Simulating Focused Ultrasound with the Boundary Element Method

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***Abstract*—Focused ultrasound is a non-invasive, non-ionizing technology with great potential for various clinical applications, including thermal ablation of tumors, targeted drug delivery, and neuromodulation. Focused ultrasound uses ultrasound energy to treat tissue deep in the body. Optimizing treatment parameters to achieve desired clinical outcomes while minimizing adverse effects remains a significant challenge. Computational simulations are powerful tools to address this challenge, develop patient-specific treatment plans and general safety guidelines, and optimize ultrasound transducers. This study presents the development of an open-source Python library, named OptimUS, for calculating ultrasound wave propagation in large computational domains in 3D using the boundary element method, specifically for focused ultrasound applications. The numerical calculations only require surface meshes at the scatterers' interfaces to define the model's geometry. Also, the computations are fast and accurate for high-frequency waves through materials with high contrast in density and speed of sound. An intercomparison exercise supports the fidelity of the simulations. Finally, simulations using anatomical models for abdominal applications of focused ultrasound reliably show the aberration of the focus from reflections by ribs and the presence of prefocal hotspots due to the lensing effect of fat layers.**

***Index Terms*—ultrasonics, computational acoustics, biomedical engineering, boundary element method**

I. Introduction

Focused ultrasound is emerging as one of the most effective non-invasive treatment modalities in biomedical engineering [1]. The working principle of therapeutic ultrasound is guiding sufficient acoustic energy towards the lesion to achieve the desired bioeffects, e.g., ablation of the malign tissue through mechanical or thermal effects. The ultrasound transducer is generally located outside the body in the operating room. This non-invasive modality has several benefits for the patient's health over traditional surgery, such as lower risks of infections, shorter recovery time, and lower costs of surgery rooms. Furthermore, the toxicities of systemic chemotherapy and ionizing radiation treatments may be mitigated.

A prime challenge in focused ultrasound treatment is configuring the ultrasound transducer to guide sufficient energy to cause ablation at the lesion while sparing surrounding healthy tissue and organs. Undesirable overheating may occur when the focusing of the acoustic beam is not correctly achieved. Furthermore, bone in the pathway may absorb energy, limit the acoustic window for treatment, aberrate the focus, or create skin burns [2]. Hence, most treatments require guidance from real-time magnetic resonance images, which extends the duration and increases surgery costs.

Clinical trials to improve therapeutic ultrasound incur significant financial costs and must follow strict ethics protocols. This also applies to experiments on animal models. Laboratory experiments on phantoms and ex-vivo tissue play a vital role in assessing the safety and efficacy of focused ultrasound as a treatment modality. Furthermore, computational simulations help streamline and optimize experimental work since numerical algorithms offer the prospect of modeling different scenarios cheaply and efficiently. Specifically, they can improve safety protocols, transducer configurations, and patient-specific treatment planning. However, most mathematical approaches suffer from numerical inaccuracies when applied to realistic models of the human body and operating frequencies in the MHz range. This study presents a computational methodology to simulate focused ultrasound in the human body efficiently.

We developed open-source Python code to simulate 3D acoustic wave propagation with dedicated functionality for ultrasound fields from commonly used transducers and scattering models at bone, organs, and soft tissue interfaces. The computations use a Boundary Element Method (BEM) with bespoke fast algorithms for high-frequency transmission at high-contrast material interfaces such as bone and soft tissue. The library, called OptimUS, is freely available on GitHub (`github. com/optimuslib`) and has a user-friendly interface via Jupyter Notebooks.

II. Methodology

Therapeutic ultrasound typically operates under continuous wave conditions at a fundamental frequency generally between 500 kHz and 5 MHz, depending on the clinical application and targeted region [3]. Modeling the linear responses of soft tissue and bone to the incident acoustic field suffices in most cases, with nonlinear solvers only necessary when the high-order

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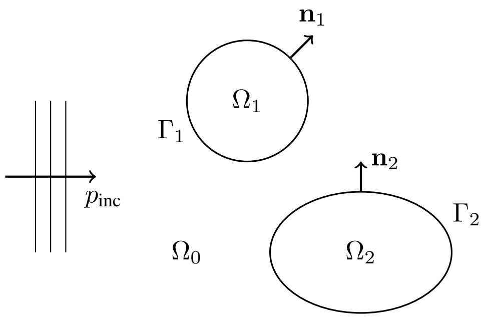

Fig. 1. A sketch of the geometry for the wave propagation model with an unbounded exterior domain Ω_0 and multiple bounded domains Ω_m for $m = 1, 2, \ldots, \ell$.

effects near the focal region must be calculated accurately. Hence, we model focused ultrasound with the Helmholtz equation for harmonic wave propagation [4]. Furthermore, we assume that each material is physically homogeneous and the exterior domain is unbounded. See Figure 1 for a sketch of a typical computational setting. Specifically,

$$-\nabla^2 p_m - k_m^2 p_m = 0 \text{ in } \Omega_m \text{ for } m = 0, 1, 2, \ldots, \ell; \tag{1}$$

for p_m the pressure field in domain Ω_m and $k_m = 2\pi f / c_m + \imath \alpha_m$ the wavenumber, where f denotes the frequency, c_m the speed of sound, and α_m the attenuation of material m. The ℓ separate scatterers are all embedded inside the unbounded domain. The interface conditions

$$p_0 = p_m, \qquad \text{at } \Gamma_m \text{ for } m = 1, 2, \ldots, \ell; \tag{2}$$

$$\frac{1}{\rho_0} \partial_n p_0 = \frac{1}{\rho_m} \partial_n p_m, \qquad \text{at } \Gamma_m \text{ for } m = 1, 2, \ldots, \ell; \tag{3}$$

model continuity of pressure and normal particle velocity, where ρ_m denotes the density of material m. Finally, the Sommerfeld radiation condition

$$\lim_{\mathbf{r} \to \infty} |\mathbf{r}| \left(\partial_{|\mathbf{r}|} p_{\text{sca}}(\mathbf{r}) - \imath k_0 p_{\text{sca}}(\mathbf{r}) \right) = 0 \tag{4}$$

forces the scattered field p_{sca} to be in outgoing direction at infinity.

A key component of the model is that the exterior domain is unbounded. This is a realistic assumption since the acoustic energy is localized in the beam path between the transducer and the focus. In this frequency range of interest, the acoustic energy decays quickly outside this region of interest so that all materials outside the targeted area can be assumed to be homogeneous and unbounded. Furthermore, millimeter-sized wavelengths are required to focus on regions of only a few centimeters, which are typical sizes in therapeutic ultrasound. At the same time, the distance between the transducer and the focus tends to be between 3 and 20 cm, depending on the clinical application [3]. Hence, realistic scenarios can require more than one hundred wavelengths across the computational domain.

We choose BEM formulations to discretize the system of Helmholtz equations because these numerical techniques accurately model high-frequency wave propagation in unbounded domains [5]. The BEM uses a Galerkin discretization of a boundary integral formulation of the Helmholtz system. The volumetric Helmholtz equation is reformulated into a boundary integral equation at each material interface. Given the surface potentials on the material interfaces, the acoustic field can be calculated at each point in space via the representation formula. Hence, unbounded domains are naturally supported, and no absorbing boundary conditions are necessary to limit the computational domain artificially. Furthermore, the BEM yields accurate approximations at high frequencies with considerably fewer elements per wavelength than volumetric methods such as finite differences and finite elements [6]. On the downside, the Green's function in the BEM yields all-to-all interactions between the surface mesh elements. Hierarchical matrix compression reduces the memory footprint of the resulting dense matrix and allows for fast matrix-vector multiplications in the iterative linear solver [7].

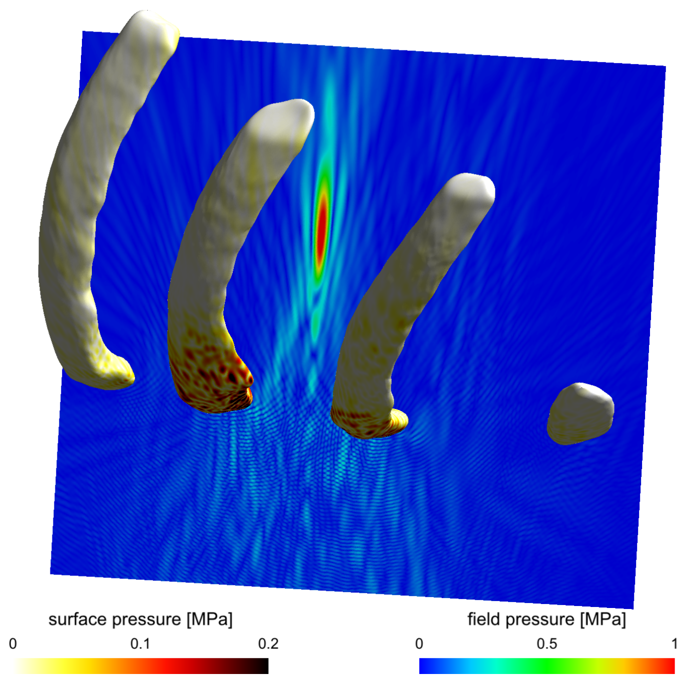

Fig. 2. Simulation of transcostal ultrasound with a model of four ribs, calculated with the BEM [7].

Figure 2 shows a BEM simulation of a typical transabdominal-focused ultrasound scenario, e.g., for treating liver or kidney tumors. The presence of the rib bone challenges the guiding of the ultrasound energy toward the intracostal region [2]. This may cause focal aberrations when liver cancer is treated with therapeutic ultrasound. The computational results effectively show a shadow region behind the bone and high acoustic energy at the surface of the ribs.

III. Contribution

We developed specific innovations to the BEM to simulate realistic scenarios of focused ultrasound. First, the large system of linear equations is usually solved with iterative linear solvers whose convergence deteriorates with increasing frequency. We designed preconditioners based on on-surface radiation conditions that reduce the iteration count considerably, especially at higher frequency ranges [8]. Furthermore, the system matrices become ill-conditioned when the contrast in density and speed of sound between materials increases. We developed specific boundary integral formulations that remain well-conditioned for high-contrast models [9]. Finally, dedicated boundary integral formulations [10], stabilized coupling with preconditioned finite element methods [11], and nonconforming meshes [12] can further improve the computational efficiency in specific scenarios.

A major stumbling block to adopting BEM simulations for focused ultrasound is the significant programming effort required to implement fast BEM algorithms. Considering this challenge, we designed the open-source OptimUS Python library. One of our research objectives is to simplify the computational pipeline of ultrasonics simulations based on the BEM. The package provides a user-friendly interface for acoustic simulations through Jupyter notebooks. The user only needs to specify the acoustic settings of the simulations, such as the geometry of the scatterers, material parameters, and transducer configuration. The library has a database with reference values for common materials and tissue types used in biomedical engineering, as well as field representations of planar, bowl, and array transducers. OptimUS then automatically chooses the correct numerical parameters and boundary integral formulations to solve the acoustic model with the BEM. Finally, a collection of postprocessing routines is available to visualize the numerical results.

The OptimUS library has a modular design with separate routines for different steps in the modeling pipeline. Hence, an interested user can access all details, settings, and computational parameters to optimize the simulations. For example, one can create user-defined materials by specifying the density, speed of sound, and attenuation and store them in a database for follow-on simulations. Also, triangular surface meshes of any scatterer can be imported into the library. Furthermore, the preconditioner type, quadrature order, and hierarchical matrix parameters can all be tweaked to accelerate the calculations of the BEM model for the problem at hand. The assembly of the system matrix is performed by an interface to the BEMPP library [5]. Finally, the postprocessing module can export the surface pressure at the material interfaces and calculate the acoustic field at any specified location in 3D space. The results can quickly be inspected inside the Jupyter notebooks or exported to external visualization packages.

IV. Results

We used the OptimUS library to solve wave propagation problems in different scenarios relevant to non-invasive ultrasound treatments. Examples include transabdominal and transcranial ultrasound. In transabdominal cases, ultrasound propagates through fat layers. Fat tends to have a higher attenuation coefficient than other soft tissue types and its lower speed of sound may cause lensing of the beam. Our simulations using OptimUS also predict the lensing effects of abdominal fat layers and the formation of prefocal hotspots [13]. Moreover, we observed that the acoustic energy delivered to the focus is reduced by half compared to free-medium propagation. These findings have crucial implications in clinical settings, confirming that propagation models can play a significant role in planning focused ultrasound interventions.

There is a strong interest in applying focused ultrasound for treating brain diseases [14]. In transcranial applications, there is no acoustic window between the transducer and the target region, and all energy is delivered through the skull. The skull bone strongly reflects and absorbs a large proportion of the energy, aberrates the beam, and reduces the amplitude at the focus. Also, thicker parts of the skull may deflect the focal spot. Indeed, simulations on a human skull model show significant aberrations of the focus, with distances of several millimeters between the geometric focus and energy peak; see Figure 3.

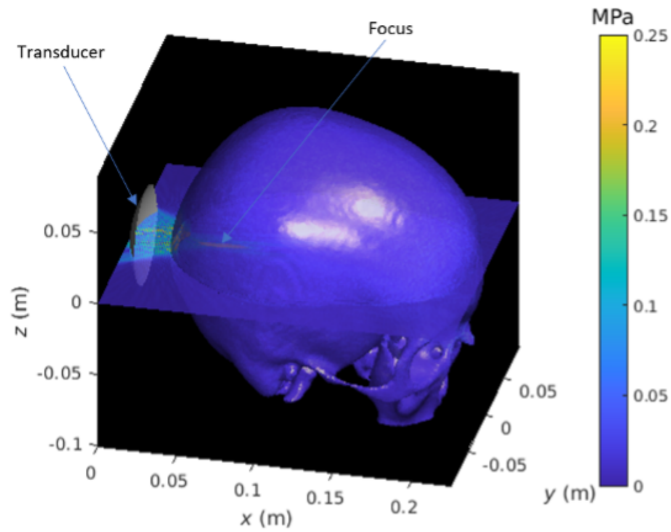

Fig. 3. Simulation of transcranial ultrasound with a human head model [15].

We verified the high fidelity of the numerical simulations of transcranial ultrasound within an intercomparison exercise of compressional wave models organized by the International Transcranial Ultrasonic Stimulation Safety and Standards (ITRUSST) consortium [15]. A range of benchmarks were defined, from free-space propagation to slabs to a full skull model. The results from the eleven participating teams provided intercomparison measures for the delivered dose in the target. The numerical methods included finite element methods, pseudospectral methods, finite-difference time-domain, hybrid angular spectrum, and our BEM. Differences between the computational approaches remained within reasonable working precisions, which builds confidence in the accuracy of numerical techniques to model therapeutic ultrasound.

V. Discussion

The computational simulations performed with the OptimUS library confirm that fast BEM calculations provide insights into the working of focused ultrasound for non-invasive cancer treatment and transcranial neuromodulation applications. Our current research efforts focus on improving the computational kernel to reduce the computational footprint and developing more elaborate models of ultrasound propagation in biomedical tissues and bone. For example, we are working on nonlinear models that improve computational realism when high intensities are present at the focal region [16]. Furthermore, we are developing volume integral equations to model piecewise heterogeneous materials. This will allow us to model bone with voxel-based information on density and speed of sound from medical images while using the fast BEM for homogeneous regions and the unbounded exterior domain. Other improvements and extensions we envision include the propagation through more general geometries, such as nested domains. Finally, new features are continuously being integrated into the OptimUS library and provided with an open-source license to the research community.

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