

Supporting Information

What do we actually see in intracellular SERS? Investigating nanosensor-induced variation

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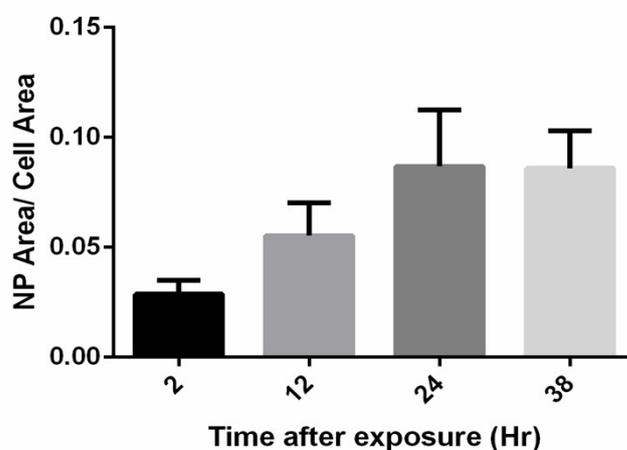


Figure S1: Optimisation of AuNP incubation period

The cellular uptake of AuNPs was observed as a percentage of cell area following incubation of SH-SY5Y cells over a 38 h period. Maximal uptake was observed at 24 h. This incubation duration was thus carried into our investigation of cellular stress events induced by AuNP internalisation.

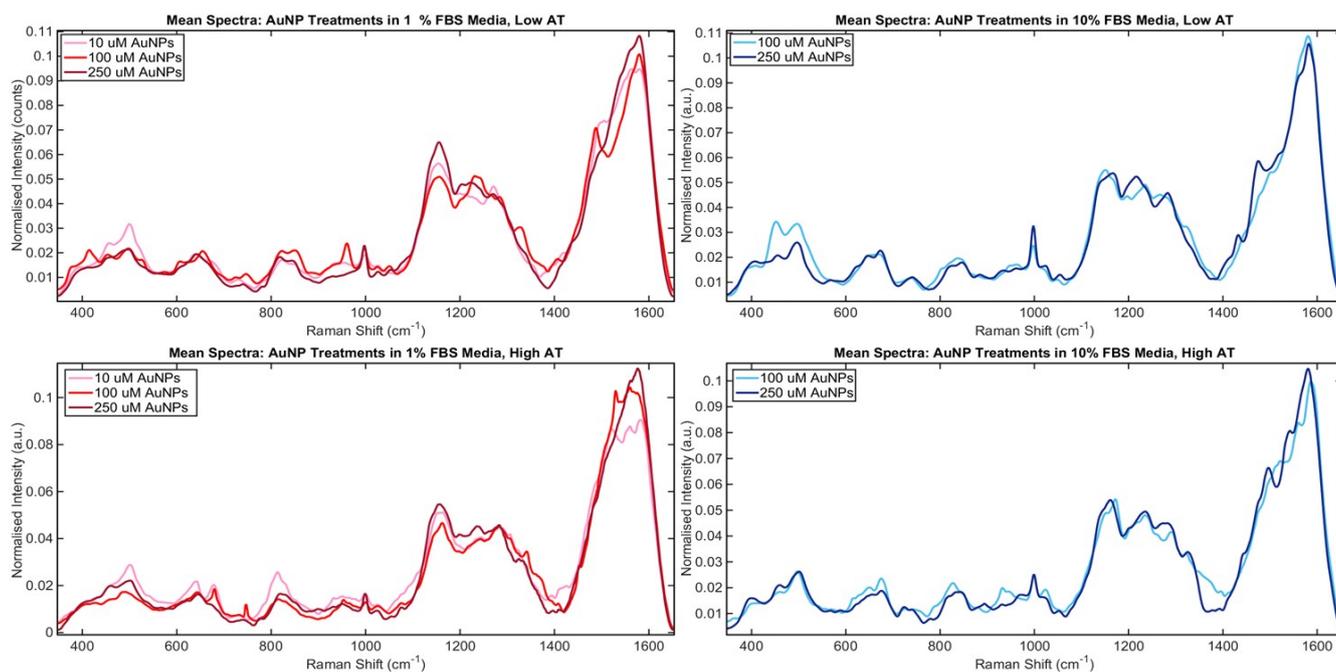
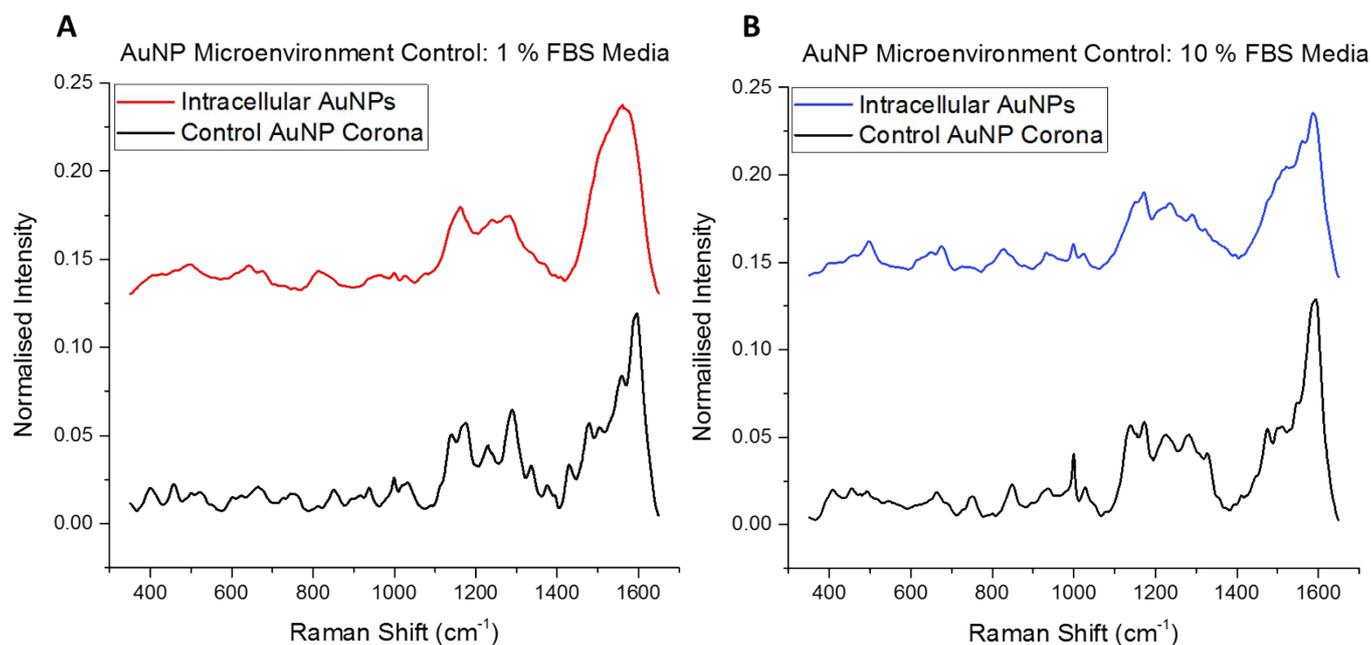


Figure S1: Effect of different acquisition times on spectra

Spectra acquired under two different acquisition conditions yield very similar spectra. Top row are SERS spectra acquired with acquisition times (AT) of 1 s with 3 averages and on the bottom are SERS spectra acquired with 10 s AT with 3 averages. Spectra for all treatments are shown. The other conditions for acquisition were exactly the same between the different acquisitions.

**Figure S3A-B**

In order to confirm SERS measurement from intracellular AuNPs, control AuNPs were incubated in 1 and 10 % FBS-media compositions for 24 h before washing, storage and taking SERS measurements in PBS. 5 spectra were recorded from different regions of AuNPs in each treatment. Acquired spectra from A) 1 % and B) 10 % FBS conditions are compared to respective spectra taken from cells incubated with 100 μM AuNPs. In both cases, distinct vibrational peaks, attributed to serum proteins forming a protein corona about the AuNPs, are observed. Cellular internalisation is confirmed by the spectral differences between control and cell spectra, primarily involving increased complexity of spectra in cellular cases which gives rise to broadened, overlapped peaks as a direct result of sampling complex cellular environments.

Table S1A-B: Tentative SERS spectral peak assignments of mean spectra

Mean spectral assignments across studied concentrations in A) 1 % FBS and B) 10 % AuNP treatments

A

Raman Shift /cm ⁻¹	Assignment
500	S-S disulfide str, collagen
543	S-S disulfide str, Cys
648	C-C twist Tyr/Phe
679	C-C DNA base ring breathing
815	Pro, HO-Pro Tyr
	PO ²⁻ str nuc acids
826	Out-of-plane ring breathing, Tyr
	O-P-O str DNA
951	CH ₃ str, proteins
1000	C-C arom ring str, Phe
1026	C-C arom str, acidified Phe
1076	Sym PO ₂ ⁻ /PO ₄ ³⁻ str DNA
	Sym C-C lipids
1150-70	C-C/C-N str, lipids/proteins
1198	Arom C-N, C-O nuc acids & phosphates
1200-1300	Amide III
1234	PO ₂ ⁻ str nucleic acids
1241	PO ₂ ⁻ Amide III/RNA
1275-80	Amide III, collagen/ α -helix
1305	CH ₂ deform, lipids
1334	CH ₃ CH ₂ wagging, proteins/nucleic acids
1395	CH rocking, lipids/proteins
1409	COO ⁻ str, proteins/Glu/Asp
1480-1575	Amide II coupling of C-N str to N-H bend
1524	C=C in plane
1543	Amide II/CH deform, Trp/NADH
1561	Ring breathing, Trp
1569	Ring breathing, DNA/RNA bases
1580	C=C bend, Phe/DNA/RNA bases

B

Raman Shift /cm ⁻¹	Tentative Assignment
500	S-S disulfide str, proteins
543	S-S disulfide str, Cys
648	C-C twist Tyr/Phe
678	C-C DNA base ring breathing
816	Pro, HO-Pro Tyr
	PO ²⁻ str nuc acids
828	Out-of-plane ring breathing, Tyr
	O-P-O str DNA
934	C-C str, Pro
1000	C-C aromatic ring stretch Phe
1028	C-C arom str acidified Phe
1070	Sym PO ₂ ⁻ /PO ₄ ³⁻ str DNA
	Sym C-C lipids
1150-70	C-C/C-N str, lipids/proteins
1198	Arom C-N, C-O nuc acids & phosphates
1200-1300	Amide III
1234	PO ₂ ⁻ str nucleic acids
1241	PO ₂ ⁻ AmideIII/RNA
1277-80	Amide III, collagen/ α -helix
1289	Amide III/CH ₂ wagging, proteins/lipids
1325	Amide III/CH ₂ deform, proteins/lipids
1409	COO ⁻ str, proteins/Glu/Asp
1480-1575	Amide II coupling of C-N str to N-H bend
1522	C=C in plane
1543	Amide II/CH deform, Trp/NADH
1561	Ring breathing, Trp
1569	Ring breathing DNA/RNA bases
1580	C=C bend, Phe/DNA/RNA bases