Experimental Section

Gold nanoparticles of 30 nm diameters were synthesized using reported method [10, 16, 18]. Gold nanoparticles of different sizes and shapes were synthesized by controlling the ratio of $HAuCl_4$, $3H_2O$ and sodium citrate concentration as we reported recently [18]. Transmission Electron Microscope (TEM) and UV-visible absorption spectrum were used to characterize the nanoparticles. The particle concentration was measured by UV-visible spectroscopy using the molar extinction coefficients at the wavelength of the maximum absorption of each gold colloid as reported recently [8] [$\varepsilon_{(15)\ 528nm} = 3.6 \times 10^8\ cm^{-1}\ M^{-1}$, $\varepsilon_{(30)\ 530nm} = 3.0 \times 10^9\ cm^{-1}\ M^{-1}$, $\varepsilon_{(40)\ 533nm} = 6.7 \times 10^9\ cm^{-1}\ M^{-1}$, $\varepsilon_{(50)\ 535nm} = 1.5 \times 10^{10}\ cm^{-1}\ M^{-1}$, $\varepsilon_{(60)\ 540nm} = 2.9 \times 10^{10}\ cm^{-1}\ M^{-1}$, and $\varepsilon_{(80)\ 550nm} = 6.9 \times 10^{10}\ cm^{-1}\ M^{-1}$]. 4 nM of thiol-substituted oligomer was added to 10 ml of ~ 15 nM gold nanoparticle solution. This solution was incubated at 50° C for 16 hours. This solution was then transferred to several small vials. After that we centrifuged the solution at 13 000 rpm for 20 minutes. The supernatant solution was removed and replaced with 10 mM of phosphate buffer and 0.1 M NaCl solution. It was centrifuged again and redissolved in 10 mM phosphate buffer containing 0.1 M NaCl. To measure the number of DNA molecules/gold nanoparticle, the fluorophore-labeled DNA strands were released from the Au NPs by a ligand exchange process induced by DTT. The solutions were centrifuged at 10 000 rpm for 15 min to isolate the Au NPs, and the supernatants containing the released fluorophore-labeled DNA strands were collected for the fluorescence analyses. The number of DNA strands per particle was calculated from the measured fluorescence intensity and the standard calibration curve. We performed the same experiment several times and the number of DNA strands per particle was 25-30. Our experiment indicates that by using the proper ratio of gold nanoparticles and fluorophore-labeled DNA strands, one can control the number of DNA strand per particle with in the error of 15-

20%. Hybridization of the probe and the target was conducted for 5 minutes in phosphate buffer solution with 0.3 M NaCl for few minutes at room temperature. To remove unhybridized complementary DNA, we centrifuged the solution at 13 000 rpm for 20 minutes. 0.06 to 0.2 U of S1 nuclease was added to gold coated DNA in presence of buffer solution. We measured the fluorescence intensity before adding the nuclease and we monitored how the fluorescence intensity changed with time to monitor the kinetics of the of the cleavage reaction.