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Imaging single molecules on nanoparticles: exploiting PSF deformations for precise localization

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Nanoparticles (NPs) have proven their applicability in biosensing, drug delivery, catalysis and photo-thermal therapy. Importantly, the exact behaviour of each NP depends heavily on the number and distribution of chemical groups on its surface. Such parameters are traditionally characterized using ensemble-averaging assays, which do not capture the particle-to-particle heterogeneity resulting from variations in particle synthesis and statistical stochasticity.

Single-molecule localization microscopy, on the other hand, is ideally suited for the study of the fluorescently-labeled surface functionalizations of individual NPs in their native, typically aqueous, environment. In this technique, sequentially, sparse subsets of the fluorophores are active, and their positions are localized with high precision by fitting a Gaussian point-spread function (PSF). However, the NP acts as a scatterer near the fluorophore and consequently distorts and displaces the point-spread function (PSF) [1,2,3]. This leads to mislocalizations, when the PSF is fitted with a two-dimensional Gaussian, which is common practice in the field.

Here, we present the first fully analytical description of the PSF of a fluorophore near a spherical NP of any material and size. In contrast to popular numerical approaches, our method is exact, 3 orders of magnitude faster, free and open source. This method 1) serves as an exact fitting algorithm for distorted PSFs and 2) reduces mislocalizations by serving as a predictive tool for optimal experimental design (e.g., NP material, size, and fluorophore). We show that by using the analytical PSF as a fitting tool for experimental DNA-PAINT data on spherical gold NPs, the position of the emitters on the NP surface can be retrieved (Figure 1). Here, we exploit that the PSF shape depends on the relative position of the emitter to the NP, thereby encoding 3D information about the functionalization of the NP surface.

We anticipate that this tool will be instrumental for future characterization of plasmonic biosensors, NP near-fields [4], NP geometry [5] and surface functionalization [6].

[1] Fu. ACS Nano *(2017)*.
[2] Lim. Nano Letters *(2016)*.
[3] Raab. Nature Communications *(2017)*.
[4] Wertz. ACS Photonics *(2016)*.
[5] Taylor. JPhysChem *(2018)*.
[6] Post. Nature Communications *(2019)*.

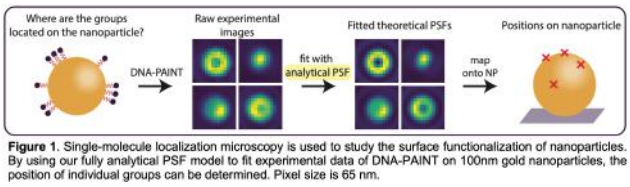

Figure 1. Single-molecule localization microscopy is used to study the surface functionalization of nanoparticles. By using our fully analytical PSF model to fit experimental data of DNA-PAINT on 100nm gold nanoparticles, the position of individual groups can be determined. Pixel size is 65 nm.

Single molecule localization on nanoparticles.png