailed chemical schemes of (1) synthesis of p(NIPAM-co-AA), (2) its maleimidization by *N*-(2-aminoethyl)-maleimide via AA protection with Boc_2O and activation with EDC and (3) grafting of p(NIPAM-co-AA) with maleimide to the 1,10-decanedithiol of the SAM of the gold pattern via deprotection and maleimide-thiol coupling. (b) ^1H NMR spectra of p(NIPAM-co-AA). (c) UV absorbance at 360 nm of 10 w/v% p(NIPAM-co-AA) in water as a function of temperature when the feed molar ratios of NIPAM and AA were 3:1 and 5:1, respectively.

(Figure 3(a)).⁷ Figure 3(b) represents the zeta (ζ) potential profile when positively charged p(NIPAM-co-AA)s were complexed with negatively charged bGNPs. As the weight ratio of p(NIPAM-co-AA) and bGNPs increased, ζ potential value of the bGNPs gradually increased from -28 mV to 10 mV, due to the strong ionic interaction of the bGNPs with positively charged p(NIPAM-co-AA). A scanning electron microscopy (SEM) image of the bGNPs complexed with p(NIPAM-co-AA) tethered on the gold pattern is shown in Figure 3(c). The thermoresponsive SERS substrates with RBITC-labeled bGNPs clearly showed that the Raman signal at 50°C above LCST was approximately three times higher than that at 25°C below LCST, due to the closer gaps between adjacent bGNPs and between bGNPs and the gold pattern above LCST. Future work will focus on controlled amplification of relative Raman intensity as a function of temperature by varying the chain length of SAM, molecular weight of p(NIPAM-co-AA) and conjugation efficiency of p(NIPAM-co-AA) on the SAM. SERS substrates with

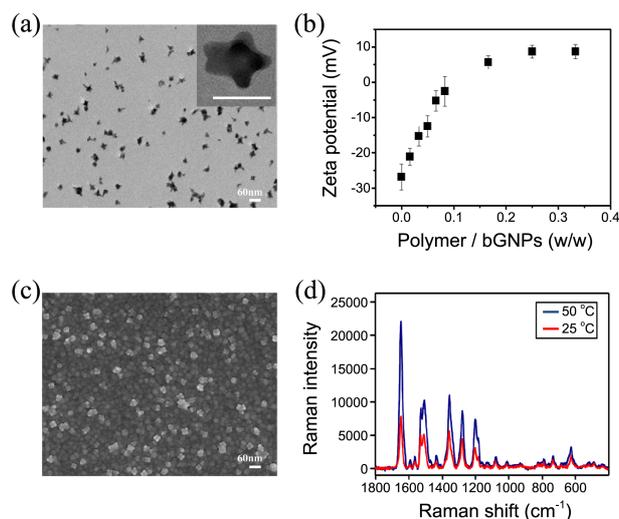


Figure 3. (a) TEM image of bGNPs prepared in HEPES buffer. (b) ζ potential profile when positively charged p(NIPAM-co-AA) was complexed with negatively charged bGNPs as the weight ratio of p(NIPAM-co-AA) and bGNPs increased. (c) SEM image of bGNPs complexed with p(NIPAM-co-AA) tethered on the pattern. (d) Relative Raman spectra of thermoresponsive SERS substrates at 25°C below LCST and 50°C above LCST. Scale bars are 60 nm in (a) and (c), and 30 nm in the inset of (a).

thermally switchable electromagnetic coupling could be useful for highly sensitive chemical detection applications.^{3,8}

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