Site-selective Functionalization of Hot-spots for Plasmonic Biosensing

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Gold nanoparticles of elongated shape display plasmon resonances that are very sensitive to the refraction index close to the particle's surface. Plasmonic sensors exploit this feature for optical detection of biomolecules.[1] The sensor specificity is built-in by chemical functionalization of the particle's surface with bioreceptors that bind a particular target molecule with high affinity. In general, the sensor response is not homogeneously distributed across the particle's surface, but instead is concentrated at regions of large plasmon-enhanced near field, or hot-spots. Such an example are the tips of gold nanorods (Fig. 1A). The site-selective functionalization of plasmon hot-spots with bioreceptors is crucial to develop plasmonic sensors with improved response by capturing the target species at the most sensitive regions of the particle. In this contribution, we show strategies developed for site-selective functionalization of a model plasmon sensor. We have used surface immobilized biotin-functionalized gold nanorods for streptavidin sensing. Selective functionalization of the nanorods tips can be achieved by protecting the side faces with a CTAB bilayer and using a thiol linker to attach the desired biotin functionality.[2] The sensor performance was characterized by measuring dose-response curves and binding kinetic assays. We find surprising differences in sensor response as a function of linker length, where intermediate linker lengths (1 - 2 nm) yield about 2-fold increase in plasmon shift compared to the shortest (0.5 nm) linker. We attribute this effect to the sparse biotin density obtained with tip-specific funcionalization that allows for the longer and flexible linkers to bind the protein with low steric hindrance, which is otherwise not possible with a non-selective full biotin coating.[3]

We also show preliminary results on the field-induced functionalization of hot-spots. This approach achieves functionalization of regions with a high field-enhancement irrespective of the ability to block certain facets with surfactant, and can therefore be generalized to any particle shape. We use a photocrosslinking reaction to attach biotin receptors onto gold nanorods immobilized on a glass surface. The photochemical reaction is performed by irradiation on resonance with the longitudinal surface plasmon. The irradiated samples in the presence of biotin-derivatized photocrosslinkers show improved responses to streptavidin compared to non-irradiated control samples (Fig. 1B). This is attributed to a two-photon absorption induced cross-linking reaction that is enhanced in the regions with a strong near-field enhancement. The generalization of the functionalization approaches described here to other type of bio-receptors, e.g. antibodies, aptamers or other nucleic acids, will be discussed.

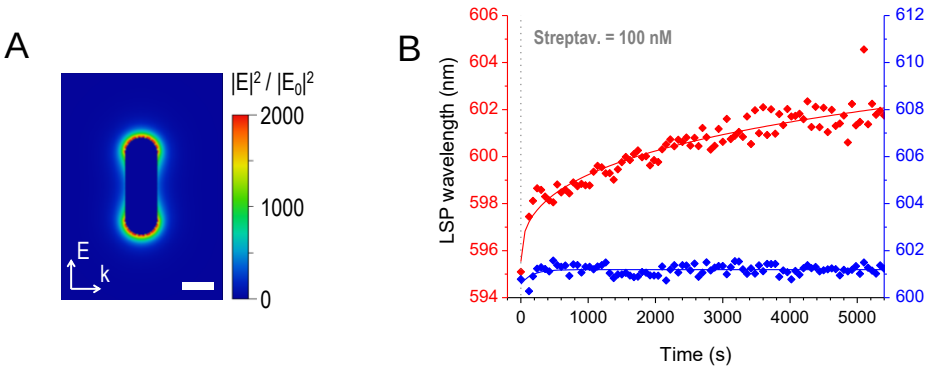

Fig. 1 A) Plasmon enhanced near field map calculated for a gold nanorod 30 nm x 10 nm excited at the longitudinal surface plasmon resonance. B) Kinetic assay of streptavidin sensing with gold nanorods 25 nm x 57 nm irradiated in the presence of a biotin-derivatized photocrosslinker (red curve) and control with a non-irradiated sample (blue curve).

1) K. M. Mayer *et al.*, *Chem. Rev.*, **2011**, *111*, 3828.
2) P. Zijlstra *et al.*, *Angew. Chem. Int. Ed.*, **2012**, *51*, 8352.
3) P. M. R. Paulo *et al.*, *submitted*.