A computational framework for investigating the feasibility of focusing light in biological tissue via photoacoustic wavefront shaping

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A computational framework for investigating the feasibility of focusing light in biological tissue via photoacoustic wavefront shaping

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ABSTRACT

Photoacoustic (PA) wavefront shaping (WFS; PAWS) could allow focusing light deep in living tissue, increasing the penetration depth of biomedical optics techniques. PAWS experiments have demonstrated focusing light through rigid scattering media. However, focusing deep in tissue is significantly more challenging. To examine the scale of this challenge, a computational model of the propagation of coherent light in tissue was developed to simulate the focusing of light via PAWS. To demonstrate the model, it was used to simulate focusing in an 800 µm thick tissue-like medium. To show the utility of the model, the focusing was repeated in different conditions illustrative of simplified PAWS experiments involving different spatial resolutions. As expected, a finer spatial resolution led to a brighter focus. By providing a simulation platform for studying PAWS, this work could pave the way to developing systems that can focus light in tissue.

Keywords: Wavefront shaping, photoacoustic imaging, computational simulation, T-matrix, scattering, biological tissue

1. INTRODUCTION

Biological tissue scatters light, limiting the penetration depth of various biomedical optics techniques. A technique that that could compensate for the deleterious effects of scattering is wavefront shaping (WFS)[1]. WFS involves spatially structuring the light field incident upon a scattering medium, so as to control the interference patterns produced in the medium. In principle, this allows creating a bright optical focus deep in scattering media, including biological tissue. By focusing light in tissue, WFS could enable increasing the penetration depth of a range of biomedical optics techniques.

The ability of focusing light through scattering layers such as optical diffusers using WFS is now well established[1]. However, focusing inside tissue is significantly more challenging. One challenge is it requires monitoring the light field inside the tissue order to provide a feedback signal[2] to guide the optimization, i.e. a so-called internal "guidestar"[3]. One possible "guidestar" involves measuring photoacoustic (PA) signals – ultrasound waves generated when light is absorbed by tissue[4]. Using PA signals to guide WFS gives rise to "photoacoustic wavefront shaping" (PAWS)[5].

Like WFS in general, PAWS has enabled focusing light through diffusers[5,6], but focusing in tissue presents challenges. One relates to the sensitivity and spatial resolution of PAWS systems. Specifically, the theoretical maximum focal enhancement (achievable increase in light intensity at the "focus") is expected to scale with N/M. Where: N is the number of independently controlled "input modes" (commonly: the number of elements on the spatial light modulator (SLM) used to structure the incident light), and; M is the number of independently observable "output modes" (independently resolvable speckle grains in the interference (speckle) pattern producing the PA signals). In static benchtop PAWS experiments, N can be made large using high-resolution SLMs. Concurrently, M can be made small because the speckle field generating the PA signals can be physically expanded (to ultrasonic length scales) to enable isolating the PA signals generated by a small number of speckles[5,6]. By contrast, when focusing in tissue, factors such as the tissue decorrelation time and finite PA detection sensitivity will limit the number of controllable input modes. Moreover, the speckle size is expected to tend towards half the optical wavelength; much smaller than the ultrasonically defined spatial resolution of PA detectors. For these reasons and others, focusing in tissue is expected to be highly demanding.

While tissue-based PAWS will be demanding, it is difficult to make firm predictions to guide experimental design and explore the expected capabilities of PAWS. One reason is it is hard to model the characteristics of coherent PA excitation light fields deep in tissue with available computational tools. Specifically, existing models based on, e.g. diffusion theory, Monte Carlo, Finite-Difference Time-Domain, or random phase screens, are typically either too simplistic to represent the

required physics (e.g. contain no deterministic phase information), or else too computationally expensive (e.g. requiring a $<\lambda/2$ discretisation of the medium) to simulate propagation through large enough volumes of tissue.

To address this challenge, a scalable computational framework for accurately simulating coherent light propagation through tissue-like media was developed and applied to simulate the evolution of light fields during PAWS. The framework is based on a discrete particle model, in which tissue is treated as a collection of spheres (of higher refractive index) embedded in a homogeneous medium (of lower index). This model has two key features. First, using appropriately chosen spheres enables designing synthetic media that have certain desired tissue-like properties. For example, one can use Mie theory to design a collection of spheres providing a desired scattering coefficient and anisotropy[7,8,9,10]. The second key feature of the model is it allows for the use of computationally efficient yet physically rigorous light field simulations. Specifically, here, the established T-matrix method is used to perform such simulations[8,9,11]. The T-matrix method directly solves Maxwell's equations and, in this way, is sufficiently physically rigorous. As such, accepting the discrete particle approximation, the solutions of the model are physically exact.

To demonstrate the model, it was applied to simulate the focusing of light in an 800 µm thick tissue-like medium. To show the potential utility of the model in studying PAWS, the focusing was repeated in different conditions illustrative of PAWS experiments involving different spatial resolutions. As expected, higher spatial resolutions led to brighter foci. By providing a simulation platform for studying PAWS, ongoing work involving this model could pave the way to developing systems that can focus light in tissue.

2. METHODS

The scenario for the PAWS simulations is shown in figure 1. A Gaussian beam incident upon a synthetic tissue-like medium is scattered, producing a speckle pattern in a plane of interest deep inside the medium.
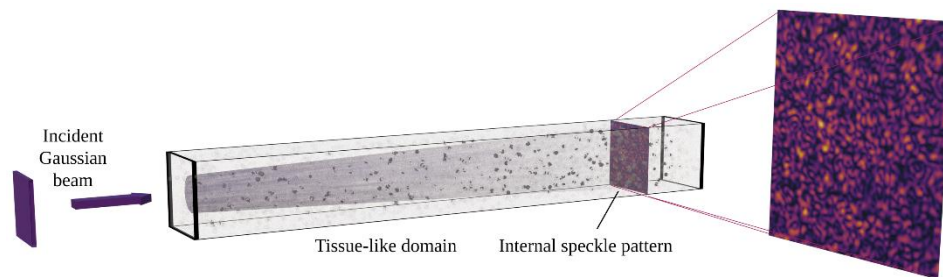

Figure 1. Illustration of the simulation scenario.

2.1 Synthetic tissue-like medium

Mie theory was used to select parameters for a discrete particle model with a scattering anisotropy of 0.95, a scattering coefficient of 15.67 mm^{-1}, and a background refractive index of 1.33. Based on these criteria, a sphere diameter of 4 µm, refractive index of 1.52, and concentration of 0.012% by volume was selected. Using this recipe, 100 by 100 by 800 µm sized scattering domains were constructed to represent 3D columnar shaped sections of tissue.

2.2 Light field calculations

The T-matrix method was used to calculate the field produced throughout the media, assuming an incident Gaussian beam of 20 µm 1/e^2 diameter. T-matrix calculations were performed using the openly available software package CELES[12].

2.3 WFS Algorithm

WFS requires optimizing the phase (and/or amplitude) of a number of optical "input modes", each producing a component of the light field in the scattering medium. Once optimized, the interference of these components can produce a focus. In practical experiments, the input modes are often defined by the independently-controlled elements of an SLM. In these conditions, a factor influencing the achievable focusing enhancement is the independence of the modes, i.e. the extent to which neighbouring SLM pixels produce uncorrelated speckle patterns. This independence is influenced by various practical factors including the specific optical configuration, optical wavelength, and properties of the medium itself, including the magnitude of correlations like so-called memory effects[13].

The presented simulation framework could be used to study the above factors. However, to first provide a simplified PAWS simulation, it was decided to eliminate these (potentially confounding) factors by adopting a different representation

of the input modes. Specifically, rather than optimizing the phase of many spatial components of the light field incident on the medium, we optimized single phase shifts applied to single spatial modes (identical Gaussian beams) incident on many different realizations of the same scattering medium (note, this is similar to the idea used to provide strict definitions of focal enhancement in traditional WFS theory[1]). Thus, multiple scattering domains were actually created as described above, each having similar parameters but with spheres in different pseudo-random positions. The field components produced in each of these domains (for the selected per-domain phase shift) were calculated as above, then summed to produce the total field.

2.4 PA signal calculations

For the purposes of simulating PAWS, PA signals were assumed to be generated directly in proportion to the sum of the optical intensity in the total field produced in the region of interest (intended location of the focus).

3. RESULTS

To demonstrate the light field calculations, a 2D cross-section through the fluence distribution calculated in a single domain (instance of the medium) was plotted in Figure 2. As expected, due to the scattering, the initially Gaussian beam is spread out and aberrated, and the intensity of the field decreases as the beam propagates deeper into the medium.
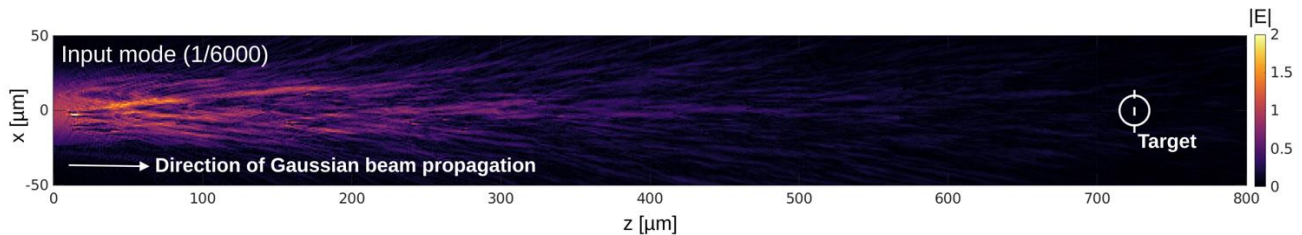

Figure 2. 2D cross-section of light propagating through the tissue-like medium. The light is incident on the left-hand side. The location of a target location for focusing light to via PAWS is shown by the white circle. A 30 by 30 μm plane of interest at this target is shown by dashed line.

To simulate a WFS experiment, a target region was defined at a location 725 μm deep in the medium (as shown by the white circle in figure 2). The region was point-like, effectively assuming the resolving of individual speckles. To shape the field, 6,000 input modes were generated as described above, and their individual input phase levels optimized using a continuous sequential algorithm[1]. The intensity of the resulting total field was plotted in figure 3a. As expected, a bright focus, the size of a single speckle, is produced. Also as expected, the field is smooth. This is a consequence of using multiple domains as input modes - effectively averaging out the aberrations observed in the individual domains.
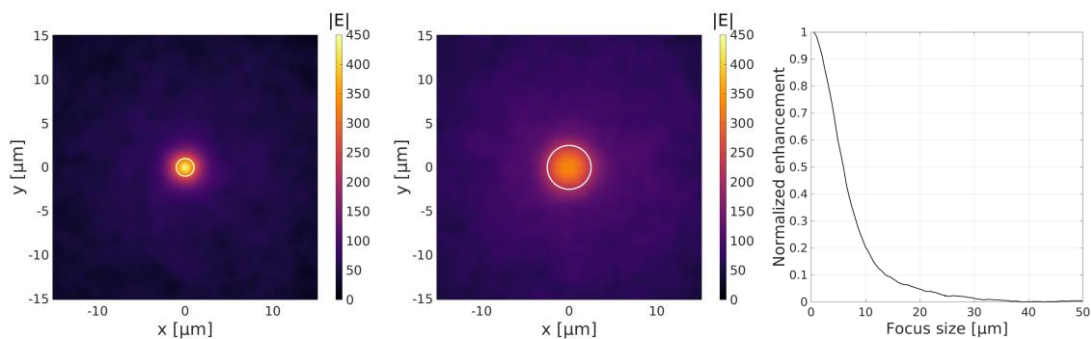

Figure 3. (a) Intensity in the plane of interest after focusing light into a single optical speckle.
(b) Intensity in the plane of interest after focusing light into a target region with a diameter of 5 μm.
(c) Normalised enhancement of optical foci at various target sizes.

To provide simple illustration of how the model might enable parametric studies relevant to PAWS, a numerical experiment was performed that was illustrative of studying the effect of changing the spatial resolution of the WFS system (i.e.

increasing M). Specifically, the above WFS simulation was repeated assuming a 5 µm diameter circular (rather than point-like) target region in the same plane of interest. The resulting light intensity distribution in the plane of interest was plotted in figure 3b. As expected, a focus is formed that is larger and less intense.

The above experiment was repeated using a range of target regions with different diameters, in the range 1-30 µm. The resulting focal enhancements - defined as the intensity of the optimised foci relative to the average intensity of the unoptimized speckles – were calculated and plotted in Figure 3c. As expected, the enhancement decreased as the size of the focal region was increased.

4. DISCUSSION

A computational framework for investigating the focusing of light in tissue via PAWS was developed. The framework couples a discrete particle model of tissue with a T-matrix method of calculating light fields. The method has a number of notable features. Primarily, it enables replicating macroscopic tissue-like optical properties, while the T-matrix method provides an accurate and complete calculation of the light fields produced inside the media. Furthermore, because a subwavelength discretization of the domain is not required (as it is by other full-wave optical models), the method is computationally efficient with respect to time and memory. This allows it to be scaled to model tissue volumes that are large, and thus to study the focusing of light in deep tissue.

The framework was demonstrated by simulating: light propagation through an 800 µm thick tissue-like scattering medium, focusing light in this medium via WFS, and; performing a parametric study of the impact of spatial resolution in a simplified version of PAWS. The latter demonstrations were intended to be illustrative and were thus simplified in several ways. The main simplification was assuming the contribution of input modes in WFS comprised the sum of light fields produced in multiple instances of the tissue-like medium (rather than the sum of the fields produced by, e.g. different pixels on an SLM, as seen in practice). While non-physical, this approach removes the impact of medium-specific correlations such as memory effects and other confounding factors, to produce more readily interpretable WFS results that can be compared to simple theory. The model can easily be adapted however, to simulate WFS in the more conventional sense[8,9]. Comparisons with the current results could then shed light on the role of various practical factors in affecting the maximum focal enhancement achievable via WFS.

In the parametric PAWS study, a second simplification was related to the size of the focal zone. Specifically, while the size of this zone was varied, it was always assumed to lie in a 2D plane inside the medium. By contrast, in practical PAWS systems PA feedback signals will be confined to 3D volumes (determined by the spatial resolution of the PA detection system). To increase the realism of the model, the work shown here can be straightforwardly adapted to sum regions of the field in 3D rather than 2D, to more accurately represent signal detection in PAWS. A final simplification in the current work was the assumption that PA signals would be generated in direct proportion to the sum of the speckle intensity within the intended focal region of interest. While, in some cases, this allowed assuming appropriately sized (ultrasonic scale; e.g. 30 µm) focal region, a more complete model could be constructed by incorporating the real response functions of ultrasonic transducers, or coupling the present model to an acoustic model such as K-wave[14] so as to model the acoustic and optical aspects of PAWS. This too will form the basis of future work.

5. CONCLUSION

A computational model was developed to simulate the focusing of light in tissue via PAWS. To demonstrate the model, we simulated focusing in an 800 µm thick medium, and performed an illustrative parametric study. By providing a simulation platform for studying PAWS, this work could pave the way to developing PAWS systems that can focus light deep in tissue.

ACKNOWLEDGMENTS

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