Biophotonic probes for bio-detection and imaging

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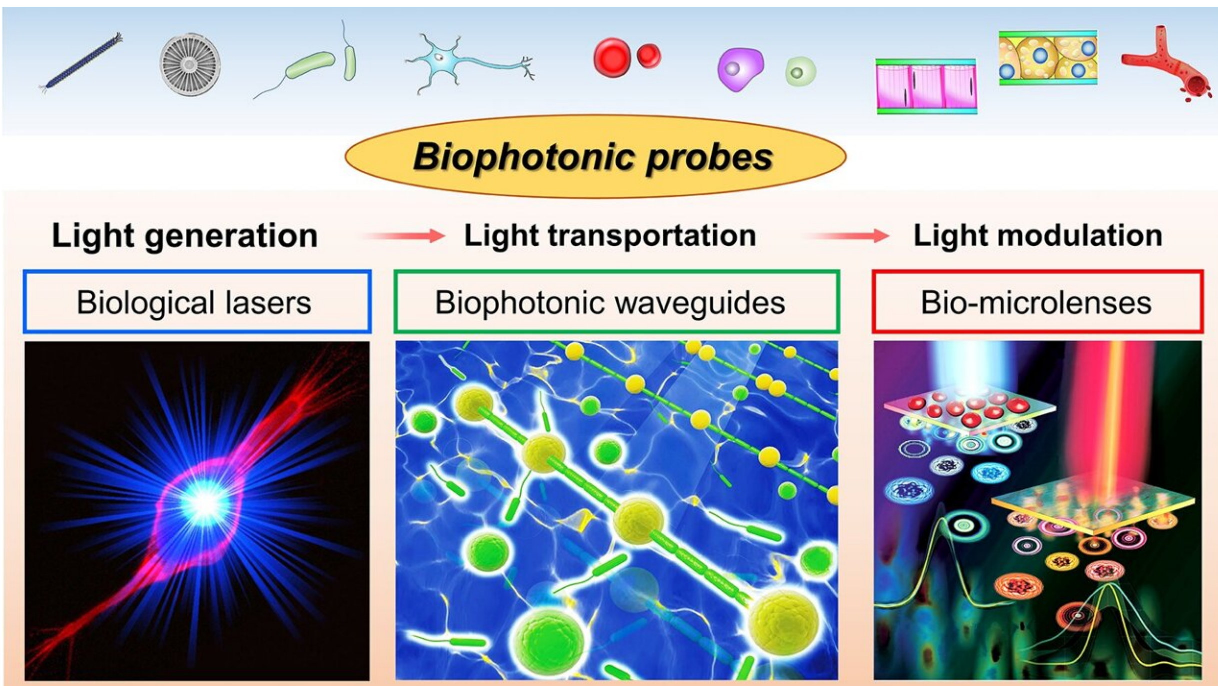

Different biological entities, such as virus, algae & bacteria, mammalian cells, and tissues, can be used for the formation of biophotonic probes, such as biological lasers, biophotonic waveguides, and bio-microlenses, with optical functions from light generation, to light transportation and light modulation. Credit: Ting Pan, Dengyun Lu, Hongbao Xin and Baojun Li

Sensitive detection and imaging in bio-microenvironment is highly desired in biophotonic and biomedical applications. However, conventional photonic materials inevitably show incompatibility and invasiveness to bio-systems. To address this issue, Scientists in China reviewed recent progresses of biophotonic probes, including bio-lasers, biophotonic waveguides, and bio-microlenses, made from biological entities with inherent biocompatibility and minimal invasiveness, with applications for bio-detection and imaging. These biophotonic probes open up entirely new windows for biophotonic researches and biomedical applications.

The rapid development of biophotonics and biomedical sciences makes a high demand on photonic structures that are capable of manipulating light at small scales for sensitive detection of biological signals and precise imaging of cellular structures in bio-microenvironment. Unfortunately, conventional photonic structures based on artificial materials (either inorganic or toxic organic) inevitably show incompatibility and invasiveness when interfacing with biological systems. The design of biophotonic probes from the abundant natural materials, particularly biological entities such as virus, cells and tissues, with the capability of multifunctional light manipulation at target sites can greatly increase the biocompatibility and minimizes the invasiveness to biological microenvironment.

In a new paper published in *Light Science & Application*, a team of scientists, led by Professor Baojun Li and Professor Hongbao Xin from Institute of Nanophotonics, Jinan University, China, reviewed the intriguing progresses of emerging biophotonic probes made from biological entities, such as virus, bacteria, cells and tissues, for bio-detection and imaging. They systematically reviewed three biophotonic probes with different optical functions, i.e., biological lasers for light generation, cell-based biophotonic waveguides for light transportation, and bio-microlenses for light modulation.

To realize their potential biomedical applications of photonic probes, effective control and modulation of light generation are particularly important in various biochemical environments. In this regard, the unique properties of light emitted by lasers, including high intensity, directionality and monochromatic emission, have rendered lasers one of the most useful tools in biomedical applications. Unlike traditional laser devices, bio-lasers utilize biological entities such as cells, tissues and virus, as part of the cavity and/or gain medium in a biological system. Bio-lasers can be categorized into three types, i.e., cell lasers, tissue lasers and virus lasers. These bio-lasers avoid the biohazards of conventional laser devices. Since their optical output is tightly related to the biological structures and activities of the biological systems, bio-lasers can serve as highly sensitive tools in a range of biomedical applications, including cellular tagging and tracking, diagnostics, intracellular sensing, and novel imaging. For example, whispering gallery modes (WGM) microdisks with slightly different diameters resulted in obviously different lasing output spectra. Intracellular cell lasers realized by incorporating these microdisks into cells enabled tagging and tracking of individual cells from large cell populations at the same time.

In addition to bio-lasers for bio-detection and imaging in biological systems, optical waveguides also play important roles in bio-microenvironments. As the main component for light transportation, optical waveguides can deliver light signals in bio-microenvironments for further real-time analysis, and optical waveguides play irreplaceable role to break the tissue penetration limit of light by transporting light into deep tissues. To solve the problem of invasiveness and low-biocompatibility of conventional materials-based optical waveguides, living cells hold huge potential for in situ formation of biophotonic waveguide that are inherently elastic, biocompatible, and biodegradable. The refractive index of biological cell (around 1.38) is slightly higher than that of water (around 1.33), thus allowing light guiding through a chain of cells by total internal reflection at the interface of the cell membrane and the water. A feasible and noninvasive approach to assemble cell-based biophotonic waveguides is optical trapping. By using laser light launched by a tapered optical fiber, biophotonic waveguides can be formed by assembling a chain of bacteria cells through optical force. Light propagation is allowed through cell chains over tens of microns. In another case, nonlinear optical effects have also been applied for biophotonic waveguides formation based on living cells, including algae and red blood cells (RBCs), achieving stable long-distance propagation of light with low loss in biological environments. These cell-based biophotonic waveguides can be performed as a biophotonic probe for cell imaging and biological microenvironment detection. For example, biophotonic waveguides formed by RBCs provide a potential detection technique for blood pH sensing and diagnosis of blood related disorders.

Optical lenses are another important optical device designed for light modulation. Interestingly, some living biological cells can confine light in biological systems, acting as bio-microlenses. One typical example is the cyanobacteria, which act as spherical microlenses, confining light into a focal spot near the plasma membrane at the rear side to the light source. On a higher level of cellular complexity, many mammalian cells also exhibit lensing behavior. The intrinsic deformability and the lack of nucleus and organelles make RBC a sort of disk-shaped microstructured envelope that is exploitable as adaptable bio-microlens. Since morphological abnormalities of RBCs are closely coupled with blood-related diseases, RBCs with biolensing property can be exploited as a noninvasive, label-free, and fast screening tool to identify abnormal RBCs from healthy cases. The biological cells have also been applied as biomagnifier for label-free imaging of living cells or other nanostructures.

These biophotonic probes open up entirely new opportunities for biophotonic researches and also for biomedical applications, e.g., bio-lasers for bio-detection, cell tagging and tissue imaging, biophotonic waveguides based on living cells for optical detection and sensing, and bio-microlenses for single-cell imaging and blood diagnostics. Compared with conventional photonic components, these biophotonic probes exhibit many remarkable advantages. First, they offer inherent and favorable opportunities for biocompatibility and biodegradability in comparison to traditional synthetic materials. Additionally, the development of biophotonic probes using biological cells/tissues let these biological entities serve simultaneously as optical components and testing samples, which facilitate in vivo and real-time sensing, detection, and imaging.

Despite the significant progresses already achieved, the authors emphasize that the overall development of biophotonic probes is still in its infancy and there is still much to be explored. They noted that more efforts are still needed to fully understand and to discover the broad and diverse family of living organisms that are suitable to serve as photonic probes. Besides, so far, most concepts and techniques have been demonstrated by in vitro or animal studies as proof on concept. Much future work is necessary to prove the feasibility in preclinical and clinical practical applications. They also suggested that biophotonic probes, for example, bio-microlenses, integrated into a smartphone-based platform has great potential in bio-detection, imaging, molecular diagnosis with clinical samples in a portable way in real time, which is of great importance in resource-limited regions.

More information: Ting Pan et al, Biophotonic probes for bio-detection and imaging, *Light: Science & Applications* (2021). DOI: 10.1038/s41377-021-00561-2

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