Upconversion Super-resolution Microscopy

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ABSTRACT

The optical microscopy resolution is limited by the physics of diffraction, $d=\lambda/2n\sin\theta$. The N-photon microscopy can theoretically improve resolution, $d=\lambda/(2n\sin\theta N^{1/2})$. However, this is a paradox that higher N always means longer λ_{ex}. To break this limit, we proposed 730-nm CW laser excited 4-photon microscopy with Nd-sensitized UCNPs, obtaining 161-nm sub-diffraction resolution[1]. Photon avalanche (PA) occurring in lanthanide-doped solids is a very important mechanism, which can arouse a giant nonlinear response in the luminescence intensity to the excitation light intensity, while not relying on intense laser pulses as in traditional nonlinear optical processes. The achievement of PA, mostly restricted to bulk materials, conventionally relies on very sophisticated excitation schemes, individual for each PA system. Recently, we established a universal PA strategy to generate huge optical nonlinearities from various lanthanide emitters, i.e., migrating photon avalanche (MPA) based on multilayer core-shell nanomaterials[2]. The core of a MPA nanoparticle is the key to activating avalanche looping cycles, where PA are synchronously achieved for both Yb^{3+} and Pr^{3+} ions under 852-nm laser excitation, exhibiting a 26^{th} order nonlinearity and a clear pumping threshold. The avalanching Yb^{3+} ions can migrate their optical nonlinear response in a long range to other emitters (e.g., Ho^{3+} and Tm^{3+}) located in the subsequent shell layer, resulting in an even higher order nonlinearity due to a further cascading multiplicative effect (as high as 46^{th} for Tm^{3+}). As a demonstration, using one low-power, 852-nm CW beam, we implemented nanoscopy with a lateral resolution down to 62 nm. Our strategy provides a facile route to achieve a giant optical nonlinearity in different nano-emitters, which holds great potential for widespread applications.

Stimulated emission depletion (STED) microscopy has become a powerful diffraction-unlimited technique for fluorescence imaging with resolution governed by $d=\lambda/(2n\sin\theta(1+I/I_{sat})^{1/2})$. However, STED fundamentally suffers from high-intensity light illumination, photobleaching, re-excitation background, sophisticated probe-defined laser schemes, and limited photon budget of the probes. In 2015, we realized emission depletion in UCNPs[3]. In 2017, using UCNPs we developed low-power CW laser enabled nonbleaching cytoskeleton STED imaging[4,5]. In our very recent progress, we have successfully broken the theoretical limit of saturation intensity itself by two orders using new mechanism, and provides background-free, contrast-enhanced imaging at $\lambda_{ex}/38$ resolution. We demonstrate a versatile strategy, stimulated-emission induced excitation depletion (STExD), to deplete the emission of multi-chromatic probes using a single pair of low-power, NIR CW lasers with fixed wavelength. With the effect of cascade amplified depletion effects, we achieve emission depletion for a wide range of emitters by manipulating their common sensitizer. We demonstrate an ultrahigh depletion efficiency of 99.3% for the 450 nm emission with a record low saturation intensity of 23.8 kW cm-2[6]. We further demonstrate nanoscopic imaging with a series of multi-chromatic nanoprobes, two-color STExD imaging, and subcellular imaging of the immunolabelled actin filaments [7].

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