3D IMAGING SUITABLE FOR CELLULAR UPTAKE OF SPHERICAL NANO PARTICLES BY ACCOUNTING FOR SPHERICAL ABERRATION
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Nanoparticle (NP) based drug delivery is a promising novel therapeutic modality. To better understand its mechanisms, 3D microscopy of cellular NP uptake is essential to precisely locate a NP and image its association with cellular organelles such as lysosomes [1]. Image resolution is reduced by spherical aberration (SA), introduced by refractive index (RI) mismatch between the heterogeneous specimen RI and imaging lens immersion medium (Fig. 1). In this study we investigate three microscopy modes available to us to determine if their resolution is suitable for cellular uptake of spherical NP: confocal microscopy (Nikon laser scanning), structured-illumination microscopy (Zeiss ApoTome) [2], and computational optical sectioning microscopy developed to account for spherical aberration (SA) using a PCA-EM algorithm [3].

Of the three imaging modes confocal does not account for SA in this case as adaptive optics methods are not employed; PCA-EM corrects for SA at all depths using depth-variant PSFs, while the approach in ZEN for deconvolution of ApoTome can use only a single aberrant PSF at a specific depth [5]. Correction of SA with the PCA-EM yields the best axial resolution. This approach, if successful, could also be applied to study protein-protein interaction by proximal ligation assays. As NPs for medical applications are particles with a size in at least one direction of 1–1000 nm [1], single molecule imaging is not always needed.

References

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