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Label-free trace detection of bio-molecules by liquid-interface assisted surface-enhanced raman scattering using a microfluidic chip

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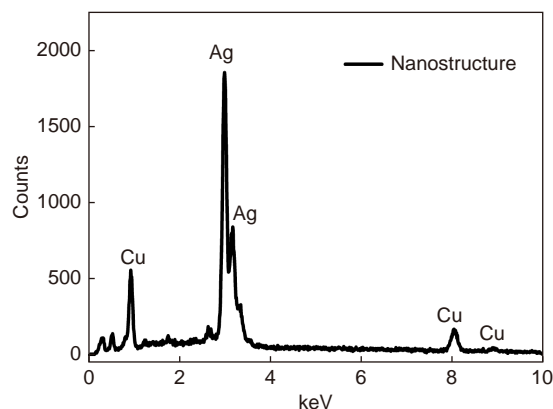


Fig. S1 | EDS spectra of 2-D Ag-Cu nanostructure fabricated by LIPSS.

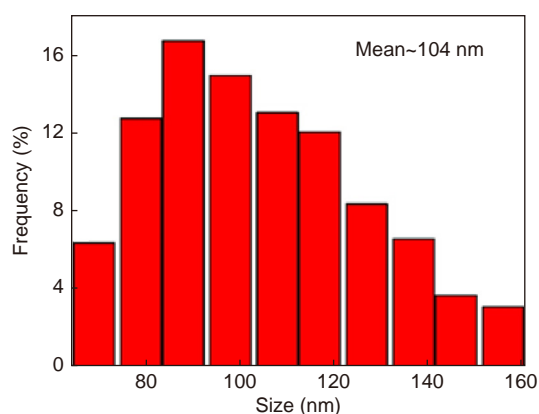


Fig. S2 | Size distribution of metal nanodots fabricated by two-step laser scanning. The mean size is about 104 nm with a standard deviation of 29 nm.

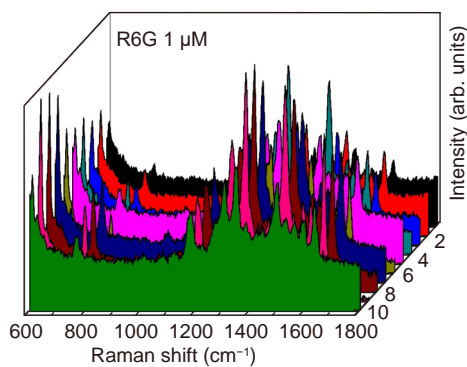


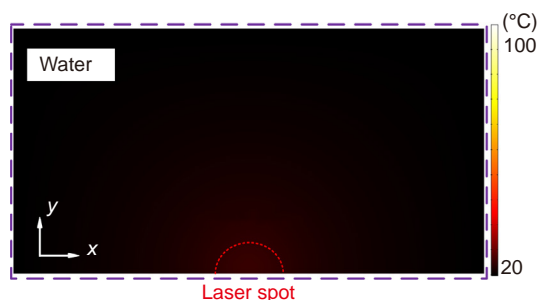
Fig. S3 | SERS spectra of 1 μM R6G solution using ten microfluidic SERS chips. The relative standard deviation of AEF calculated based on the ten spectra was 10.1% (at 604 cm^{-1}).

Table S1 | Relative standard deviation (RSD) of the main Raman peaks of R6G (1 μM).

Raman peak (cm^{-1})	RSD (%)
604	10.1
765	9.2
1177	8.9
1305	13.5
1354	16.2
1502	14.5
Average	11.7

Table S2 | The DNA sequence for LI-SERS measurements used in Figure 5(a).

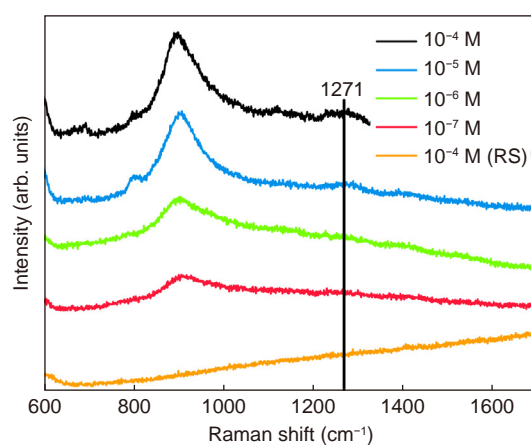
Sequence	A	T	C	G
TATAAATACAAGTACCATCAGGCGAAACACAAACAGCATAAG (42 mer)	50% (21 mer)	14.29% (6 mer)	21.43% (9 mer)	14.29% (6 mer)

**Fig. S4 | Simulation of the fluid temperature in the liquid on the SERS substrate. The laser beam irradiates into the liquid and the initial temperature is 20 °C.****Table S3 | DNA sequences for discrimination used in Figure 5(b).**

Sequence	A	T	C	G
S1:TCCACAACCATGTCCTGATAGTTTTTCAGC (30 mer)	23.33% (7 mer)	33.33% (10 mer)	30% (9 mer)	13.33% (4 mer)
S2:TAAATACAAGTACCATCAGGCGAAACACAAACAGC (35 mer)	48.57% (21 mer)	11.43% (6 mer)	25.71% (9 mer)	14.29% (6 mer)

Table S4 | Recently developed SERS platforms for the trace detection of A β .

SERS platform	Capping agents/Linker	Detection limit	Ref.
Au nanoshell	Sialic acid	1 pM	1
Hollow Au/Ag nanostar	Thioflavin	10 nM	2
Au nanoparticle	Anti-A β antibody	1 μ M	3
Au nanoparticle	Rose Bengal	2 μ M	4
Ag nanogap shell	A β antibody	55 fM	5
Graphene oxide - gold shell nanoparticle	A β antibody	22 fM	6
Au nanoparticle	Label-free	70 pM	7
3D Au nanowire array	Label-free	1 nM	8
Au nanoparticle in nanochannel	Label-free	10 pM	9
Ag-Cu nanostructure in microchannel	Label-free	<1 pM	Present work

**Fig. S5 | Raman spectra of A β (29-40) measured by the regular SERS method for different concentrations (10^{-4} M to 10^{-7} M) and Raman spectroscopy (RS) on glass surface for 10^{-4} M.**

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