

Raman Active Jagged-Shaped Gold-Coated Magnetic Particles as Novel Multimodal Nanoprobe

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Materials

$\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, diethylene glycol, sodium hydroxide (NaOH), $\text{NH}_2\text{OH} \cdot \text{HCl}$, gold salt (HAuCl_4) Poly-L-histidine (PLH), and Poly (2-vinylpyridine) were purchased from Sigma-Aldrich. It is noteworthy that PLH and Poly (2-vinylpyridine) were used as the templates to direct gold nucleation and growth. Phospholipid-polyethylene glycol terminated with carboxylic acid (PL-PEG-COOH) was purchased from Avanti polar lipids. Pyridine was obtained from Sinopharm Chemical Reagent Company.

Experimental Section

In order to obtain nanoparticles with a narrow size distribution, the polyol route was employed.^{8, 37, 38} Briefly, 5 mL of an aqueous solution of $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (0.045 mol) and FeCl_3 (0.0375 mol) were added to 250 mL of diethyleneglycol. The mixture was heated to 170°C and maintained at this temperature for 15 min before addition of the base (i.e. solid NaOH, 0.375 mol). Afterward, the temperature was maintained at 170°C for a period of 1 h before cooling at 60°C. The synthesized SPIONs were collected with neodymium magnet and washed with 100 mL of the HNO_3 1N solution.

The smooth gold-shell SPIONs were prepared according to the previous report.²² Briefly, the prepared SPIONs were mixed with PLH(Poly-L-histidine)-PEG-COOH (ratio of 1:1.5 W/W) in chloroform, and remained till the solvent were evaporated slowly. The residual coated SPIONs were heated to 80 °C for 5 min and redispersed in deionized (DI) **water** with sonication. The obtained materials were collected with a strong magnet and washed several times with DI water. PLH was added to the solution of SPIONs and the pH was adjusted in the range 5-6, using 0.1 N.HCl. After incubation for 60 min, the magnetic NPs were collected with magnet and washed several times with DI water. The obtained solution was mixed with HAuCl_4 (w/w 1%), for 20 min where the pH was adjusted in the range 9-10 with NaOH. Afterward, $\text{NH}_2\text{OH} \cdot \text{HCl}$ was added to the solution and mixed well till the colour of colloidal suspension turned to dark blue. It is noteworthy that the observed colour was cleared in a few minutes. The achieved solution was washed several times, redispersed in DI water using sonicator, and kept in the range 2-8 °C.

In order to create the jagged-shaped gold-coated SPIONs, the prepared SPIONs were mixed with Poly (2-vinylpyridine) and PL-PEG-COOH (ratio of 1:1.5 (the same concentration of polymers were employed) W/W) and the same other stages of preparation of smooth-shaped gold shell were followed except the final section (i.e. addition and reduction of gold salts). More specifically, the solution containing Poly (2-vinylpyridine) and PL-PEG-COOH coated SPIONs, after PLH addition, was mixed with HAuCl_4 (w/w 1%), for 20 min where the pH was adjusted in the range 4-5 with NaOH. In this pH, Poly (2-vinylpyridine), which is the pH sensitive polymer, has folded formation where PL-PEG-COOH has stranded shape.⁴⁵ After reduction of gold with $\text{NH}_2\text{OH} \cdot \text{HCl}$, the jagged-shaped gold-coated SPIONs were obtained (see **Figure S1 and S2**). The achieved solution was washed several times, redispersed in DI water using sonicator, and kept between 2-8 °C.

Measurements and Instrumentation

Characterization of particles. Dynamic light scattering (DLS) measurements were performed with a Malvern PCS-4700 instrument equipped with a 256-channel correlator. The 488.0 nm line of a Coherent Innova-70 Ar ion laser was used as the incident beam. The laser power used was 250 mW. The scattering angles, θ , employed ranged between 40° and 140°. The temperature was maintained at 25°C with an external circulator. Zeta potential determination was performed using a Malvern Zetasizer 3000HSa. Each measurement was an average of six repetitions of one minute each and repeated five times. Data analysis has been performed according to the standard procedures, and interpreted through a cumulant expansion of the field autocorrelation function to the second order. Moreover, in order to obtain a distribution of decay rates, a constrained regularization method, CONTIN, was used to invert the experimental data.

The size and shape of the NPs were evaluated with a Phillips CM200 transmission electron microscope (TEM) equipped with an AMT 2 x 2 CCD camera at an accelerating voltage of 200 kV. To prepare samples for TEM, a drop of the suspension was placed on a copper grid and dried. High-resolution surface imaging studies were performed using atomic force microscopy (AFM) to estimate surface morphology and particle size distribution. The samples were imaged with the aid of Dualscope/Rasterscope C26, DME, Denmark, using DS 95-50-E scanner with vertical z-axis resolution of 0.1 nm. Raman spectra were achieved by employing a confocal microprobe Raman system (HR800, Jobin Yvon), which is a single spectrograph instrument equipped with a holographic notch filter and a CCD detector. The size of the silt and pinhole were 100 and 400 μm , respectively. A long working distance 50 \times objective was used to collect the Raman scattering signal. The excitation wavelength was 632.8 nm from a He-Ne laser, and the greatest laser power was 10mW.

The obtained results are summarized in Table S1.

Magnetometry measurements. Magnetization measurements were performed using a Quantum Design Superconducting Quantum Interference Device (SQUID) MPMS-XL7 magnetometer. The temperature dependence of the magnetization was studied in the temperature range 5-300 K by zero-field-cooling (ZFC) and field-cooling (FC) curves collected at an applied magnetic field $H = 50$ Oe (see Figure S8). Table S2 presents the parameters obtained from ZFC/FC and hysteresis curves.

NMR relaxometry measurements. The ^1H nuclear magnetic resonance dispersion (NMR-D) profiles were determined, physiological temperature $T = 37^\circ\text{C}$, by measuring the longitudinal T_1 and transverse T_2 nuclear relaxation times at 20 MHz and 60 MHz. The corresponding relaxivities, i.e. r_1 and r_2 , are given in Table S2.

Simulation. In order to simulate interaction of light with gold-coated SPIONs, we used 3D-FDTD method.⁴⁵ The method is based on solving Maxwell's equations by replacing derivative with differentiation. We considered Drude model in order to consider dispersion behavior of permittivity (Equation 1).

$$\varepsilon(\omega) = \varepsilon_\infty - \frac{\omega_D^2}{\omega^2 + i\gamma_D\omega} \quad (1)$$

Where ε_∞ is dielectric constant at frequencies far above plasma frequency, ω_D is plasma frequency and γ_D is intrinsic damping parameter. Material parameters are obtained by fitting equation 1 with parameters which are obtained from measurement. The software was developed in MATLAB and contains Total Field /Scatter Field formulation for excitation and Mur's absorbing boundary condition. Results of electric field enhancement were performed for two cases of smooth and corrugated gold-coated SPIONs (as depicted in Figure 6).

Remarks

The DLS and zeta potential results are displayed in Figure S3. The zeta potential for jagged-shaped gold shell has two various populations confirming the formation of keen edge of gold shell.

It is notable that the optimized presented concentrations of materials are crucial to achieve the smooth- and jagged- shaped gold shell, with polymeric gap, on the surface of SPIONs. For instance, if the concentration of PLH is higher than a defined amount (see experimental section of the paper), the surface of SPIONs would be covered by multilayer of PLH (see Figure S4); in this case, the Chinese script structure (see Figure S5) would be formed by reduction of the gold salts which are attached at the PLH outer layer. The concentration of the gold salt is another key role for the formation of well-defined gold ring shell, with polymeric gap, at the surface of SPIONs. Using higher gold salt and lower PLH amounts, the gold nanoparticles would be prepared individually (see Figure S6).

The cartoon of employed method for Raman spectroscopy is shown in Figure S9.

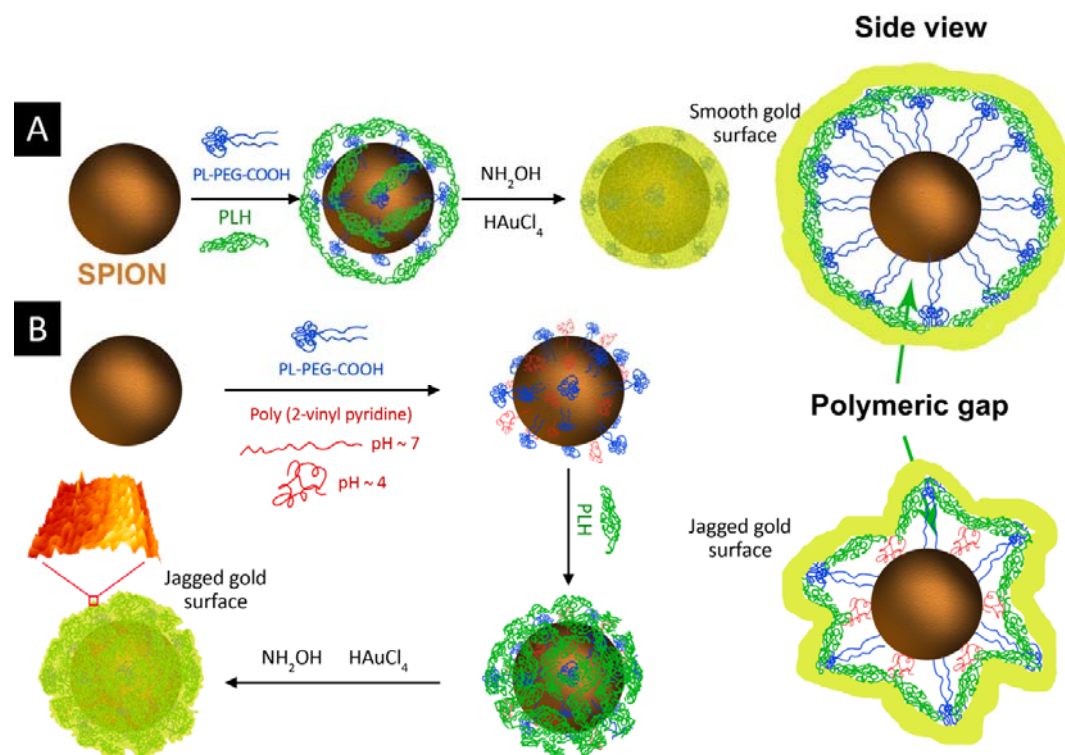


Figure S1: Cartoon showing the key steps involved in synthesis of (A) smooth- and (B) jagged-shaped gold-coated SPIONs with a polymeric gap, diagram is not in scale in representing the proportions of the different objects.

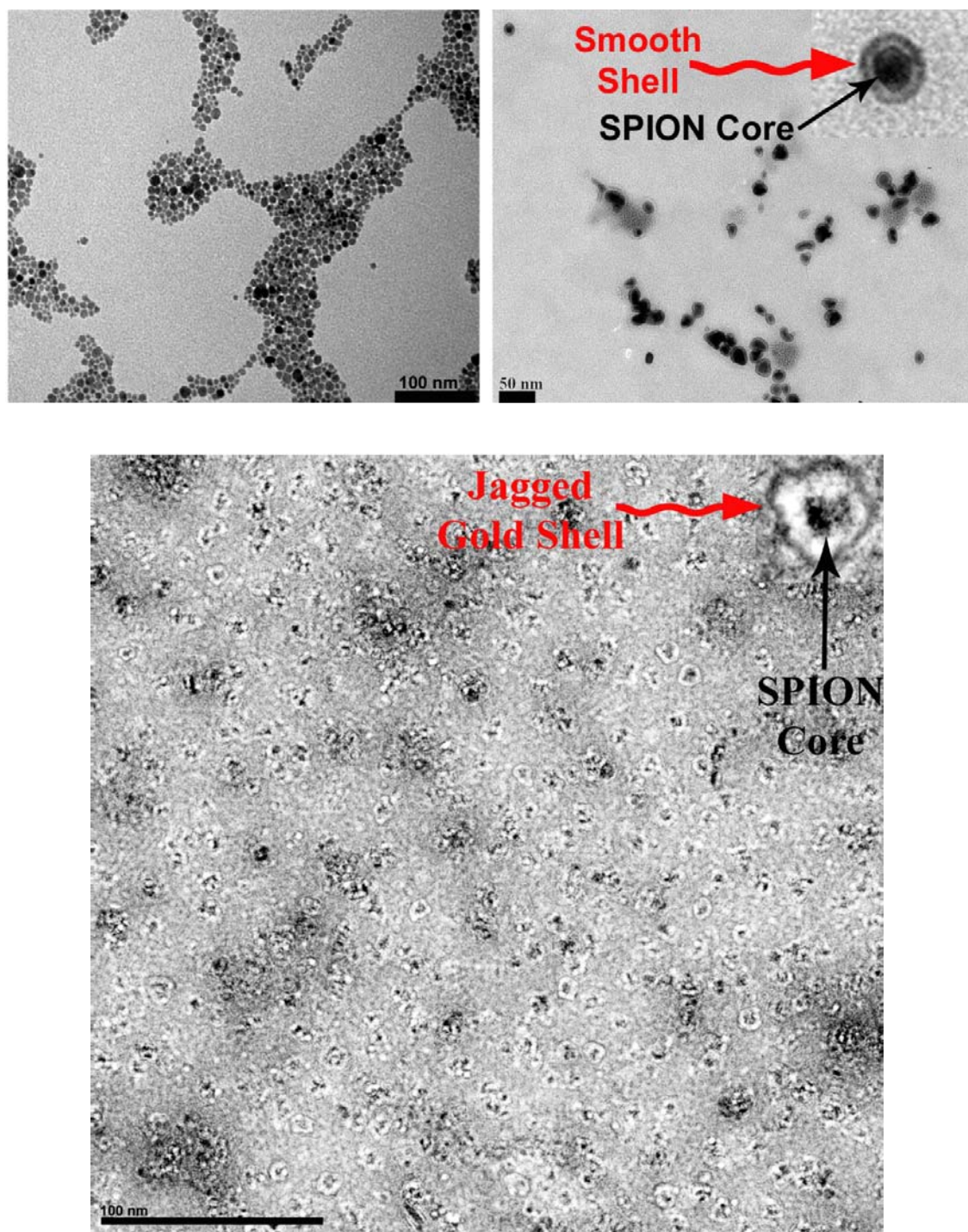


Figure S2: TEM images of bare SPIONs (displays a formation of magnetic NPs with very narrow size distribution), smooth- and jagged-shaped gold-coated SPIONs (illustrates the existence of polymeric gap between the SPION core and gold ring together with the existence of the smooth and rough (top right panels) surface morphologies), respectively.

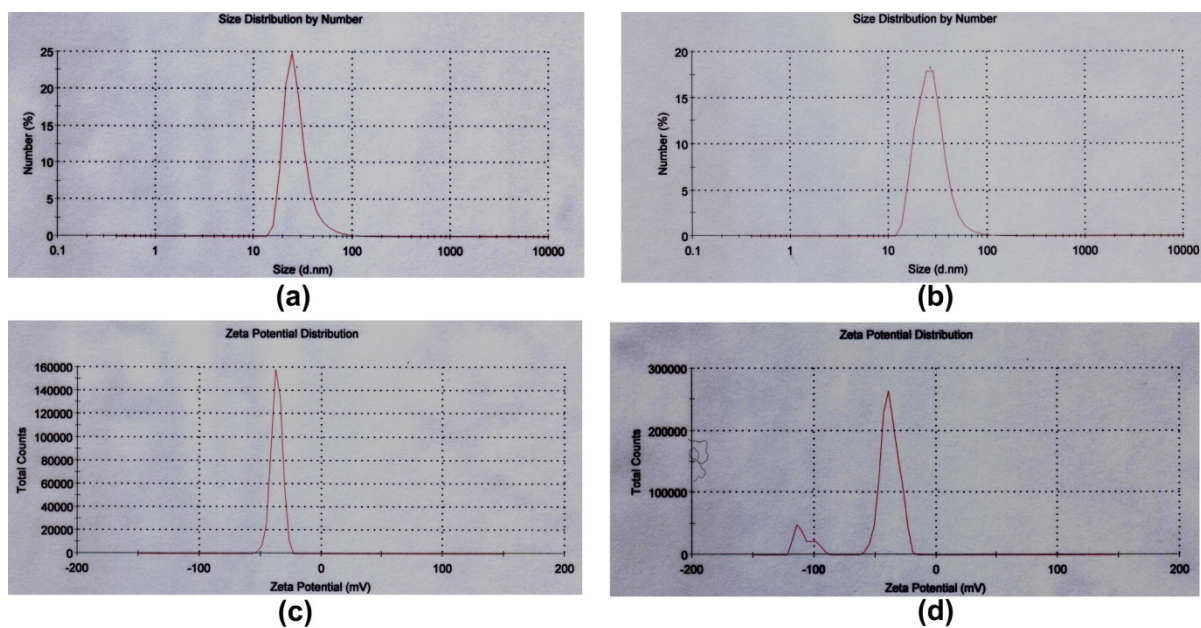


Figure S3: DLS data of (a) smooth- and (b) jagged-shaped gold-coated SPIONs; (c) and (d) shows the zeta potential data for smooth- and jagged-shaped gold-coated SPIONs, respectively.

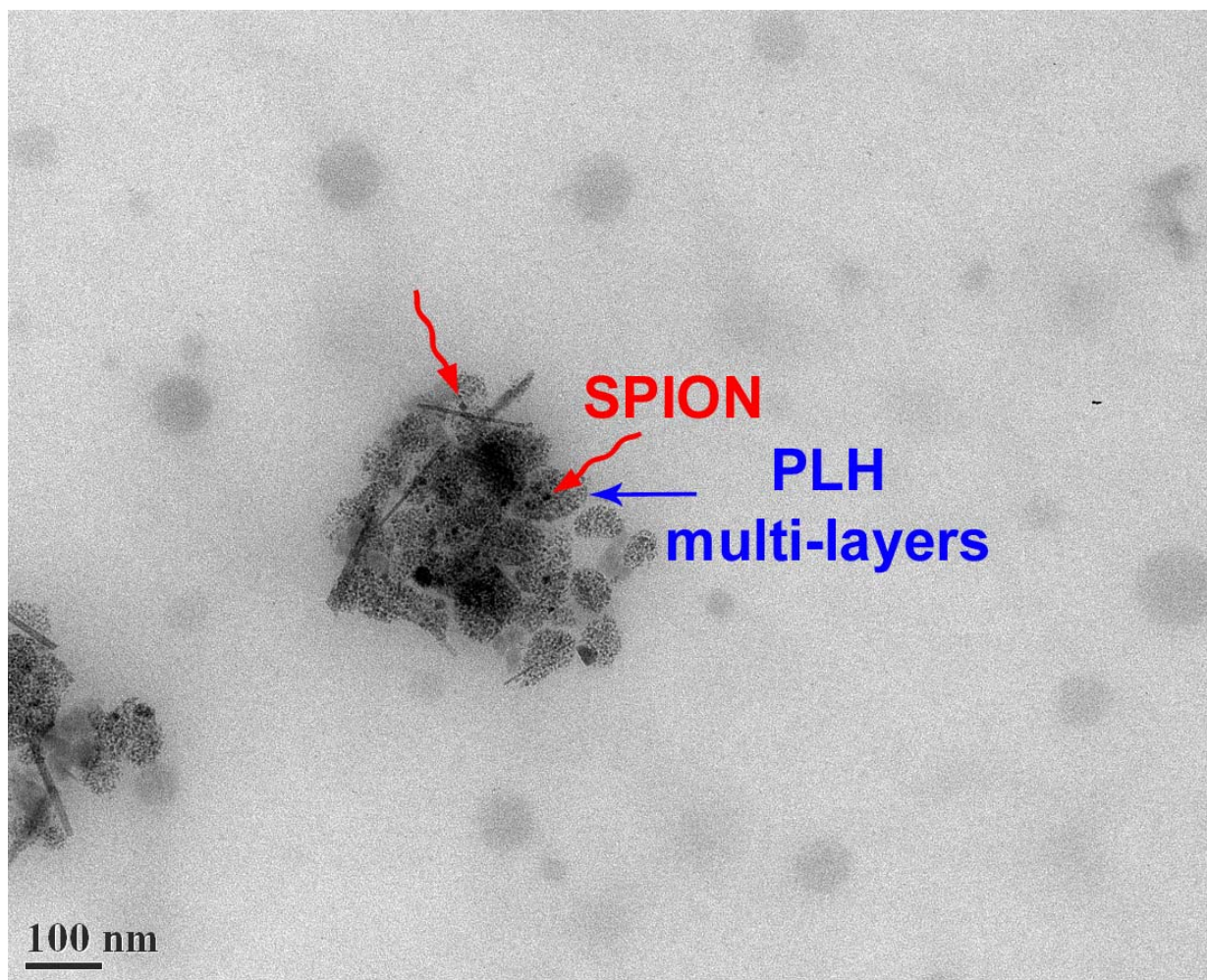


Figure S4: TEM image of bare SPIONs (i.e. dark spots) covered by PLH multilayers.

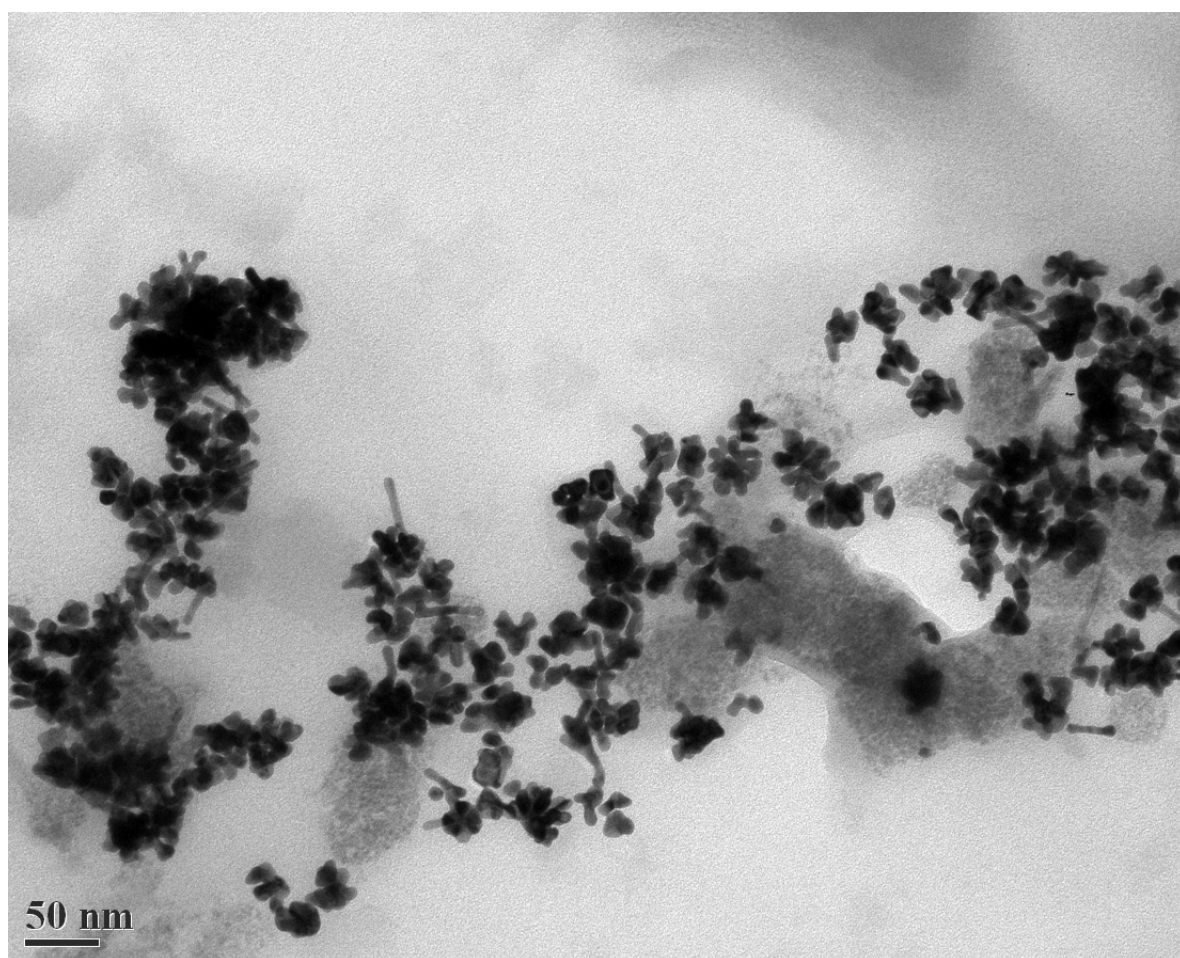


Figure S5: TEM image of gold@SPIONs with chinese script structure.

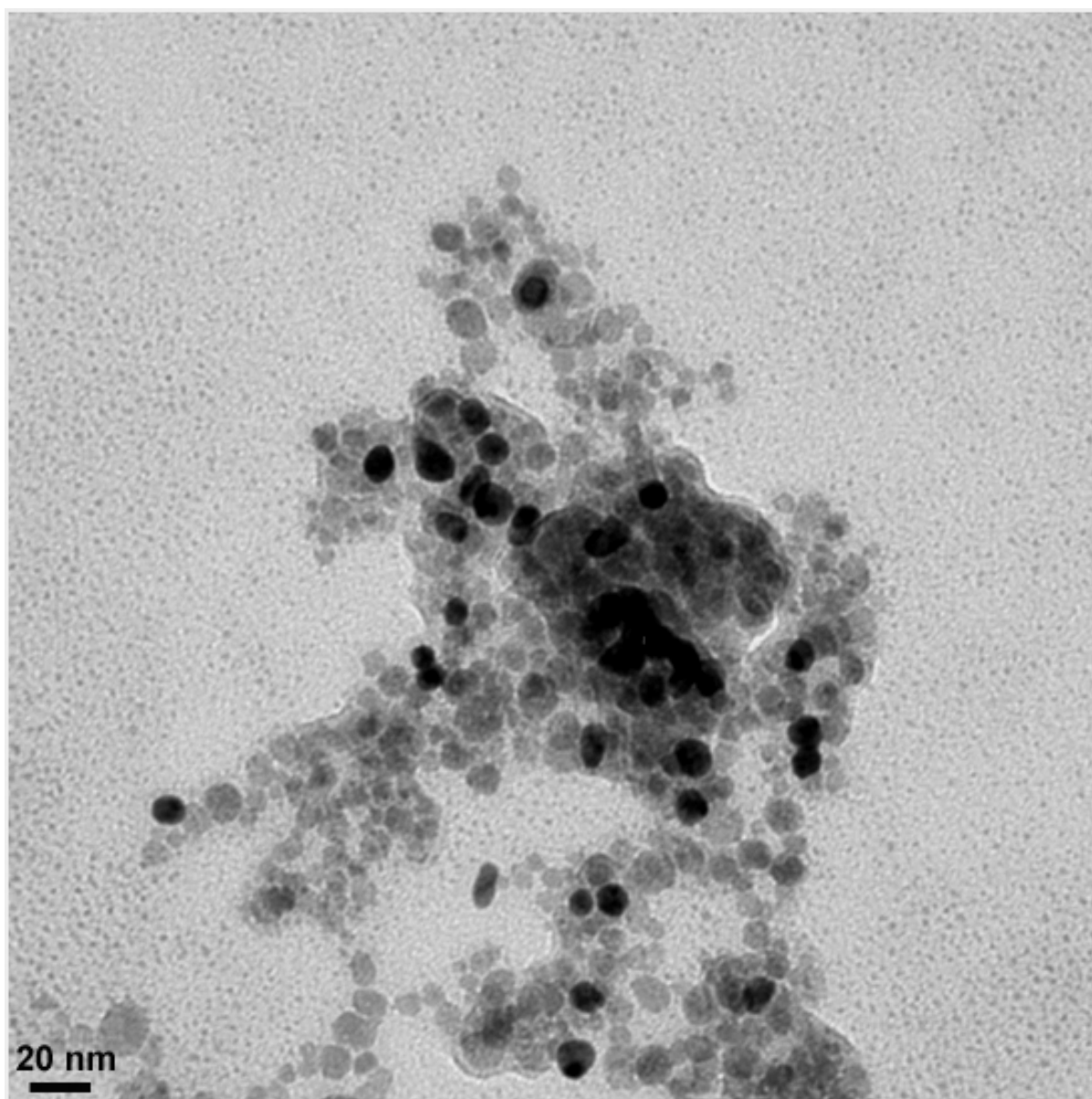


Figure S6: TEM image of the mixture of both gold@SPIONs and individual gold NPs; the particles with less defined shape and darker contrast are gold nanoparticles, whereas the other particles are the SPIONs.

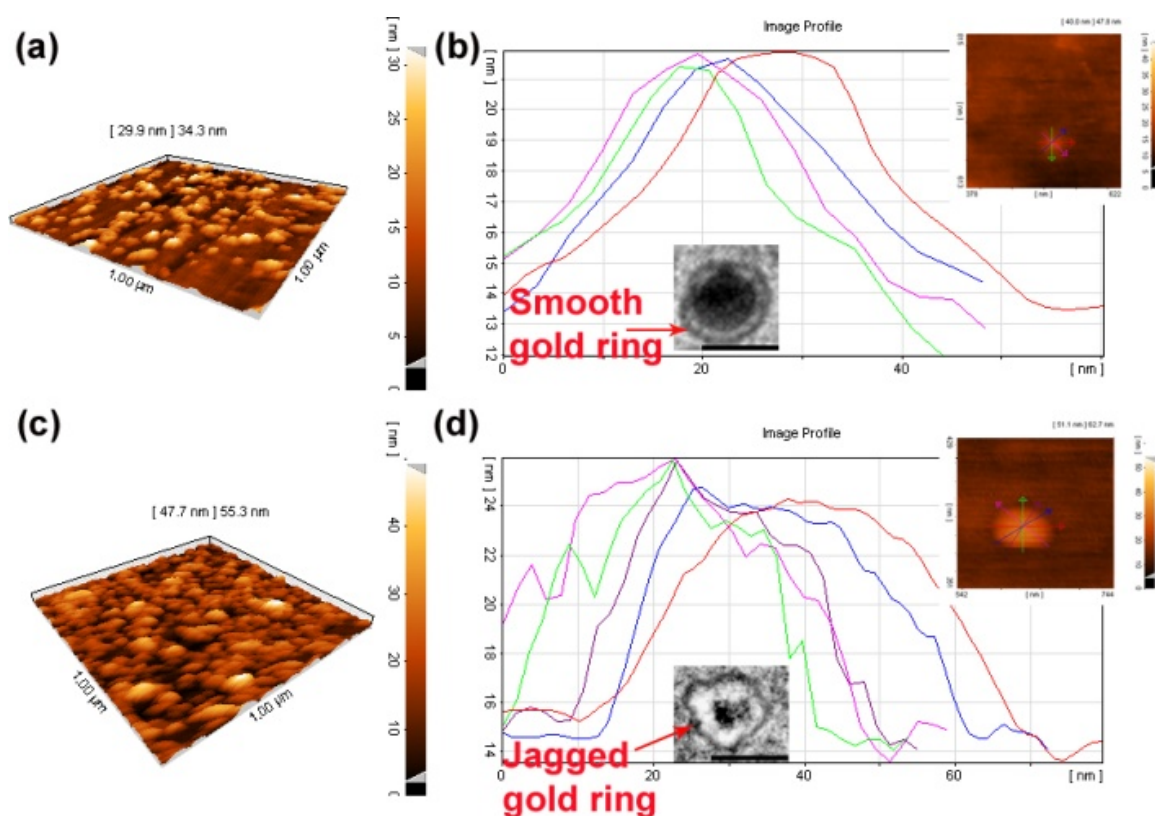
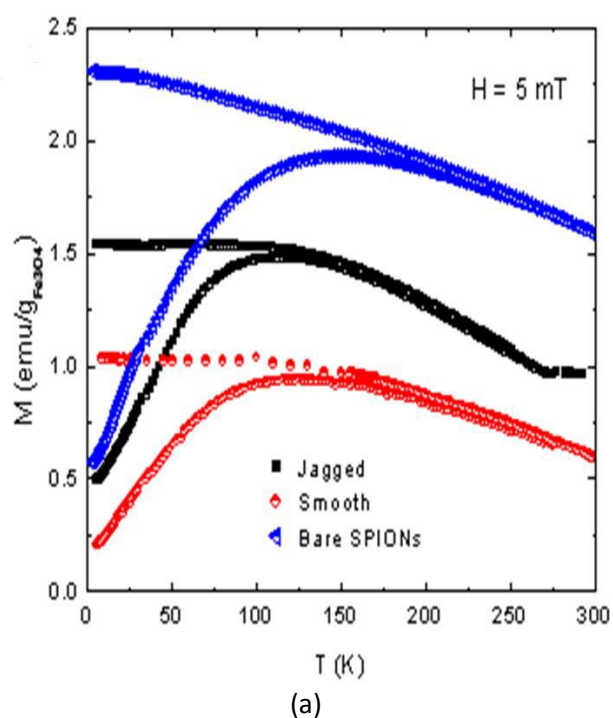


Figure S7: AFM images of (a) smooth- and (c) jagged-shaped gold-coated SPIONs; (b) and (d) show the image profiles of selected NPs in various spherical directions (upper inset panel) showing smooth and jagged morphologies of the particles; lower inset panel shows the corresponding TEM images of the NPs with various surface shapes (the TEM scale bar is 15 nm).



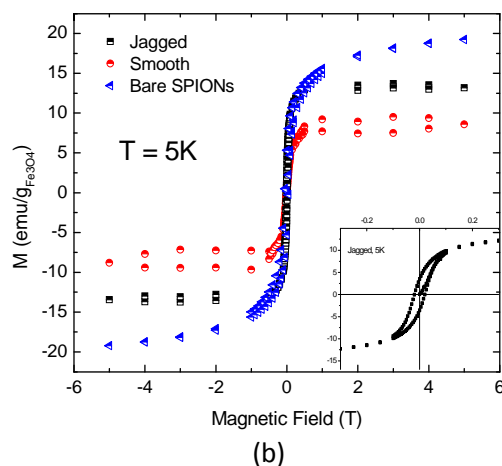


Figure S8: (a) ZFC/FC magnetization curves and (b) magnetization as a function of applied magnetic field, i.e. hysteresis, at low temperature for both smooth- and jagged-shaped gold shell samples together with the bare SPIONs. The inset in (b) (with the same units) shows a zoom of the Jagged-shaped gold-coated NPs.

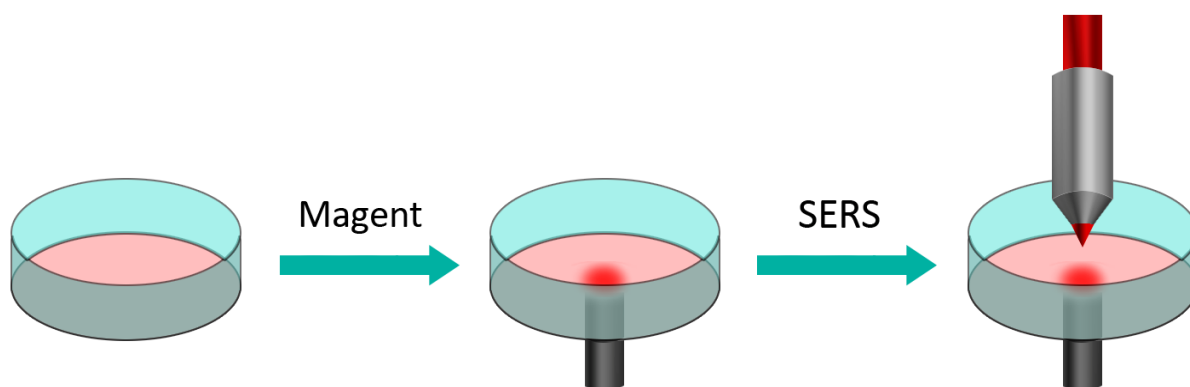


Figure S9: Cartoon showing the SERS detection of pyridine which is absorbed on the surface of magnetic NPs.

TABLE S1: SPIONs size by dynamic light scattering and zeta potential by particulate microelectrophoresis for the differently coated SPIONs. Sizes are presented as mean \pm SD.

^a z-average hydrodynamic diameter extracted by cumulant analysis of the data. ^b Polydispersity Index. ^c Average hydrodynamic diameter determined from CONTIN size distribution.

NPs coating	D_H (nm) ^a	PDI ^b	$\langle D_H \rangle$ (nm) ^c	Zeta potential (mV)
Bare SPIONs	13.7 ± 2.1	0.29	18.3 ± 3.2	$+43.7 \pm 1.7$
Smooth –shaped gold	27.8 ± 2.6	0.19	34.2 ± 2.2	-36.5 ± 1.56
Jagged-shaped gold	28.1 ± 2.8	0.17	7.4 ± 2.7	-37.6 ± 1.29
				-108 ± 3.54

TABLE S2: Blocking temperature (T_B), coercive field (H_C), and remanent magnetization (M_r) obtained from magnetization experiments together with the longitudinal (r_1) and transverse (r_2) relaxivities at 20MHz and 60MHz.

NPs Coating	T_B (K)	H_C (mT)	M_r (emu/g _{Fe})	r_1 (mM.s) ⁻¹		r_2 (mM.s) ⁻¹	
				20 MHz	60 MHz	20 MHz	60 MHz
Smooth-shaped gold	137.45	16.64	1.3	21.97	10.09	192.4	201.5
Jagged-shaped gold	115.54	20.0	3.53	22.35	10.76	193.7	202.2
Bare SPIONs	148.54	53.8	5.31	3.41	1.98	42.72	40.96