Supporting Information

Facile synthesis of high-performance SiO_2@Au core-shell nanoparticles with high SERS activity

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Experimental section

1.1 Materials and chemicals

Chlorauric acid tetrahydrate ($HAuCl_4 \cdot 4H_2O$), trisodium citrate dehydrate, and ammonia solution (28%) were purchased from Sinopharm Chemical Reagent Co., Ltd., (China). Tetraethoxysylane (TEOS), polyethyleneimine branched (PEI, MW 25 kDa), 5,5-dithiobis-(2-nitrobenzoic acid) (DTNB), N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (EDC), MES monohydrate, N-hydroxysuccinimide (NHS), sodium borohydride ($NaBH_4$), polyvinylpyrrolidone (PVP, MW 40 kDa), Human immunoglobulin M (IgM), goat anti-human IgM, donkey anti-goat immunoglobulin G (IgG), and bovine serum albumin (BSA) were purchased from Sigma-Aldrich (USA). The nitrocellulose (NC) membrane (Hi-flow plus HF135) with 6 μm pore size was obtained from Millipore Corporation (USA). The sample pad, conjugate pad, and absorbent pad were obtained from GE Healthcare (UK). Ultrapure water purified with a Millipore Milli-Q system (18.2 $M\Omega \cdot cm^{-1}$) was used to prepare the aqueous solutions. All chemicals used in this study were analytical reagent grade.

1.2. Instruments

The morphologies of the SiO_2@Au NPs were characterized by Hitachi H-7650 microscope at an accelerating voltage of 80 kV. The HRTEM imaging of monodisperse SiO_2@Au NPs were charactered by Philips Tecnai G2 F20 microscope at an accelerating voltage of 200 kV. Elemental mapping images were recorded by energy-dispersive X-ray spectroscopy (EDS) using another JEOL JEM-2100 electron microscope equipped with a STEM unit. Scanning electron microscopy

(SEM) images were obtained with a JEOL JSM-7001F microscopy at an accelerating voltage of 5 kV. The XRD patterns of products powder were characterized on investigated on a Japan Rigaku D/max 2550 VB/PC rotation anode X-ray diffractometer. UV-visible spectra of the samples were measured in the range of 200-800 nm using a Shimadzu 2600 spectrometer. Zeta potential of samples were recorded by a dynamic light scattering with Zetasizer Nano ZS (Malvern, UK). All the measurements were performed at room temperature. Raman signals from the test zone of the SERS-based LFA strips were recorded on a Renishaw inVia plus Raman system with an excitation laser at 785 nm. Incident radiation was coupled to an Olympus BX51 optical microscope and focused to a 2 μm diameter spot through a 50× objective. The data acquisition time at each spot was 5 s, and the peak intensities of the samples were normalized with respect to the silicon wafer at 520 cm^{-1}.

1.3. Synthesis of monodispersed SiO_2 NPs

Monodispersed SiO_2 NPs were prepared according to a modified Stöber method. Typically, 4 mL of ammonia solution and 6 mL of deionized water were added to 100 mL ethanol under magnetic stirring (600 rpm/min). Subsequently, 4 mL of TEOS were added into the above mixture solution, and the reaction was kept at room temperature for 4h. Finally, the resulting SiO_2 NPs were centrifuged and redispersed in 20 mL of ethanol.

1.4. Synthesis of SiO_2@PEI-Au seed NPs

The SiO_2@PEI NPs were synthesized through a PEI self-assembly process under sonication condition. First, 0.5 g PEI was dissolved in 100 mL of deionized water by ultrasonication for 10 min. Next, 0.1 mL of prepared SiO_2 NPs (10 mg/mL) was dispersed in the PEI solution under sonication at room temperature for 30 min, during which PEI gradually self-assembled on the silica cores. The obtained SiO_2@PEI NPs were separated by centrifugation at 7000 rpm for 6 min. After washing three times with deionized water to remove the excess PEI, the PEI-modified SiO_2 particles were mixed with previously prepared small Au NPs (3-5 nm) by sonication for 20 min. The resulting SiO_2@PEI-Au seed NPs were separated and dispersed in 10 mL ethanol.

1.5. Synthesis of high-performance SiO_2@Au NPs

5 mg of SiO_2@PEI-Au seed NPs were dispersed in 100 mL of 0.02 mM $HAuCl_4$ aqueous solution containing 0.2 wt% PVP and then 1mL of hydroxylammonium chloride (10 mg/mL) was added. The SiO_2@Au core-shell NPs were obtained within 5 min under sonication. Finally, the products were washed twice with deionized water and finaly resuspended in ethanol.

1.6. SERS detection of DTNB

A series of DTNB ethanol solutions with concentrations ranging from 10^{-4} M to 10^{-11} M was prepared. About 500 μL of DTNB solution of different concentrations was mixed with 10 μL of SiO_2@Au NPs (1 mg/mL) and incubated under sonication for 1 h. The mixture was separated and

washed three times with ethanol to remove excess DTNB. The precipitate was resuspended in 5 μL of ethanol. The suspension was dropped on a silicon substrate, air dried, and subjected to recording of SERS spectra.

1.7. Preparation of SiO_2@Au NPs SERS tags

DTNB-labelled SiO_2@Au NPs were prepared by attaching the DTNB molecules on the Au shell. In brief, 100 μL of DTNB ethanol solution (10 mM) was added to 10 mL of the as-prepared SiO_2@Au NPs. The mixture was vigorously sonicated at room temperature for 1 h. The product was centrifuged at 3000 rpm for 6 min to remove the excess DTNB molecules, and the precipitate was redispersed in 1 mL of MES solution (100 mM, pH 6.0). The carboxyl groups of DTNB on the surface of the SiO_2@Au NPs were reacted with a mixture of 100 μL of EDC (10 mM) and 10 μL of NHS (100 mM) for 15 min. The mixture was then added with 5 μL of goat anti-human IgM (2 mg/mL) and shaken for 2 h (800 rpm, 25 °C). The nonspecific absorption sites on the SiO_2@Au NPs SERS tags were blocked with 100 μL of BSA (5%, v/v) for 2 h. After separating by centrifugation and washing twice with PBS (10 mM, pH 7.4), the final obtained SERS tags were dispersed in 500 μL of PBS and stored at 4 °C before use.

1.8. Preparation of SERS-based LFA strips

The LFA strip is composed of five parts: a sample pad, a conjugate pad, an NC membrane, an absorbent pad, and a plastic backing card. Each component was fabricated on a plastic backing card, and both ends of the component were overlapped (around 2.5 mm) in sequence to ensure solution migration. A desired volume of the as-prepared SiO_2@Au SERS tags was added to the conjugate pad, which was then dried in an incubator at 37 °C for 4 h. Donkey anti-goat IgG (1 mg/mL) was sprayed in the control line, and goat anti-human antibody IgM (1 mg/mL) was sprayed in the testing line in the nitrocellulose membrane by the bio-dot spraying-membrane machine at a rate of 1.0 $\mu L \cdot cm^{-1}$ and dried for 2 h at 37 °C. The prepared strips were cut in 3.5 mm width by using a programmable cutter and stored in a sealed falcon tube with desiccant before use.

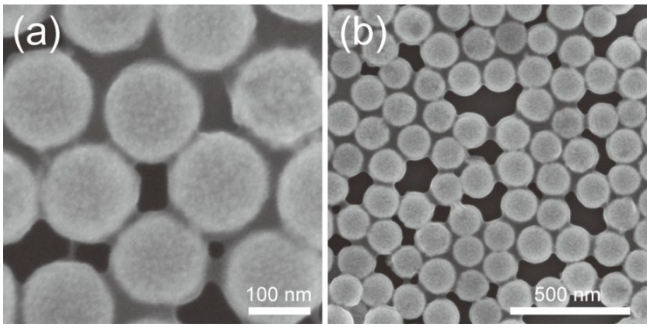

Fig. S1 SEM images of the fabricated monodisperse SiO_2@Au NPs.

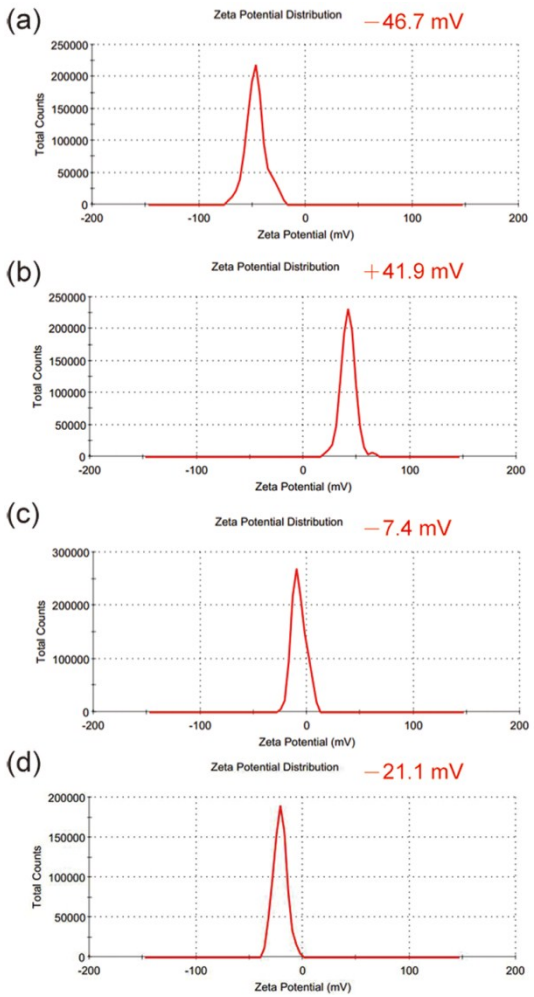

Fig. S2 Zeta potentials of (a) SiO_2, (b) SiO_2@PEI, (c) SiO_2-Au seed, and (d) SiO_2@Au NPs in aqueous solution.

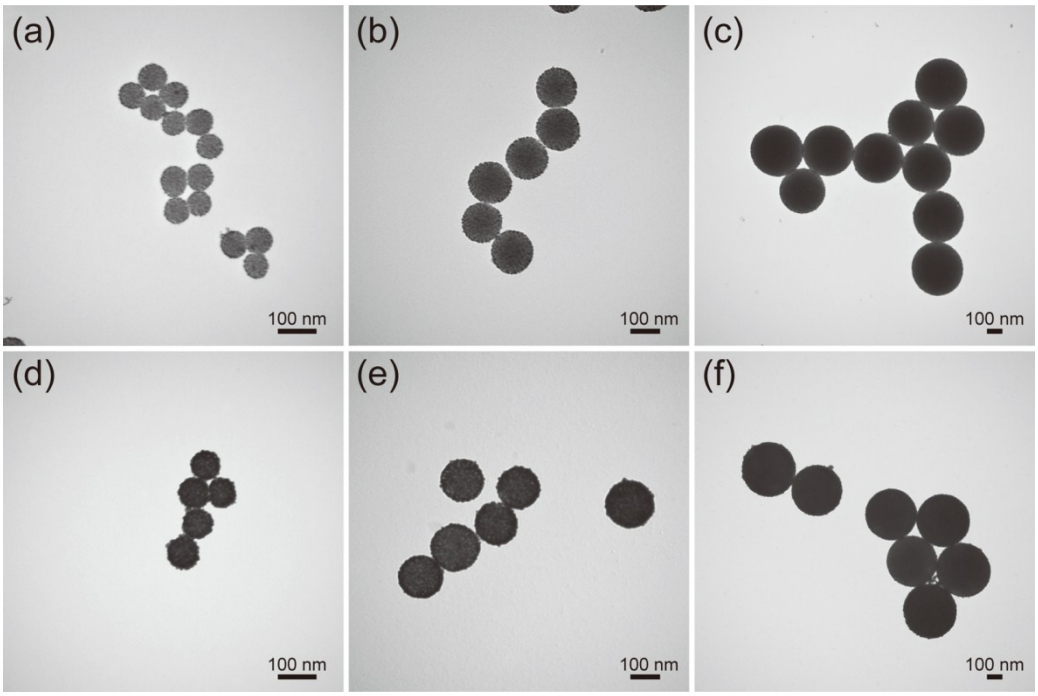

Fig. S3 TEM images of multiple SiO_2-Au seed with different sizes: (a) 70 nm, (b) 150 nm, (c) 300 nm, and their corresponding fabricated SiO_2@Au MNPs (d), (e), and (f) respectively.

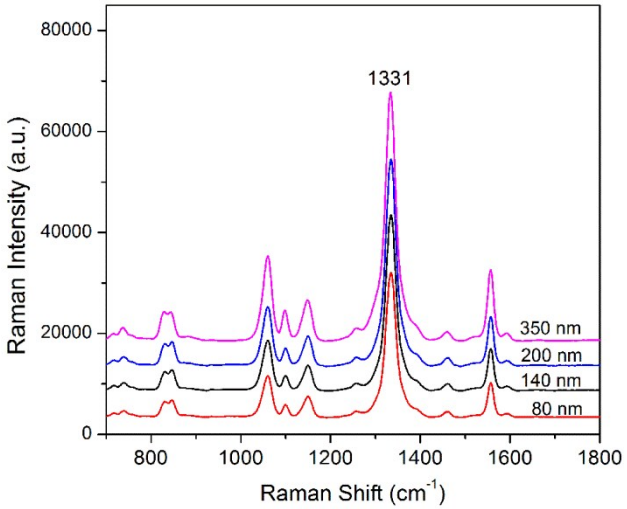

Fig. S4 SERS spectra of DTNB (10^{-5} M) adsorbed on SiO_2@Au NPs with different particle sizes.

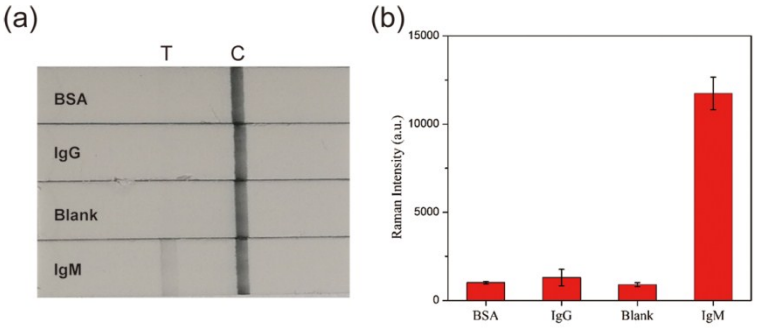

Fig. S5 Specificity of the SiO_2@Au tags based SERS-LFIA. (a) Photograph of the SERS-LFIA strip after applying human IgM solution (100 ng/mL) as a positive test, other proteins (1000 ng/mL) as a negative test, and PBST buffer as a blank control. (b) Raman spectra at the test lines of SERS-LFIA strip. Error bars are the standard deviation of three independent experiments.