Imaging and tweezing under a nonlinear optical endoscope

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Abstract: We show the recent progress on super resolution multiphoton imaging and tweezing of micro/nano fluorescent particles in a fibre-optical nonlinear optical endoscope.

OCIS codes: 170.6900 Three-dimensional microscopy; 110.2350 Fiber optical imaging; 170.5810 Scanning microscopy

1. Introduction

High resolution imaging and manipulation of micro/nano objects that cannot be seen by eyes are two important functions in biological and biomedical studies. The integration of femtosecond laser beams and optical microscopy has led to the invention of nonlinear optical microscopy which provides a revolutionary tool for three-dimensional (3D) imaging through thick tissue media [1]. The recent development of fibre optics including photonic crystal fibre and its application into this new microscopy method has facilitated the emerging of nonlinear optical endoscopy for in vivo diagnosis and therapeutic studies [1-3]. It has been shown recently that a functional handheld fibre-optical nonlinear endoscopy system can be used as a minimal invasive method for simultaneous diagnoses and treatment of cancer cells when transferrin-conjugated gold nanorods that are specifically labelled to cancer cells are adopted [4, 5]. In this paper, we will report on a novel nonlinear optical endoscope design using laser beams at two wavelengths for 3D superresolution imaging. In addition, the application of the nonlinear optical endoscope for trapping and tweezing micro/nano fluorescent particles [6] will be present.

2. Superresolution multiphoton endoscopy

Despite its incredible advantages, the resolution of optical nonlinear endoscopy is still limited by optical diffraction by a low numerical lens used for imaging. It can hardly resolve most protein complexes and subcellular organelles. Recently photo-activated localization microscopy (PALM), stochastic optical reconstruction microscopy (STORM) and stimulated emission depletion (STED) microscopy have been chosen to overcome the optical diffraction barrier. However, the major problem with PALM and STORM techniques is that formulating the image takes on the order of hours to collect the data, which limits the study of dynamics. In addition, these techniques require the relative position between molecules or nanoparticles being fixed during data collection, which is not feasible for imaging live biological specimens. STED microscopy has been broadly used in imaging bio-molecules of cells, and fluorescent nanoparticles with ultra-high resolution of tens of nanometres. However STED microscopy is based on a space transmitted bench-top microscope system. Such a system does not have the movement flexibility and it is bulky. Therefore it is limited for in vivo imaging or viewing inner organs. Perfectly overlapping excitation beam and STED beam at focal plane is technically challenging for such a system. Here, we use double clad fibre (DCF) for superresolution nonlinear endoscopy. The alignment of the excitation beam with the STED beam is guaranteed by the structure of the DCF. This nonlinear endoscope can be used for 3D two-photon-excited fluorescence imaging with resolution breaking diffraction limitation barrier.

3. Nonlinear endoscopic tweezing

The nonlinear optical endoscopy system with a small probe can enter hollow organs or blood vessel is not only useful in in vivo imaging and detection but also capable of providing a local force to manipulate micro/nano-particles. Here we, for the first time, demonstrate that optical nonlinear endoscopy can be used to move fluorescent particles with diameters from nanometres to micrometres in a 3D liquid environment within a large volume of through two-photon absorption. Two-photon absorption in small particles not only provides a nonlinear signal for showing the particle moving trace but also enhances the trapping efficiency of small particles by orders of magnitude. Nonlinear endoscopy tweezing is promising to be used for efficient drug delivery.
4. References


