Creating Molecularly-Reconfigurable Plasmonic Surfaces for Biosensing

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Abstract

We report a new plasmonic manipulation technique which employs biomolecular interactions as active building blocks in the construction of novel surfaces which gains optical functionality due to individual molecular binding events. We demonstrate two novel biosensors which combine direct-write fabrication with molecular nanopatterning to position individual nanoparticles around single, complex plasmonic nanostructures due to molecular binding. In doing so, we demonstrate both an extremely sensitive naked-eye biosensor which relies on a plasmonic colour-shift to report on antibody-binding events, and a surface-enhanced Raman sensor which relies on the completion of a simple plasmonic circuit by a DNA-conjugated nanoparticle to detect an individual DNA-hybridisation event.

Method

To create the molecularly-reconfigurable plasmonic surfaces we use a novel combination of electron-beam lithography and molecular surface nanopatterning, which allows us to control individual molecular interactions such that we can dictate, with protein-scale resolution (~5 nm), the placement of single nanoparticles (NPs) around individual nanostructures, **Figure 1**. After defining a nanostructure using electron-beam lithography, a second electron-beam step is carried out in order to define a "window" at a particular point around the structure. The surface beneath this window can then be molecularly modified and the polymer resist material removed, leaving a nanophotonic surface that has been molecularly patterned at specific points. Molecularly conjugated NPs can then be bound to these areas in a controlled manner (the initial surface modification is large enough such that only a single particle can bind to any one area).

Naked-eye detection of antibody-binding

Our understanding of biological systems is dependent on our ability to visualise and measure biomolecules and biological events with high spatial and temporal resolution. Plasmonic colorimetry is a biosensing technique which relies on visible plasmon resonance shifts in nanostructures due to some biological event or process. Scattered plasmonic colours are highly sensitive to environmental changes surrounding the nanostructures, making the effect ideal for sensing applications. Any metallic nano-object brought into proximity with the array will influence its resonance, shifting the plasmon frequency and causing a change in structural colour, which can be observed by eye.

To date, biosensors based on plasmonic colour shifts have relied on random, molecularly driven aggregation of chemically synthesized colloid, or blanket binding of NPs to pre-fabricated structures [1-4] and thus have demonstrated little or no control over the number and location of binding events. Although there has been great progress in recent years in molecular lithography techniques, there remains significant problems in terms of the control, placement and spacing of individual particles in order to create arbitrary structures. Here, we bridge the gap between the versatility of direct-write nanolithography, and the resolution and selectivity of molecular self-assembly, combining both techniques for the first time. Precise positioning of single particles around pre-fabricated plasmonic structures allows us to manipulate the plasmon supported by the resultant structure, altering the colour of the light scattered by the surface in an engineered fashion. In large arrays (>100μm, comprising of several thousand structures) the homogeneous colour-shifts can be seen with the naked-eye, without the need for any spectroscopy or microscopy equipment (**Figure 2(a)**).

Completing a plasmonic bowtie with a DNA nanoparticle for extreme Raman detection

The use of metallic NPs in surface enhanced resonance Raman spectroscopy (SERRS) applications is well-known[5]**.** By aggregating discrete NPs, exceptionally large field enhancement values can be realised due to interparticle plasmonic-coupling, creating electromagnetic "hot-spots" in the nanometre gaps between particles.[6] However, controlling this coupling is problematic; common NP aggregation techniques produce randomly coupled particles, where neither the hot-spot number, location or resonance can be controlled. This leads to non-repeatable spectra, and requires large amounts of NPs and analyte to ensure a signal is obtained.

We describe a novel, molecularly reconfigurable plasmonic structure capable of detecting single DNA-binding events via SERRS. By positioning single NPs within plasmonic bowties (**Figure 2(b)**) we can generate intense hot-spots at known locations and known plasmonic frequencies. This novel approach to DNA-driven plasmonic tuning directly addresses one of the fundamental challenges of NP SERRS; control over the localization and frequency of EM-hotspots in NP assemblies. Using NPs modified with both DNA and a Raman reporter, we show an improvement of 2 orders of magnitude *above* the existing SERRS effect, allowing us to pinpoint and measure single DNA-NP binding events.

References

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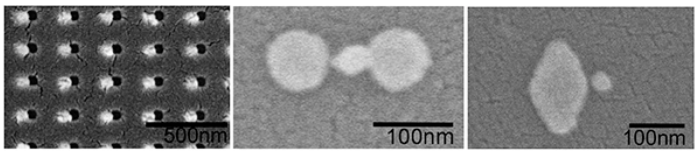

Figure 1. From left; SEM of Au plasmonic structures aligned to resist "windows" which allow molecular surface modification; Individual NP molecularly bound between 2 discs; Individual NP bound at specific point around nano-diamond structure.

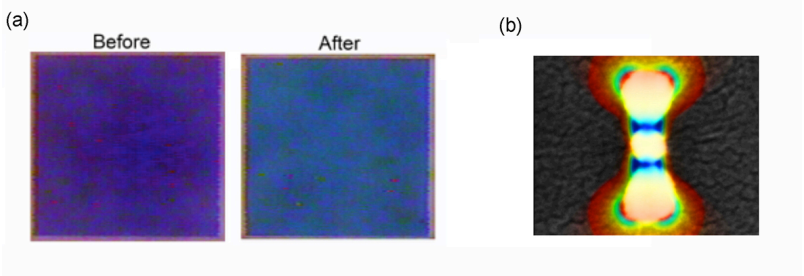

Figure 2. (a) Bright-field images of a plasmonic sensor array before and after antibody affinity binding. (b) A superimposition of an SEM and a finite-element simulation of localized electric-field for a nanoplasmonic bowtie structure with a DNA bound NP in its centre.