

Plasmonic Nanoparticle Dimer Sensors

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Abstract:

We explored actuatable nanoparticle dimers as sensors for small molecules, employing the distance dependence of the hybridized plasmon resonance. By linking the nanoparticles with oligonucleotides that can undergo geometric changes, we detected the analyte via its intercalation into the deoxyribonucleic acid (DNA) linker. The resulting spectral blue shift in the dimer plasmon resonance confirmed that this sensing modality can detect small molecules via their interactions with DNA.

Introduction:

In metal nanoparticles, free electrons in the material move in a collective oscillation known as a surface plasmon. When two nanoparticles are close together, their plasmons interact to form two hybridized modes of different energy. The strength of this coupling depends on the distance between the particles [1]. We considered the lower-energy dimer plasmon mode, which displays a red shift as the particles move together and the coupling strengthens, and a blue shift as the particles move apart and the coupling weakens.

We applied this relationship for sensors by assembling nanoparticle dimers with linkers that extend geometrically in the presence of the target molecule. For example, linking gold nanoparticles with hairpin DNA allowed us to sensitively and selectively detect oligonucleotides based on the blue shift in the plasmon resonance wavelength [2].

These dimer sensors represent a potential improvement over single-particle plasmonic sensors, which rely on refractive index changes and are susceptible to interfering species.

We demonstrated this sensing modality for small molecules using daunorubicin, an anticancer drug that intercalates into right-handed-DNA, binding specifically to the CGA base sequence. Upon intercalation, daunorubicin distorts the structure of DNA, unwinding the helix by 8° and lengthening the DNA by 0.34 nm per molecule intercalated [3].

We hypothesized that the intercalation of daunorubicin into DNA-linked gold nanoparticle dimers would produce a blue shift in plasmon resonance. By varying the number of CGA base repeats in the DNA linker, we confirmed that this spectral response is specific for sequences containing these repeats and dependent on the number of repeats. We also showed that the spectral response is selective for daunorubicin vs. its enantiomer.

Experimental Procedure:

We attached 100 nm gold nanoparticles (GNP) to a silanized glass substrate, then functionalized them with single-stranded DNA (Figure 1a).

We coupled these to 60 nm GNP that had been functionalized in solution with the complementary DNA strand (Figure 1b).

We identified dimers based on color changes seen in darkfield optical images, in which single nanoparticles appear green while dimers appear yellow or brown. We collected darkfield scattering spectra for these individual dimers in buffer, as well as one hour and 24 hours after the addition of daunorubicin (1 μ M; Figure 1c). The peak positions were determined using a Lorentzian fit in a selected interval around the peak.

We used DNA sequences containing 6, 10, and 15 CGA repeats (denoted as CGA6, CGA10, and CGA15 respectively), as well as a random control sequence.

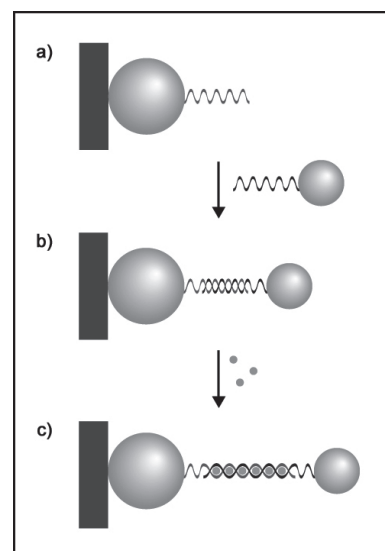


Figure 1: Schematic showing dimer formation and drug intercalation.

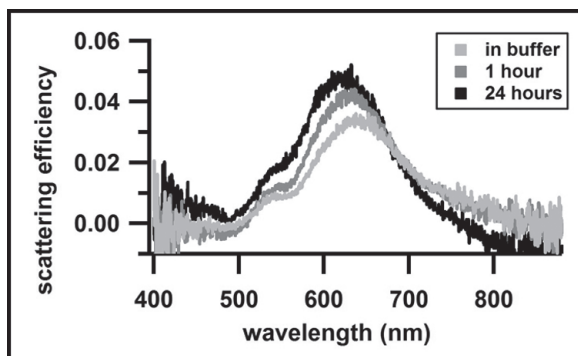


Figure 2: Spectra collected for a CGA15 dimer.

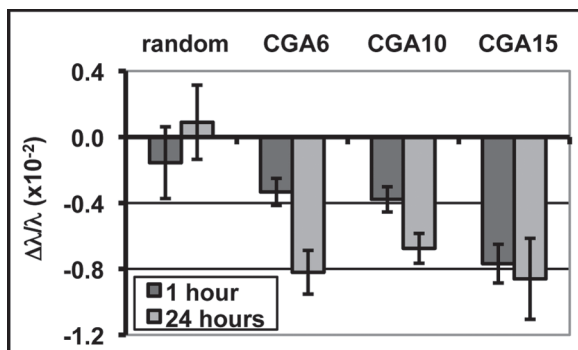


Figure 3: Average fractional shifts for different DNA sequences.

DNA sequence	Calculated change in interparticle distance (nm)	Number of intercalation sites (theoretical)	Number of molecules intercalated (experimental)
CGA6	1.22	6	3.6
CGA10	1.85	10	5.4
CGA15	3.27	15	7.9

Table 1: Theoretical vs. experimental number of molecules intercalated.

Results:

Figure 2 shows scattering spectra for a dimer linked with CGA15 in buffer and after incubation with daunorubicin for one hour and 24 hours. The average fractional shifts (defined as $\Delta\lambda/\lambda$) for dimers using different DNA sequences are shown in Figure 3. The CGA15 sequence displayed the largest blue shift after one hour (average $\Delta\lambda/\lambda$ -0.0077 ± 0.0012). The CGA10 sequence displayed an intermediate shift (-0.0038 ± 0.0008). Finally, the CGA6 sequence displayed the smallest shift (-0.0033 ± 0.0008). The cause of the large shift for these sequences after 24 hours is still under investigation. Dimers using a random DNA sequence did not display a significant shift in either direction after one hour or 24 hours.

We extrapolated the average change in particle separation distance for each type of dimer after one hour, using a calibration curve that relates the dimer peak position to the particle separation distance [4]. We then estimated the average number of molecules intercalated into each dimer, based on crystal structure data which suggests that each daunorubicin molecule lengthens DNA by 0.34 nm. We found that the experimental number of daunorubicin molecules intercalated scales linearly with the theoretical number of intercalation sites (Table 1).

Additionally, we tested the chiral selectivity of the dimers by monitoring their response to daunorubicin vs. its enantiomer WP900, which does not intercalate into right-handed DNA. Introducing WP900 to CGA15 dimers did not produce a significant shift, in contrast to the large blue shift induced by daunorubicin.

Conclusions:

We conclude that monitoring the plasmon resonance of gold nanoparticle dimers is a viable method for the detection of daunorubicin. A significant blue shift is displayed when daunorubicin is added to dimers whose DNA linkers contain CGA repeats, with the magnitude of the shift dependent on the number of repeats. In addition, this response is selective for daunorubicin over its enantiomer, WP900.

Future Work:

The next steps in our specific project are to determine the detection limit of this dimer sensor and evaluate its performance in complex media.

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