Microfluidic-SERS Devices for One Shot Limit-of-Detection

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Supporting Information (SI) – Supplemental Data, nanoparticle synthesis procedure, and enhancement factor (E.F) calculation

1. Supplemental Data
Figure S-1. (a) Device design and (b) Fluorescence response analysis for intra-device variation assessment.

Figure S-2. 1 mM (a) BPE and (b) benzenethiol spectra obtained using the flexible SERS sensor prototype (i.e. with incorporated nanospheres).
Figure S-3. Representative LSPR measurement performed on a AuNR-containing flexible SERS sensor.

Figure S-4. SERS response analysis before (a and c) and after (b and d) the use of a PDMS peak as an intensity correction standard. (a) and (b) are from AuNR flexible SERS sensors and (c) and (d) are from AuNC flexible SERS sensors.
Figure S-5. MATLAB baseline fit (green line) of a BPE spectrum (red line) of a 10 nm solution of BPE. The peaks at 1610 and 1640 wavenumbers are not correctly resolved because of the overlapping nature of the peaks. The baseline fit of the peaks is not accurately fitting both peaks and therefore skews the area under the curve and does not yield the correct response. *Note: The x-axis was programmed to give the pixel number instead of the relative Raman shift in wavenumbers, however adding 200 to the x-axis gives the relative wavenumbers.
2. Au nanosphere synthesis

Au nanospheres (AuNSs) for use in initial flexible SERS devices were synthesized under a nitrogen atmosphere while sonicating (Branson, Model 2510) using equimolar amounts of aqueous hydrogen tetrachloroaurate and sodium citrate for half an hour. The resulting purple solution was aged in the dark for 16 hours, with a final $\lambda_{\text{max}}$ of 524 nm.$^1$

3. Enhancement factor calculation

Enhancement factor calculation followed the method published by Wustholz et al (Eq. 1).$^2$

$$\text{Enhancement Factor (EF)} = \frac{(N_{\text{NRS}} \times I_{\text{SERS}})}{(N_{\text{SERS}} \times I_{\text{NRS}})} \quad (\text{Eq. 1})$$

where $N_{\text{NRS}}$ is the number of analyte molecules contributing to the normal Raman scattering measurement, $N_{\text{SERS}}$ is the number of analyte molecules contributing to the SERS measurement, $I_{\text{NRS}}$ is the normal Raman scattering intensity of the analyte at a particular cm$^{-1}$ shift, and $I_{\text{SERS}}$ is SERS intensity of the analyte at an analogous cm$^{-1}$ shift. In this calculation, we assume all molecules in the probe volume contribute equally to the measured signal. The
value of $N_{SERS}$ was estimated two different ways to account for potential variations in nanoparticle distribution in the PDMS layer: (1) uniformly using the in-device probe volume, considering excitation laser spot size (25-µm-diameter) and the microfluidic channel heights (100 µm) and (2) based on the nanoparticle coverage seen in the figure 4 SEM image (assuming that this coverage is representative and that the revealed nanoparticle surface area is hemispherical). Calculating the enhancement factor both ways presents a reasonable enhancement factor range for the flexible SERS microfluidic device. For the simple consideration of all molecules in the cylindrical probe volume experiencing enhancement (estimation #1): the laser spot size for SERS measurement (25-µm-diameter) was 490.9 µm$^2$ and the height of the microfluidic channel was 100 µm, yielding a probe volume (disregarding the possibility of sub-monolayer nanoparticle coverage) is:

$$490.9 \mu m^2 \times 100 \mu m = 4.9 \times 10^4 \mu m^3$$

Using this probe volume:

$$N_{SERS} = 4.9 \times 10^4 \mu m^3 \times (10^{-6})^3 m^3 \mu m^{-3} \times \frac{1 \times 10^{-3} mole}{10^{-3} m^3} \times 6.02 \times 10^{23} \frac{molecules}{mole} = 2.9 \times 10^{10} molecules$$

Using the SEM image in figure 4 and ImageJ software to calculate nanoparticle surface coverage (estimation #2): the nanoparticle surface area is 325.4 nm$^2$, and assuming each nanoparticle presents a hemispherical surface protruding from the PDMS layer, we have a nanoparticle surface area within this imaged region of 650.8 nm$^2$. With a total imaged area of 4,385,700 nm$^2$, this yields a surface coverage of nanoparticles on the PDMS surface of 0.014%. With the laser spot size of 490.9 µm$^2$, the surface area of nanoparticles within the excitation laser spot is:

$$= 490.9 \mu m^2 \times 0.00014 = 0.068 \mu m^2$$
Assuming, optimistically, that all BPE molecules in the microfluidic channel can interact with the nanoparticles, we can get an estimated cylindrical probe volume of:

\[ V = 0.068 \mu m^2 \times 100 \mu m = 6.8 \mu m^3 \]

Thus,

\[ N_{SERS} = 6.8 \mu m^3 \times (10^{-6})^3 m^3 \mu m^{-3} \times \frac{1 \times 10^{-3} mole}{10^{-3} m^3} \times 6.02 \times 10^{23} \frac{molecules}{mole} = 4.1 \times 10^6 \text{molecules} \]

So, for the two assumptions, the number of molecules contributing to the measured SERS intensities range from \(4.1 \times 10^6\) to \(2.9 \times 10^{10}\). \(I_{SERS}\) for the 1200 cm\(^{-1}\) shift band, collected at 3 mW incident power for 10 seconds (matched to collection conditions for normal Raman spectra), was measured to be 4813 adus.

For normal Raman measurement on a 100 mM BPE solution, probe volume was determined using the scanning knife edge method\(^3\) to be 0.0024 mm\(^3\), and thus:

\[ N_{NRS} = 1.4 \times 10^{14} \]

\[ I_{NRS} = 4175 \text{ adus} \]

Thus, our estimated EF range for nanoparticles within the microfluidic device is:

\[ EF = \frac{(1.4 \times 10^{14} \text{molecules}) \times (4813 \text{ adus})}{(4.1 \times 10^6 \text{ or } 2.9 \times 10^{10} \text{molecules}) \times (4175 \text{ adus})} = 5.9 \times 10^4 - 4.1 \times 10^7 \]
