Smart light touch and optical antennas: from optical manipulation to cellular exploration

Hongbao Xin[a]*, Baojun Li[a], and Luke P. Lee[b]
(*hongbaoxin@jnu.edu.cn)
[a]Guangdong Provincial Key Laboratory of Optical Fiber Sensing and Communications, Institute of Nanophotonics, Jinan University, Guangzhou 511443, China
[b]University of California, Berkeley, USA

ABSTRACT

We present some recent developments using smart optical tools, such as optical fiber tweezers (OFTs) and plasmonic optical antennas, to explore the biological world. Using OFTs, which act as a smart light touch, we realized the stable trapping and flexible manipulation of single particles, bacteria, and cells. The trapping and multifunctional manipulation is demonstrated using different samples varying from mammalian cells to bacteria, nanotubes and to biomolecules, with sizes changing from several tens of micrometer to a few nanometer. The OFTs is also used for the stable trapping and patterning of multiple particles and cells, with the ability of biophotonic waveguides formation based on bacteria. In addition to the trapping and manipulation of cell individuals, we also demonstrated that smart optical tools, such as plasmonic optical antennas, are capable of cellular exploration.

Keywords: Optical fiber tweezers, optical trapping, optical manipulation, nanoplasmonic optical antennas, cellular exploration

1. INTRODUCTION

The rapid development of biophotonics has improved our better understanding of the biological world. Smart optical tools, such as optical tweezers[1,2] and nanoplasmonic optical antennas[3], have constantly uncovered mysteries and provided new insights throughout cellular society. Outside the cell, optical tweezers act as a smart touch, enabling the precise and flexible capture, manipulation, and analysis of single cells and biomolecules[4]. Particularly, optical fiber tweezers allow us to form biocompatible and implantable optical components to explore the biological world. Inside of the cell, plasmonic nanoparticles act as smart optical antennas, enabling the exploration of intracellular world.

Since the first introduction[5], conventional optical tweezers (COTs), where the core part is a focused laser beam, has been widely used in different areas. However, there are some limitations of COTs, such as the bulky system and manipulation inflexibility. OFTs formed with a single tapered optical fiber have solved these problems and served as a versatile smart tool for optical trapping and manipulation[6,7]. Compared with COTs, OFTs have the advantages of easy fabrication, high flexibility, increased manipulation precision and high levels of integration. Launching of laser beams with different wavelength into the fiber allowed the trapping and manipulation of particles and cells by either

Optoelectronic Devices and Integration VII, edited by Xuping Zhang, Baojun Li, Changyuan Yu, Xinliang Zhang, Proc. of SPIE Vol. 10814, 108140D · © 2018 SPIE · CCC code 0277-786X/18/$18 · doi: 10.1117/12.2503548

photothermal effect[8] or optical force trapping[7,9,10]. The evanescent fields at the surface of a subwavelength optical fiber also allow the trapping and long-range delivery of particles and bacteria[11-13]. The OFTs now can be used for the stable trapping, targeted pushing, and precise arrangement of singe particles[7]. It can also be used for the trapping and analysis of a single motile bacteria in a non-contact manner[14]. In addition, OFTs also allowed the cotrapping of single upconversion nanoparticles and bacteria for single bacteria labeling and analysis[15]. Compared with conventional cell/bacterium labeling methods, which are based on large number of cells, this single-bacteria labeling is a better candidate for further single cell analysis, because different cells have different properties due to the cellular heterogeneity. Based on OFTs, trapping and manipulation of single carbon nanotubes[16] and single DNA molecules[17] have also been demonstrated by overcoming the diffraction limit. In addition to single particle or cell trapping and manipulation, OFTs have also shown the fantastic ability for multiple particle/cell trapping and patterning. By combining the optical scattering force and gradient force, optical binding has been used for multiple trapping and patterning of particles and cells using OFTs[18]. By simply using the optical gradient force, multiple trapping and alignment of bacteria and different cells have also been demonstrated[19,20]. This multiple trapping and alignment of bacteria has provided an important way for the formation of biophotonic waveguides directly using the material of bacteria[21]. By modifying the end of the fiber, light output from the fiber can be divided into three beams, which can be further used for the formation of branched biophotonic components[22]. Compared with traditional photonic components, these biophotonic components are highly biocompatible and implantable, because they are directed assembled with biological materials. OFTs have been widely used for the trapping, manipulation, and further analysis of cell individuals. However, to get the information inside a cell, a smart tool capable of stepping into the cell for information acquisition is very necessary. Plasmonic nanoparticles, which act as smart optical antennas, are such a tool for cellular exploration[3]. In this paper, we will demonstrate the stable trapping, flexible manipulation of single particle and cells using OFTs. Multiple cell trapping, arrangement, and biophotonic waveguides formation will also be demonstrated using OFTs. We will also demonstrate the cellular exploration using nanoplasmonic optical antennas.

2. RESULTS

2.1 Flexibly manipulation of single particle/cell

Fig. 1a shows the experimental setup of OFTs for single particle trapping and manipulation. The tapered optical fiber can be flexibly manipulated in three dimensions (3D) using a six-axis manipulator with a manipulation resolution of 60 nm. A laser beam at a wavelength of 980 nm was launched into the fiber for particle trapping and manipulation. Fig. 1b shows a microscopic image of the tapered optical fiber, which was fabricated using a flame-heating and pulling technique. Fig. 1c shows a simulation result of the light distribution output from the fiber end, showing a light focusing at the fiber end, which is similar to the light focus in COTs. Fig. 1d schematically shows the trapping, pushing, and manipulation of a single particle with different distance to the fiber end[7]. By calculation, the optical force exerted on a single particle was obtained, and is shown in Fig. 1e and f. Near the fiber end, the force in the *x* direction is negative, which is a trapping force, and the particle can be trapped. While away from the fiber, the force is positive, and the particle can by pushed away. By combining the trapping and pushing ability, flexible manipulation and precise arrangement of particles can be achieved as shown in Fig. 2. This method can also be used for the trapping and manipulation of other samples, such as bacteria and cells. By modify the fiber end, non-contact trapping and manipulation of single bacteria can also be realized[14].

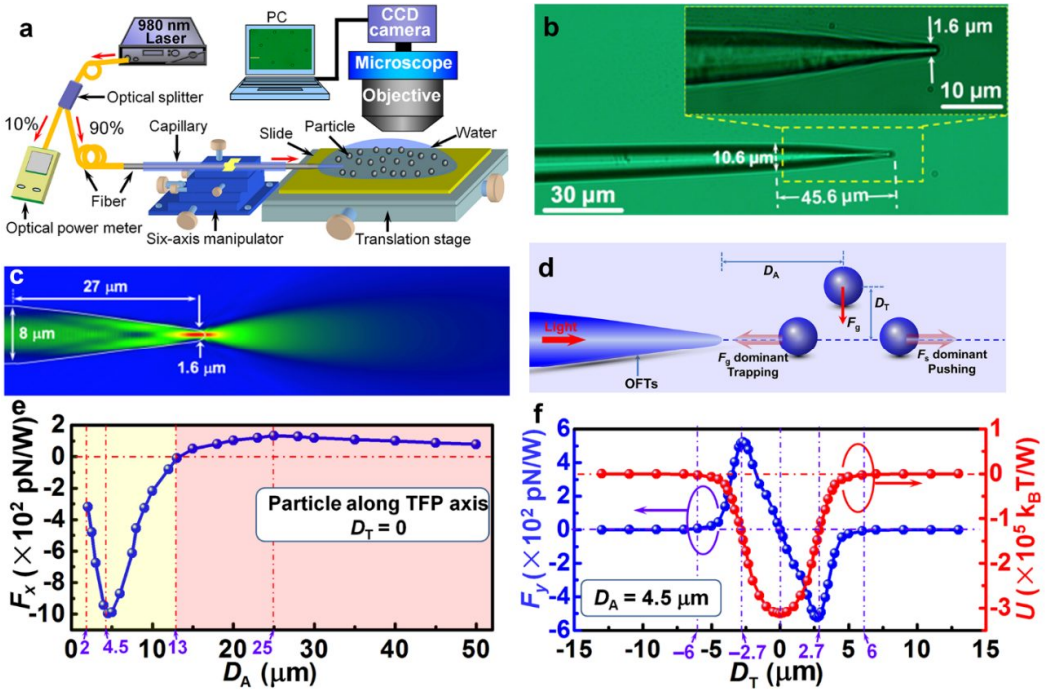

Figure 1 (a) Schematic illustration of OFTs experiment setup for single particle/cell trapping and manipulation. (b) Optical microscopic image of a tapered optical fiber for the use of OFTs. (c) Simulation results of the light distribution output from the fiber. (d) Schematic illustration of single particle trapping, pushing and manipulation with different distance to the fiber end. (e,f) Calculation results of the optical force exerted on a single particle in (e) *x* and (f) *y* direction.

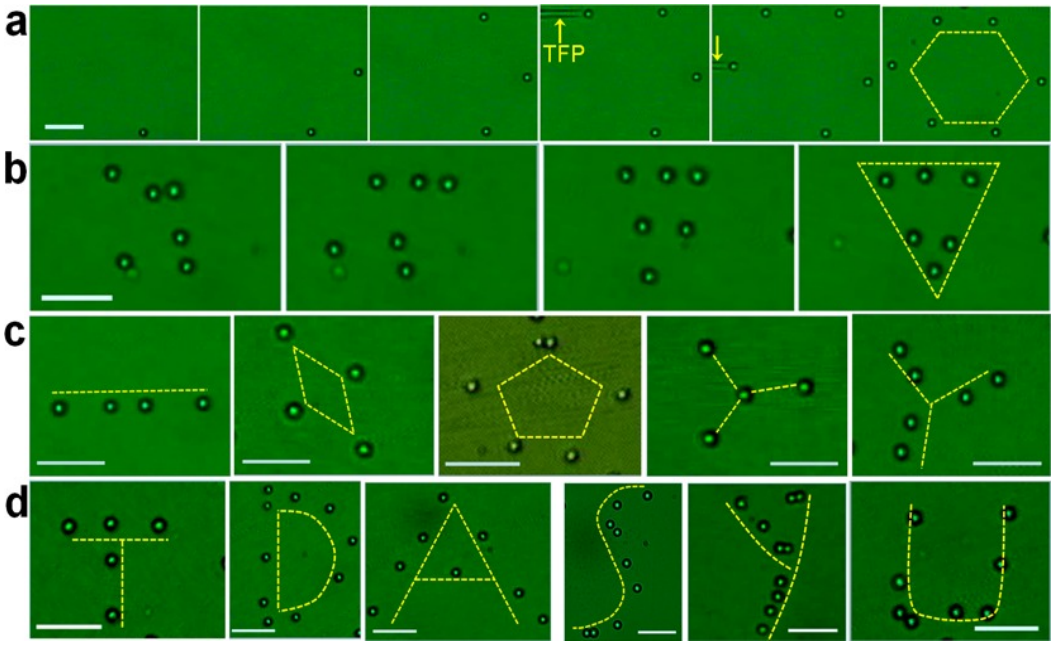

Figure 2. Experimental results of particle arrangement using OFTs by combining the trapping and pushing ability. Scale bar: 20 μm.

2.2 Single upconversion nanoparticle-bacterium contrapping for single bacteria labeling

In addition to the single particle and cell trapping and manipulation, the OFTs can also be used for the cotrapping of single upconversion nanoparticle (UCNP) and bacterium, and further be used for single bacteria labeling and analysis. As shown in Fig. 3a, a single UCNP (120 nm) was first trapped by the OFTs with the laser of 980-nm wavelength. The UCNP emitted green light under the excitation of 980 nm wavelength light. After the trapping of UCNP I, a single bacterium and UCNP II were subsequently trapped. The single bacterium was then labelled by the two UCNPs at both ends. Fig. 3b and 3c show the cotrapped and labelled *Escherichia coli* (*E. coli*) with different sizes under bright field and dark field, respectively. During the cotrapping process, the real-time light signal was detected as shown in Fig. 3d. The final light response properties for bacteria with different sizes were different, this signal change can be used for single bacteria analysis[15].

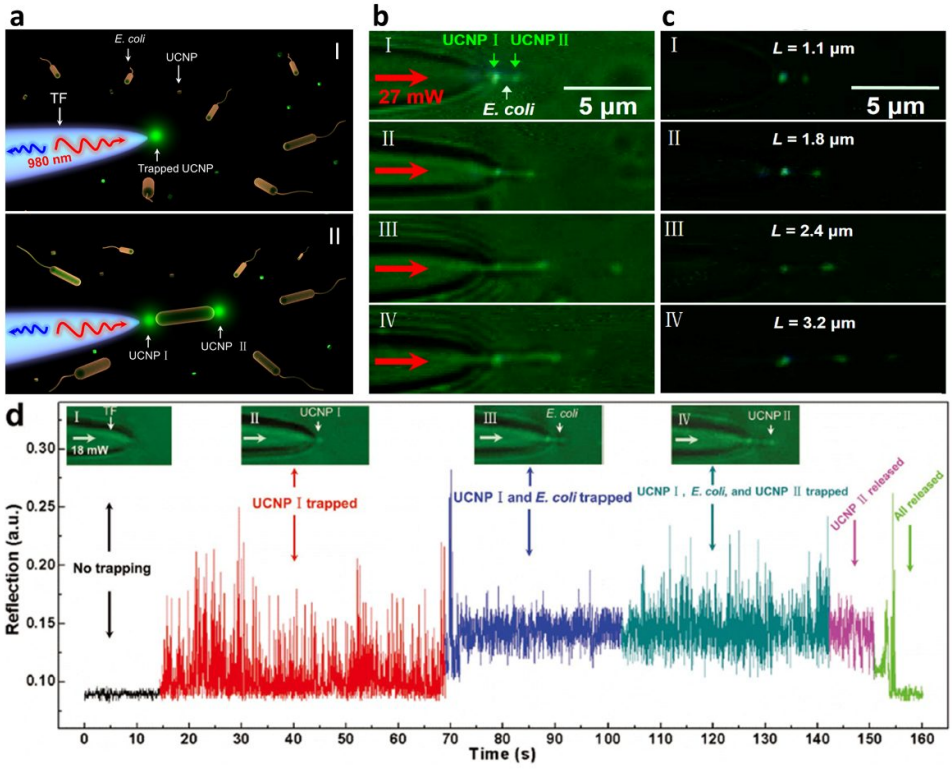

Figure 3 (a) Schematic illustration of cotrapping of single UCNP-bacterium for single bacterium labeling. (b) Bright-field image and (c) dark-field image for single bacteria labeling. (d) Real-time reflected signal in the cotrapping process.

2.3 Single carbon nanotube trapping and manipulation using fiber nanotip

In addition to the trapping and manipulation of particles and cells in the micrometer scale, OFTs-based technique can also be used for the trapping and manipulation of objects with nanometer size[16,17], which are conventional very difficult for trapping and manipulation due to the strong Brownian motion and diffraction limit. We fabricated a nanotip at the end of a tapered optical fiber for the trapping and manipulation of a single multiwalled carbon nanotube (MWCNT, outer diameter: 50 nm, average length 0.9 μm), the size of the fiber tip is shown in Fig. 4a. A single MWCNT was oriented and targeted shifted by the optical torque and scattering force with a laser beam at a wavelength of 980 nm launched into the fiber (Fig. 4b). With two fiber nanotip, a single MWCNT was stably trapped (Fig. 4c-e).

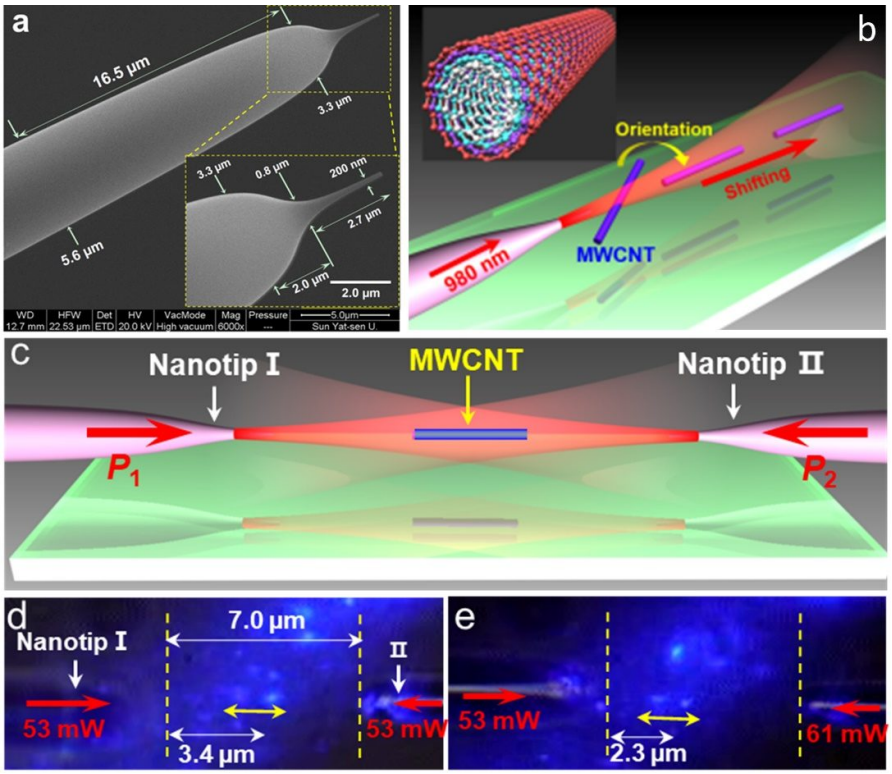

Figure 4. (a) Scanning electron microscope (SEM) image of the fiber nanotip. (b)Schematic of the optical orientation and shifting of a single MWCNT using a laser beam at a wavelength of 980 nm launched into the nanotip. (c) Schematic illustration of two fiber nanotip for the stable trapping of a single MWCNT. (d,e) Dark-field optical microscope images of the orientation, trapping and shifting of a single MWCNT.

2.4 Multiple particle/cell trapping and assembly by optical binding

In addition to single particle/cell trapping and manipulation, the OFTs can also be used for multiple particle/cell trapping and assembly[18]. For single particle/cell trapping, the target is trapped near the fiber tip, where the optical gradient force is larger than the scattering force. Here, we consider the situation with a distance of several micrometer away from the fiber tip, where the gradient force is smaller than the scattering force. In this case, a single particle will be pushed away[7], but multiple particles will be bound together (Fig. 5a). For multiple particles, light will propagate along the particles, and refocus at the particle end (Fig. 5b). The force exerted on the end particle is changed from pushing force to trapping force in the *x* direction (Fig. 5c), and the force in the *y* direction is increased compared with a single particle (Fig. 5d). Multiple particles are then bound together by the cooperation of optical gradient force and optical scattering force. Using this principle, silica particles (diameter: 3.2 µm) were assembled into one dimensional (1D) with different particle numbers with the laser beam at 980 nm wavelength launched into the fiber (38.8 mW) (Fig. 5e). Two-dimensional (2D) particle arrays were also assembled (Fig. 5f). In addition, this method can also be used for the assembly of multiple cells[18].

.

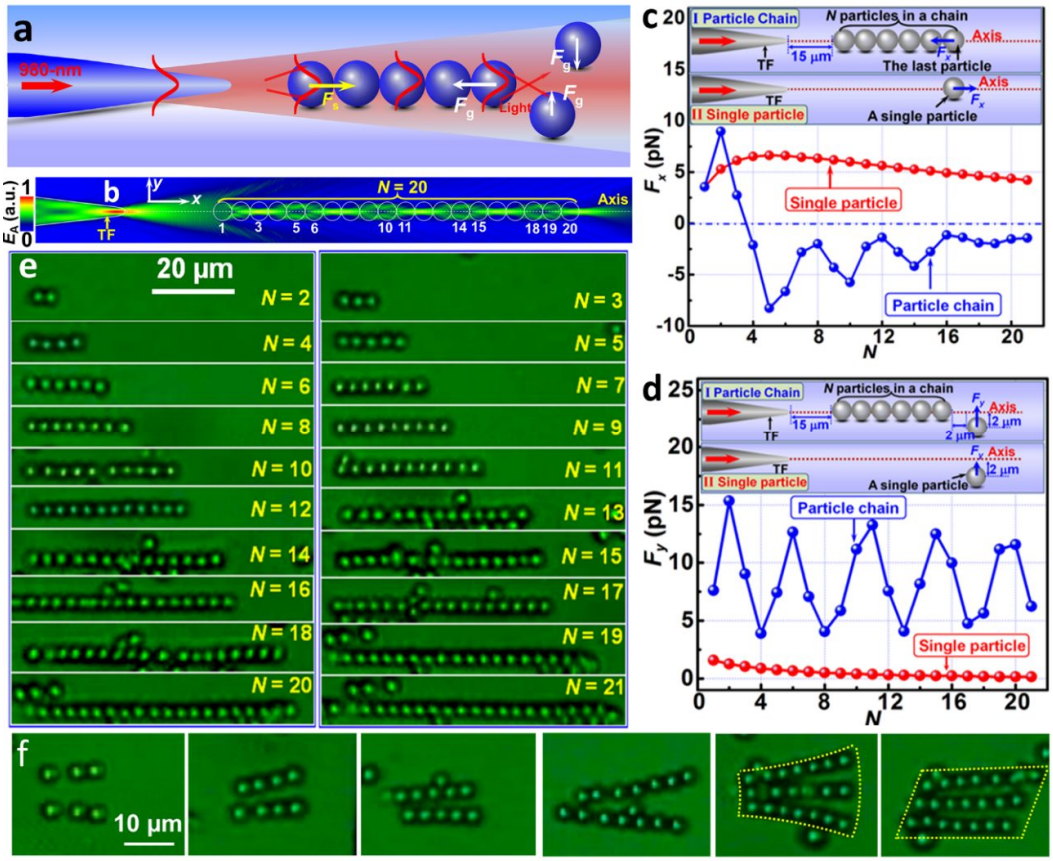

Figure 5. (a) Schematic illustration of multiple particle trapping and assembly by optical binding. (b) Simulation result of light propagation along multiple particles. (c,d) Calculation results of optical force exerted on particles in the (c) *x* and (d) *y* direction. (e) Optical microscopic image of assembled 1D particle chains with different particle numbers. (f) Optical microscopic image of assembled 2D particle arrays with different particle numbers.

2.5 Multiple cell trapping and patterning

In addition to the multiple particle/cell trapping and assembly by the cooperation of optical gradient force and scattering force, simply using optical gradient force can also result in multiple cell trapping[19,20]. As shown in Fig. 6a, multiple bacteria (*E. coli*) can be trapped one after another at the end of the OFTs by the optical gradient force (Fig. 6b). Light propagating along the trapped bacteria can be further refocused at the bacterium end, and generate an optical gradient force to other bacteria, resulting in multiple bacteria trapping and alignment. *E. coli* chains with different bacteria number were formed with different optical power (Fig. 6c). This method can also be used for the trapping and assembly of other cells, such as yeast cells (Fig. 6d) and human cells (Fig. 6e). In addition to the trapping and assembly of same cells at one time, this method can also be used for the trapping and assembly of cells with different types for cell patterning[20]. For example, we used the OFTs for the patterning of rod-shaped *E. coli* and spherical *Chlorella* cells. 1D cell patterns with different structures were assembled using this method (Fig. 6f). And light can still propagate along these cell patterns. This optical patterning strategy provides a new approach for cell patterning with controllable cell locations at single-cell resolution control.

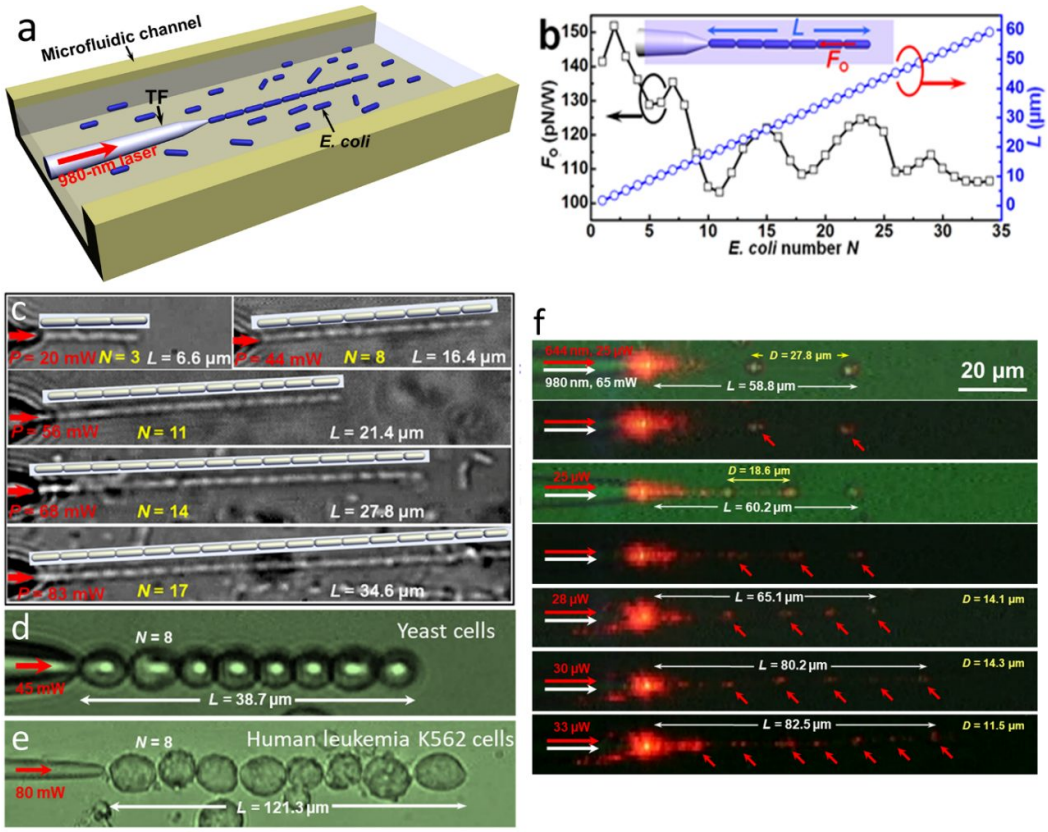

Figure 6. (a) Schematic illustration of multiple bacteria trapping and assembly by OFTs in a microfluidic channel. (b) Calculation results of optical force exerted on the last bacterium in the assembled bacteria chain as a function of bacteria number. (c) Optical microscopic image of assembled *E. coli* chains with different length. (d) Multiple trapping of yeast cells. (e) Multiple trapping of human leukemia K562 cells. (f) Multiple trapping and patterning of *E. coli* and *Chlorella* cells.

2.6 Biophotonic waveguides formation based on multiple *E. coli* trapping

The multiple cell trapping and assembly results indicate that light can propagate along cells and bacteria. Using this phenomenon, we fabricated biophotonic waveguides based on multiple trapped *E. coli*[21]. By simulation, we find that light can propagate along the *E. coli*-based biophotonic waveguide with a high efficiency (Fig. 7a), with a minimum energy larger than 60% of the input at the waveguide end with different lengths (Fig. 7b). With different optical power of the trapping laser beam (980 nm wavelength), waveguides with different lengths can be formed (Fig. 7c, left panel). The light propagation along these waveguides were observed using a visible laser (644 nm wavelength) (Fig. 7c, right panel). Compared with conventional optical waveguides based on silicon, the most important advantages of these biophotonic waveguides are that these waveguides are highly biocompatible and implantable, because these waveguides are directly formed with biological cells.

By modifying the end of the tapered optical fiber (Fig. 8a), the output light at the fiber end can be divided into three individual beams (Fig. 8b). Using these individual beams, we can form branched biophotonic structures based on multiple trapped *E. coli*[22]. For example, we can form biophotonic

structures with single branch, two branches, and three branches (Fig. 8c). Using a visible laser beam, we can observe the light propagation along these branched structures. These branches structures can be used as biophotonic splitters.

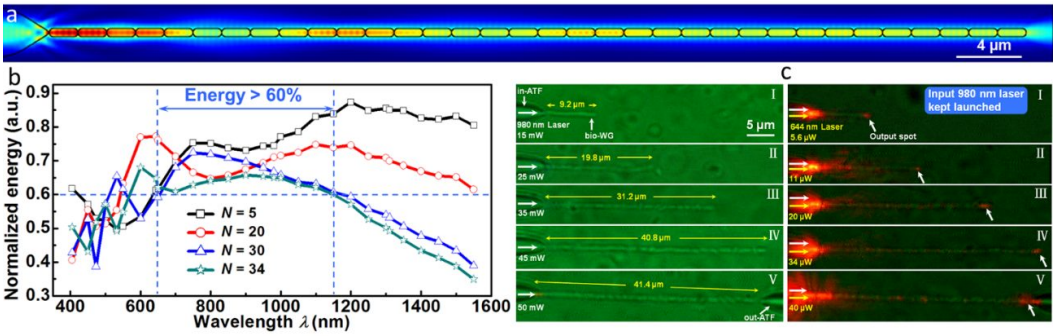

Figure 7. (a) Simulation result of light propagation along the *E. coli*-based biophotonic waveguide. (b) Simulation result of the energy at the end of waveguides with different lengths. (c) Optical microscope image of formed biophotonic waveguides with different lengths. Left panel: bright field, right panel: dark field showing the propagation of visible light.

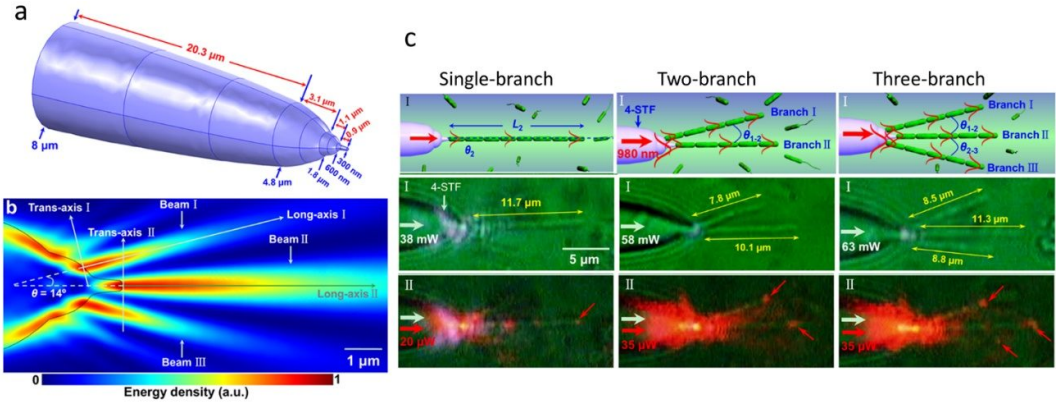

Figure 8. (a) Schematic illustration of modified tapered optical fiber. (b) Simulation result of light distribution with three individual beams output from the fiber end. (c) Formed branched biophotonic structures.

2.7 Plasmonic nanoparticles as optical nanoantennas for cellular exploration

The OFTs can be used for the manipulation and further analysis of cell individuals. However, if we want to get the information inside a cell, we need to go inside the cell to see what happens in the cell. Plasmonic nanoparticles can act as optical antennas for cellular exploration[3]. Using plasmonic nanoparticles, one

can get the molecular information inside the cell.

When a plasmonic nanoparticle is irradiated with light at the resonant wavelength (Fig. 9a), the free electrons in the conduction band are excited from the Fermi Level to a higher-energy surface plasmon state (Fig. 9b), and the far-field light is localized at the particle surface within a few nanometers. This local field enhancement enables the nanoparticle to act as an ultrasensitive receiving optical antenna. When this localized light interacts with a biomolecule near the particle surface, the molecule will be excited from the ground state (E_0) to an exited state (E_1). This excitation includes electronic excitation and vibrational excitation. This excitations are characteristic of the molecules, and therefore this molecular information serves as the molecular fingerprint for identification and can be detected from the light signal. In this case, the plasmonic nanoparticle acts as an optical antenna, by receiving the light signal, and then transmitting the molecular signal.

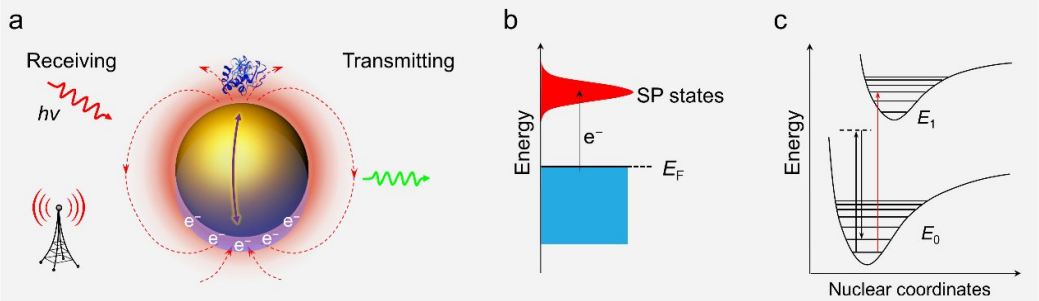

Figure 9. Plasmonic nanoparticle as optical nanoantenna. (a) Schematic illustration of a plasmonic nanoparticle as an optical nanoantenna when irradiated with resonant light.

When the optical nanoantenna interacts with a cell, it can be used for cellular exploration with different applications (Fig. 10). For example, outside the cell, it can be used for ion channel control. The high degree of spatial and temporal control of light by the plasmonic nanoparticles make them attractive candidates for regulating photothermal receptors at the cell membranes[23]. The plasmonic nanoparticles also enables ultrasensitive cellular targeting and imaging via the surface enhanced Raman spectroscopy (SERS)[24]. It can also control the endocytosis pathway, after internalized into the cell, it can be used for gene delivery by the controlled photothermal effect[25]. The intracellular molecular fingerprints can be detected by SERS or plasmon resonance energy transfer (PRET)[26] for in vivo molecular imaging. The plasmon coupling between individual optical antennas enables the real-time detection of mRNA in living cell[27].

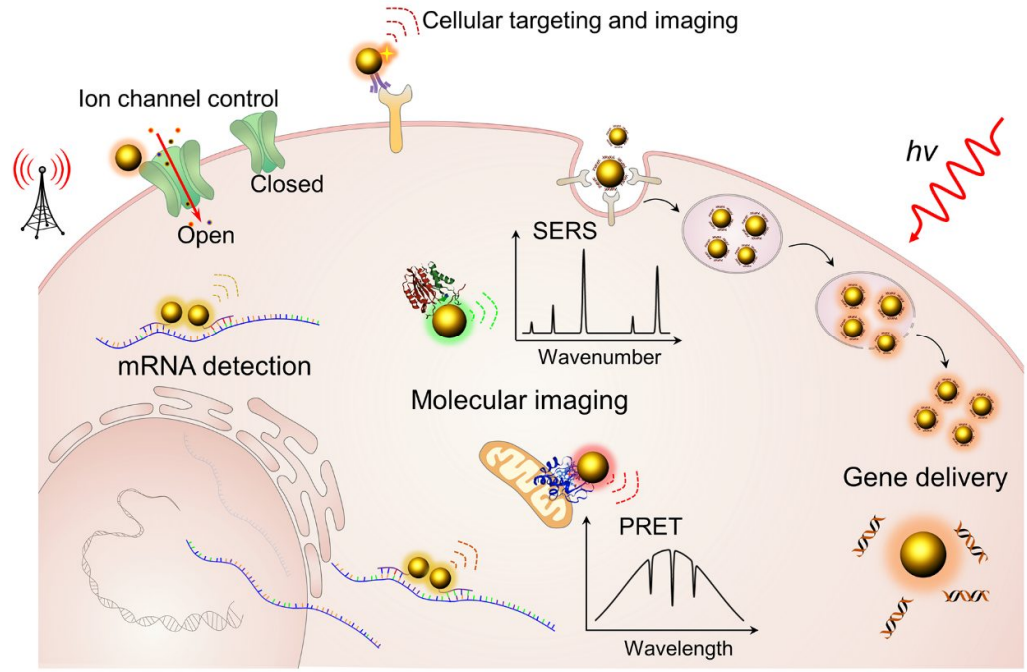

Figure 10. Plasmonic nanoparticle as an optical nanoantenna for cellular exploration with different functions.

3. CONCLUSIONS

In conclusion, we used different smart optical tools to explore the biological world. Using OFTs, we realized the stable trapping and flexible manipulation of particles, carbon nanotubes, cells and bacteria. The OFTs were also used for multiple trapping and assembly of cells. Based on multiple trapping of *E. coli*, we formed biophotonic waveguides and branched biophotonic structures with *E. coli*. We also discussed plasmonic nanoparticles as optical antennas for cellular exploration. These smart optical tools will provide huge possibilities to manipulate and explore the biological world.

REFRENCES

1 Grier, D. G. "A revolution in optical manipulation." Nature **424**(6950), 810 (2003).

2 Moffitt, J. R., Chemla, Y. R., Smith, S. B. and Bustamante, C. "Recent advances in optical tweezers." Annu. Rev. Biochem. **77**, 205-228 (2008).

3 Xin, H., Namgung, B. and Lee, L. P. "Nanoplasmonic optical antennas for life sciences and medicine." Nature Reviews Materials **3**, 228-243 (2018).

4 Goldman, D. H., Kaiser, C. M., Milin, A., Righini, M., Tinoco, I. and Bustamante, C. "Mechanical force releases nascent chain–mediated ribosome arrest in vitro and in vivo." Science **348**(6233), 457-460 (2015).

5 Ashkin, A., Dziedzic, J. M., Bjorkholm, J. and Chu, S. "Observation of a single-beam gradient force optical trap for dielectric particles." Optics letters **11**(5), 288-290 (1986).

6 Liu, Z., Guo, C., Yang, J. and Yuan, L. "Tapered fiber optical tweezers for microscopic particle trapping: fabrication and application." Optics express **14**(25), 12510-12516 (2006).

7 Xin, H., Xu, R. and Li, B. "Optical trapping, driving, and arrangement of particles using a

tapered fibre probe." Scientific reports **2**, 818 (2012).

8 Xin, H., Li, X. and Li, B. "Massive photothermal trapping and migration of particles by a tapered optical fiber." Optics Express **19**(18), 17065-17074 (2011).

9 Berthelot, J., Aćimović, S., Juan, M., Kreuzer, M., Renger, J. and Quidant, R. "Three-dimensional manipulation with scanning near-field optical nanotweezers." Nature nanotechnology **9**(4), 295-299 (2014).

10 Gong, Y., Huang, W., Liu, Q.-F., Wu, Y., Rao, Y., Peng, G.-D., Lang, J. and Zhang, K. "Graded-index optical fiber tweezers with long manipulation length." Optics Express **22**(21), 25267-25276 (2014).

11 Brambilla, G., Murugan, G. S., Wilkinson, J. and Richardson, D. "Optical manipulation of microspheres along a subwavelength optical wire." Optics letters **32**(20), 3041-3043 (2007).

12 Xin, H.and Li, B. "Targeted delivery and controllable release of nanoparticles using a defect-decorated optical nanofiber." Optics express **19**(14), 13285-13290 (2011).

13 Xin, H., Cheng, C. and Li, B. "Trapping and delivery of Escherichia coli in a microfluidic channel using an optical nanofiber." Nanoscale **5**(15), 6720-6724 (2013).

14 Xin, H., Liu, Q. and Li, B. "Non-contact fiber-optical trapping of motile bacteria: dynamics observation and energy estimation." Scientific reports **4**, 6576 (2014).

15 Xin, H., Li, Y., Xu, D., Zhang, Y., Chen, C. H. and Li, B. "Single Upconversion Nanoparticle–Bacterium Cotrapping for Single-Bacterium Labeling and Analysis." small **13**(14), 1603418 (2017).

16 Xin, H.and Li, B. "Optical orientation and shifting of a single multiwalled carbon nanotube." Light: Science & Applications **3**(9), e205 (2014).

17 Li, Y.-C., Xin, H.-B., Lei, H.-X., Liu, L.-L., Li, Y.-Z., Zhang, Y. and Li, B.-J. "Manipulation and detection of single nanoparticles and biomolecules by a photonic nanojet." Light: Science & Applications **5**(12), e16176 (2016).

18 Xin, H., Xu, R. and Li, B. "Optical formation and manipulation of particle and cell patterns using a tapered optical fiber." Laser & Photonics Reviews **7**(5), 801-809 (2013).

19 Xin, H., Zhang, Y., Lei, H., Li, Y., Zhang, H. and Li, B. "Optofluidic realization and retaining of cell–cell contact using an abrupt tapered optical fibre." Scientific reports **3**, 1993 (2013).

20 Xin, H., Li, Y. and Li, B. "Controllable patterning of different cells via optical assembly of 1D periodic cell structures." Advanced Functional Materials **25**(19), 2816-2823 (2015).

21 Xin, H., Li, Y., Liu, X. and Li, B. "Escherichia coli-based biophotonic waveguides." Nano letters **13**(7), 3408-3413 (2013).

22 Xin, H., Li, Y. and Li, B. "Bacteria-based branched structures for bionanophotonics." Laser & Photonics Reviews **9**(5), 554-563 (2015).

23 Rivnay, J., Wang, H., Fenno, L., Deisseroth, K. and Malliaras, G. G. "Next-generation probes, particles, and proteins for neural interfacing." Science Advances **3**(6), e1601649 (2017).

24 Pallaoro, A., Hoonejani, M. R., Braun, G. B.,Meinhart, C. D. and Moskovits, M. "Rapid identification by surface-enhanced Raman spectroscopy of cancer cells at low concentrations flowing in a microfluidic channel." ACS Nano **9**(4), 4328–4336 (2015)

25 Lee, S. E., Sasaki D. Y., Park, Y., Xu, R., Brennan, J. S., Bissell, M. J., and Luke, P. L. "Photonic gene circuits by optically addressable siRNA-Au nanoantennas." ACS Nano **6**(9), 7770–7780 (2012).

26 Liu, G. L., Long, Y.-T., Choi, Y., Kang, T. and Lee, L. P. "Quantized plasmon quenching dips

nanospectroscopy via plasmon resonance energy transfer." Nature Methods **4**(12), 1015–2017 (2007).

27 Lee, K., Cui, Y., Lee, L. P. and Irudayaraj, J. "Quantitative imaging of single mRNA splice variants in living cells." Nature Nanotechnology **9**(6), 474–480 (2014).