Editorial

Photoacoustics special issue 'Photoacoustic image reconstruction: Theory and practice'

Photoacoustic imaging is a coupled-physics imaging modality that exploits the spatially-varying optical absorption within biological tissue for contrast [1–3]. When biological tissue is illuminated by a short pulse of light, the light is scattered and eventually absorbed by light-absorbing molecules, chromophores, each type of which will have a characteristic optical absorption spectrum. The absorbed energy is typically thermalised, generating increases in pressure in regions of high optical absorption (often blood vessels). This excess pressure is known as the *initial acoustic pressure distribution* and it acts as a pulsed, distributed, acoustic source. This optically-generated acoustic pulse travels through the tissue and can be detected at the tissue surface: this is the data that is used to generate photoacoustic images. Many different arrangements of acoustic sensors have been proposed for photoacoustic imaging, but two broad categories are worth highlighting here. When the measurements are made with an array, or synthesised array, of sensors that are sensitive to waves incident from a wide range of angles, and a numerical algorithm must be used to generate the photoacoustic image, this is known as *photoacoustic tomography* (PAT). When the measurements are made with a sensor that is focussed along a line (albeit imperfectly) such that the measured time series can be used directly to form an image, this is known as *photoacoustic microscopy* [4] (PAM). (When the light is unfocussed this is known as *acoustic resolution* PAM).

In photoacoustic imaging, the optical pulse must be short for there to be efficient acoustic generation, and this allows the problems of modelling the optical propagation and the acoustic propagation to be decoupled. The output of the optical modelling (including, for sake of argument, the thermalisation step) is the initial acoustic pressure distribution, and it is this which is the input to the acoustic model. There are therefore two related inverse problems: first, an acoustic inversion from the measured acoustic time series to the initial acoustic pressure distribution [5,6], and, second, an optical inversion from the initial acoustic pressure distribution to the distributions of the chromophores [7]. The former is what is usually referred to as *photoacoustic image reconstruction*, and the latter as *quantitative* or *spectroscopic photoacoustic reconstruction*. For some applications, the optical inversion is an important problem to solve because it is the chromophore distributions, and not the initial acoustic pressure distributions, which give direct information about the tissue and which can therefore facilitate molecular [8], genetic [9] and functional imaging [10] using photoacoustics. The essential task in this regard is to estimate the (wavelength-dependent) light fluence in the tissue, which is complicated by the fact it is affected by the unknown chromophore distributions. However, for many practical applications it is sufficient to solve just the acoustic inversion. Many different ways to do this have been proposed, including analytical formulas, in particular backprojection formulas,

and schemes based on computational models such as time reversal and iterative approaches. Despite this progress, in almost all practical cases these methods are only approximate because (1) the measurement data is incomplete, and (2) the forward operator - the acoustic model – relies on approximations. The measured data can be incomplete because for some applications it is not possible for the sensor array to surround the object of interest, and real-world sensors are not sensitive to all directions or frequencies. It may also be too expensive or too time-consuming to record complete data, eg. when a high image frame-rate is essential. One reason why most forward models are approximate is because the speed of sound in soft tissue is heterogeneous [11], although there can also be other issues to deal with, especially in vivo, such as absorption and tissue motion. One approach to ameliorating these problems is to incorporate additional prior information into the reconstruction, but this can lead to computationally intensive, time-consuming, reconstructions, which can restrict their practical usability. There is a need, therefore, for novel approaches to photoacoustic image reconstruction that can mitigate the incomplete knowledge of the data and the forward operator, without sacrificing reconstruction speed. The framework of Deep Learning, and data-driven approaches more generally, seem to offer great potential in this regard [12–14], but bring their own challenges, not least how to ensure accuracy and generalisability.

The papers in this Special Issue touch on all aspects of photoacoustic image reconstruction. Pattyn et al. [1] tackle problems in both the acoustic and optical reconstructions: the heterogeneity of the sound speed, and the problem of the unknown light fluence. Zuo et al. [2] are also interested in both the acoustic and optical reconstructions; they study how wavelength-dependent errors in the acoustic reconstruction affect the spectroscopic optical reconstruction, a problem they call *spectral crosstalk*. Continuing the concern with quantitative PAT, Zhang et al. [3] propose an iterative approach for fluence correction scheme. Four of the papers in this Special Issue are concerned with how Deep Learning can be brought to bear on photoacoustic image reconstruction problems. Hsu et al. [4] examine different Deep Learning approaches for PAT reconstruction, specifically comparing learned post-processing steps with learned model-based reconstructions. Feng et al. [5] demonstrate the use of Deep Learning for deconvolving the point-spread-function of an acoustic resolution PAM imaging system to improve the image resolution. Two papers [6,7] address the speed with which image reconstruction can be performed: Lan et al. [6] use a learned approach to facilitate image reconstruction from a low channel count measurement system and demonstrate its real-time performance, and Hsu et al. [7] use a learned model to replace the conventional numerical model of the physics in an iterative reconstruction in order to

speed it up.

1. Abstracts of the papers in the special issue

[1] Alexander Pattyn, Zackary Mumm, Naser Alijabbari, Neb Duric, Mark A. Anastasio, Mohammad Mehrmohammadi. Model-based optical and acoustical compensation for photoacoustic tomography of heterogeneous mediums. *Photoacoustics*, 100275, 2021.

Photoacoustic tomography (PAT) is a non-invasive, high-resolution imaging modality, capable of providing functional and molecular information of various pathologies, such as cancer. One limitation of PAT is the depth and wavelength dependent optical fluence, which results in reduced PA signal amplitude from deeper tissue regions. These factors can therefore introduce errors into quantitative measurements such as oxygen saturation (sO2) or the localization and concentration of various chromophores. The variation in the speed-of-sound between different tissues can also lead to distortions in object location and shape. Compensating for these effects allows PAT to be used more quantitatively. We have developed a proof-of-concept algorithm capable of compensating for the heterogeneity in speed-of-sound and depth dependent optical fluence. Speed-of-sound correction was done by using a straight ray-based algorithm for calculating the family of iso-time-of-flight contours between the transducers and every pixel in the imaging grid, while fluence compensation was done by utilizing the graphics processing unit (GPU) accelerated software MCXCL for Monte Carlo modeling of optical fluence variation. This algorithm was tested on a polyvinyl chloride plastisol (PVCP) phantom, which contained cyst mimics and blood inclusions to test the algorithm under relatively heterogeneous conditions. Our results indicate that our PAT algorithm can compensate for the speed-of-sound variation and depth dependent fluence effects within a heterogeneous phantom. The results of this study will pave the way for further development and evaluation of the proposed method in more complex in-vitro and ex-vivo phantoms, as well as compensating for the wavelength-dependent optical fluence in spectroscopic PAT.

[2] Hongzhi Zuo, Manxiu Cui, Xuanhao Wang, Cheng Ma. Spectral crosstalk in photoacoustic computed tomography. *Photoacoustics*, 100356, 2022.

Multispectral photoacoustic (PA) imaging faces two major challenges: the spectral coloring effect, which has been studied extensively as an optical inversion problem, and the spectral crosstalk, which is basically a result of non-ideal acoustic inversion. So far, there is no systematic work to analyze the spectral crosstalk because acoustic inversion and spectroscopic measurement are always treated as decoupled. In this work, we theorize and demonstrate through a series of simulations and experiments how imperfect acoustic inversion induces inaccurate PA spectrum measurement. We provide detailed analysis to elucidate how different factors, including limited bandwidth, limited view, light attenuation, out-of-plane signal, and image reconstruction schemes, conspire to render the measured PA spectrum inaccurate. We found that the model-based reconstruction outperforms universal backprojection in suppressing the spectral crosstalk in some cases.

[3] Shuangyang Zhang, Jiaming Liu, Zhichao Liang, Jia Ge, Yanqiu Feng, Wufan Chen, Li Qi. Pixel-wise reconstruction of tissue absorption coefficients in photoacoustic tomography using a non-segmentation iterative method. *Photoacoustics*, 100390, 2022.

In Photoacoustic Tomography (PAT), the acquired image represents a light energy deposition map of the imaging object. For quantitative imaging, the PAT image is converted into an absorption coefficient (μa) map by dividing the light fluence (LF). Previous methods usually assume a uniform tissue μa distribution, and consequently degrade the LF correction results. Here, we propose a simple method to reconstruct the pixel-wise μa map. Our method is based on a non-segmentation-based iterative algorithm, which alternately optimizes the LF distribution and the μa map. Using simulation data, as well as phantom and animal data, we implemented our algorithm and compared it to segmentation-

based correction methods. The results show that our method can obtain accurate estimation of the LF distribution and therefore improve the image quality and feature visibility of the μa map. Our method may facilitate efficient calculation of the concentration distributions of endogenous and exogenous agents in vivo.

[4] Ko-Tsung Hsu, Steven Guan, Parag V. Chitnis. Comparing Deep Learning Frameworks for Photoacoustic Tomography Image Reconstruction. *Photoacoustics*, 100271, 2021.

Conventional reconstruction methods for photoacoustic images are not suitable for the scenario of sparse sensing and geometrical limitation. To overcome these challenges and enhance the quality of reconstruction, several learning-based methods have recently been introduced for photoacoustic tomography reconstruction. The goal of this study is to compare and systematically evaluate the recently proposed learning-based methods and modified networks for photoacoustic image reconstruction. Specifically, learning-based post-processing methods and model-based learned iterative reconstruction methods are investigated. In addition to comparing the differences inherently brought by the models, we also study the impact of different inputs on the reconstruction effect. Our results demonstrate that the reconstruction performance mainly stems from the effective amount of information carried by the input. The inherent difference of the models based on the learning-based post-processing method does not provide a significant difference in photoacoustic image reconstruction. Furthermore, the results indicate that the model-based learned iterative reconstruction method outperforms all other learning-based post-processing methods in terms of generalizability and robustness.

[5] Fei Feng, Siqi Liang, Jiajia Luo, Sung-Liang Chen. High-fidelity deconvolution for acoustic-resolution photoacoustic microscopy enabled by convolutional neural networks. *Photoacoustics*, 100360, 2022.

Acoustic-resolution photoacoustic microscopy (AR-PAM) image resolution is determined by the point spread function (PSF) of the imaging system. Previous algorithms, including Richardson–Lucy (R–L) deconvolution and model-based (MB) deconvolution, improve spatial resolution by taking advantage of the PSF as prior knowledge. However, these methods encounter the problems of inaccurate deconvolution, meaning the deconvolved feature size and the original one are not consistent (e.g., the former can be smaller than the latter). We present a novel deep convolution neural network (CNN)-based algorithm featuring high-fidelity recovery of multiscale feature size to improve lateral resolution of AR-PAM. The CNN is trained with simulated image pairs of line patterns, which is to mimic blood vessels. To investigate the suitable CNN model structure and elaborate on the effectiveness of CNN methods compared with non-learning methods, we select five different CNN models, while R–L and directional MB methods are also applied for comparison. Besides simulated data, experimental data including tungsten wires, leaf veins, and in vivo blood vessels are also evaluated. A custom-defined metric of relative size error (RSE) is used to quantify the multiscale feature recovery ability of different methods. Compared to other methods, enhanced deep super resolution (EDSR) network and residual in residual dense block network (RRDBNet) model show better recovery in terms of RSE for tungsten wires with diameters ranging from 30 μm to 120 μm. Moreover, AR-PAM images of leaf veins are tested to demonstrate the effectiveness of the optimized CNN methods (by EDSR and RRDBNet) for complex patterns. Finally, in vivo images of mouse ear blood vessels and rat ear blood vessels are acquired and then deconvolved, and the results show that the proposed CNN method (notably RRDBNet) enables accurate deconvolution of multiscale feature size and thus good fidelity.

[6] Hengrong Lan, Daohuai Jiang, Feng Gao, Fei Gao. Deep learning enabled real-time photoacoustic tomography system via single data acquisition channel. *Photoacoustics*, 100270, 2021.

Photoacoustic computed tomography (PACT) combines the optical contrast of optical imaging and the penetrability of sonography. In this work, we develop a novel PACT system to provide real-time imaging,

which is achieved by a 120-elements ultrasound array only using a single data acquisition (DAQ) channel. To reduce the channel number of DAQ, we superimpose 30 nearby channels' signals together in the analog domain, and shrinking to 4 channels of data ($120/30 = 4$). Furthermore, a four-to-one delay-line module is designed to combine these four channels' data into one channel before entering the single-channel DAQ, followed by decoupling the signals after data acquisition. To reconstruct the image from four superimposed 30-channels' PA signals, we train a dedicated deep learning model to reconstruct the final PA image. In this paper, we present the preliminary results of phantom and in-vivo experiments, which manifests its robust real-time imaging performance. The significance of this novel PACT system is that it dramatically reduces the cost of multi-channel DAQ module (from 120 channels to 1 channel), paving the way to a portable, low-cost and real-time PACT system.

[7] Ko-Tsung Hsu, Steven Guan, Parag V. Chitnis. Fast Iterative Reconstruction for Photoacoustic Tomography Using Learned Physical Model: Theoretical Validation. *Photoacoustics*, ??, 2023.

Iterative reconstruction has demonstrated superior performance in medical imaging under compressed, sparse, and limited-view sensing scenarios. However, iterative reconstruction algorithms are slow to converge and rely heavily on hand-crafted parameters to achieve good performance. Many iterations are usually required to reconstruct a high-quality image, which is computationally expensive due to repeated evaluations of the physical model. While learned iterative reconstruction approaches can reduce the number of iterations through convolutional neural networks, it still requires repeated evaluations of the physical models at each iteration. Therefore, the goal of this study is to develop a Fast Iterative Reconstruction (FIRe) algorithm that incorporates a learned physical model into the learned iterative reconstruction scheme to further reduce the reconstruction time while maintaining robust reconstruction performance. The results demonstrate comparable reconstruction performance to learned iterative reconstruction methods with a 9x reduction in computation time and a 620x reduction in computation time compared to variational reconstruction.

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Ben Cox, Mark Anastasio

E-mail addresses: b.cox@ucl.ac.ukb, cox@ucl.ac.uk (B. Cox).