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Three-dimensional single-cell imaging with x-ray waveguides in the holographic regime"

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Commentary on "Three-dimensional single-cell imaging with x-ray waveguides in the holographic regime"

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This article, published in the current issue of Acta Crystallographica A, is by Martin Krenkel et. al. in the group of Tim Salditt from Georg-August-University in Go¨ttingen [1]. The work represents a significant advance in full-field X-ray imaging of biological samples, demonstrating a significant improvement of the classical "Transport of Intensity" (TIE) method of Paganin and Nugent [2], called "Holo-TIE" in the new paper.

Following the original development of Cloetens et al [3], the new work combines data measured at multiple detector distances to fill holes of missing frequencies in the contrast transfer function. This idea is presented using the language of variation of Fresnel numbers, which is quoted as the justification.

The results also clearly show the respective advantages of different staining strategies relevant to biological imaging, where both resolution and contrast are key metrics. In X-ray imaging science, "resolution" is defined as the highest spatial frequency capable of being measured by the *instrument*, limited by the solid angle passed by some aperture, or by the detector, for example. The "contrast", on the other hand, is a property of the *sample*, measured in an analogous way as the presence of density (or phase) modulations of a given spatial frequency within the sample. Both the instrument and the sample have to deliver the performance in order for the resulting image to contain the fine features needed for biological interpretation. In the current work, reporting holo-TIE imaging of Human macrophage cells [1], Os was found to create a uniform background that identifies only the approximate shape of the cytoplasm filled regions, while Ba particles were found to stand out nicely. However, while the Ba particles are seen with high resolution, they are markers that may or may not report on the biological state of the sample, depending on the method of attachment and introduction to the cells. Observing the markers with high resolution does not necessarily mean that the biological functions are determined with the same level of detail.

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[1] "Three-dimensional single-cell imaging with x-ray waveguides in the holographic regime", Martin Krenkel, Mareike To¨pperwien, Frauke Alves and Tim Salditt, Acta Cryst. A xxx (2017)

[2] Paganin, D. and Nugent, K. A. Phys. Rev. Lett. 80, 2586–2589 (1998)

[3] "Holotomography: Quantitative phase tomography with micrometer resolution using hard synchrotron radiation x rays", P. Cloetens, W. Ludwig, and J. Baruchel, D. Van Dyck, J. Van Landuyt, J. P. Guigay and M. Schlenker, Appl. Phys. Letts. **75** 2912 (1999)