Large scale sub-1-nm random gaps approaching the quantum upper limit for quantitative chemical sensing

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Metallic nanostructures with nanogap features can confine electromagnetic fields into extremely small volumes. In particular, as the gap size is scaled down to sub-nanometer regime, the quantum effects for localized field enhancement reveal the ultimate capability for light-matter interaction. Although the enhancement factor approaching the quantum upper limit has been reported, the grand challenge for surface enhanced vibrational spectroscopic sensing remains in the inherent randomness, preventing uniformly distributed localized fields over large areas. Here we report a strategy to fabricate high-density random metallic nanopatterns with accurately controlled nanogaps defined by atomic-layer-deposition and self-assembled-monolayer processes. As the gap size approaches the quantum regime of ~ 0.78 nm, we demonstrate its potential for quantitative sensing based on a record-high uniformity with the relative standard deviation of 4.3% over a large area of $22\text{ mm} \times 60\text{ mm}$. This superior feature paves the way towards more affordable and quantitative sensing using quantum-limit-approaching nanogap structures.

Significantly enhancing localized optical fields enable investigation of light-matter interaction within deep-subwavelength dimensions [1-4]. Smaller gaps between metallic structures will generally result in stronger localized field towards the quantum enhancement upper limit determined by the tunneling current introduced by free electrons across the gap [5-10]. For instance, it has been recognized that nano-bowtie-antenna can support highly enhanced localized fields at the 20-nm-wide gap between tips [11]. To reveal the enhancement upper limit of the localized field, researchers explored nonlocality effects between nanospheres and metal films [12-14] or between nanotips with sub-1-nm-scale gaps [15, 16]. Experimental results down to 0.3~0.5-nm scale demonstrated the nonlocality effect [17]: When the gap distance decreases into the subnanometer quantum regime, coherent quantum tunneling becomes more profound and the system enters a regime of extreme nonlocality. This quantum upper limit revealed the ultimate capability to explore the light-matter interaction. In the past decades, many works reported impressive enhancement factors in surface enhanced Raman spectroscopy sensing (SERS, e.g., [18-22]), using the boosted localized field to excite the vibrational signatures of chemicals/biomolecules. Although the enhancement factor approaching the quantum upper limit was reported (e.g., [23-27]), the grand challenge for this sensing technology is the inherent randomness of the strongly localized field over large areas. Due to this inherent randomness, it is challenging to compare the absolute intensities of SERS signal from chip to chip for quantitative sensing. In this article, we will report a high density random metallic nanopatterns with atomic-layer-deposition- (ALD) and self-assembled-monolayer- (SAM) defined nanogaps approaching the quantum plasmonic enhancement limit and demonstrate its potential for quantitative sensing based on its uniform response over large areas.

Here we first explain the nature of the randomness in light-matter interaction within extremely small volumes. SERS is a typical process using localized optical fields to boost the light-matter interaction with chemical- and bio-molecules. Due to the intrinsically weak signal of Raman processes, researchers developed various metallic nanostructures to realized strongly localized fields to boost Raman signal. Although localized field enhancement can be boosted up to $10^{14}\sim 10^{15}$ [28], their spatial controllability is very limited: one cannot freely tune the localization region in an accurate manner. Therefore, random metallic structures usually suffer from this spatial randomness in localized field enhancement. Researchers can only demonstrate very strong signal enhancement at given local regions by running a raster scanning over a large area. This ‘brute force’ observation is not quite repeatable on another chip fabricated by identical procedures. To overcome this challenge, periodic metallic structures were proposed to better control the spatial distribution of the localized field [29]. Using highly ordered nanopatterns, one can get a better spatial sampling rate over a given area. However, most periodic metallic nanostructures still cannot address the uniformity issue in a satisfactory manner since the spatial distribution of chemical/biomolecule binding is another equivalently important factor. Especially, for sensing of low concentration samples, the sparse and random binding of chemical- or bio-molecules over the nanostructure surface will introduce another uncontrollable factor to affect the uniformity. In this case, high-density spatial sampling is desired. Unfortunately, the spatial sampling rate of periodic nanostructures is heavily constrained by the resolution of top-down nanofabrication procedures. The fabrication cost and scalability to realize high-density periodic metallic nanostructures impose a tough barrier for further development of practical sensing applications. To overcome this challenge in spatial sampling rate and fabrication cost, we will discuss a strategy to fabricate high-density random metallic patterns with accurately controlled nanogaps. By approaching the quantum regime to enable quantum sensing capability, we will demonstrate the sensing of a record low concentration of 4-methylbenzenethiol (4-MBT) molecules down to 1 pM, three orders of magnitude better than previously reported performance of the same molecule. The relative standard deviation (RSD) of Raman intensities

of the observed SERS signal of 4.3% will also be realized on a large sample with a dimension of 22 mm × 60 mm, equivalent to the best results reported on periodic nanopatterns for SERS sensing.

Atomic layer lithography is an emerging nanomanufacturing technology to fabricate deep-subwavelength uniform features [30-33]. According to previous reports [30, 34, 35], this process began with an ordered metal grating patterned by focused ion beam (FIB) milling [30, 34] or electron beam lithography (EBL) [35], followed by the deposition of a dielectric film controlled by ALD or SAM processes (e.g., [36, 37]). Building on this strategy, here we first extend this process to fabricate high-density random metallic patterns with no need for prefabricated nanostructures using FIB or EBL processes. As illustrated in **Figure 1a**, our structure started from the direct deposition of random metallic nanoparticles (NP) [38]: a silver (Ag) film was deposited onto a pre-cleaned glass substrate using electron-beam evaporation. Following previously reported lithography-free fabrication technique [39, 40], thermal annealing was used to manipulate the average morphology (e.g., size, spacing) of the first layer of Ag NPs. Then, these NPs were covered by a 1-nm alumina (Al_2O_3) film deposited by ALD. With subsequent evaporation of the second metal layer (e.g., a 10-nm-thick Au film in our experiment), the original gaps will be filled. Therefore, a tiny gap introduced by the ALD layer can be obtained between the first and the second metal patterns. After that, an optical adhesive (NOA 71, Norland Products Inc.) was applied to attach the surface of the film to a glass slide, and cured under a UV lamp. Finally, the entire film was peeled off to obtain the proposed random nanogap structure. Although these directly deposited NPs are random in shape and local spatial distribution, the gaps were independently controlled by the ALD process.

Figure 1. (a) Schematic of the device fabrication process. Direct deposition of metal followed by thermal annealing is used to pattern the first layer of random nanostructure on the glass substrate. These patterns are conformally encapsulated with a thin Al_2O_3 spacer using ALD. Next, a gold (Au) film is deposited on the existing nanopattern, and the whole structure is stripped off the glass substrate using UV cured epoxy and a glass slide. (b-e) Top-view scanning electron microscope (SEM) images of different buried random nanopatterns. Red dotted squares: Further zoomed-in images show a 1 nm nanogap surrounding the existing nanopatterns. Scale bar: 300 nm. (f) Cross-sectional TEM of a 10-Å-wide Al_2O_3 layer between Ag and Au layers. Scale bar: 100 nm (Up), 30 nm (Middle), 10 nm (Bottom).

Following this procedure, we fabricated 4 representative samples with different dimensions and densities for the first metal NP layer. As shown in **Figures 1b-1d**, the initial thicknesses of the first Ag metal layer are 10 nm, 12 nm, and 15 nm, respectively, followed by thermal annealing of 300 °C to form different nanopattern templates. As a result, the continuous metal films were transferred to isolated nanoislands/nanoparticles with various lateral dimensions. The initial metal can also be Au (or other metals) to obtain different morphologies (e.g., an 8-nm-thick Au film followed by thermal annealing of 400 °C as shown in **Figure 1e**). One can see that these metallic NPs were clearly surrounded by a dark line, i.e., the 1-nm-thick dielectric film defined by ALD processes as shown in **Figures 1b-1e**. To characterize and quantify the high density random metallic NPs, we analyzed the particle number in a given area by extracting the geometric information from the SEM image shown in **Figures 1b-1e** and obtained the particle density of 11~77 NPs/ μm^2 . This particle density obtained through the lithography-free process is higher than previously reported results on periodic structures fabricated by various lithography methods including e-beam lithography [35, 41], nanosphere lithography [42], nanoimprint lithography [43], and optical interference lithography [44, 45]. To reveal the microscopic features, we employed the high-resolution transmission electron microscopy (TEM) to verify the 10-Å-thick Al_2O_3 layer on the sidewall of a cross-sectional Ag/ Al_2O_3 /Au nanogap (**Figure 1f**). Due to this lithography-free process, these random nanogap structures can be fabricated over large areas in foundry facilities to overcome the cost barrier. Importantly, since the gap size is close to the quantum regime (e.g., [15-17, 23-27]), these inexpensive random nanogap structures are attractive to realize boosted field enhancement for vibrational sensing applications.

Figure 2. (a) Schematic illustration of the nanogap structures. (b) Cross-sectional (xz plane, up panel) and top-view (xy plane, low panel) electric field distribution in the buried nanogap of random NPs nanostructure with uniform 10 nm gaps (b), 5 nm gaps (c), and 1 nm gaps (d).

To reveal the optical feature of these nanogap structures, here we use a hemisphere-shaped NP as an example to analyze its localized field distribution (see the schematic in **Figure 2a**). The diameter and period of the hemisphere-shaped Ag NP are 65 nm and 100 nm, respectively. The thickness of the second Au film is 10 nm. The gap sizes are tuned from 10 nm to 1 nm. The metal-insulator-metal nanostructures can function as optical antennas to excite hot spots in the nanogaps. When this NP is surrounded by a uniform nanogap with a width of 10 nm, the incident light at 785 nm can be coupled into the nanogap between this NP and the adjacent metal structures, as shown by the up panel of **Figure 2b**. However, the strongest hot spots are only distributed and located at the edges of NPs. When the nanogap size decreases to 5 nm in **Figure 2c**, stronger hot spots are excited within the nanogap. Intriguingly, when this gap is scaled down to ~1-nm (see the up panel of **Figure 2d**), the optical field is squeezed into a strongly confined region, resulting in a boosted field intensity. To further reveal the localized field intensity and

distribution, we plot the electric field from the cross-sectional view, as shown by the low panel of **Figures 2b-2d**. One can see that the overall field intensity within the 1-nm-gap is enhanced significantly, which is helpful for enhanced light-matter interaction. Extra modeling results with square-shaped NPs (e.g., [30, 34-36], **Figure S1**), different particle lateral dimensions of 45 nm and 75 nm (**Figure S2**), different period of 150 nm (**Figure S3**), under the excitation wavelengths of 633 nm and 514 nm (**Figure S4**) are presented in **Section S1** in the Supporting Information, demonstrating that this phenomenon is universal, insensitive to the particle size, shape, period or excitation wavelength. Importantly, using these nanopatterns with ALD-defined gaps, the spatial density of the hot spots can be increased significantly, and therefore, resulting in increased sampling rate and improved sensing signal produced by light-matter interaction within these extreme regions. Next, we will analyze the spatial density of this nanogap region with boosted optical fields.

Figure 3. (a) Chemical structures of (i) BZT, (ii) 4-MBA, (iii) BPT, and (iv) TPT. (b) Schematic illustration of molecular self-assemblies between the NP and the adjacent metal structures. (c) SERS spectra of the nanogap structures with different molecules within the nanogaps. (d) Relationship between the Raman intensities at the peak of $\sim 1081\text{ cm}^{-1}$ and different molecule nanogaps. Error bars indicate standard deviations from 4 spectra. (e) Raman mapping of the nanogap structure with molecule ii within an area of $180\text{ }\mu\text{m} \times 180\text{ }\mu\text{m}$ under the 20 $\times$ objective lens. (f) Direct comparison of SERS signal uniformity obtained by previously reported nanostructures (data from refs [42, 49-57]) and the nanogap structures with molecule ii under different objective lenses.

To demonstrate how these high-density nanogaps influence the performance in enhanced light-matter interaction, we then employed SAMs with different chain lengths to tune the gap size between two metal layers (i.e., to replace the ALD layer in **Figure 1a**). As illustrated in **Figures 3a** and **3b**, the gap size was tuned from a few angstroms to a few nanometers using monolayers of benzenethiol (BZT) (molecule **i**), 4-mercaptobenzoic acid (4-MBA) (molecule **ii**), biphenyl-4-thiol (BPT) (molecule **iii**), and 1,1,4,1'-Terphenyl-4-thiol (TPT) (molecule **iv**), respectively. These four types of molecules all

include a phenyl ring which will generate signature Raman signals corresponding to the breathing mode and stretching motion [25]. To form a SAM film on the first layer of Ag NPs, all samples were incubated in glass vials containing methanol solutions with different molecules at the concentration of 1mM for 3 hours. Then, these samples were copiously rinsed with methanol to remove unbounded molecules. Afterward, they were coated by a 10-nm-thick Au film to form the nanogap. As shown in **Figure 3b**, the chemical bonding occurs through the thiol groups reaction with the metal during the SAM formation process. The advantage of using molecules with one thiol group is to avoid multilayer chemical formation. The gap sizes can then be estimated by considering the theoretical length of different chemical groups (i.e., BZT is composed of a benzene ring and a thiol group; 4-MBA includes a benzene ring, a thiol group, and a carboxyl group; BPT consists of two benzene rings and a thiol group; TPT is made up of three benzene rings and a thiol group). Accordingly, the estimated gap sizes of these four different molecules are 566 pm, 780 pm, 994 pm, and 1422 pm based on the online database [46].

To reveal the gap-dependent light-matter interaction, we then measured the SERS signals of these four samples using microscopic Raman spectroscopy (Renishaw inVia™). All samples were excited by a 785 nm laser (35 mW) with an integration time of 1 s. As shown in **Figure 3c**, the characteristic Raman bands at ~ 1081 and 1588 cm^{-1} can easily be resolved from all samples, corresponding to the breathing mode (CH in-plane bending and CS stretching) and stretching motion of the phenyl ring, respectively. In particular, as shown in **Figure 3d**, the amplitude of the Raman peak at 1081 cm^{-1} of molecule ii (i.e., 4-MBA with the estimated size of 780 pm) is the strongest among the four samples. In contrast, this phenomenon cannot be observed from the Raman spectra of their bulk counterparts (see control experiment shown in **Figure S5** in the Supporting Information), indicating that the enhanced signal is not an intrinsic property of molecule ii. Instead, the gap distance of 780 pm close to the quantum upper limit resulted in this boosted Raman signal, agreeing well with a previously reported boundary of quantum regime [47, 48] (see **Figure S6** for another experimental validation of this gap-dependent enhancement in SERS signal).

Importantly, due to the high-density NP arrays fabricated by the lithography free processes, we observed the overall response of ~ 150 NPs over the area of $4.9\text{ }\mu\text{m}^2$ using the $20\times$ objective lens. In this experiment, a two-dimensional Raman mapping at the peak of $\sim 1081\text{ cm}^{-1}$ was performed using a $20\times$ objective lens over a $180\text{ }\mu\text{m} \times 180\text{ }\mu\text{m}$ area with a step size of $6\text{ }\mu\text{m}$ (**Figure 3e**). A record relative standard deviation (RSD) of 2.15% was obtained. This uniformity of the observed Raman signal generated within the 1-nm gap is much better than previously reported works: in **Figure 3f**, we compared the uniformity of the SERS signals of different structures observed under the objective lens with the same magnification (i.e., $20\times$) [42, 49, 50]. It should be noted that under the high magnitude objective lens, the observation area will be much smaller (i.e., $1.4\text{ }\mu\text{m}^2$ for $50\times$ and $1.1\text{ }\mu\text{m}^2$ for $100\times$, see more calculation details in the Methods Section). Larger RSD of 5.13% (under the $50\times$ objective lens) and 5.65% (under the $100\times$ objective lens) were obtained due to the random nature of the directly deposited NPs. But the uniformity performance of the high-density nanogap structure is still better than many nanopatterns including those periodic nanostructures fabricated by expensive top-down lithography processes (e.g., [42, 49-57] as shown in **Figure 3f**). This uniform response enables quantitative sensing of molecules, which is considered as one of the major challenges for practical SERS sensing applications [58-60].

Conventional quantitative SERS sensing usually requires precisely engineered plasmonic periodic nanostructures manufactured by expensive top-down lithography processes [61]. Here we will

demonstrate that the proposed random nanogap structure can address this challenge in fabrication cost and scalability to enable high-performance quantitative sensing.

As illustrated in **Figure 4a**, we fabricated a new sample on a glass slide (22 mm $\times$ 60 mm) using a SAM of 4-methylbenzenethiol (4-MBT) molecules as the isolation layer and cut it into 12 pieces (11 mm $\times$ 10 mm). The estimated chain length of the 4-MBT molecule is $\sim$ 701 pm [46], close to the quantum regime [23, 62, 63]. In this experiment, a 12-nm-thick Ag film was first deposited onto a pre-cleaned glass substrate using electron-beam evaporation followed by 300 $^{\circ}$ C thermal annealing process for 1 hour, as shown by the left panel of **Figure 4a**. Next we placed 10 μ L 4-MBT methanol solutions with the concentrations ranging from 100 mM to 1 pM onto each piece to control the effective thickness of the molecule layer thickness (middle panel of **Figure 4a**). Then, these chips were air-dried for the second 10-nm-thick Au layer deposition to form the ultimate nanogap chips for SERS sensing (i.e., the right panel of **Figure 4a** with the surface SEM image). As shown in **Figure 4b**, the signature Raman peaks of 4-MBT at $\sim$ 1078 and $\sim$ 1592 cm^{-1} were observed clearly through a 20 $\times$ objective lens. Remarkably, low concentration down to 1 pM is still observable as shown by the inset of **Figure 4b**, representing the record high performance of SERS sensing of this particular molecule, 3 orders of magnitude better than previous literature based on ordered nanopillar SERS chips [64].

Figure 4. (a) The whole process of sample preparation. Left panel: Photo of the random NPs on glass, and surface SEM image of surface NPs. Middle panel: Photo of molecule drop-casting on the sample using pipette and drying process. Right panel: Photo of the nanogap structure after 2nd metal layer coating, and surface SEM image of the nanogap structure. Scale bar: 300 nm (b) SERS spectra of 4-MBT solutions with different concentrations on the nanogap structure. (c) Relationship between the Raman intensities at the peak of $\sim$ 1078 cm^{-1} and different concentrations of 4-MBT methanol solutions. Inset: Illustrated molecule distributions at different concentration levels.

In this experiment, SERS signals from 4 randomly picked areas were recorded on each sample. By extracting their peak intensities at $\sim$ 1078 cm^{-1} in **Figure 4c**, we also plotted the error bars to indicate the

standard deviation of 4 measured spectra at each concentration. The most intriguing phenomenon is that the signal amplitude maximized at the concentration of ~1 mM (see **Figure S7** for Raman signal comparison from drop-casting method and immersion method in the Supporting Information). The signal amplitude decreases for both higher (i.e., region I) and lower molecule concentrations (i.e., region II), indicating that quantum enhancement limit regime was approached at this concentration, agreeing well with previously reported literature [65]: i.e., this concentration of 1 mM was mostly used to form a SAM of 4-MBT molecules in previous works [66, 67]. In particular, in the low concentration region II, those measured data points can be fitted using the Langmuir model [68]:

$$I = \alpha \frac{KC^n}{1+KC^n} \quad (1)$$

Here I is the SERS intensity related to the surface molecule coverage and distribution. C , K , and n are the molecule concentration, the equilibrium constant of adsorption, and a factor related to the adsorption steric hindrance, respectively. This adsorption model has been widely used to quantify the amount of substance adsorption (usually less than a monolayer) on a surface as a function of solution concentration [69]. For instance, this model was used to describe the low surface coverage of the antibiotic sulfamethoxazole molecule on the gold island template structure [70]. Ref. [71] also used this model to perform the quantitative detection of 1,2-bis(4-pyridyl)ethylene molecule on the inkjet-printed paper-based SERS substrate. In our experiment, the concentration-dependent SERS signal intensity profile can be fitted by the Langmuir adsorption isotherm very well with the fitting degree, R^2 , of 0.9978 (here $\alpha=18512.57$, $K=0.0001869$, and $n=0.488$), as shown by the solid curve in **Figure 4c**. Importantly, this ideal fitting degree indicates the potential for quantitative sensing of 4-MBT at a low concentration range (i.e., region II).

To validate the quantitative sensing capability shown in **Figure 4**, small and large area uniformity over the fabricated sample is essential (i.e., the 22 mm $\times$ 60 mm glass slide). In addition, batch-to-batch repeatability is another key factor to enable practical quantitative sensing applications. In this experiment, we submerged the entire 22 mm $\times$ 60 mm sample into the 1mM 4-MBT solution for 3 hours to introduce the spacer layer and then fabricated the nanogap structure (see **Figure S8** for SAM validation of 4-MBT molecules and **Supplementary Section S6** for surface density and intermolecular spacing calculation of 4-MBT SAM at the concentration of 1 mM). As shown in **Figure 5a**, we still cut the sample into 12 pieces. On each small piece, a two-dimensional Raman mapping at the peak of $\sim 1078\text{ cm}^{-1}$ was performed using the 20 $\times$ objective lens (i.e., the same experiment shown in **Figure 3e**), resulting in 900 data points collected on each small sample. Raw data from all 12 samples were listed in **Table S1** in the Supporting Information. One can see that the RSD ranges from 1.80% (**Figure 5b**) to 2.60% (see all 12 data in batch 1 of **Table S1**). To our best knowledge, this uniformity is much better than previously reported SERS substrates (e.g., [42, 49-57]) due to the high-density hot spots in our nanogap sample. Since our proposed method can be used to fabricate cost-effective SERS chips over large areas, the overall data variation on these 12 pieces will reflect the uniformity of the entire slide. By analyzing all 10800 points from all 12 pieces listed in **Table S1** (batch 1), the RSD of Raman intensities on this 22 mm $\times$ 60 mm slide is 4.3%. This slightly larger RSD can be attributed to the surface molecule distribution difference and the fabrication variation of random NPs over large areas on the entire slide. However, this value is much better than most previously reported results on different SERS nanostructures fabricated by various advanced nanomanufacturing methods (e.g., nanosphere/electron-beam lithography [42, 54], mask/maskless reactive-ion etching [50, 52, 53, 57], chemical synthesis [51, 55], see **Table S2** in the Supporting Information).

To reveal the batch-to-batch repeatability, we fabricated another two batches of nanogap structures in the same deposition cycle (see **Figure 5c**) and characterized them under identical experiment conditions (i.e., another 24 pieces from batch 2 and batch 3). On each small piece, we repeated the small area uniformity characterization experiments and collected 900 data points over a $180\ \mu\text{m} \times 180\ \mu\text{m}$ area (see batch 2 and 3 in **Table S1**). As shown in **Figure 5d**, we plotted 32400 data from all 36 pieces. The variation is below 10%, indicating great batch-to-batch repeatability of this large area nanostructure manufacturing process. For better comparison, two commercial substrates (i.e., QSERS®, RAM-SERS®) were prepared under the same procedure and measured using identical experimental conditions, as shown in **Figure 5e**. One can see that the Raman signal from our nanogap sample is 5 and 17 times stronger than those from QSERS and RAM-SERS, respectively. Importantly, by plotting the Raman signal maps of these three samples over identical scales in **Figure 5f**, it is obvious that the uniformity of the random nanogap structure is much better than the other two commercial SERS substrates, revealing the promise of the nanogap structure for cost-effective quantitative SERS sensing.

Figure 5. (a) Photograph of the fabricated random nanogap structures on a glass slide ($22\ \text{mm} \times 60\ \text{mm}$). Inset: 12 pieces cut from the whole sample on a glass slide. (b) Raman mapping of random nanogap structure over a $180\ \mu\text{m} \times 180\ \mu\text{m}$ area. (c) Photograph of batch-to-batch comparison of the nanogap structures on the glass slide, showing different University at Buffalo logos clearly visible and lying underneath. (d) Raman spectra from 32400 data points on all batches of three samples. (e) SERS spectra of 4-MBT methanol solutions on the nanogap structure and two commercial substrates. (f) Raman mappings of random nanogap structure and two commercial substrates.

Enhancement factor (EF) and shelf time are another two important factors to evaluate the performance of SERS chips. Following the general calculation strategy [51, 72], the EF of the random nanogap structure shown in **Figure 5** is estimated to be 6.6×10^8 considering the surface density of SAM molecules and nanogaps producing SERS signals (see more calculation details in **Section S9** in the Supporting Information). This remarkable EF achieved by our nanogap sample is similar to the values obtained by advanced lithography processes [31, 73-75]. However, our lithography-free process is superior in fabrication cost to achieve high performance SERS sensing. To test the shelf time of the proposed structure, we characterized the same chip after 6 months storage in ambient environment. As shown in **Figure S9** in the Supporting Information, the degradation rate of the peak intensity at $1078\ \text{cm}^{-1}$ is less

than 10%, which is much better than previously reported nanostructures [76-80]. This comparison demonstrated that the embedded molecular nanogap improved the reliability of the chip.

It should be noted that the major objective to introduce different thiol molecules with different lengths is to precisely control the nanogap size, revealing the gap-dependent quantum regime light-matter interaction. The sensing performance and uniformity are expected to decrease for sensing of molecules with no thiol groups. Here we performed extra experiments using two frequently used molecules for SERS sensing, i.e., 1,2-bis(4-pyridyl)-ethylene (BPE) and Rhodamine 6G (R6G). BPE molecules include a highly delocalized π -electron system with chemically active pyridyl nitrogen atoms for relatively strong binding with metal surfaces, while R6G molecules do not contain such chemical groups for chemical binding with metal surfaces [81]. Therefore, one can predict that the uniformity for BPE molecules should be better than that of R6G molecules since the uniformity for molecule binding is better for BPE. In this experiment, we placed two droplets of 10 μ L BPE and R6G molecular methanol solution (with the concentration of 1 mM) onto two samples of Ag NPs, respectively. Then, these samples were air-dried for the second 10-nm-thick Au layer deposition to form the ultimate nanogap chip for SERS sensing. As shown in **Figure S10**, we performed the mapping using the excitation laser of 785 nm over a $180\text{ }\mu\text{m} \times 180\text{ }\mu\text{m}$ area and obtained the RSD of 3.3% for the BPE sample, better than the R6G sample (i.e., 4.4%), validating the prediction of the chemical binding. On the other hand, it has been reported that introducing thiol groups to existing molecules or using thiol molecules as a bridge to connect molecules with sensing chips [82-84] can improve the sensing performance of non-thiol-based molecules. These emerging strategies are promising to expand the impact of the proposed nanogap sensing architectures. In addition, by etching Al_2O_3 in the gap and backfilling molecules (e.g., [85]) will also expand the capability for practical sensing applications of the proposed nanogap sensor chips.

In conclusion, we developed a high-density random metallic nanogap structure based on lithography-free ALD and SAM procedures to approach the quantum plasmonic enhancement limit. Four different molecules (i.e., BZT, 4-MBA, BPT, and TPT) with different lengths were employed to precisely control the nanogap size in a range of 0.5-1.5 nm, revealing the gap-dependent light-matter interaction and boosted Raman signal near the quantum regime. Importantly, due to the high-density NP arrays fabricated by the lithography free processes and high sampling rate generated by the nanogaps, the uniformity performance of the high-density nanogap structure sets a new record of uniformity with the RSD of 1.8% on a chip with the size of $\sim 11\text{ mm} \times 10\text{ mm}$, 4.3% for chip-to-chip uniformity over a large area of $22\text{ mm} \times 60\text{ mm}$, and below 10% for batch-to-batch uniformity over three $22\text{ mm} \times 60\text{ mm}$ slides, better than previously reported nanopatterns including many periodic nanostructures fabricated by expensive top-down lithography processes. This superior feature paves the way towards quantitative sensing using SERS technology. In particular, we have demonstrated that the random metallic nanogap structure is capable of quantitative detection of 4-MBT molecule down to $\sim 1\text{ pM}$ level. It will enable the development of low-cost high-performance SERS chips for the emerging portable Raman spectroscopy systems. We also anticipate that our unique designs could provide a new platform for further understanding quantum mechanical effects as well as gap-dependent light-matter interaction and be developed to meet the emerging needs in ultrasensitive biomedical diagnosis, environmental pollution monitoring, food safety evaluation, security defense, anti-counterfeiting, and healthcare monitoring applications.

Experimental Section

Fabrication of random nanogap structures: The 22 mm × 60 mm glass slides (Fisher Scientific, 12-545-J) were cleaned subsequently in acetone, methanol, and deionized water (DI water) with 10 minutes sonication for each step. Ag and Au films were both deposited using an electron beam evaporator (Kurt J. Lesker AXXIS). During the deposition, the pressure in the chamber was set below 10^{-6} Torr with no heating on the substrate. The deposition rate of Ag and Au were set 0.2 Å/sec. The thermal annealing process was finished in the commercial ALD system (Ultratech/Cambridge Nanotech Savannah S100) chamber in vacuum at 300 °C for 60 minutes. Al₂O₃ was deposited using ALD at the temperature of 80 °C with a deposition speed of 0.09 nm/cycle.

SEM and TEM characterization: SEM images were taken using the Zeiss CrossBeam® Workstation system. High-resolution transmission electron microscopy (HRTEM) was applied to investigate the specimen by operating Thermo Scientific FEI Titan ST at an acceleration voltage of 300 kV, and the image process was taken by Gatan DigitalMicrograph. The TEM specimen was prepared by using Thermo Scientific FEI's Helios G4 dual-beam focused ion beam scanning electron microscope (DBFIB-SEM) system equipped with an Omniprobe and a Gallium ion source.

Raman measurement of random nanogap structures: Raman spectra were measured using a bench-top Renishaw inVia Raman microscope equipped with a 785 nm laser. The power was set to be 35 mW with an integration time of 1 second. Three different objective lenses (i.e., 20×, 50×, 100×) were used to focus the excitation lasers onto the sample and collect the emitted Raman signals.

COMSOL simulations: Full-field electromagnetic simulations were performed using a commercial modeling package COMSOL Multiphysics®. Periodic boundary conditions were employed and only a single Ag hemisphere-shaped NP was placed in a unit cell to form the random nanogap structure. The circularly polarized illumination was used to mimic the unpolarized light since the proposed structure has no circular dichroism response.

Laser beam focus area calculation: The 785 nm laser beam was focused to be a Gaussian spot with the diameter of $\omega_0 = (4 \times \lambda) / (\pi \times NA)$, where NA is the numerical aperture of the objective lens (i.e., 0.4 for 20× objective lens, 0.75 for 50× objective lens, and 0.85 for 100× objective lens in this experiment). In this case, the detection beam radiuses are estimated to be ~1.25 μm, ~0.67 μm, and ~0.59 μm, respectively. The surface areas of the beam are therefore ~4.9 μm², ~1.4 μm², and ~1.1 μm², respectively.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

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