Label-Free Nanoscopy Enabled by Photonic Chip Fourier ptychography

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Abstract: Label-free nanoscopy encompasses optical imaging with resolution in the 100nm range using visible wavelengths, vastly exceeding the Abbe limit of diffraction [1]. A direct transfer of common approaches known from conventional, fluorescence-based nanoscopy is not feasible due to a lack of access to non-linear sample responses. Thus, implementations so far have proven challenging.

Here, we present a label-free nanoscopy method based on a purpose-built super-condenser for sample illumination. Our approach combines Fourier ptychography [2] with waveguide-based microscopy [3] to realize maximally inclined darkfield illumination with artificially stretched wavevectors due to the large refractive index of the selected waveguide material.

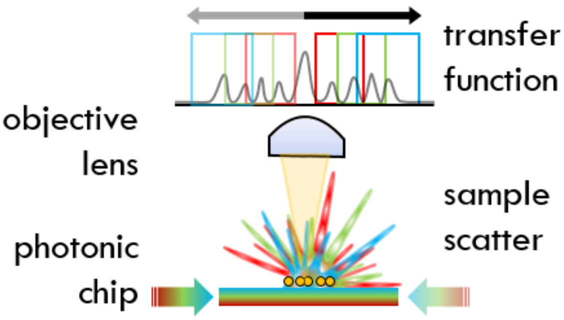

Figure 1: Artificially elongated illumination wavevectors grant access to higher spatial frequency information.

Illumination at oblique angles "re-positions" the sample's field in the aperture, in effect down-modulating the sample information with the illumination's spatial frequency. Since this occurs before the objective low-pass filtering, access to information far beyond the diffraction limit is possible due to the high spatial frequencies of the waveguide illumination.

To extract those fine, down-modulated details, Fourier ptychography is used. This technique computationally combines several raw images, taken sequentially with illumination directions spanning the condenser numerical aperture, into a super-resolved image.

Thus, the then achievable resolution is given by the illumination wavelength divided by the sum of numerical aperture and waveguide refractive index, which in our implementation allows visualization of details approaching 100nm.

We validate the method via extensive in silico and in vitro experiments and provide details on the underlying image formation theory, the employed waveguide chips, the microscopy system, as well as the reconstruction algorithm.

References

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