Supplementary Information for

Super resolution label-free dark-field microscopy by deep learning

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Reconstruction method

Various techniques exist for recovering high spatial frequency details embedded in low-resolution images. Notably, structured illumination microscopy (SIM) and Fourier ptychography microscopy (FPM) are widely recognized methods in the super-resolution imaging field. SIM employs sinusoidal illumination patterns projected onto the object, creating diffraction-limited moiré fringes images which encode the high spatial frequency information of the object. Analytical extraction of high spatial frequency information from these moiré fringes sets SIM apart from dark-field microscopy (DFM), where a different illumination method renders the information retrieval method inapplicable for DFM.

FPM aligns more closely with our research. Using an LED array, FPM illuminates the object to capture a sequence of diffraction-limited images, each containing specific high spatial frequency information. These images overlap in Fourier space. Traditional super-resolution image reconstruction relies on iterative phase retrieval methods like the Gerchberg-Saxton algorithm and convex relaxation. Although deep learning approaches also exist for high spatial frequency information retrieval, they still depend on multiple frames of diffraction-limited images acquired under diverse illumination angles.

In DFM, simultaneous illumination from various angles results in the detection of only one image, posing a greater challenge for information retrieval. The inverse problem to solve for the high resolution image is much more ill-posed. Analytical solutions is impossible for such problem. Consequently, we made the decision to involve deep learning algorithms trained with simulation data based on a forward model.

Network architecture

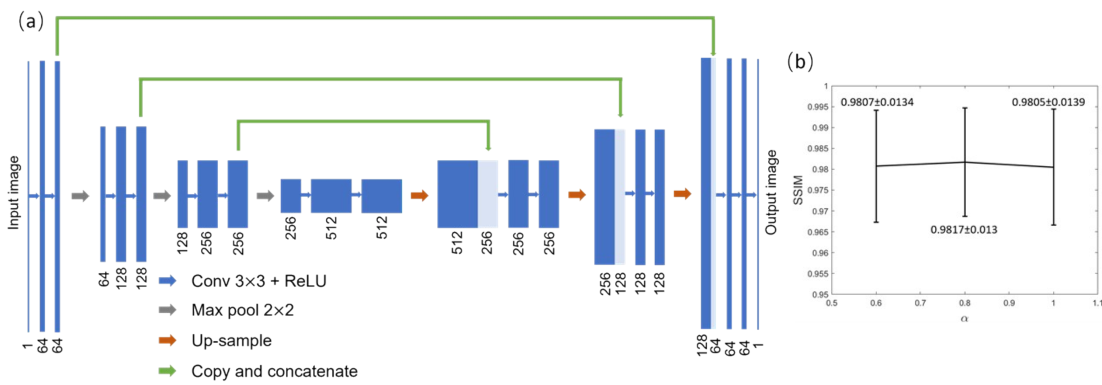

Fig. S1. (a) Architecture of the neural network. (b) SSIM statistics between reconstructed images and ground truth images under different α in the loss function.

Resolution improvement characterization

In order to confirm the resolution improvement achieved by the neural network, we calculated the Fourier spectrums of the low resolution dark field image and network output image, as shown in Figure S2a and S2b. The size of the red circle in network output Fourier spectrum is twice as it in the low resolution one, which roughly outlines the twice resolution improvement achieved by the network. Figure S2c shows the Fourier ring correlation (FRC) between the network ouput images added with different noise. Considering 1/7 threshold in FRC, ~190 nm resolution was confirmed.

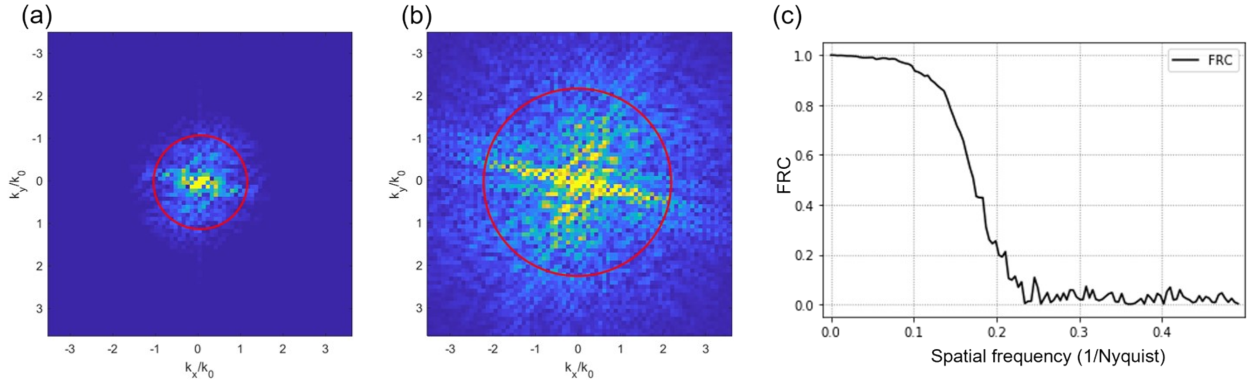

Fig. S2. Resolution characterization. (a) Fourier spectrum of low resolution dark field image. (b) Fourier spectrum of network ouput image. (c) Fourier ring correlation curve of network ouput image with different noise.