Mathematical and numerical modeling of elastic waves propagation in the heart

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Abstract: The objective of this thesis is to develop a rigorous mathematical and numerical background for the extension and dissemination of imaging modalities by ultrasound, i.e. elastic waves, applied to the cardiac settings. The problems treated will concerned the topics of mathematical modeling, numerical analysis and scientific computing. More precisely we plan to define a linearized model for the propagation of elastic waves in the heart, study approximations of these models and define adapted numerical methods for the discretization of the resulting partial differential equations. Our end-objective is to be able to do high performance computing of the underlying multi-scale and multi-physics phenomena.

Context and positioning of the thesis

Cardiovascular diseases are the leading worldwide cause of death and the second in France. One of the precursor symptoms of these diseases is the local modification of the mechanical properties of the heart. Therefore, patient-specific monitoring of these mechanical properties has a strong potential to help medical doctors in the construction of a reliable diagnosis. Among many existing medical imaging modalities we want to develop a mathematical and numerical background for a new transient ultrasound elastography modality: the 3D shear-wave imaging with 3D ultrafast ultrasound (as experimented in [2] on living tissue). The principle of this modality is to use emitted and back-scattered ultra-sound (pressure waves) at a very high frequency to image the propagation of a generated shear waves in the tissue. The propagation speed of these shear wave can then be correlated with the mechanical properties of the probed medium at a (really) fine scale. These properties can be recovered in a second step using for instance data assimilation based strategies, or more specifically observer-based strategies.

Experimental preliminary studies presented in [1] show the potential of the extension of transient elastography to cardiac imaging. However there does not exist in the applied mathematic literature studies of this modality for the application in a cardiac setting. It can be explained since realistic mechanical models for the heart contraction are relatively new (see [3]) and are of fundamental importance to define a relevant modeling background for the elastic wave propagation.

The objective of this proposal is to develop a rigorous mathematical and numerical background for the extension of shear-wave imaging with ultrafast ultrasound techniques to the cardiac settings. More precisely, in this proposal oriented towards applied mathematics, we propose to study the elastic waves propagation (pressure and shear waves propagation) in the beating heart and wish to offer some well-defined mathematical modeling and numerical strategy as well as scientific computations of the involved phenomena. This will hopefully improve the dissemination of the transient ultrasound elastography technique, and this project will present a major step forward in the modeling and simulation of a multi-scale (pressure and shear waves) and multi-physics phenomenon (beating heart and wave propagation) for life sciences.

Scientific and technical description

We aim at developing a rigorous mathematical and numerical background for the extension and improvement of a transient ultrasound elastography modality in the context of non-invasive cardiac imaging. Some intrinsic difficulties related to our application have to be addressed. More precisely:

- **The heart contraction**, in its fastest phase, has a velocity of the same order of magnitude than the speed of the shear wave propagation. Therefore the transient elastographic measurements (directly related to the propagating shear wave) are coupled with the heart mechanics.

- **The heart constitutive laws** consist of an active stress and a passive stress. The active stress results from an electrophysiological excitation and may be predominant compared to the passive stress that respects more standard non-linear mechanical law. Active and passive stress has to be carefully taken into account when modeling wave propagations.
- **The heart is a nearly incompressible material.** As most living tissue, the heart is an heterogeneous nearly incompressible viscous medium. The speed of the pressure wave (around 1500 m/s in soft tissues) is two orders of magnitude higher than the speed of the shear waves (around 1-10 m/s in soft tissues).

We can distinguish three kinds of intertwined *topics* that we wish to tackle with this proposal:

- **Mathematical modeling:** It consists in writing a set of partial differential equations that best describe the complex mechanical phenomena that are relevant for our study. We want to show that these equations satisfy some mathematical properties, like energy balance and well-posedness, that will drive the numerical analysis. However, solving the full set of equations will turn out to be intractable from a numerical point of view. Therefore some simplified approximate models have to be defined, their level of accuracy analyzed, and their relevance in term of scientific computing evaluated.
- **Numerical analysis:** The mathematical models obtained in the previous stage have to be discretized in time and in 3-dimensional space before implementation. Original numerical schemes have to be developed and analyzed in terms of stability or accuracy to guarantee the adequate behavior of the computations; these analyses are done relying on properties proven at the continuous level (i.e. at the modeling stage).
- **Scientific computing:** Finally, relatively large scale, parallel finite element computations strategy have to be carried out to take into account the 3-dimensional aspect of the problem as well as the small scale of the phenomena (i.e. the high frequency behavior of the waves).

We now list some *problems* that will be represent the main milestones of the thesis:

[*Mathematical modeling*] **Linearization of the elastodynamic equations of the heart**. The heart large deformations are governed by non-linear mechanical laws coupled with electrical activation laws (see Figure 1 for snapshots of a typical heartbeat simulation). The elastic wave propagations satisfy the same physical laws, but with small displacements of the material. Therefore, a linearization around a time-dependent mechanical state (representing a large deformation) can be carried out to derive relevant linear equations. This is a non-trivial step that is model-dependent (see [7, 8] and their reference for a study in soft passive media and definition of the resulting linear acoustoelastic equations). We will then consider the relevance of simplified quasi-static models, which they consist in assuming small time variations of the average deformation compared to the time variations of the wave propagation.

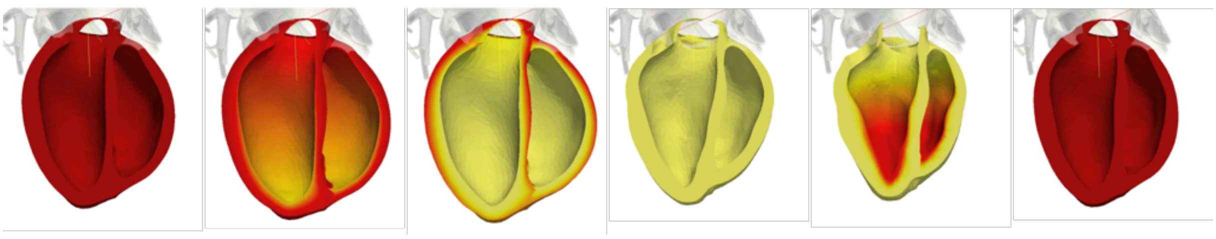

Figure 1: *Snapshots of the numerical simulation of a contraction cycle, the color representing a propagation of activating electric potential (model from [3], team Inria MΞDISIM).*

[*Mathematical modeling & Numerical analysis*] **Approximate model for pressure and shear waves decoupling**. As already mentioned, the heart is a nearly-incompressible medium and this results in a large difference in propagation speed between pressure and shear waves. This has the consequence of approximately decoupling the different wave propagations. Depending on which phenomenon we want to focus on (pressure or shear wave propagation), to avoid numerical issues or to give more simplified description of the involved physics, we want to derive a simplified model and corresponding numerical scheme that takes into account this approximate decoupling (see [4] in which a numerical scheme decoupling the shear and pressure waves in a simple configuration is derived). The derived numerical schemes will enable us to simulate the underlying multi-scale phenomena (because of the wave velocity differences) while guarantying a reasonable computational cost.

[*Numerical analysis*] **Truncation of the computational domain**. In ultrasound elastography, only a small region of interest is investigated although the wave propagates everywhere. To be efficient our numerical scheme and computations have to be restricted to this small region of interest. It can be done using either transparent boundary conditions or perfectly matched absorbing layers. Depending on the newly derived linearized equations we plan to use existing approaches (see [5] or [6] for anisotropic acoustic media). The proper definition of the specific configuration of the heart (geometry, heterogeneity, viscosity,...) and the mathematical analysis of the obtained equations are the key steps to define variants of the previously mentioned methodologies.

[*Numerical analysis & scientific computing*] **Multi-scale and multi-physics finite element simulations**. The previously presented development will end up with the definition of numerical schemes that will be implemented. The resulting software will be coupled with an existing software (developed by the team MΞDISIM) that simulate the cardiac beats. Specific numerical coupling procedures will be defined to use the time dependent large deformation occurring during a simulated heartbeat. These deformations will be used as parameters for the newly developed wave propagation code. We plan to use specific high-order efficient finite elements as well as a parallel implementation written in C++.

Work-environment and required skills

The thesis will be supervised within the team Inria MΞDISIM by D. Chapelle whose area of expertise is the mechanical modeling of the heart. It will be done in collaboration with P. Moireau and S. Imperiale, (Inria, MΞDISIM), whose area of expertise are respectively: the mechanical and numerical modeling of the heart; the modeling and numerical aspects of elastic wave propagations. The definition of the most adapted method for the truncation of the computational domain and the study of numerical implementation aspects will be done jointly by S. Imperiale and S. Fliss (Inria-CNRS-Ensta, POems) who are expert in this field. Software developments will be incorporated into the computational platform *HappyHeart* developed by the team MΞDISIM. It is written in C++, oriented towards finite element multi-physics cardiac simulation and is fully interfaced with the PetSc library to allow for high performance computing. The proposed thesis subject will require from the candidate to have a strong knowledge of applied mathematic tools (functional analysis and theory of finite elements), some fundamentals in mechanics and programming skills oriented towards scientific computations (object-oriented programming in C++).

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