## Quantitative Surface-enhanced Raman Spectroscopy of Single Bases in Oligodeoxynucleotides

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## **Supplementary Information**



Figure S1. Illustration of scaled subtraction in SERS difference spectra. (a), (b) Raw SERS spectra of GCA-TAC-CGT-GAT-C and GCA-TAC-CGT-GAT-CG. (d) is the scaled difference spectrum showing the additional G bands only. (c) is undersubtracted by 10% and (e) oversubtracted using a factor which is 10% larger than that used in (d).



Figure S2. (a), (b) SERS spectra of the same ODN taken at 2 different times on the same day. (c) is the unscaled difference spectrum created by direct subtraction of the 2 spectra. All spectra are shown on the same vertical scale except that (a) was shifted vertically for clarity. The largest residual feature in (c) at 1335 cm<sup>-1</sup> has intensity -170 cts, which is slightly above the noise in that region which is ca. 125 cts and arises from shot noise on the ca. 15,000 cts signal.



Figure S3. Figure illustrating the relative intensities of the raw spectra and the difference spectrum created by subtracting them. (a), (b) SERS spectra of 25 mer ODNs with either C or A at the 3' end. (c) is the unscaled difference spectrum created by direct subtraction of the 2 spectra. The difference, although small compared to the parent spectra, is considerably larger than the residual found in the control case, shown in Figure S2.



Figure S4. Illustration of the reproducibility of SERS difference measurements. (a), (b) SERS difference spectra of 25-mer ODNs for A to C substitution at the 3' end recorded for 2 different samples. (c) is the difference spectrum for A to C substitution at the 3' end of a 25-mer ODN taken from ref 6 (E. Papadopoulou, S. E. J. Bell, *Angew. Chem. Int. Ed.* **2011**, 50, 9058-9061).