

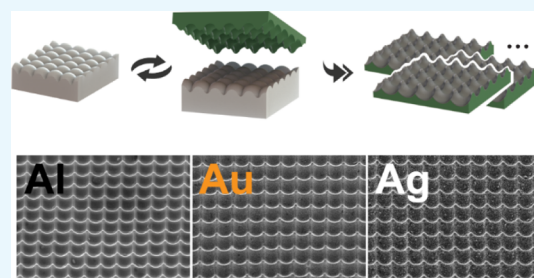
Reproducible Plasmonic Nanopyramid Array of Various Metals for Highly Sensitive Refractometric and Surface-Enhanced Raman Biosensing

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Supporting Information

ABSTRACT: Localized surface plasmon resonance (LSPR) biosensors show great potential for practical/commercial use in clinical diagnosis, home healthcare, environmental analysis, and public healthcare. However, two main issues, that is, low refractometric sensitivity and low reproducibility (large-area uniformity and batch-to-batch consistency), hinder the extensive applications of LSPR biosensors. Therefore, plasmonic nanostructures with high sensitivity and excellent reproducibility are desirable for preparing reliable LSPR sensors. Herein, we have fabricated plasmonic nanopyramid arrays (NPAs) for several batches with reproducible morphology and optical properties by elastic soft lithography and metal thermal evaporation. NPAs of various metals (i.e., Al, Au, and Ag) were also prepared by thermal evaporation with the according metals. The transmission spectra of these NPAs showed several narrow LSPR peaks in the visible-infrared wavelength region. The refractometric sensitivities of the LSPR peaks were systematically studied, and high refractometric sensitivities of 774.0, 472.8, and 421.0 nm/RIU were achieved on Al, Au, and Ag NPAs, respectively. To demonstrate the potential of the NPAs for multiplex applications, we first applied this highly sensitive Al NPA biosensor to monitoring the process of proliferation of HeLa cancer cells, in situ and in real time. Then, we demonstrated that the Au NPA was able to identify the absorbed analytes on its surface through the surface-enhanced Raman scattering spectrum. In addition, the finite difference time domain simulations were performed to reveal the electromagnetic field enhancement on NPAs. Because of the properties of high sensitivity and excellent reproducibility of the metal NPA LSPR substrates, as well as the simplicity and cost efficiency of the fabrication method, our proposed work will accelerate the practical use of LSPR sensors.



INTRODUCTION

Plasmonic metal nanostructures have attracted increasing attention because of their wide applications in metamaterials,^{1,2} sunlight harvesting,^{3,4} photocatalyst,⁵ color display,⁶ and optical sensing.^{7–9} Plasmonic biosensors have been appreciated as the advancing and promising optical sensors in recent years because of their properties of ultrasensitivity, high spatial resolution, and label-free detections.^{10–13} Plasmonic biosensors are mainly divided into propagating surface plasmon resonance (PSPR) and localized surface plasmon resonance (LSPR) biosensors.¹⁴ Compared to PSPR biosensors, LSPR biosensors are remarkable in measuring local refractive index (RI) changes caused by the adsorption of targeted molecules.^{8,15} Moreover, the optical system for LSPR sensing is simpler, whereas SPR system requires coupler (i.e., prism or grating) to activate plasmons. It makes the LSPR sensor more promising in the construction of miniaturized biomedical devices.^{16,17} With the outstanding merits of high spatial resolution, simple optical framework, and capacity of label-free detection, LSPR

biosensors show great potential for practical/commercial use in clinical diagnosis,^{18,19} home healthcare,²⁰ environmental analysis,²¹ and public healthcare.²²

However, there are two main issues that hinder the extensive applications of LSPR biosensors, that is, low refractometric sensitivity and low reproducibility (large-area uniformity and batch-to-batch consistency). On the one hand, the refractometric sensitivity of the LSPR biosensor is still low because the LSPRs generally exhibit broad resonance peaks owing to strong radiative damping.²³ According to the physical principles, LSPR nanostructures exhibiting a shorter decay length and more enhanced electromagnetic field (EF) in a smaller volume than the planar metallic surface can respond better to the local RI (n) changes near the metallic surfaces. To enhance the local EF, many efforts have been made such as changing the size and

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shape^{24–26} and/or the spatial arrangement^{27,28} of the metal nanoparticles and nanostructures. To obtain largely enhanced EF at confined small sites (so-called “hotspots”), deliberately designed sharp tips, sharp edges,²⁹ and narrow gaps between the two nanostructures³⁰ on LSPR substrates are highly desirable.

On the other hand, the nanostructures are inhomogeneous in large area and vary from batch to batch. The spot-to-spot and batch-to-batch consistency of the nanostructures is the key to reproducible LSPR response among the measurements of all sensing substrates, which is essential for the practical use of LSPR sensors.³¹ There are mainly two conventional approaches to fabricate the LSPR nanostructures: chemical synthesis and physical preparation. In chemical methods, nanocrystals were synthesized in the solution phase and then deposited on a flat substrate to prepare a LSPR sensor. In this case, chemical methods are facing problems of the difficulty in controlling the interdistance between the nanocrystals and eliminating the inconsistency of the nanostructures between different batches.³² Compared to chemical synthesis, physical preparation is more promising for LSPR sensors because of the controllable interspace of nanostructures and non-contamination of the metal surface. In physical preparations, e-beam lithography,³³ focused ion beam lithography,³⁴ and photolithography³⁵ can realize the precise control of size, shape, and interspace among the metal nanostructures, but they still can not provide low-cost production of large-area nanostructures. Nanosphere lithography,^{36,37} template stripping,³⁸ elastic soft lithography (ESL)³⁹ are the next-generation approaches that provide cheap production of large-area nanostructures. However, some efforts are still required to obtain a satisfactory LSPR sensor with spot-to-spot and batch-to-batch consistency by these approaches.

Herein, to address these two issues, we proposed a well-designed metal nanopyramid array (NPA) with high refractometric sensitivity and high reproducibility prepared by ESL and metal thermal evaporation. In the ESL procedures, NPAs with geometries of tapering nanostructure can be easily detached from the template stamp without damage. Therefore, we have fabricated NPAs with excellent reproducibility in large area and in different batches. In the metal thermal evaporation procedure, Al, Au, and Ag NPAs were obtained, respectively. Their transmission spectra showed several narrow LSPR peaks in the visible-infrared wavelength region, and the spectra of NPAs from different batches were consistent. The refractometric sensitivities of the LSPR peaks were systematically investigated, and the Al NPA held a highest refractometric sensitivity of 774.0 nm/RIU. This highly sensitive Al NPA was applied to monitoring the process of proliferation of HeLa cancer cells. In addition, the Au NPA with enhanced local EF was used to provide a surface-enhanced Raman scattering (SERS) spectrum of the 4-methylbenzenethiol (4-MBT) monolayer. Furthermore, the finite difference time domain (FDTD) simulations were performed to investigate the EF enhancement of the NPAs. This work will accelerate the practical process of LSPR sensors on the basis of the simplicity and cost efficiency of the fabrication method, as well as the properties of excellent reproducibility and high sensitivity of the NPA LSPR substrate.

RESULTS AND DISCUSSION

Fabrication of Reproducible Metal NPAs. Figure 1 shows the scheme of fabricating metal NPAs by two steps: ESL

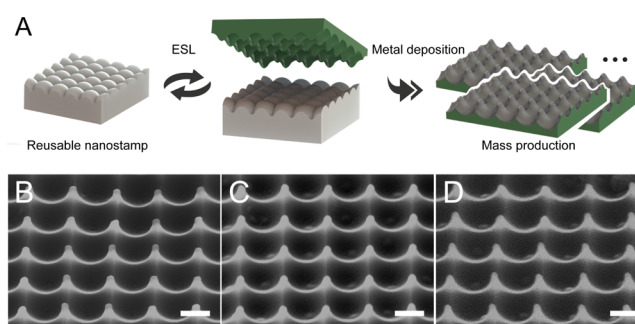


Figure 1. (A) Fabrication procedure of the NPA using ESL and subsequent metal thermal evaporation. (B–D) Side-view SEM images of Al NPAs at 45°. These Al NPAs were obtained from different batches. The scale bars in (B–D) are 1 μm .

and subsequent metal thermal evaporation. The as-prepared metal NPA is composed of a transparent polymer substrate and a 50 nm thick metal deposition. ESL was performed by a polydimethylsiloxane (PDMS) nanostamp and an UV-cured norland optical adhesive (NOA). The PDMS nanostamp is flexible and reusable for more than 50 times, which can reduce the costs for mass production. We are able to measure the transmission spectra of such a NPA because the NOA substrate is transparent, which greatly simplified the detection system.⁴⁰ On the basis of the tapering shape of the nanopyramid, the NPA substrate was easily detached from its complementary nanostamp in the ESL procedure, which enabled the uniformity in a large area and the consistency between different batches. The uniformity of the NPA in a large area (0.25 cm²) is demonstrated in Figure S1, and the consistency of NPAs from five batches in morphologies and optical properties are shown in Figures 1B–D and S2, respectively. Various types of metal NPAs (Al NPA, Au NPA, and Ag NPA) were prepared by the subsequent thermal evaporation (Figure S3). Figures 1B–D and S4 show the morphologies of NPAs through the 45° side-view scanning electron microscope (SEM) images and top-view SEM images. The lattice constant of the array (l) is 1.4 μm , the height of the nanopyramid (h) is 590 nm, and the depth of the nanoconcave (d) is 368 nm. This nanopyramid possessed geometries of nanotips and nanoedges (Figure S4), which enabled the presence of hotspots for high sensitivity of refractometric sensing and SERS. This two-dimensional (2D) NPA features a morphology similar to that of bulk NPA in our previous work.⁷ However, in contrast to the fabrication technique of electrochemical etching used in the previous work, the technique of ESL used here was simple, cost-efficient, and accessible to reproducible NPAs.

Optical Properties of Al, Au, and Ag NPAs. Figure 2A shows the normal transmission spectra of the as-obtained Al, Au, and Ag NPAs in air at the wavelength region from 400 to 1100 nm. The transmission spectra of corresponding metal flat films were also measured as references (Figure 2B). Multiple characteristic peaks were observed on the spectra of metal NPAs in contrast to those of flat films. Our previous work of bulk Al NPAs with similar morphologies displayed several LSPR peaks in the whole UV–visible–infrared region as well.⁷ The troughs at 700 nm and at ~ 990 nm (equals to $\frac{1}{2}l$ and $\frac{1}{2}\sqrt{2}l$, respectively) of all three metal NPAs mainly resulted from the second-order Rayleigh diffraction anomaly between the adjacent nanopyramids and between the diagonally adjacent nanopyramids, respectively.⁴¹ It is noteworthy mentioning that

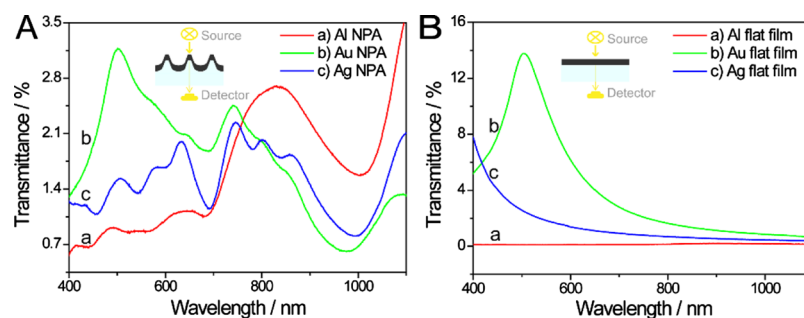


Figure 2. Transmission spectra of Al, Au, and Ag NPs (A) and flat films (B) exposed in air (curve a for Al, curve b for Au, and curve c for Ag). The insets show the perpendicular transmission system employed in the sensing process.

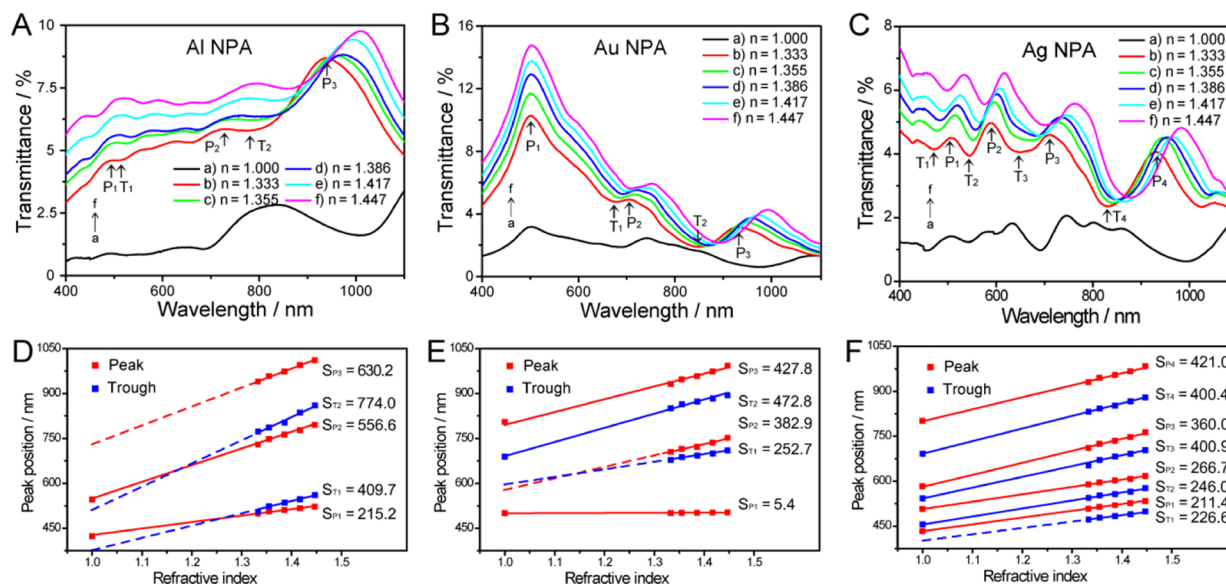


Figure 3. Refractometric sensitivities of Al, Au, and Ag NPs. (A–C) Transmission spectra of Al, Au, and Ag NPs when the superstrates were air and glycerol/water mixtures with different RIs (n), respectively. (D–F) Relationships between the position of the peak/trough and corresponding n of the superstrate. The troughs and peaks are arrowed in (A–C). The slopes of the linear fitting curves indicate the refractometric sensitivities, whose unit is nm/RIU. Error bars for each point are too small to be seen.

the peak of the Al NPA at 827 nm located in the region of bio-optical window (700–1100 nm), which made it a promising candidate for biosensing involving tissues and cells. For both Au NPA (curve b, Figure 2A) and Au flat film (curve b, Figure 2B), the large resonance peak at 502 nm was the characteristic PSPR peak.⁴² All of these peaks here presented relatively narrow bandwidth, in which the smallest full width at half-maximum was 21.7 nm from the Ag NPA, benefiting the refractometric sensing of NPs based on the LSPR peak shift.⁴³

Refractometric Sensitivities of Al, Au, and Ag NPs.

We have measured the transmission spectra of NPs when they were covered by superstrates with different RIs. The superstrates were air ($n = 1$) and glycerol/water mixtures with different ratios ($n = 1.333, 1.355, 1.386, 1.417, \text{ and } 1.447$). A normal transmission optical path was used during the measurements to eliminate systematic errors caused by the RI variation of superstrates.³⁹ As the RI increased, the resonance peaks and troughs of the NPs red shifted and the transmittance increased as well, as shown in Figure 3A–C. The relationships between the peak/trough position and the corresponding RI (n) for Al, Au, and Ag NPs were exhibited in Figure 3D–F, respectively. Linear fitting results of these relationships were demonstrated with high goodness of fit ($R^2 > 0.99$), and the slopes of the linear fitting curves indicated the

refractometric sensitivities. The refractometric sensitivities of these peaks tended to augment with the increase of the peak wavelength, and the refractometric sensitivities of these troughs also exhibited the similar phenomenon (Figure S5). Notably, high refractometric sensitivities of 774.0, 472.8, and 421.0 nm/RIU were observed on Al, Au, and Ag NPs, respectively. A summary of Al nanostructures for refractometric biosensing is provided in Table S1. To our best knowledge, this refractometric sensitivity of 774 nm/RIU was the highest one among those of Al nanoparticles and 2D Al nanostructures. In addition, it is closed to the refractometric sensitivity of the bulk Al NPA (819 nm/RIU).⁷ Besides the similar high sensitivity, this 2D Al NPA exceeded the bulk Al NPA in the mass-producing procedure based on the high reproducibility and the cost efficiency of its preparing methods. These advantages made the 2D NPA a competing candidate as LSPR biosensor for practically biomedical applications.

Semiquantitative Detection of Cell Concentration by the Al NPA. Monitoring the proliferation of cancer cells is significant for investigating the growth, infiltration, recurrence, and migration of tumors. We integrated the as-prepared Al NPA with a high refractometric sensitivity into a LSPR sensing platform for monitoring the proliferation of HeLa cancer cells in situ and in real time. To avoid the influence of the optical

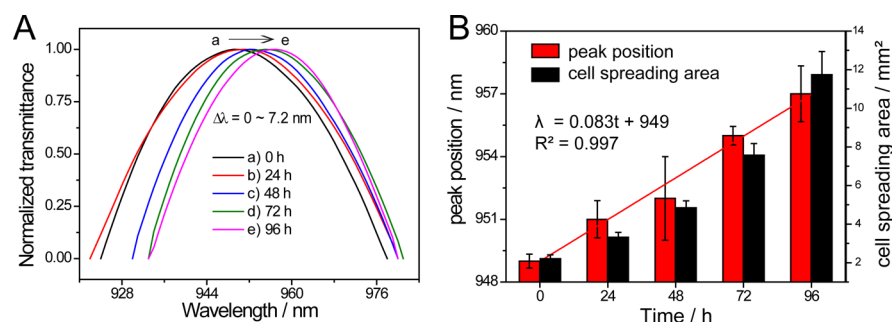


Figure 4. (A) Normalized transmission spectra of P_3 for an Al NPA biosensor when monitoring HeLa cell's proliferation for 0, 24, 48, 72, and 96 h (curve a to curve e). The maximal peak shift ($\Delta\lambda_{\max}$) is about 7.2 nm. (B) Relationship between the LSPR peak position and the proliferation time (red columns) and the relationship between the cell spreading area and the proliferation time (black columns). The red line indicates the linear relationship between the peak position and time. Using the Pearson correlation coefficient, a significant correlation was observed between the cell spreading area and the LSPR peak position ($r = 0.979$, $P = 0.004$).

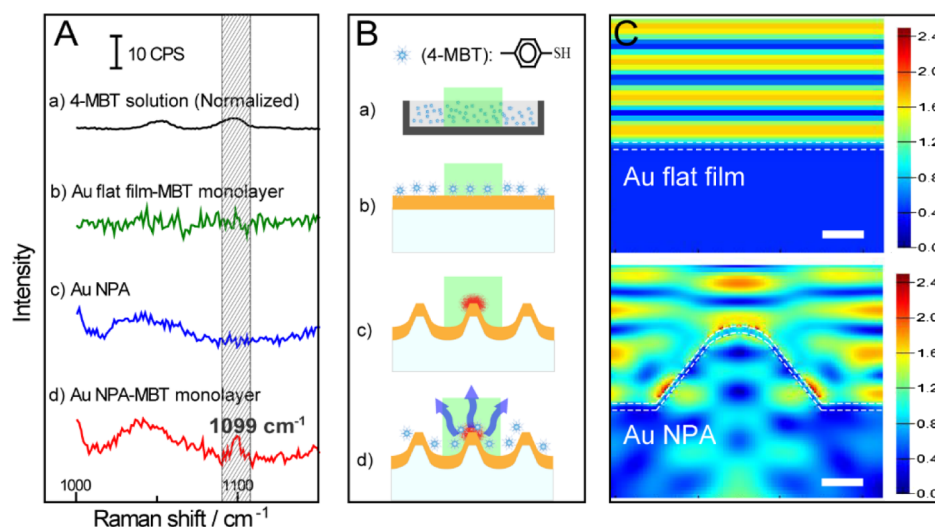


Figure 5. (A) Raman spectra of the 4-MBT solution (normalized, curve a), a Au flat film adsorbed with 4-MBT (curve b), a bare Au NPA (curve c), and a Au NPA adsorbed with 4-MBT (curve d). A peak at 1099 cm^{-1} was observed at the Raman scattering spectra of the 4-MBT solution and the Au NPA adsorbed with 4-MBT. (B) Schematic diagrams illustrating the structure of 4-MBT and the Raman scattering process of the 4-MBT solution (a), a Au flat film adsorbed with the 4-MBT monolayer (b), a bare Au NPA (c), and a Au NPA adsorbed with the 4-MBT monolayer (d). (C) FDTD simulations of EF distribution for the Au flat film and the Au NPA with light at normal incidence. The dashed lines and curves outline the 50 nm thick Au layers of the Au flat film and the Au NPA. EF enhancement was observed at the nanotip and the nanoedge. The scale bars in (C) are 200 nm.

absorption spectra of cellular components, P_3 at the infrared region with a high refractometric sensitivity ($630.2\text{ nm}/\text{RIU}$) was used for the measurements. Healthy HeLa cells with controlled amount (30 000 cells per mL) were seeded on the Al NPA and constantly proliferated for 96 h without fully covering the metal surface. The cells have higher RI ($n_{\text{cytoplasm}} = 1.38$, $n_{\text{membrane}} = 1.48$) than that in the culture medium ($n_{\text{medium}} = 1.33$). With the proliferation of cells, increasing cells replaced the culture medium and occupied more sensing area of the Al NPA. As a result, the RI near the surface of the Al NPA increased constantly. In addition, this variation of the local RI was demonstrated by the shift of the LSPR peak. As shown in Figure 4A, transmission spectra (from 920 to 990 nm) of this Al NPA were measured every 24 h. In addition, the resonance peak red shifted for $\sim 7.2\text{ nm}$ (from 949.4 to 956.6 nm) in 96 h. A linear relationship between the peak position (λ) and time (t) was observed (Figure 4B, red line). Micrographs of the cells were recorded at the same time points (Figure S6), to certify the enlarging amount of cells and the cells partly covering the NPA. From the micrographs, we recorded the cell spreading

area at different times (Figure 4B, black columns). Using the Pearson correlation coefficient, a significant correlation was observed between the cell spreading area and the LSPR peak shift ($r = 0.979$, $P = 0.004$).

Cell proliferation can be detected by other experimental methods (such as microscope, piezoelectric sensing, electric cell-substrate impedance sensing, and surface plasmon resonance sensing). However, our method based on the LSPR biosensor has two advantages compared to the above methods. The equipment that we need is a spectrometer, which is low-cost. In addition, information such as cell-substrate interaction is able to be obtained by LSPR sensors while it is not provided by other sensors. Since the LSPR sensor is sensitive to the RI in the vicinity of the metal surface, only the alive cells contact closely to the substrate and induce the LSPR signals, whereas the dead cells suspend in the culture medium without interfering the signals. Therefore, our LSPR sensors mainly obtained the signals caused by the alive cells on the sensor surface.

Qualitative Identification of Molecules on the Au NPA. The enhanced localized EF induced by LSPR has not only been utilized in refractometric biosensing but also in surface-enhanced assays such as surface-enhanced fluorescence⁴⁴ and SERS.^{45–47} SERS can provide a structural fingerprint of an analyte, which can be applied to identifying the molecules functioning in the process of the cell-substrate interaction.^{48,49} Here, we demonstrate the capacity of the NPA to work as a SERS substrate. We immersed the Au NPA substrate in a solution of the model analyte, 4-MBT. This molecule was adsorbed on the NPA based on the strong Au–S linkage between the molecule and the Au surface. Figure 5A shows the Raman spectra of 4-MBT solution (normalized, curve a), 4-MBT monolayer-absorbed Au flat film (curve b), bare Au NPA (curve c), and 4-MBT monolayer-absorbed Au NPA (curve d). The characteristic peak at $\sim 1100\text{ cm}^{-1}$ was attributed to a combination of the phenyl ring breathing mode, CH in-plane bending, and CS stretching.⁵⁰ There was no peak appeared at around 1100 cm^{-1} on the Raman spectrum of the 4-MBT-absorbed Au flat film, whereas an enhance peak at 1099 cm^{-1} was observed on the Raman spectrum of the 4-MBT-absorbed Au NPA. A schematic diagram in Figure 5B indicates how 4-MBT absorbed on the Au flat film (scheme b) and the Au NPA (scheme d), and then responded to the Raman exciting laser. Compared to the flat film, there were hotspots (localized enhanced EF) induced by LSPRs occurring on the nanotips and nanoedges of NPAs; therefore, these hotspots enhanced the Raman scattering signals.

To investigate the mechanism of SERS capacity and high refractometric sensitivity of NPAs, we have simulated the EF distribution of the Au flat film and the Au NPA by using the FDTD solutions (Figure 5C). Band-shaped EF distribution was observed above the Au flat film, resulting from the interference between the incident and reflected light. In contrast, localized hotspots at both tip and edges of the nanopillar were attained on the Au NPA. The localization and intensification of EF on the NPA can improve the performance of the LSPR biosensor for refractometric and surface-enhanced Raman biosensing.

In conclusion, we have prepared a type of plasmonic NPA with excellent reproducibility (large-area uniformity and batch-to-batch consistency) by using ESL and metal thermal evaporation, which obtained high refractometric sensitivity based on hotspots at nanotips and nanoedges. Specific detection of molecules such as cancer biomarkers or thrombin could be achieved on such a LSPR biosensor after chemical modification.^{7,51} In addition, the Au NPA-based SERS illustrated that this NPA LSPR nanosubstrate is capable to be applied in molecular identification, such as the detection of glucose.⁵² In comparison to the existing LSPR biosensors, our proposed work exhibit the following advantages: (1) the NPA with the geometry of the tapering nanostructure is very suitable for ESL. Compared to the nanopillar and nanomushroom, a nanopillar is much easier to be detached from its complementary nanostamp without damage. This characteristic makes the NPA biosensor prepared by ESL approaches highly reproducible, which indicates the remarkable reliability of LSPR biosensors for practical use; (2) the fabricating technique combining ESL and metal thermal evaporation has provided various types of metal NPAs (e.g., Al, Au, and Ag NPAs), meeting the demands of different situations. This fabrication technique could also utilize other non-noble metal materials such as Cu to fabricate NPAs. Moreover, these non-noble metal

NPAs including Al NPA with properties of low cost, ease to process, and abundant mineral reserve have great potential in constructing high-performance LSPR biosensors; (3) the NPAs with deliberately designed sharp tips and edges confine light into nanoscale regions and create dense hotspots for highly sensitive refractometric biosensing and surface-enhanced spectroscopies, certifying the potential of the NPAs for multiplex applications; (4) the NPA will enable the combination of quantitative LSPR sensing and qualitative SERS analysis, where the transmittance changes of UV–visible spectra (light through the NPA) that involve the information of the concentrations and the Raman scattering signals (light backward from the NPA surface) reveals the molecular structure. Considering the simplicity and cost efficiency of the fabrication method, as well as the properties of excellent reproducibility and high sensitivity, this NPA LSPR substrate will accelerate the process of applying the LSPR sensor into practical use such as clinical diagnosis, home healthcare, environmental analysis, and public healthcare.

METHODS

Materials. PDMS (SYLGARD 184) was purchased from Dow Corning (US). NOA61 was obtained from Norland Products (US). Gold, silver, and aluminum particles for metal thermal evaporation were from ZhongNuo Advanced Material Technology Company (Beijing, China). Ethanol and glycerol were supplied by Damao chemical reagent (Tianjin, China). For cells' experiments, the Dulbecco's modified Eagle's medium was purchased from HyClone (US). Bovine serum was from Gibco (Singapore). For SERS experiments, 4-MBT was obtained from Aladdin (Shanghai, China). All chemicals and solvents used were of analytical grade and were used as received. Deionized water was used for all experiments.

Fabrication of Metal NPAs. A bulk Al NPA template was previously fabricated through denting and subsequent electrochemical etching on a flat aluminum sheet.⁷ A well-mixed liquid PDMS prepolymer was poured onto the template, degassed, and solidified in an oven ($80\text{ }^{\circ}\text{C}$, 30 min). The solidified PDMS nanostamp was then peeled off from the template. During the next ESL process, the solution was dripped onto the PDMS nanostamp. To increase the sharpness of the nanopillar, a type of NOA61 solution with lower viscosity was employed and a 12 h standing in the vacuum was operated. The NOA61 substrate was then solidified under UV light (Kinsten KVB-30D, Taiwan) (15 W, 5 min) and peeled off. After that, 50 nm thick Al, Au, or Ag layers were deposited onto the NOA61 substrate through thermal evaporation.

It is worth mentioned that a stable native oxide layer of aluminum on the Al NPA was formed in hours, with a thickness stabilizing at 2.5–3 nm.⁵³ In addition, the workability of the passivated aluminum nanostructure as an optical biosensor has also been proved.⁵⁴

Characterization of NPAs and Nanofilms. SEM images of metal NPAs were captured by a SEM (Zeiss Auriga). The transmission spectra of Al, Au, and Ag NPAs under different superstrates of air ($n = 1$) and glycerol/water mixtures were measured using a UV–visible spectrophotometer (Inesa L3S). The mixing ratios of the above mixtures are 0, 25.96, 41.46, 62.50, and 86.57 wt %, whereas the according RIs are 1.333, 1.355, 1.386, 1.417, and 1.447, respectively. To determine the standard deviation (SD) of the peak position, three measurements were performed at each RI. The appearance of the NPA chip was captured by cell phone (iPhone 5S).

In the cell experiment, the Al NPA was previously immobilized on the inner wall of the cell culture flask. The whole flask was then sterilized and washed by phosphate-buffered saline. Transmission spectra of the NPA biosensor were measured every 24 h after healthy HeLa cancer cells were seeded on the surface of the nanostructure. To determine the SD of the peak position, three measurements were performed at each time. In the meantime, micrographs of cells on the Al NPA were taken from an inverted fluorescence microscope (Nikon Eclipse Ti-U). The area of each micrograph is 1/300 of the area of Al NPA. We counted the pixel points in the micrograph and multiplied 300 to estimate the whole cell spreading area on Al NPA.

In the SERS experiment, the Au NPA and the Au film were both immersed in the 4-MBT/ethanol solution (0.05 M, 3 mL) in a Petri dish ($\Phi = 3.5$ cm) for 15 min, respectively. Then, they were washed by ethanol and dried in air. The Raman spectra of 0.05 M 4-MBT solution, 4-MBT-adsorbed Au film, bare Au NPA, and 4-MBT-adsorbed Au NPA were measured on a Raman spectrometer (Renishaw inVia Reflex). The Raman spectrum of the 4-MBT solution (0.05 M) was normalized for further analysis. The wavelength of the excitation laser was 532 nm. The laser power and signal acquisition time were 1 mW and 10 s, respectively.

FDTD Simulation. The EF distribution of the Au film and the Au NPA under a 532 nm light source was simulated using FDTD solutions (Lumerical Solutions). The NPA was simplified as a combination of two vertical gradient grating arrays and one nancone array. All of the dimension parameters were set according to the SEM images. Mesh size for the metal region was 3 nm (x -, y -, and z -directions). The RI of NOA61 was 1.56.

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acsomega.7b02016](https://doi.org/10.1021/acsomega.7b02016).

SEM image showing the large-area uniformity of an Al NPA chip; transmission spectra showing the batch-to-batch consistency of optical properties of NPAs; SEM images of Al NPA, Au NPA, and Ag NPA; top-view SEM image of Al NPA and magnification image of a single nanopillar; the increasing tendency of refractometric sensitivity with a peak or trough position; microscopic images of cell proliferation; and summary of aluminum nanostructures for refractometric biosensing (PDF)

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Notes

The authors declare no competing financial interest.

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