

NONLINEAR FOCAL MODULATION MICROSCOPY

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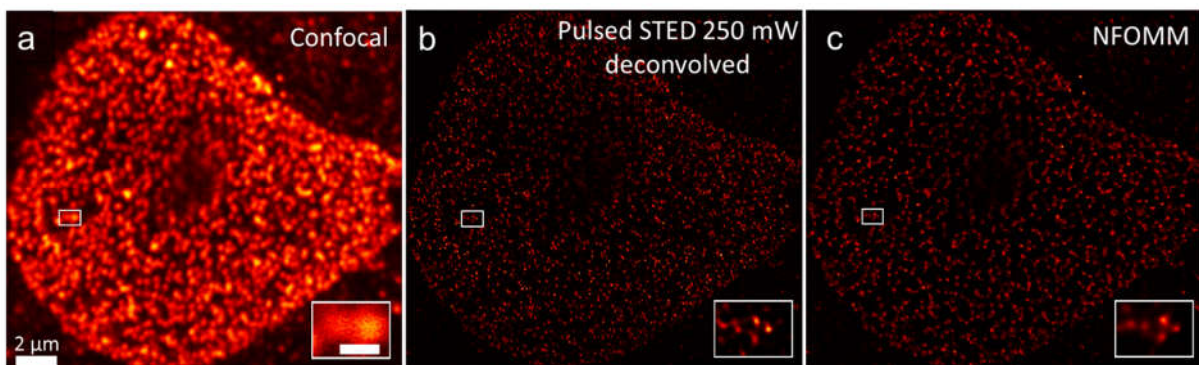
KEY WORDS: Super resolution, Fluorescence saturation, Frequency shifting.

1. PRINCIPLE

Here we report nonlinear focal modulation microscopy (NFOMM) [1] to achieve super-resolution imaging. Abandoning the previous persistence on minimizing the size of Gaussian emission pattern by directly narrowing (e.g. Minimizing the detection pinhole in Airyscan, Zeiss) or by indirectly peeling its outer profiles (e.g., Depleting the outer emission region in STED, stimulated emission microscopy) in pointwise scanning scenarios, we stick to a more general basis—— maximizing the system's frequency shifting ability. In NFOMM, we implement a nonlinear focal modulation by applying phase modulations with high-intensity illumination, thereby extending the effective spatial-frequency bandwidth of the imaging system for reconstructing super-resolved images. NFOMM employs a spatial light modulator (SLM) for assisting pattern-modulated pointwise scanning, making the system single beam path while achieving a transverse resolution of ~ 60 nm ($\sim \lambda/10$) on imaging fluorescent nanoparticles. Since NFOMM is implemented as an add-on module to an existing laser scanning microscope and easy to be aligned, we anticipate it will be adopted rapidly by the biological community.

2. IMAGING VERIFICATION

We conducted experiments with Vero cells to verify the resolution of NFOMM. As shown below, NFOMM was successfully applied to studying details of nuclear pore complex. Nuclear pores that appear clustered together in confocal image (a) can be individually identified in NFOMM image (c), and also well examined in the pulsed STED (b) result after deconvolution. Insert scale bar in (a) is 500 nm.



REFERENCE

1. G. Zhao, C. Zheng, C. Kuang, R. Zhou, M. M. Kabir, K. C. Toussaint Jr, W. Wang, L. Xu, H. Li, and P. Xiu, "Nonlinear focal modulation microscopy," arXiv preprint arXiv:1711.01455 (2017).