Chapter

Optical Fiber Tweezers for the Assembly of Living Photonic Probes

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Abstract

Optical fiber tweezers, as a versatile tool for optical trapping and manipulation, have attracted much attention in cell trapping, manipulation, and detection. Particularly, assembly of living cells using optical fiber tweezes has become a significant attention. Advanced achievements have been made on the assembly of fully biocompatible photonic probes with biological cells, enabling optical detection in biological environment in a highly compatible manner. Therefore, in this chapter, we discuss the use of optical fiber tweezers for assembly of living photonic probes. Living photonic probes can be assembled by the trapping and assembly of multiple cells using optical fiber tweezers. These photonic probes exhibit high biocompatibility and show great promise for the bio-applications in bio-microenvironments.

Keywords: Optical fiber tweezers, living photonic probes, optical trapping, optical manipulation, cell assembly

1. Introduction

The development of optical fiber tweezers (OFTs) makes it a versatile candidate for optical trapping and manipulation of targets ranging from different dielectric particles to biological cells and biomolecules [1–3]. This is because OFTs possess exceptional advantages in manipulation flexibility, due to the simple structure with only optical fibers. This simple structure also avoids the use of a high numerical-aperture objective which is necessary for the light focusing in conventional optical tweezers system [4, 5]. It is much easier to handle and manipulate the microscopic objects after trapped with OFTs [6, 7]. And it is much more suitable for practical use such as in trapping, levitating and rotating of microscopic particles in different environments [8–10]. The OFTs tip can be inserted into thick samples and turbid media, which greatly increases the sample applicability. In addition, OFTs exhibit a low-cost manipulation technique and can also be integrated into small devices, such as optofluidic channels [11]. OFTs enable the trapping and manipulation of different single targets. For the further biological detection in bio-environments, it is highly desired to form biocompatible photonic probes that can minimize the physical damage to the biological samples. Unfortunately, most photonic probes are made from inorganic and artificial materials, which are incompatible and invasive when interfacing with biological systems. It is still a big challenge to find out a biomaterial to assemble biophotonic probes that are noninvasive and highly biocompatible to

biological systems. Fortunately, it is found that living cells, which are abundant in the natural world, show the capability for light manipulation and propagation with high biocompatibility, and can thus be used for the assembly of living photonic probes. In this chapter, recent advances of OFTs in trapping and manipulating of cells, particularly in assembly of living photonic probes based on biological cells, were discussed. These formed living photonic probes provide a promising approach for bio-detection in biological environments with highly biocompatibility [12, 13].

2. Working principle of OFTs

OFTs, generally based on a tapered fiber probe, can be fabricated by drawing a commercial single-mode optical fiber through a flame-heating technique. The shape of OFTs tip can be controlled by controlling the heating temperature and the drawing speed. The operation principle of typical OFTs has been detailedly analyzed and described [14]. As schematically shown in **Figure 1a**, an OFT is immersed in water. D_A means the axial distance of a dispersed particle to the OFTs tip, while D_T means the transverse distance. With a laser beam launched into the OFTs, particle will be trapped and manipulated by the generated optical force. There two components of the optical force, *i.e.*, gradient force (F_g) and scattering force (F_s). F_g is directed to the region with stronger light intensity and

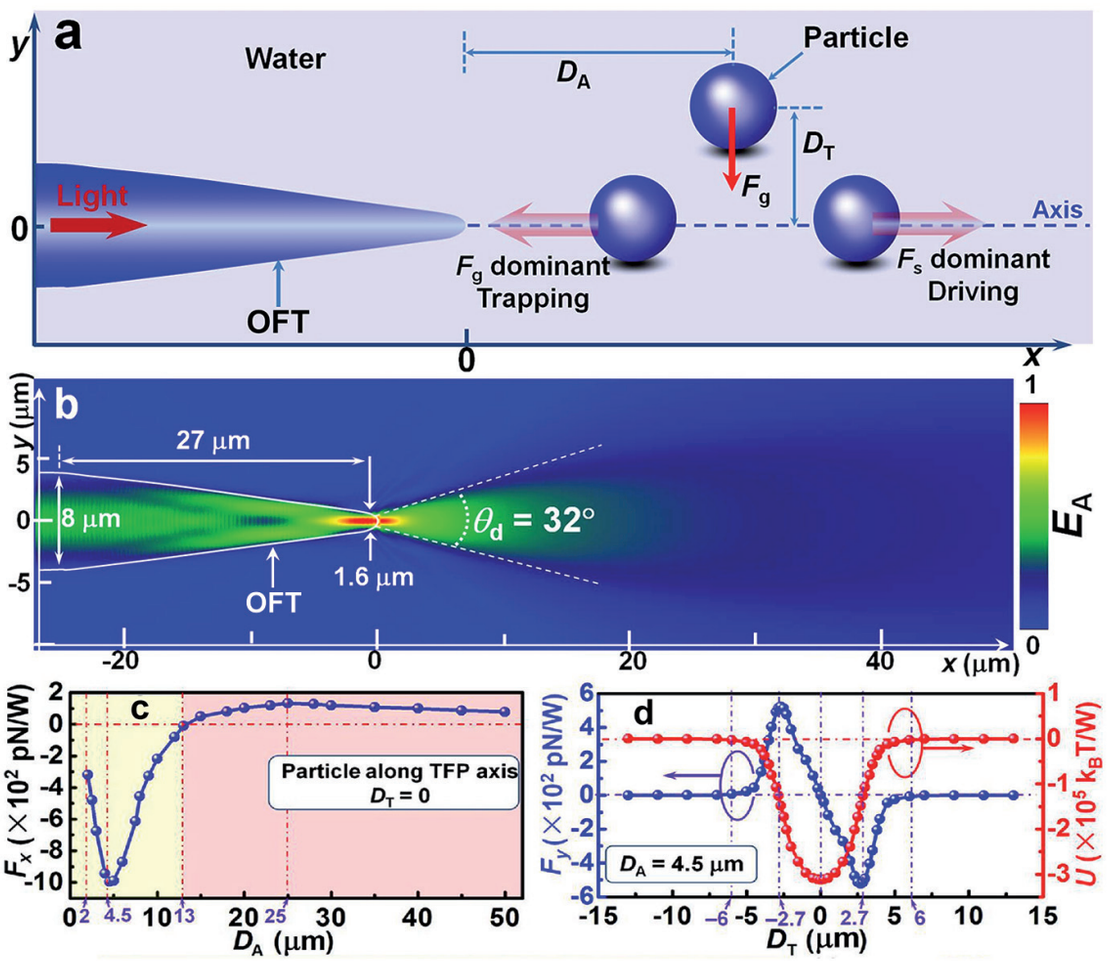

Figure 1.
Principle of a single optical fiber tweezers for trapping of particles [14]. (a) Schematic of particle manipulation by an OFT with light launched. (b) Simulated electric field amplitude (E_A) distribution by FDTD method. (c) Calculated optical force exerted on particles along the x direction. (d) Calculated optical force and trapping potential along the y direction.

is responsible to trap the particle, while F_s is directed along the light propagation and can push particles away from the OFTs tip. When a particle is near the axial axis of the OFTs, it will be trapped to the axis by F_g. For particle near the OFTs tip, the dominated F_g can trap the particle to the fiber tip. As the distance to the tip increases, F_s will become larger than F_g, and the dominated F_s will push the particle away from the fiber tip. The electric field amplitude (E_A) distribution around the OFTs was shown in **Figure 1b**, with a laser beam at a wavelength of 980 nm launched into the fiber probe. It can be seen that the light outputted from the OFTs is firstly focused at the tip and subsequently diverged out in water with a divergence angle of 32°. **Figure 1c** shows the calculated optical force exerted on a 3-μm silica particle along the x direction. It can be seen that, near the fiber tip, the force is negative, indicating a trapping force for particles. Therefore, particles near the fiber tip can be trapped by the OFTs. As the distance increases, the force is positive, indicating a driving force for particles. Therefore, particles can be pushed away by the OFTs. **Figure 1d** shows the calculated force and trapping potential in the y direction. It can be seen that the trapping potential on the axis is the smallest, and therefore particles beside the axis can be trapped at the axis. These optical forces enable the trapping capability of OFTs. By simply moving the fiber probe, the trapped particles can be manipulated in a highly flexible manner.

3. Manipulation of single cell and multiple cells by OFTs

OFTs can serve as a powerful tool for the trapping and manipulation of cells. Using *Escherichia coli* as an example, both single and multiple motile bacteria have been trapped and manipulated in a non-contact manner [15]. **Figure 2a** shows the experimental schematic for non-contact trapping of *E. coli* using OFTs. In this scenario, a laser beam at a wavelength of 980 nm was launched into the OFTs. A *E. coli* bacterium that was randomly swimming in the suspension was then trapped by the OFTs. The trapping was a non-contact trapping, and the bacterium was in the trapping position with several microns to the tip of the OFTs. During the trapping, the highly active bacterium was struggling around the trapping region. **Figure 2b–d** shows the detailed process for the trapping and struggling dynamics. The bacterium was trapped by the OFTs in a non-contact manner. However, due to the motility, the trapped bacterium was struggling after trapping. This phenomenon provides a new method for the studying of bacteria dynamics using OFTs.

In addition to the trapping and manipulation of single cells, OFTs can also be used for the trapping and assembly of multiple cells. For example, **Figure 3a** shows a schematic for the trapping and assembly of multiple *E. coli* cells in a microfluidic channel using OFTs [16]. Light output from the OFTs can trap the *E. coli* bacteria delivered by microfluidics. After a single bacterium was trapped, light can further propagate along the cell, and can be used for the trapping of other bacteria. Therefore, multiple bacteria can be trapped and assembled into cell chains with different lengths. To show the multiple trapping capability, **Figure 3b** shows the simulated light propagation along multiple cells. It can be seen that, light can propagate along the trapped cells, and the exerted optical force can be used for further trapping of other bacteria (**Figure 3c**). To experimentally demonstrate stable trapping and connecting of multiple *E. coli* cells with highly organized orientation, i.e., realization and retaining of *E. coli* cell–cell contact, the 980-nm wavelength laser with an optical power was launched into the fiber probe. **Figure 3d** shows the trapped multiple cells and formed cell chains with different numbers of cells at different input optical powers. By moving the fiber probe, the assembled cell chains can further be flexibly manipulated.

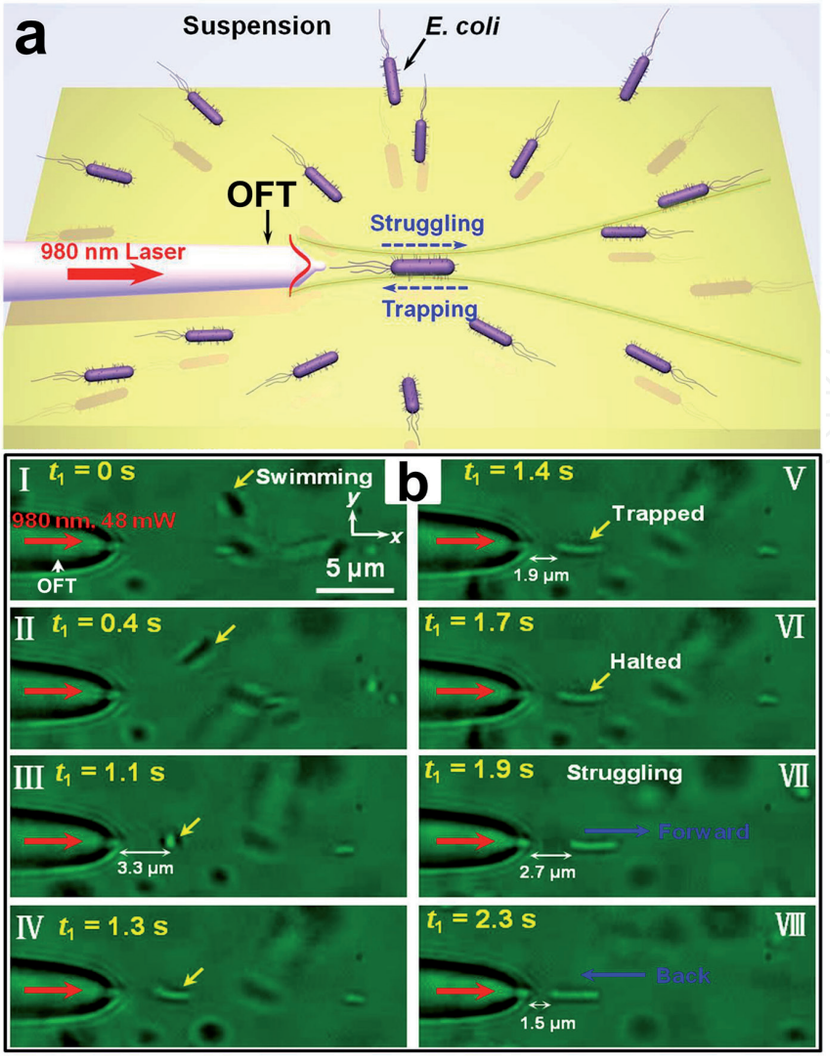

Figure 2.
Optical trapping of a single bacterium using OFTs [15]. (a) Schematic illustration of the non-contact optical trapping of a single bacterium and the struggling dynamics. (b) Optical microscope images of the trapping and struggling process of a single bacterium.

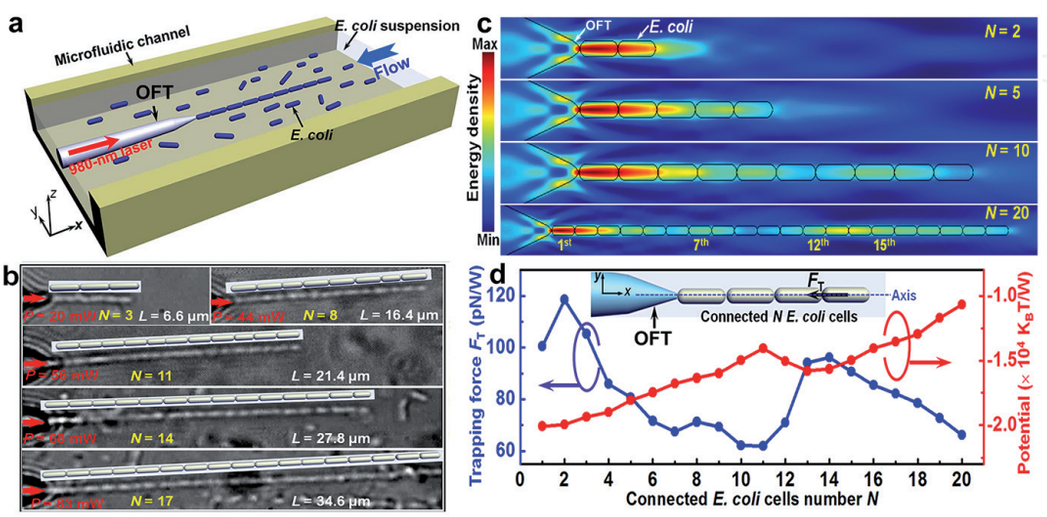

Figure 3.
Optical trapping of multiple cells using OFTs [16]. (a) Schematic of multiple E. coli trapping using OFTs. A laser at 980 nm wavelength was launched into the fiber probe which was placed in a microfluidic channel with a flowing suspension of E. coli cells. Multiple E. coli cells were trapped and connected orderly at the tip of the fiber probe. (b) Simulated light propagation along multiple bacteria. (c) Simulated light distribution along the assembled cell chains. (d) Calculated optical trapping force exerted on the last cell of each cell chain and the trapping potential.

4. Assembly of cell-based biophotonic waveguides by OFTs

Based on the multiple cell trapping capability of OFTs, direct formation of biophotonic waveguides with *E. coli* were reported [17]. By launching a laser of 980 nm wavelength into the OFTs, multiple *E. coli* were trapped and connected together with highly ordered organizations, forming biophotonic waveguides with different lengths (**Figure 4a**). By coupling a visible laser beam into the formed biophotonic waveguides, light propagation along these biophotonic waveguides can be directed observed as indicated by the red-light spots at the end of the waveguides (**Figure 4b**). The light propagation loss along the formed waveguides can be measured using an optical power meter by coupling another tapered optical fiber at the end of the formed biophotonic waveguide. As shown in **Figure 4c** and **d**, the measured propagation loss was measured to be 0.23 dB/μm.

In addition to the linear biophotonic waveguides, using OFTs, branched photonic probes can also been assembled. For example, **Figure 5** shows the assembled branched photonic probes with *E. coli* bacteria [18]. By designing a specially segmented tapered optical fiber, light output from the fiber can be divided into three individual beams, and *E. coli* bacteria can be trapped by the individual beams, further forming into branched biophotonic probes with different lengths (**Figure 5**). These branched photonic probes show strong stability, and can be used for further applications. By moving the OFTs, the formed biophotonic probes can be flexibly manipulated to different designated positions for further applications. These results show that the OFTs offer a seamless interface between optical and biological worlds for biophotonic probes formation with natural

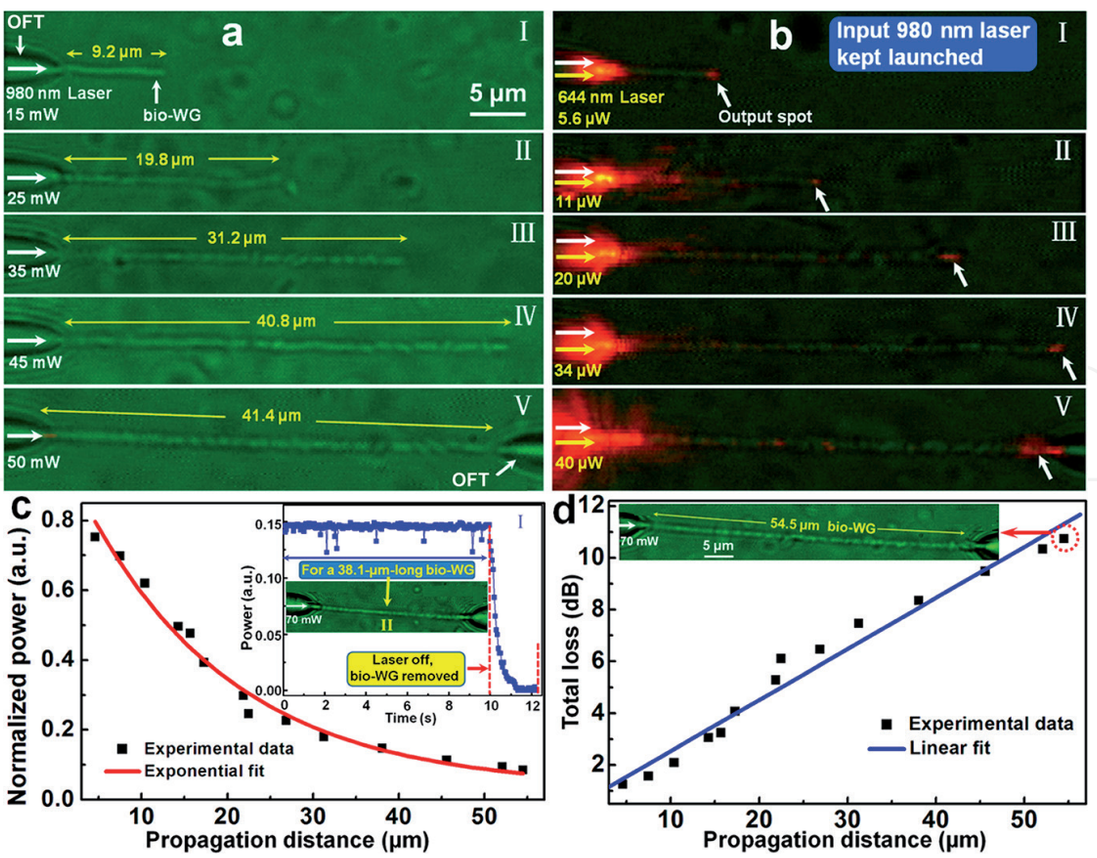

Figure 4.
Biophotonic waveguides formation [17]. (a) Optical microscope images of formed bio-waveguides (bio-WGs) with different lengths. (b) Light propagation observation along the formed biophotonic waveguides. (c) Normalized optical power measured at the end of each waveguides. (d) Measured optical loss of the waveguides.

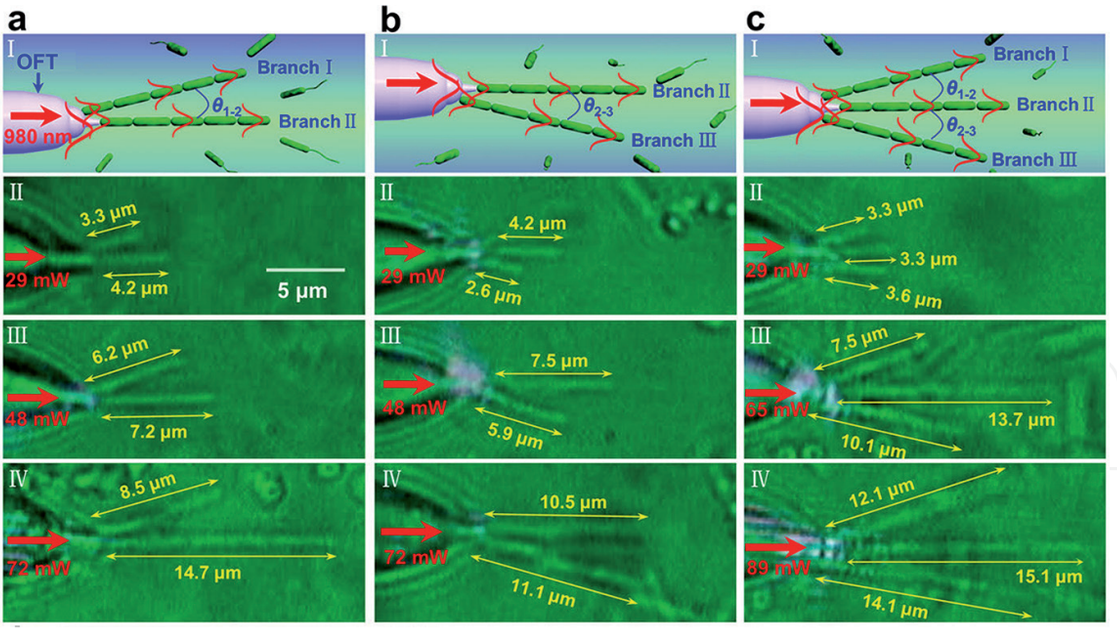

Figure 5.
Optical assembly of branched biophotonic structures [18]. (a, b) Assembly of two-branch structures. (c) Assembly of three-branch structures.

materials, and provides a new opportunity for direct sensing and detection of biological signal and information in biocompatible microenvironments.

5. Assembly of cell-based periodical structures by OFTs

In addition to the assembly of biophotonic waveguides with one type of cells, assembly of periodical structures of different types of cells was also demonstrated using OFTs [19]. Using *E. coli* cells and *Chlorella* cells as examples, different cells are flexibly patterned into one-dimensional (1D) periodic cell structures with controllable configurations and lengths (**Figure 6**), by periodically connecting one type of cells with another by optical force. Further demonstration shows that the structures show good performance for light propagation and can be moved flexibly. Real-time light signals can be detected from these photonic structures. These features make these photonic structures excellent candidates for the detection of signals transducing among different patterned cells. This assembly and patterning technique can also be applicable for other cells, such as mammalian cells and human cells.

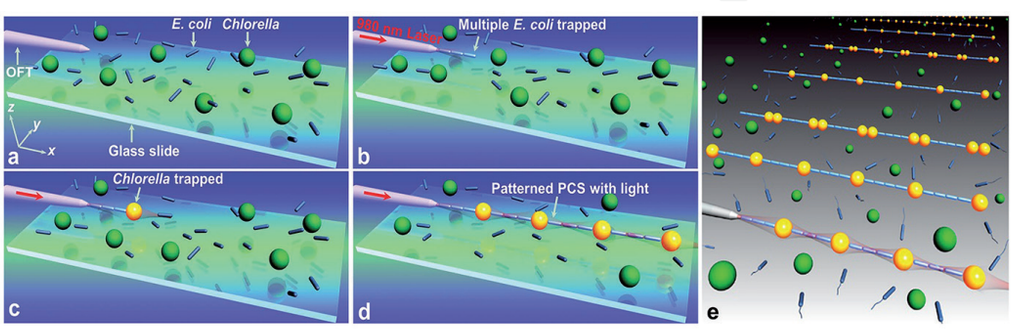

Figure 6.
Experimental schemes for cell assembly into periodical structures [19]. (a) an OTF is placed in cell suspensions. (b) Laser launched, multiple E. coli cells trapped. (c) a Chlorella cell is trapped and connected to the former trapped E. coli cells. (d) a periodical structure is formed, and light propagates along the periodical structure. (e) Schematic shows the assembled periodical biophotonic structures.

6. Assembly of cell-based structures in vivo by OFTs

The assembly capability can also be used for in vivo applications. For example, a non-contact intracellular binding and controllable manipulation of chloroplasts *in vivo* was demonstrated using OFTs [12]. By launching a laser beam at 980 nm wavelength into the tapered fiber, which was placed above the surface of a living plant (*Hydrilla verticillata*) leaf with a gap of about 3 μm to the leaf surface, chloroplasts with different numbers were stably bound and arranged into one-dimensional chains and two-dimensional arrays inside the leaf by optical force without damage to the chloroplasts, by the cooperation of scattering force F_s and gradient force F_g (**Figure 7**). The formed chloroplast chains were controllably transported inside the living cells. This non-invasive and non-contact method of organelle binding and manipulation could provide a way for biological and biochemical research *in vivo*, especially for investigating signal transduction and communication between intracellular organelles via organized organelle-organelle contact.

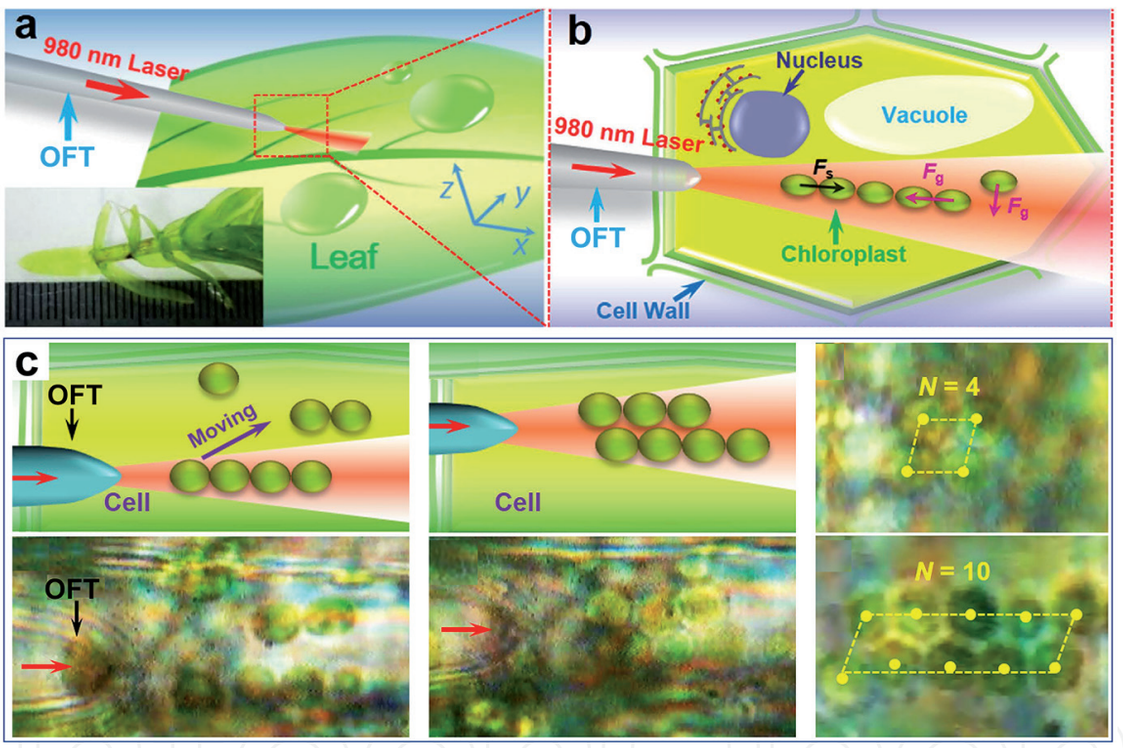

Figure 7.
Assembly of biophotonic probes in vivo [12]. (a) Schematic illustration of biophotonic probe assembly inside a leaf using OFTs. (b) Schematic illustration of biophotonic probe assembly based on a chain of chloroplasts. The chloroplasts inside a leaf are trapped and assembled by the cooperation of F_g and F_s. (c) Schematics and microscope images of the manipulation and assembly of organelle-based biophotonic probes in vivo.

7. Assembly of living photonic probe by OFTs for bio-probing and detection

Recently, using OFTs, a fully biocompatible living photonic probe for subwavelength probing of localized fluorescence from leukemia single-cells in human blood has been created [13]. The high-aspect-ratio living photonic probe based on a yeast cell (1.4 μm in radius) and Lactobacillus acidophilus (*L. acidophilus*) cells (2 μm in length and 200 nm in radius) is formed at the tip of a tapered optical fiber by optical trapping (**Figure 8a**). In the assembly, the authors have precisely moved the fiber to approach a yeast cell. Benefited from the spherical shape of the yeast,

the trapping laser beam was focused into a tiny region and exerted a strong optical force on a *L. acidophilus* cell that traps it behind the yeast. With this alignment, the trapping laser beam propagates through the *L. acidophilus* cell and exert an optical force on other *L. acidophilus* cells, which were orderly bound together by optical binding effect and finally formed the living photonic probe. **Figure 8b** shows a formed probe assembled with a yeast and five *L. acidophilus* cells. To view the light propagation, after assembly of the probe, the trapping laser remained on, and a visible illumination light was launched into the probe. **Figure 8c–e** show the illumination light propagating along the tapered fiber. At the output port of the probe, a tiny light spot was observed with full width at half maximum (FWHM) of 345, 282, and 248 nm for the illumination wavelengths of 644, 532, and 473 nm, respectively.

As a benefit of the highly focused effect of the living cells, the living photonic probe can also deliver subwavelength excitation light to biological samples, and detect optical signals with a subwavelength spatial resolution. Moreover, within human blood, selective probing of the localized fluorescent signals on single leukemia cell surface can be realized via the precise manipulation of the living photonic probe. Due to the high biocompatibility and resolution, these photonic probes hold great promises for biosensing and imaging in bio-microenvironment. Furthermore, the living photonic probe can be integrated in the available near-field scanning optical microscopy, functioning as a biocompatible and non-invasive scanning probe for near-field imaging of living cells. **Figure 9**, as an example, shows the use of the living photonic probe in probing localized fluorescence of leukemia cells in human blood [13]. **Figure 9a–d** shows the spot excitation capability by manipulating the living photonic probe to approach the cell membrane. As shown in **Figure 9a**,

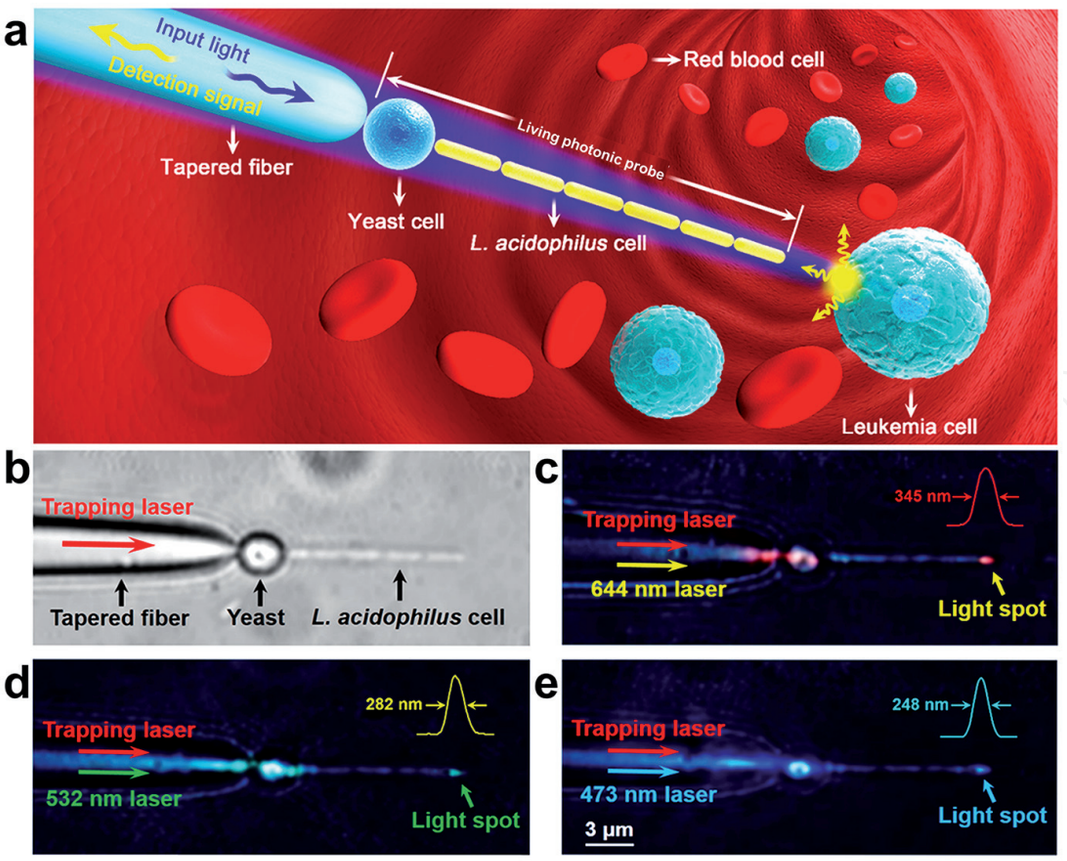

Figure 8.
Assembly of living biophonic probes for bio-probing [13]. (a) Schematic illustration for assembly of living photonic probe by OFTs. (b) Image of a formed living photonic probe. (c)-(e) images showing light propagation along the formed living photonic probes. Light spots can be observed at the end of each photonic probes.

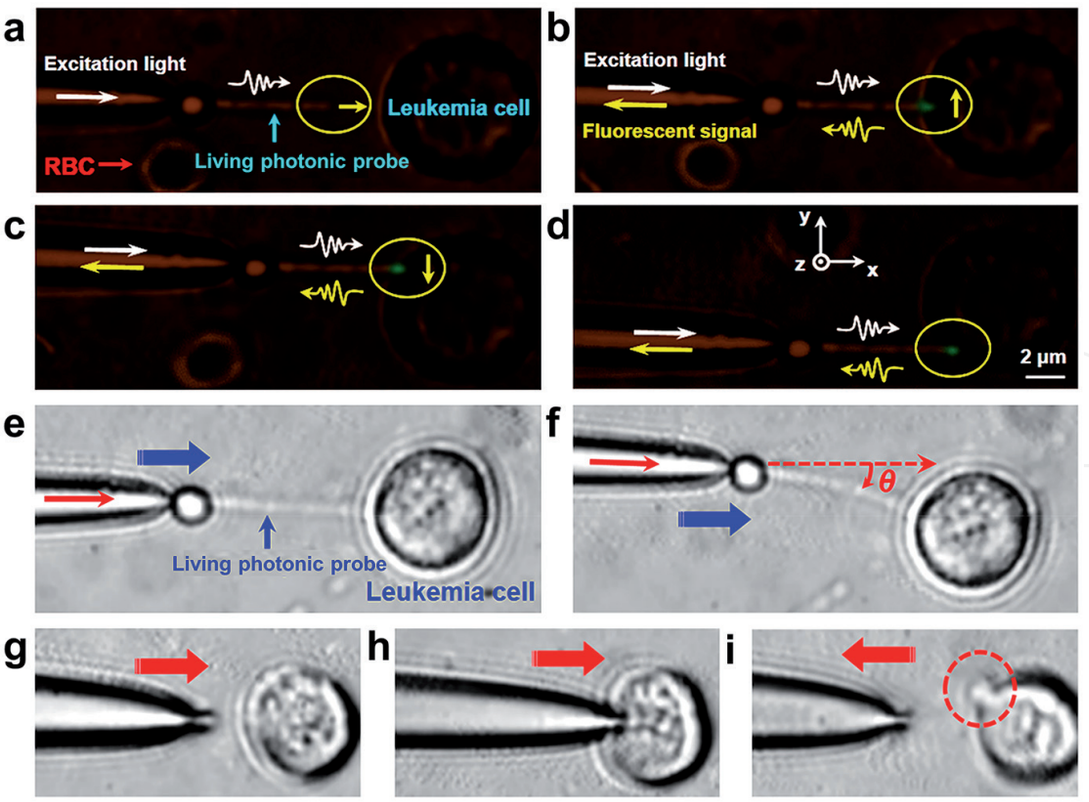

Figure 9.
Living photonic probe for single-cell probing and detection [13]. (a-d) Excitation and detection of local fluorescence from a leukemia cell in human blood by manipulating the living photonic probe to scan a cell. (e,f) Flexibility testing of the probe by pushing the probe against the leukemia cell membrane. (g-i) Touching and punching of the cell directly using a tapered optical fiber tip, to compare the flexibility of the living photonic probe.

there was no fluorescent signals when the distance between the living photonic probe and the surface of a leukemia cell was 3 μm. But the fluorescent signal was detected with a distinct fluorescent spot observed at the cell membrane when the probe was in contact with the cell (**Figure 9b**). The fluorescent signals at other locations were also detected by scanning the cell surface via precisely moving the probe (**Figure 9c** and **d**). Flexibility and deformability of the living photonic probe have also been demonstrated by interacting with biospecimens. As shown in **Figure 9e** and **f**, the living photonic probe was forced against a leukemia cell, then the living photonic probe was bent to an angle θ of 15° without puncture to the cell membrane. A certain degree of the deformability of the probe has no obvious influence on the scanning capabilities. For comparison, the authors pushed a fiber probe with a sub-micrometer tip, which is commonly used in scanning probe microscopes, against the leukemia cell (**Figure 9g**). As a result of the relatively large dimension and rigid structure, the fiber probe could easily insert into the cell (**Figure 9h**), and rupture the cell membrane (**Figure 9i**).

8. Conclusions

In this chapter, we reviewed the trapping and assembly of biological cells using OFTs, and finally extended the trapping capability for the assembly of living photonic probes such as cell-based biophotonic waveguides, cell-based periodical structures, cell-based structures in vivo, and living photonic probe for bio-probing and detection. These living photonic probes exhibit extremely high biocompatibility for further biological applications in bio-environment. As a benefit of the

light focusing ability of the cells, the biocompatible living photonic probes allow the trapping, manipulation, sensing, and diagnostics in vivo. Furthermore, the living photonic probes assembled using OFTs offer an biophotonic bridge between optical and biological worlds with natural materials. With the advantages of its biocompatibility, the living photonic probes are envisioned to provides a new opportunity for direct sensing and detection of biological signal and information in biocompatible microenvironments.

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Conflict of interest

The authors declare no competing financial interests.

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References

[1] Ashkin A, Dziedzic JM, Bjorkholm J. Observation of a single-beam gradient force optical trap for dielectric particles. Opt. Lett. 1986;11:288-290. DOI: 10.1364/OL.11.000288

[2] Ashkin A, Dziedzic JM. Optical trapping and manipulation of viruses and bacteria. Science. 1987;235:1517-1520. DOI: 10.1126/science.3547653

[3] Zhao X, Zhao N, Shi Y, Xin H. Optical fiber tweezers: a versatile tool for optical trapping and manipulation. Micromachines. 2020;11:114. DOI: 10.3390/mi11020114

[4] Fuh MRS, Burgess LW,Hirschfeld T. Single fiber optic fluorescence pH probe.Analyst. 1987;112:1159-1163. DOI: 10.1039/an9871201159

[5] Hu Z, Wang J, Liang J. Manipulation and arrangement of biological and dielectric particles by a lensed fiber probe. Opt. Express. 2004;12:4123-4128. DOI: 10.1364/OPEX.12.004123

[6] Lyons ER, Sonek GJ. Confinement and bistability in a tapered hemispherically lensed optical fiber trap. Appl. Phys. Lett. 1995;66:1584-1586. DOI: 10.1063/1.113859

[7] Taguchi K, Ueno H, Hiramatsu T. Optical rapping of dielectric particle and biological cell using optical fiber. Electron. Lett. 1997;33:413-414. DOI: 10.1049/el:19970247

[8] Taguchi K, Ueno H, Ikeda M. Rotational manipulation of a yeast cell using optical fibers. Electron. Lett. 1997;33:1249-1250. DOI: 10.1049/el:19970827

[9] Taguchi K, Atsuta K, Nakata T. Levitation of a microscopic object using plural optical fibers. Opt. Commun. 2000;176:43-47. DOI: 10.1016/S0030-4018(00)00499-5

[10] Frick M, Haller T, Dietl P. Combined optical tweezers and optical stretcher in microscopy. SPIE. 2001;4434:227-232. DOI: 10.1117/12.446684

[11] Ribeiro RSR, Soppera O, Oliva AG. New trends on optical fiber tweezers. J. Lightwave Technol. 2015;33:3394-3405.

[12] Li Y, Xin H, Liu X. Non-contact intracellular binding of chloroplasts in vivo. Sci. Rep. 2015;5:10925. DOI: 10.1038/srep10925

[13] Li Y, Xin H, Zhang Y. Living nanospear for near-field optical probing. ACS Nano. 2018;12:10703. DOI: 10.1021/acsnano.8b05235

[14] Xin H, Xu R, Li B. Optical trapping, driving, and arrangement of particles using a tapered fiber probe, Sci. Rep. 2012;2:818. DOI: 10.1038/srep00818

[15] Xin H, Liu Q, Li B. Non-contact fiber-optical trapping of motile bacteria: dynamics observation and energy estimation. Sci. Rep. 2014;4:6576. DOI: 10.1038/srep06576

[16] Xin H, Zhang Y, Lei H. Optofluidic realization and retaining of cell-cell contact using an abrupt tapered optical fiber. Sci. Rep. 2013;3:1993. DOI: 10.1038/srep01993

[17] Xin H, Li Y, Liu X. Escherichia coli-based biophotonic waveguides. Nano Lett. 2013;13:3408. DOI: 10.1021/nl401870d

[18] Xin H, Li Y, Li B. Bacteria-based branched structures for bionanophotonics. Laser Photonics Rev. 2015;9:554. DOI: 10.1002/lpor.201500097

[19] Xin H, Li Y, Li B. Controllable patterning of different cells via optical assembly of 1D periodic cell structures. Adv. Funct. Mater. 2015;25:2816. DOI: 10.1002/adfm.201500287