

## Supplementary Information for:

**Label-free detecting the compaction and decompaction of ctDNA**

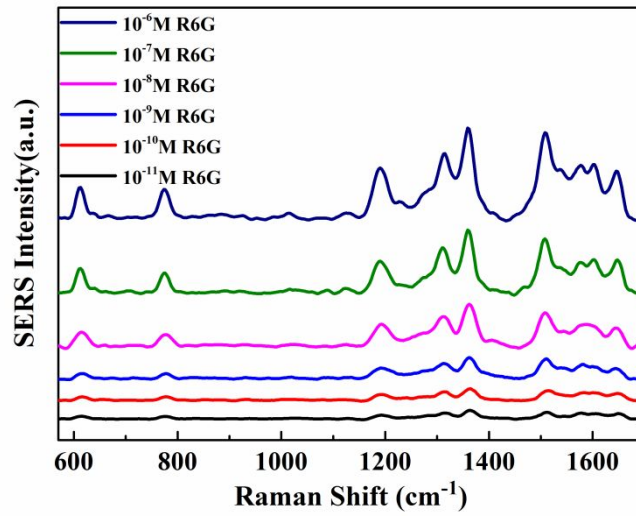
**molecules induced by surfactants with SERS based on**

**nanoPAA -ZnCl<sub>2</sub>-AuLs solid substrate**

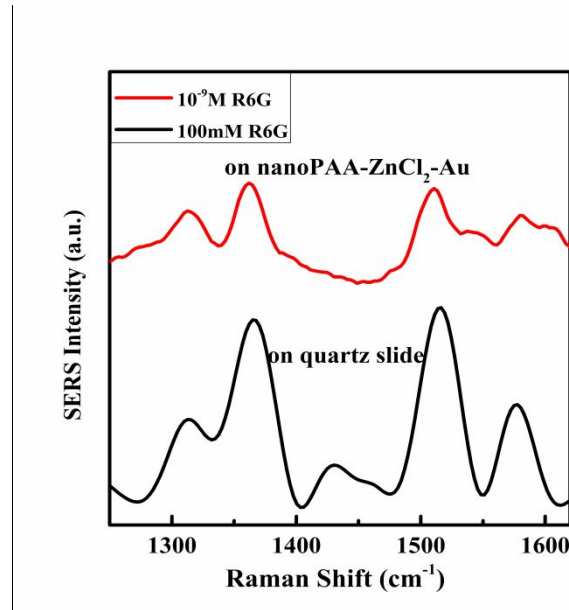
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**Figure S1.** SERS Spectra of R6G solution with concentration changed from  $10^{-6}$  M to  $10^{-11}$  M on nanoPAA-ZnCl<sub>2</sub>-AuLs substrate.



**Figure S2.** Spectrum of  $10^{-9}$  M R6G collected on nanoPAA-ZnCl<sub>2</sub>-AuLs substrate for Enhancement factors (EFs) calculation with a Raman spectrum of 100 mM R6G collected on quartz slide as a reference.

For enhancement factors, the scientific fomula commonly used definition is:

$$EF = \frac{I_{surf}/N_{surf}}{I_{bulk}/N_{bulk}} , \quad (1)$$

where  $I_{surf}$  and  $I_{bulk}$  represent the intensities of SERS and the normal

Raman scattering, respectively, while  $N_{surf}$  and  $N_{bulk}$  are the corresponding number of molecules able to be irradiated by laser, respectively.

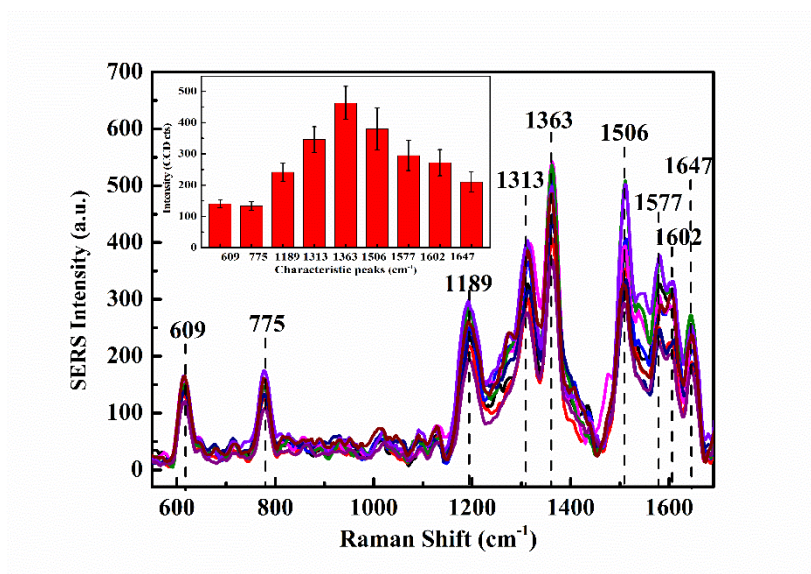
$$\bar{N} = C \cdot V \cdot N_A \cdot \frac{S_2}{S_1}, \quad (2)$$

where  $C$  represents concentration of probe solution,  $V$  represents droplet volume,  $N_A$  is Avogadro's number,  $S_1$  represents droplet size and  $S_2$  represents irradiation area size of laser, respectively.

In the experiment, the parameters  $V$ ,  $S_1$  and  $S_2$  were precisely controlled to be constant. Therefore, the ratio of molecule number is equal to ratio of probe concentration, EFs for each characteristic SERS peak could be estimated according to the deformation of formula (1):

$$EF = \frac{I_{SERS}/C_{SERS}}{I_{Raman}/C_{Raman}}, \quad (3)$$

where  $I_{SERS}$  and  $I_{Raman}$  are the SERS and the normal Raman scattering intensities, respectively, while  $C_{SERS}$  and  $C_{Raman}$  are the corresponding concentration, respectively.



**Figure S3.** SERS spectra of  $10^{-9}$ M R6G aqueous solution collected from 9 different spots on nanoPAA-ZnCl<sub>2</sub>-AuLs substrate. The inset shows mean  $\pm$  standard deviation of SERS intensity for each characteristic peak.