Supporting Information

Experimental

Locked nucleic acid (LNA) and DNA oligonucleotides were purchased from Eurogentec, Belgium and ATD Bio, Southampton, respectively. The isothiocyanate dyes were purchased from Invitrogen, Paisley and Victoria Blue was purchased from Sigma Aldrich, UK.

Thiol modified LNA (10 nmoles) was added to 35 nm citrate-reduced silver nanoparticles (1 mL, 0.4 nM) and salt-aged as previously reported.[1] The sequences used were: 5' SH C_6 $(HEG)_3$ $T^mctCtCt$ 3' (probe 1); 5' CccTtTt $(HEG)_3$ C_3 SH 3' (probe 2); 5' SH C_6 $(HEG)_3$ C^mc^mcTtTt 3' (probe 3) where uppercase letters represent LNA modified nucleotides and ^{m}c represents 5-deoxymethylcytidine. Nanoparticle conjugate concentrations were evaluated using extinction spectroscopy ($\varepsilon = 2.87 \times 10^{10}$ M^{-1} cm^{-1} at 400 nm).[2] Probe 1 (500 μL, 0.67 nM) was added to 500 μL, 1 μM solution of either ROX isothiocyanate (ROX ITC), Tamra isothiocyante (TRITC), Victoria Blue, or 3,5-dimethoxy-4-(6'-azobenzotriazolyl)phenylamine (DABT PA).[3] Cy5 labelled oligonucleotide sequences (5' SH C_6 Cy5 $(HEG)_3$ TCTCTCT 3') were immobilised onto the silver nanoparticles for quantitation using a DTT displacement method.[4] Following labelling with TRITC, the number of oligonculeotides per nanoparticle was estimated to be 934 ± 49. If TRITC labelling was omitted, the number of oligonculeotides was estimated to be 1069 ± 63. The number of TRITC molecules was estimated for non-fluorescent oligonucleotide (probe 1) functionalised nanoparticles and was found to be 1205 ± 84.

The 1 μM dye concentration produced optimal discrimination in the SERRS spectra against control samples for ROX ITC labelled nanoparticles and so was applied to the other dye labels, however the method is also successful if a larger excess of dye is incubated with the oligonucleotide nanoparticle conjugates (~ 10 μM). The oligonucleotide nanoparticle conjugates were incubated for 16 hours in the dark, and then centrifuged and resuspended in 0.3 M PBS. Head-to-head nanoparticle assembly was initiated upon the addition of the complementary target: 5' AGA GAG AAA AAG GG 3' (20 nM) to Probe 1 (20 pM) and Probe 2 (20 pM) in 0.3 M PBS. Head-to-tail assembly was achieved using Probe 1 and Probe 3 with 5' AAAAGGGAGAGAGA 3', and tail-to-tail assembly was achieved using Probe 1 and Probe 2 with 5' AAAAGGGAGAGAGA 3' in the same probe:target concentration ratios as for the head-to-head assembly. The non-complementray sequence used was: 5' ATC CTG AAT GCG TAC GAG TTG AGA 3'. SERRS spectra were recorded 5 minutes after the addition of the target sequence using a Renishaw Probe Spectrometer with a 514.5 nm argon ion laser.

1 McKenzie, F.; Faulds, K.; Graham, D. *Small* **2007,** *3*, 1866-1168.
2 Yguerabide, J.; Yguerabide, E. E. *Anal. Biochem.* **1998,** *262*, 137-156.
3 McAnally, G.; McLaughlin, C.; Brown, R.; Robson, D. C.; Faulds, K.; Tackley, D. R.; Smith, W. E.; Graham, D. *Analyst* **2002,** *127*, 838–841.
4 Demers, L. M.; Mirkin, C. A.; Mucic, R. C.; Reynolds, R. A.; Letsinger, R. L.; Elghanian, R.; Viswanadham, G. *Anal. Chem.* **2000,** *72*, 5535-5541.

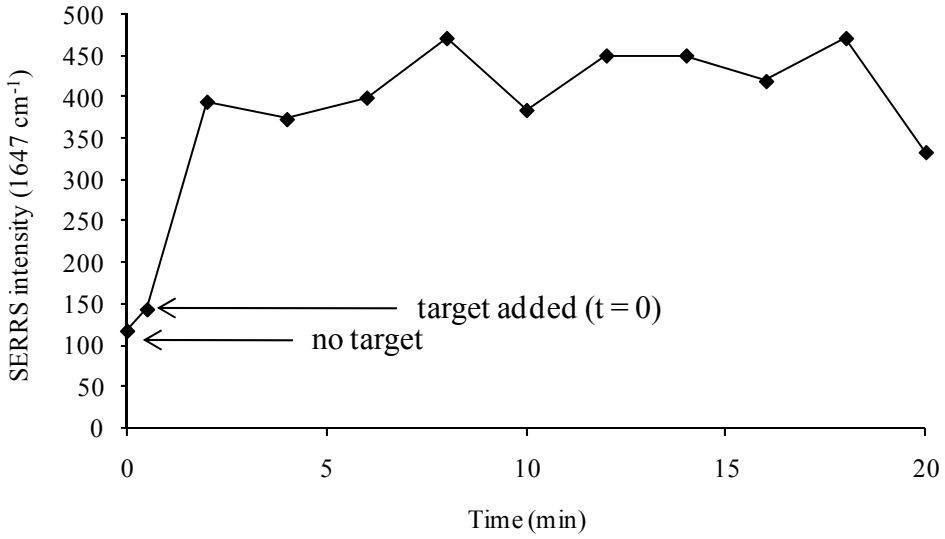

Figure S1. SERRS intensity of TRITC-labelled duplex over time

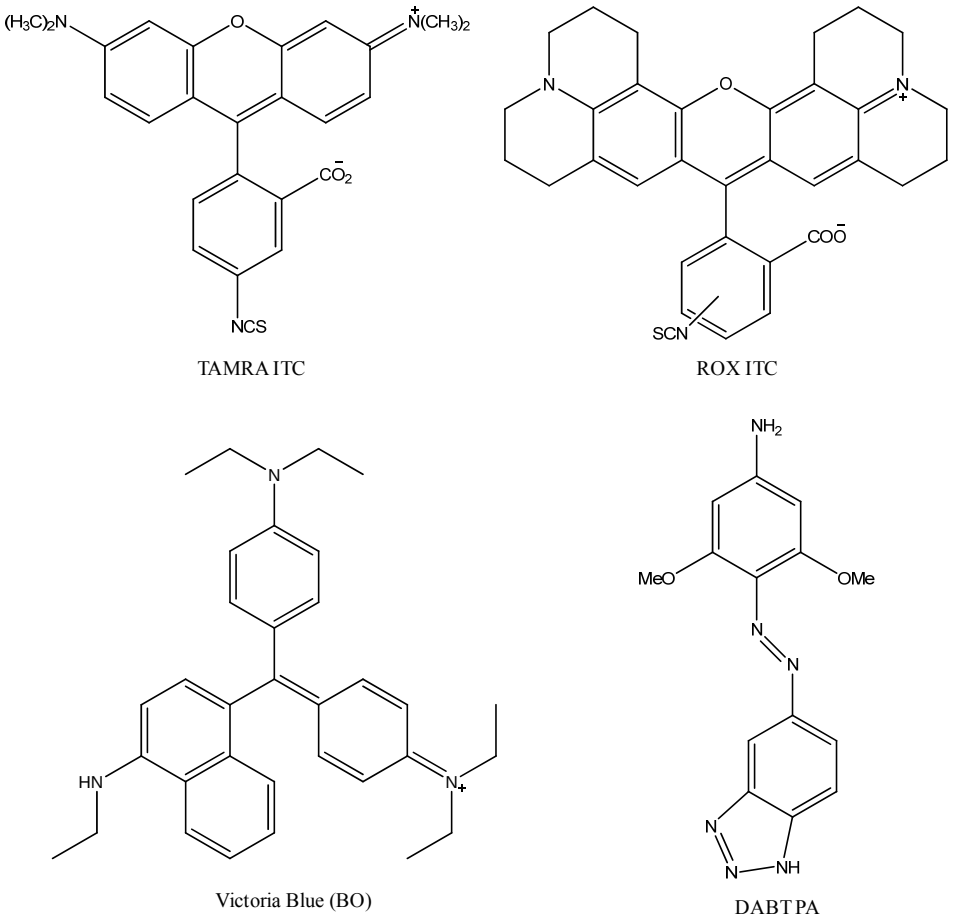

Figure S2. Structures of the dyes used for labeleling the DNA functionalised nanoparticles.

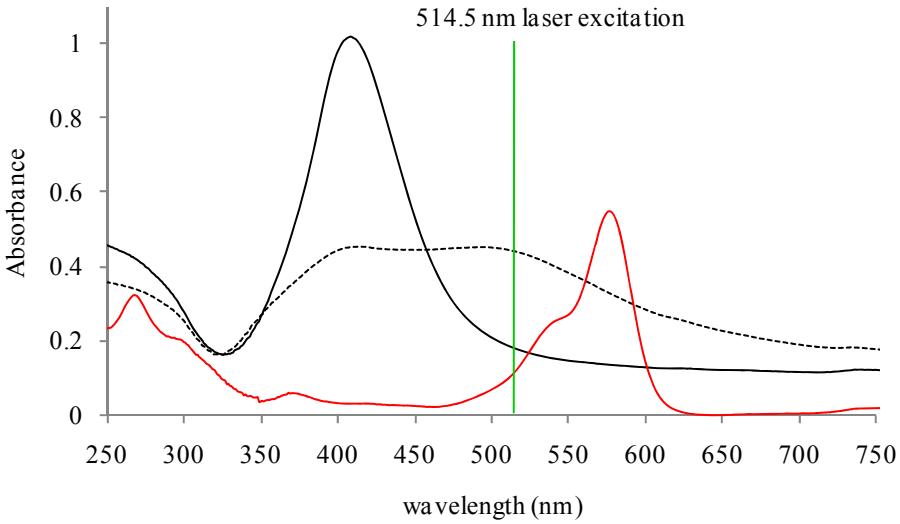

Figure S3. UV-visible spectra of ROX ITC-labelled DNA functionalised nanoparticles in the absence (solid black line) and presence (dashed black line) of the target DNA. The UV-visible spectrum of ROX ITC is shown in red.