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Editorial: Breaking the speed limits in photoacoustic microscopy

As a major implementation of photoacoustic imaging, photoacoustic microscopy (PAM) has become increasingly popular in both fundamental research and (pre)clinical applications, taking advantage of its superior resolution, significant imaging penetration, and rich contrast over traditional optical imaging methods. Recent breakthroughs in PAM technologies have enabled the visualization of the biological structures and functions with unprecedented details and new capabilities. However, the traditionally low imaging speed has prevented PAM from obtaining tissue's dynamic information, such as fast drug responses and brain functions. In the last decade, many efforts from the PAM community have been attempted to speed up PAM. Creative applications of high-speed PAM technologies in preclinical and clinical settings are also ongoing and will remain active for years to come. In this special issue, we have collected a total of eleven original research articles and two review articles that can reflect the strong momentum of high-speed PAM, highlighting the acoustic, optical, mechanical and mathematical breakthroughs that allow for breaking the speed limits in PAM. This special issue also includes high-speed PAM-enabled life sciences and human studies applications.

First of all, Wang et al. (https://doi.org/10.1016/j.pacs.2021.100294) contribute a comprehensive review article that summarizes the technological history and fast development of high-speed PAM, as well as a variety of representative biomedical applications [1]. This review article shall provide the readers with a broad overview of the key components of high-speed PAM technologies, and set the foundations for a better understanding of the other original research articles that focus on more specific technical aspects.

One of the major challenges in high-speed PAM is the laser's limited pulse repetition rate, which determines the maximal number of one-dimensional signals acquired per unit time, and thus the imaging speed. The existing high-speed pulsed lasers used in PAM often suffer from low pulse energy, large power fluctuation, and/or limited wavelength turnability. In a comprehensive review article, Cho et al. (https://doi.org/10.1016/j.pacs.2021.100291) introduce the technical details of developing and applying high-speed pulsed lasers for PAM [2]. In particular, this article describes the working principles, implementation, and limitations of multi-wavelength Raman-shifter-based light sources that have become increasingly popular in high-speed PAM.

Similarly, ultrasound detection with a large receiving aperture and high sensitivity is critically important for accelerating the PAM. The ultrasound transducer's effective detection zone often limits the field of view (or scanning range) of high-speed PAM. To this end, two original research articles in this collection aim to develop novel ultrasound detection methods for high-speed PAM. Chen et al. (https://doi.org/10.1016/j.pacs.2022.100417) report a cylindrically-focused transparent high-frequency ultrasound transducer, which is made of lithium niobate coated with indium-tin-oxide as electrodes [3]. The transparent ultrasound transducer enables a large scanning range and high detection sensitivity. Yang et al. (https://doi.org/10.1016/j.pacs.2021.100305) develop a broadband surface plasmon resonance sensor with an acoustic bandwidth of ~125 MHz [4]. This broad bandwidth is highly beneficial for improving the axial resolution of high-speed PAM. In addition, the large acceptance angle of the resonance transducer provides a wide field of view. Both transducers allow for the fast optical scanning of the excitation laser beam without requiring acoustic beam steering.

The third critical component of high-speed PAM is the fast-scanning mechanism of the excitation light beam and the resultant acoustic waves. With point-by-point image formation, traditional PAM systems rely on slow motorized scanning stages to provide three-dimensional imaging, which cannot achieve the needed scanning speed for the target temporal resolution. Three original research articles are included in this collection to overcome this limitation, focusing on different high-speed scanning strategies. Chen et al. (https://doi.org/10.1016/j.pacs.2021.100292) report a novel scanning method that uses an MEMS scanner steering two optical foci simultaneously, and has achieved a B-scan rate of 2 kHz over a 3 mm scanning range [5]. Hirasawa and colleagues (https://doi.org/10.1016/j.pacs.2022.100364) have achieved high-throughput spectroscopic PAM with a single scan, utilizing two broadband optical pulses with wavelength-dependent time delay [6]. Chen et al. (https://doi.org/10.1016/j.pacs.2021.100309) developed a novel two-axis MEMS scanner with torsion and bending scanning as the fast and slow axis, respectively, which can effectively decouple the two axes and improve the scanning stability [7].

One inherent technical challenge of the high-speed PAM is spatial undersampling, due to the high scanning frame rate, the limited laser pulse repetition rate, and the laser safety limit. The spatial undersampling leads to reduced spatial resolution and deteriorated image quality. While it becomes increasingly challenging to address the undersampling issue via better hardware, two original research articles aim to tackle this issue through the state-of-the-art deep-learning approaches. Vu et al. (https://doi.org/10.1016/j.pacs.2021.100266) report an iterative deep-image-prior based model to improve the undersampled PAM image quality using less than 2% fully-sampled pixels, without the need for a large training data [8]. Seong et al. (https://doi.org/10.1016/j.pacs.2022.100429) developed a 3D deep-learning method to restore the undersampled PAM images with as much as 800 times fewer pixels than the fully sampled images [9].

All of the technical advances in high-speed PAM have collectively enabled studies of dynamic functions and behaviors on small animal models and humans that are not possible for traditional slow PAM. In

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this collection, a total of four original research articles have demonstrated proof-of-concept applications of high-speed PAM. Chen et al. (https://doi.org/10.1016/j.pacs.2022.100411) use a handheld PAM probe to perform freehand scanning of mouse skin lesion with real-time image stitching capability [10]. Xu et al. (https://doi.org/10.1016/j.pacs.2022.100342) utilizes high-speed PAM to study the mouse tumor angiogenesis and margin, at both the microscopic and mesoscopic scales [11]. For human studies, Ahn et al. (https://doi.org/10.1016/j.pacs.2021.100282) demonstrate high-speed PAM in tracking the blood perfusion and oxygenation on human fingers [12], and for the first time (https://doi.org/10.1016/j.pacs.2022.100374), integrates high-speed PAM with photoplethysmography to provide the human skin blood volume and vasculature movement during cardiac functions [13].

All in all, although the exciting papers include in this special issue are only a small sample of the ongoing research on high-speed PAM, we expect they will become a valuable reference for the professionals working on PA technologies and relevant applications. It is also our hope that this collection will inform the broad biomedical community of the field of high-speed PAM, and so more researchers can capitalize on these advances. Sometimes, breaking the speed limits can lead to significant breakthroughs in biomedical science. We hope this work inspires investigators to break more speed limits to enable high temporal resolution 3-dimensional photoacoustic functional imaging of tissues.

Declaration of Competing Interest

None.

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