Optical-resolution photoacoustic microscopy innovation enables simultaneous multicontrast imaging

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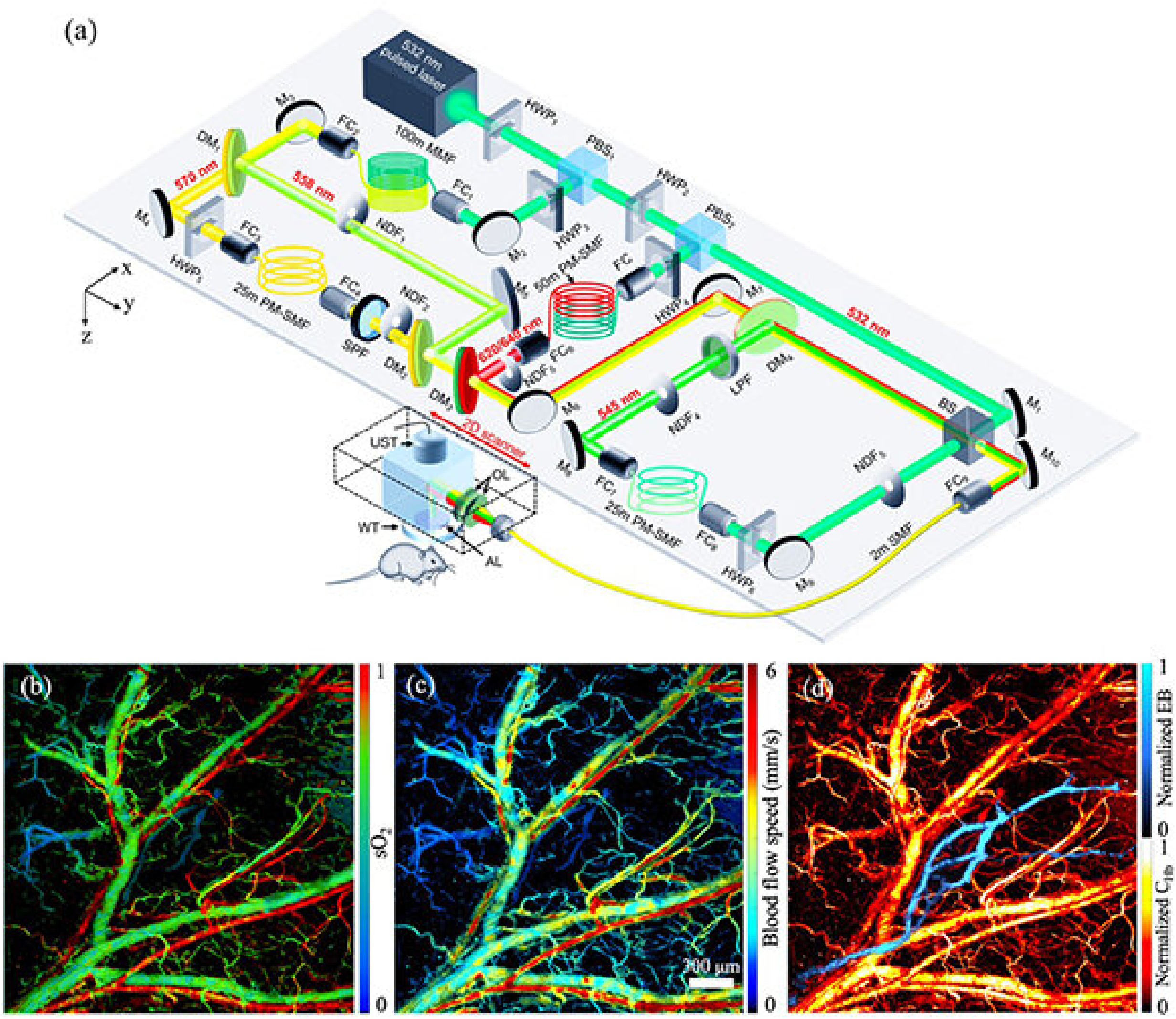


OR-PAM system (a) and image of (b) sO2, (c) BF, and (d) CHb and lymphatic concentration. Credit: SPIE

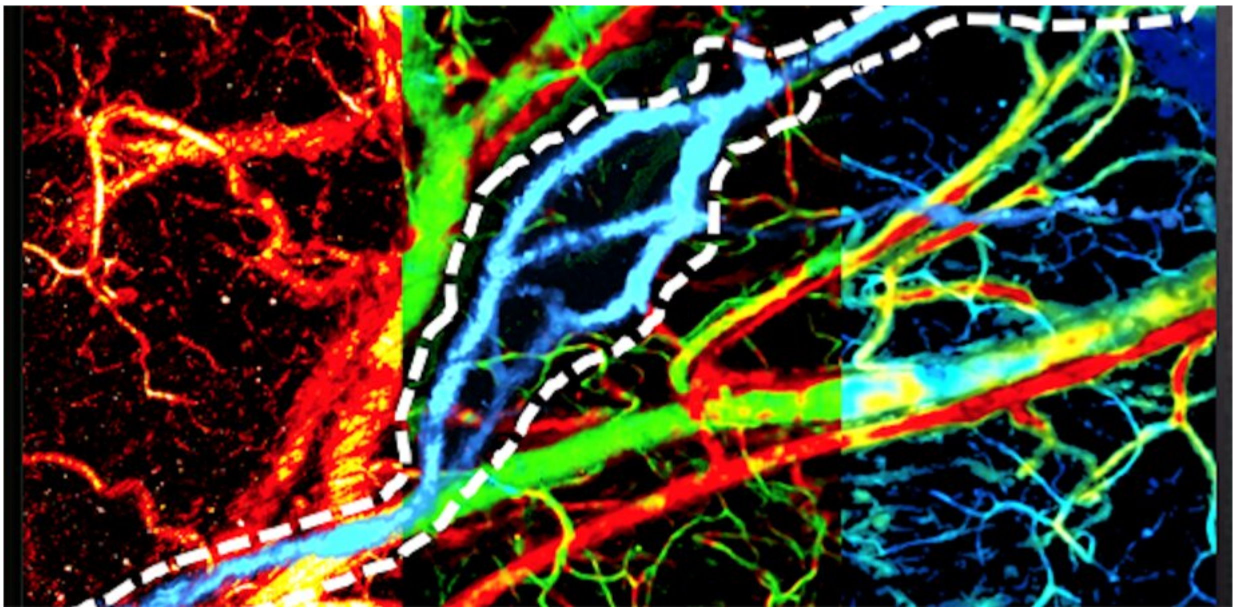
Optical-resolution photoacoustic microscopy (OR-PAM), a new hybrid imaging technique, allows us to listen to the sound of light and see the color of biological tissue itself. It can be used for live, multicontrast functional imaging, but the limited wavelength choice of most commercial lasers and the limitations of the existing scanning methods have meant that OR-PAM can obtain only one or two different types of contrast in a single scan. These limitations have made multicontrast functional imaging time-consuming, and it's been difficult to capture the dynamic changes of functional information in biological tissues.

To overcome these limitations, Lidai Wang and his research team at City University of Hong Kong recently developed a multiwavelength OR-PAM system based on a single laser source. As reported in *Advanced Photonics*, the novel system enables simultaneous multicontrast imaging of hemoglobin concentration, blood flow speed, blood oxygen saturation, and lymphatic concentration. This functional information can provide significant subcellular insights for scientists studying disease models, for instance in cancer research.

Optical-resolution photoacoustic microscopy

Based on the intrinsic absorption properties of the targeted biological tissue, photoacoustic imaging takes advantage of the fact that when tissue is targeted by a pulsed laser beam, it absorbs the light and generates instantaneous heat. That heat causes thermal expansion, which generates a mechanical ultrasonic wave, known as the photoacoustic (PA) wave. After collecting the PA wave by ultrasonic transducer and reconstructing the signal, scientists can acquire an image showing the light absorption distribution in biological tissue.

Optical-resolution photoacoustic microscopy provides high-resolution and high contrast image information for the structure, morphology, function, and metabolism of biological tissues, with prospects for broad applications in biomolecular imaging.



Simultaneous multicontrast OR-PAM of hemoglobin concentration, oxygen saturation, blood flow speed, and lymphatic concentration. Credit: doi 10.1117/1.AP.3.1.016002

Five-wavelength fiber laser source

Wang's team has improved OR-PAM by developing a five-wavelength fiber laser source based on a single-wavelength nanosecond laser source. The switching time among different wavelengths happens on a submicrosecond timescale, which opens possibilities for simultaneous multifunctional OR-PAM. Wang's team validated the system stability by measuring the energy fluctuation and drift, and tested the imaging depth, as well as the lateral and axial resolution for OR-PAM imaging.

According to Wang, the system is based on the stimulated Raman scattering (SRS) effect. Basically, the pumped laser source can generate a scattered laser beam with a longer wavelength than the original incident beam through the optical fiber. When the energy of the pumped laser source exceeds a certain threshold, the generated SRS wavelength maintains high directivity, high monochromaticity, and high coherence, which makes it very suitable as the laser source of OR-PAM. The multiple scattered wavelengths can be used for multicontrast photoacoustic imaging.

Multifunctional imaging and disease modeling

Wang's team also developed a multiparameter image processing method for calculating the diameter, depth, tortuosity, and other physiological parameters in microvascular vessels, providing an image analysis basis for modeling disease. Using the five-wavelength OR-PAM, the research team further carried out multifunctional imaging of tumor development, lymphatic clearance, and brain imaging.

In their first step, they performed multifunctional microscopic imaging of small animals in vivo, including hemoglobin concentration, blood flow speed, oxygen saturation, and lymphatic concentration. They also analyzed morphological and functional differences (including diameter, blood flow, blood oxygen level, etc.) of different blood vessels in the imaging area.

Since traditional multifunctional OR-PAM requires multiple scanning and multiple laser sources to achieve such results, their work has addressed two significant problems. One is that the microenvironment of blood vessels in the tissue changes with time, so multiple long-term scanning causes inconsistencies in functional imaging. The other is the asynchrony among the different laser sources. Such fluctuations cause systematic errors in calculation. This new method can realize multifunctional imaging with a single laser source and in a single scanning, which not only greatly shortens the imaging time, but also improves the imaging accuracy.

Wang remarks, "In the future, by optimizing the scanning method, and combining with the multiwavelength OR-PAM in this work, real-time imaging of the dynamic changes for physiological parameters in some disease models can be realized."

More information: Chao Liu et al, Five-wavelength optical-resolution photoacoustic microscopy of blood and lymphatic vessels, *Advanced Photonics* (2021). DOI: 10.1117/1.AP.3.1.016002

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