

## Supplementary Information

### **Flexible plasmonic substrate for sensitive surface-enhanced Raman scattering-based detection of fentanyl**

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## Materials

Gold chloride trihydrate ( $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ ), hexadecyltrimethylammonium bromide (CTAB), sodium borohydride ( $\text{NaBH}_4$ ), silver nitrate ( $\text{AgNO}_3$ ), ascorbic acid, fentanyl (1.0 mg/mL in methanol), potassium chloride (KCl), sodium chloride (NaCl), citric acid, and uric acid were purchased from Sigma-Aldrich. Hexadecyltrimethylammonium chloride (CTAC) was purchased from Tokyo Chemical Industry Co., Ltd (TCI). Artificial urine was purchased from Biochemazone. All the chemicals were used as received without further purification. Nanopure water (18.2 M $\Omega$ -cm) was used for all the experiments.

## Characterization Techniques

A Shimadzu UV-1900 spectrophotometer was used to collect Vis-NIR extinction spectra. SEM images were captured using a JEOL JSM-7610F field emission instrument. TEM images were acquired with a JEOL JEM-2100 field emission TEM. STEM imaging was performed with a HAADF detector. Energy-dispersive X-ray spectroscopy (EDS) is affiliated with TEM.

## Synthesis of Au Nanorods

Au nanorods were synthesized by using a seed-mediated method and our previous reports.<sup>1-4</sup> Seed solution was synthesized by adding 0.6 mL of an ice-cold  $\text{NaBH}_4$  (10 mM) solution into the solution containing 0.25 mL of  $\text{HAuCl}_4$  (10 mM) and 9.75 mL of CTAB (0.1 M) under vigorous stirring at room temperature. The color of the seed solution changed from yellow to brown. The growth solution was prepared by mixing 5 mL of  $\text{HAuCl}_4$  (10 mM), 95 mL of CTAB (0.1 M), 1 mL of  $\text{AgNO}_3$  (10 mM), and 0.55 mL of ascorbic acid (0.1 M), consecutively. The solution was homogenized by gentle shaking. To the colorless solution, 0.12 mL of freshly prepared seed solution was added and kept in the dark overnight.

## Synthesis of AuNR@Ag

Four milliliters of twice-centrifuged AuNR and 8 mL of CTAC (20 mM) were mixed at 60 °C under stirring for 20 min. After stirring, 1.6 mL of  $\text{AgNO}_3$  (2 mM), 2 mL of CTAC (20 mM), and 0.8 mL of ascorbic acid (0.1M) were added under stirring at 60 °C for 4 h. The

as-synthesized AuNR@Ag was centrifuged at 8,000 rpm for 10 min and re-dispersed CTAC solution (20 mM).

### **Synthesis of Yolk-Shell AuNR@Au/Ag Nanomaterials**

Yolk-shell AuNR@Au/Ag nanomaterials were synthesized by transforming the Ag shell of Au@Ag NRs into the porous shell of Au/Ag via a galvanic replacement reaction. The as-synthesized AuNR@Ag were centrifuged and re-dispersed in CTAC (20 mM). H<sub>2</sub>AuCl<sub>4</sub> aqueous solution (0.5 mM) was injected into the AuNR@Ag solution at a rate of 0.5 mL/min under magnetic stirring until the desired LSPR wavelength was achieved.

### **Preparation of Flexible SERS Substrates**

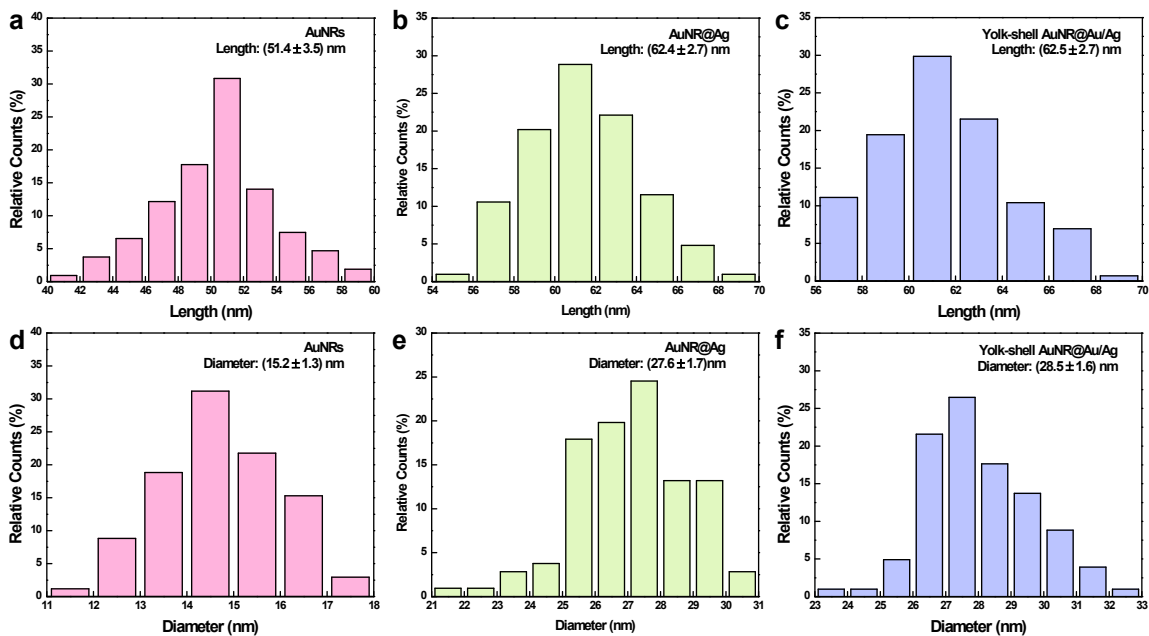
Cellulose microfiber filter paper (Whatman, grade 1) was selected for the adsorption of yolk-shell AuNR@Au/Ag nanomaterials to form the flexible SERS substrates. Briefly, filter paper with a diameter of 5 mm was immersed in the solution of yolk-shell AuNR@Au/Ag nanomaterials (OD around 2.0) in a 96-well plate and left overnight.

### **SERS Measurements**

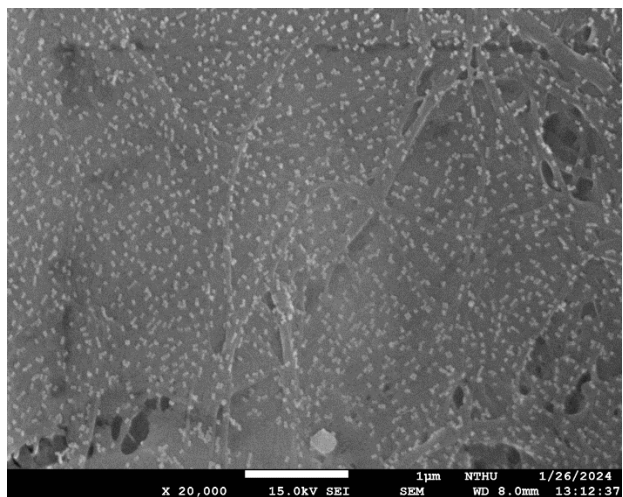
Raman spectra were acquired using a Horiba Raman spectrometer (LabRAM HR 800 UV) with a 50X objective and 632.8 nm HeNe laser. For the fentanyl-exposed SERS substrates, various concentrations of fentanyl were spiked into artificial urine before being applied to the SERS biochips for analysis.

### **Selectivity Test**

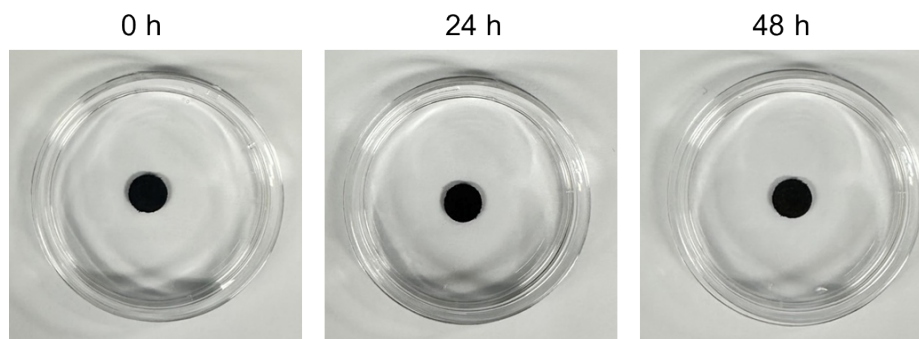
Non-target molecules, including KCl (1.17 mg/mL), NaCl (2.07 mg/mL), citric acid (0.3 mg/mL), and uric acid (0.25 mg/mL) in artificial urine were exposed to the flexible SERS substrates followed by the SERS measurements.



**Fig. S1** The histogram shows the size distribution of the AuNRs, AuNR@Ag NRs, and yolk-shell AuNR@Au/Ag nanomaterials. (a) Length of AuNRs. (b) Length of AuNR@Ag NRs. (c) Length of yolk-shell AuNR@Au/Ag nanomaterials. (d) Diameter of AuNRs. (e) Diameter of AuNR@Ag NRs. (f) Diameter of yolk-shell AuNR@Au/Ag nanomaterials.



**Fig. S2** SEM image of the yolk-shell nanomaterial-decorated flexible substrate.



**Fig. S3** Optical images of the yolk-shell nanomaterial-decorated flexible substrate in water at different time points show the stability of the substrate.

## References

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