

Deep learning based direct aberration phase retrieval in stimulated emission depletion (STED) microscopy

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STED microscopy is a laser scanning method, in which super-resolution is achieved by confining the fluorescence emission to a region much smaller than the focused laser beam size [1]. As the high resolution optical system, STED microscopy suffers from aberration. The aberration caused by the refractive index mismatch of the specimen especially when a laser beam is focused deeply into it. Systematic aberration arises from optical beam paths in a STED microscope decreasing the image quality, and even the resolution and illumination efficiency.

In a STED microscope, classical indirect approaches to phase retrieval are parameterized point spread function (PSF) fitting methods such as image based quality metric [2]. Although PSF fitting methods are simpler in hardware compared with a direct sensing approach, it is complicated on software configuration and the iteration is relatively slow. Recently, several studies demonstrated that deep learning (DL)-based phase retrieval can produce results at fast processing speeds [3, 4]. But neural network performance still needs to be improved.

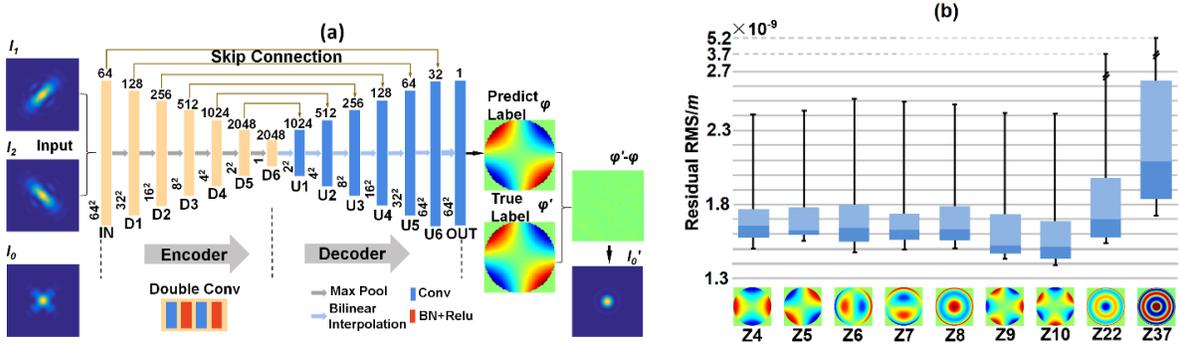


Fig. 1(a) The structure of neural networks and the process of aberration compensation. Here, I_1, I_2 are PSFs of off-focal planes, I_0 is the PSF in afocal plane, and I_0' is the reconstructed PSF. **Fig. 1(b)** The comparison of the residual root mean square (RMS) phase magnitude.

Here, we demonstrate a fast and accurate Unet based method for direct aberration correction on the illumination path in a STED microscope. As shown in Fig. 1(a), the inputs I_1 and I_2 are intensities of 9000 paired aberrated PSFs at two out-of-focus positions. The network is the general encoder-decoder Unet structure. The outputs are predicted phase aberrations for coma, astigmatism, trefoil and 1st, 2nd and 3rd order spherical aberrations. The trained network is then tested with 2700 PSF pairs. Fig. 1(b) is the comparison of the residual RMS phase magnitude for all 9 Zernike polynomials. The network determined a high performance phase aberration compensation and enabled a drastically reduction in the RMS median range from $(5.9937 \times 10^{-8}, 7.6357 \times 10^{-8})$ m to $(1.5146 \times 10^{-9}, 2.0963 \times 10^{-9})$ m.

In conclusion, we have proposed a accurate and fast aberration correction method for the illumination path of a STED microscope based on DL. Our approach could be further implemented in the depletion beam path of a STED microscope to improve the imaging resolution and illumination efficiency.

References

- [1] S. W. Hell, J. Wichmann, "Breaking the diffraction resolution limit by stimulated emission: stimulated-emission-depletion fluorescence microscopy," *Opt. Lett.* **19**, 780 (1994).
- [2] T. J. Gould, D. Burke, J. Bewersdorf, and M. J. Booth, "Adaptive optics enables 3D STED microscopy in aberrating specimens," *Opt. Express.* **20**, 20998 (2012).
- [3] D. Saha, U. Schmidt, Q. Zhang, A. Barbotin, Q. Hu, N. Ji, M. J. Booth, M. Weigert, and E. W. Myers, "Practical sensorless aberration estimation for 3D microscopy with deep learning," *Opt. Express.* **28**, 29044 (2020).
- [4] B. P. Cumming, and M. Gu, "Direct determination of aberration functions in microscopy by an artificial neural network," *Opt. Express.* **28**, 14511 (2020).