Pyheart-lib: A Python Library For LS-DYNA Multi-Physics Heart Simulations

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Abstract: Physics-based computer simulations of the heart are gaining rising interest for optimizing the design of medical devices and for its treatment prediction and planning. LS-DYNA offers a powerful framework for modeling cardiac electrophysiology, mechanics, and fluid dynamics, as well as the coupling between the three physics. However, its wider adoption is hindered by several requirements among which: knowledge in cardiac function in health and pathology, expertise in numerical simulation, appropriate right modeling choices for the target application, availability of realistic heart geometries. In this paper, we present a free to use python package that allows for the generation of physiologically accurate heart models in an automatic and modular fashion. The architecture is organized in an abstract form that allows users to easily choose between the different physics, anatomical chambers of interest and parameters of interest and export the LS-DYNA keyword files ready for simulation. We also introduce the relevant heart modeling features that are available in LS-DYNA and present two exemplary models generated by the package: a full electrophysiology heart model and a bi-ventricular mechanical model.

1 Introduction

It is widely recognized that numerical methods-based computer simulations of the heart has tremendous potential, both for the medical device industry as for clinical practice [19].

Over the years several tools dedicated to heart modeling were proposed [13]. However, heart modeling is not yet common practice in the medical device industry. Specific expertise, knowledge, and experience is required to set up workflows that link various tools. E.g. segmentation tools to obtain a suitable geometry, a meshing tool to create a simulation-ready mesh, and a finite element analysis tool for solving the governing equations. Moreover, heart modeling features such as material laws, electrophysiology models, and coupling schemes may not be available in the tool of preference, which further inhibits adoption. Recently, various relevant heart modeling features were added to LS-DYNA, a commercial general-purpose finite element code known for its (highly) non-linear finite element analysis capabilities. Added features include mono- and bidomain solvers for electrophysiology modeling, advanced fluid-structure interaction capabilities as demonstrated by [4,15], as well as Purkinje network and fiber generation methods. Nevertheless, creating LS-DYNA heart simulation models still requires an experienced user and manual work. Therefore, we propose a python library – pyheart-lib – dedicated to heart modeling, that should help new and existing LS-DYNA users to efficiently set up and post-process these heart models.

2 Methods

The following section is divided into two main parts. The first part describes the available heart modeling features in LS-DYNA, and the second part gives a brief introduction to the python library that was developed to exploit these features (see e.g., Fig. 1). Finally, we give two potential user applications: a full heart electrophysiology model, and a bi-ventricular model of cardiac mechanics.

2.1 LS-DYNA heart modeling features

A heartbeat is the result of three physics that are inherently coupled: electrophysiology (EP), the mechanical response of the tissue, and blood flow [21]. EP drives mechanical deformation by excitation of the myocardial fibers leading to contraction, this mechanical deformation acts to drive blood flow in and out of the cavities. Deformation is however also a function of the pressure exerted by the fluid inside the cavity. Since the influence of the mechanical deformation to the electrophysiological states is less significant, we essentially have a combined one-way (EP-mechanics) and two-way (mechanics-fluids) coupling problem.

Electrophysiology The bidomain and the monodomain models are widely used to simulate cardiac electrical propagation and accepted for their physiological relevance [18]. Briefly, the bidomain model assumes that cardiac tissue can be partitioned into two separate conducting media: the intracellular space, located inside the cardiac cells, and the extracellular space that connects cells between them. The monodomain model is a simplification of the bidomain model obtained by assuming an equal anisotropy ratio between the intracellular conductivity tensor and the intracellular conductivity tensor. This assumption considerably reduces the size of the system to be solved while keeping a comparable accuracy for the targeted application [20]. LS-DYNA offers the possibility of using either the bidomain, monodomain, or a mix of both models. In this paper we focus on the monodomain formulation which reads:

$$\beta C_m \frac{\partial V_m}{\partial dt} + \beta I_{ion}(V_m, u) - \nabla \cdot (\sigma \nabla \mathrm{V_m}) = \beta \mathrm{I}_{stim}$$

where V_m is the transmembrane potential that measures the potential difference between the intracellular and extra-cellular space at time t, β is the cell surface to volume ratio, Cm is the cell membrane capacitance, $I_{ion}(V_m, u)$ is the resulting ionic currents flowing from the extracellular to the intracellular space through cell membranes, σ is an electrical conductivity tensor that expresses the anisotropic inhomogeneous character of the heart tissue, and I_{stim} is the stimulation current applied on a small region of heart tissue in order to initiate the electrical wavefront. Finally, u is a set of variables that satisfy a set of ordinary differential equations that describe how ionic currents evolve with time through a cardiac cell membrane. Such a system can be expressed by the following equation:

$$\frac{\partial u}{\partial dt} = f(u, V_m)$$

The choice of the expression of f determines which type of cell model is used to describe ionic kinetics. The monodomain and bidomain models can be triggered using **`*EM_MAT_003`**. Regarding cell models, users can choose from for instance: Fitzhugh Nagumo, ten Tusscher, ToR-Ord [14] or define their own by providing the expression of *f* (**`*EM_EP_CELLMODEL_*`**). These equations are completed by Neumann boundary conditions at the domain surface in case of an electrically isolated model, or by flux continuity boundary conditions in the presence of bath. The EP system of equations can be solved using direct or iterative solvers, with several options of operator splitting techniques, for more details see [16].

Mechanics Cardiac tissue can be characterized by a hyperelastic, nearly incompressible, orthotropic material with a nonlinear stress-strain relationship [9] (**`*MAT_295`**.). The orthotropic property is due to the presence of the myocardial fibers. The deformation is governed by boundary conditions (pericardial constraints), external loads (blood pressure), and active stresses generated along the fiber direction upon contraction. The total stress can be decomposed into passive and active parts as:

$$\boldsymbol{\tau} = \boldsymbol{\tau}_p + \boldsymbol{\tau}_A$$

Passive stress $\boldsymbol{\tau}_p$ designates the passive stress which is derived from the strain energy function Ψ. In this work we used the nearly in-compressible Holzapfel- Ogden model with one fiber family [9]:

$$\begin{aligned}\Psi &= \Psi_1(I_1) + \Psi_F(I_F) + \Psi_V(J) \\ &= \frac{a}{2b}(\exp[b(I_1 - 3)] - 1) + \frac{a_f}{2b_f}\left(\exp\left[[b_f(I_f - 3)\right] - 1\right) + \frac{K}{2}(J-1)^2\end{aligned}$$

Active stress Active stress describes the excitation-contraction from the EP model. Multiple active models are available within LS-DYNA, including those presented by [8, 10, 17]. For the mechanical model presented here, we used the classic model of active stress proposed by Guccione et al. [7]. This "Hill"-type active model describes the relationship between the evolution of cytosolic calcium ion concentration and tension developed in the tissue, calcium concentration can be either defined explicitly or can come from a coupled EP simulation.

Circulation model The opening/closing state of the heart valves strongly influences the pressures inside the cavity, leading to the characteristic pressure-volume loops with two iso-volumetric phases (iso-volumetric contraction and iso-volumetric relaxation). Fully resolving blood flow and behavior of the heart valves is, however, not a strict requirement for all applications where the overall cardiac function is of interest. Hence, a uniform cavity pressure is typically assumed [1, 3, 25]. Similarly, a lumped-parameter approach is available in LSDYNA, where blood flow in/out of the cavity – represented by an in-compressible volume – can be added as an additional constraint to update the pressure of the cavity (**`*DEFINE_CONTROL_VOLUME, *DEFINE_CONTROL_INTERACTION`**).

Fiber orientation, the spatial arrangement of the ventricular myocytes is crucial for the physiological conduction of the electrical wave and mechanical response. To obtain this typical fiber structure, LS-DYNA uses the rule-based method proposed in [2]. Briefly, the user specifies Laplace-Dirichlet problems for which the solutions gradients define the apex base direction and the transmural direction, for each element of the mesh. These two local vectors are rotated by an angle that varies depending on the transmural depth. The obtained local coordinate system serves as the basis for defining electrical conduction properties and active stress components (**`*EM_EP_LAPLACE_DIRICHLET`**, **`*EM_EP_CREATEFIBERORIENTATION`**).

Purkinje network The Purkinje network allows for a more appropriate electrical activation sequence. LS-DYNA offers the possibility to construct a set of beams that play the role of Purkinje fibers in EP simulations. LS-DYNA implements a fractal tree algorithm like [5] that takes a set of faces and a starting point as inputs in order to construct a set of beam elements that lie on the given surface (**`*EM_EP_PURKINJE_NETWORK`**).

2.2 A pythonic interface to LS-DYNA for heart modeling

Python is popular in the scientific community due to the large number of third-party libraries that are available. Similarly, we developed a python library that integrates some of these third-party libraries, such as the Visualization Toolkit [23], and exploits the implemented heart-modeling features in LS-DYNA. Consequently, this library provides pythonic access to LS-DYNA's heart-modeling capabilities, while at the same time reducing complexity by using an abstracted representation of a heart model. In this preliminary work, we introduce two modules: a preprocessor module and a simulator module. *preprocessor* The main purpose of the preprocessor module is to generate a heart model that contains all geometric heart features relevant for the simulation model, and currently supports models of the isolated left ventricle, bi-ventricular models, and full-heart models (Fig. 1). Moreover, this module provides methods to filter the parts of interest, extract relevant geometric features, and (re)mesh surfaces and volumes if necessary. Examples of relevant heart features include: the endo/epi-cardial, and septal surfaces, apical points, and cavities. For example, this preprocessor can currently download and process models from the virtual cohorts of full-heart models by Strocchi et al. [24] and Rodero et al. [22] but can be extended to other sources.

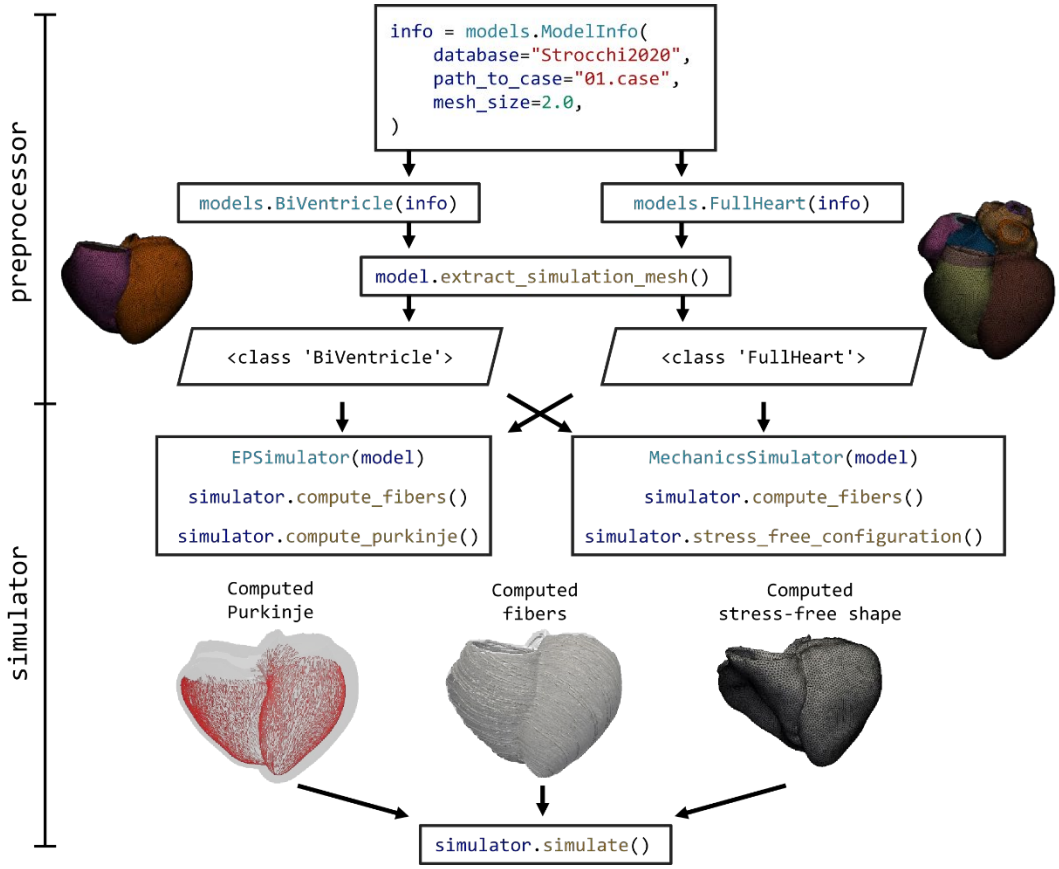

Fig.1: Flow chart demonstrating the preprocessor and simulator modules. The preprocessor is used to instantiate a model of a certain geometric type. Consequently, this instantiated model can be used to instantiate a simulator class that defines the physics of interest.

simulator Models defined by the preprocessor module can be consumed by the simulator module. The simulator module contains different simulators, e.g. for EP simulations and electro-mechanics simulations (Fig. 1). Consequently, these simulators contain essential methods for these types of simulations, and include computation of 1) the fiber orientation, 2) the Purkinje network, and 3) the stress-free configuration. Finally, any main simulation can then easily be launched by *simulator.simulate()*. Methods for convenient visualization of resulting fibers or constructed Purkinje networks are also available. A typical code-snippet to generate a full heart Electrophysiology model from [24] is included below.

3 Model examples

Section 2.2 describes the preprocessor and simulator modules. In the following section two example models are presented that were generated with these modules: a full-heart EP model, and a bi-ventricle mechanical model to simulate cardiac mechanics.

3.1 Full heart electrophysiology

Methods The full-heart geometry was obtained from [24], and was re-meshed with an average edge length of 2mm. The model uses the monodomain framework (Eq. 1) with a 1ms time step and the ten Tusscher cell model with a finer time step of 0.2ms and exploited the implicit first order operator splitting scheme (see appendix D in [16]). The conductivity values in atria and ventricles were 0.5 mS/mm in the fiber direction and 0.1mS/mm in the normal and sheet directions. The conductive beams were assigned with a conductivity value of 10 mS/mm and the atrioventricular node area with a value of 7 mS/mm. A stimulation current of 50μA/mm3 was applied at the sinoatrial node for a duration of 20ms.
Results Fig. 2b demonstrates that the obtained activation sequence follows a typical healthy wavefront. The initiation of the wavefront occurs at the sinoatrial node, propagates through the right and left atria, is delayed at the atrioventricular node, spreads through the branches, Purkinje network and finally within the ventricular myocardium. The total activation times at the atria and ventricles are 235ms and 222ms respectively.

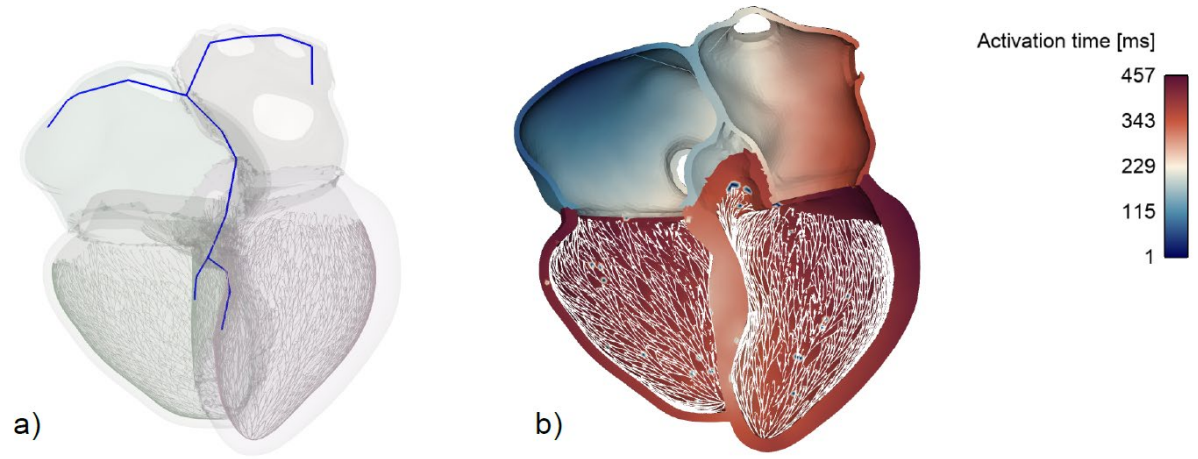

Fig.2: Flow chart demonstrating the preprocessor and simulator modules. The preprocessor is used to instantiate a model of a certain geometric type. Consequently, this instantiated model can be used to instantiate a simulator class that defines the physics of interest.

3.2 Bi-ventricular mechanical model

Methods The bi-ventricular geometry is extracted from a healthy full heart of [22], and represents a healthy case segmented at end-diastole. Fibers were generated on the end-diastolic geometry using a rule-based method [2]. The stress-free configuration was computed using a left-ventricular and right-ventricular end-diastolic pressure of 15 mmHg and 4 mmHg respectively. The presence of the pericardium was modeled using springs defined in the normal direction of the epicardial surface and

was similar to the implementation by [25]. A constant pre-load (left: p_{venous} = 15mmHg, right: p_{venous} = 4mmHg) and Windkessel afterload was added to both cavities, see also [25]. Passive material parameters were based on literature, and chosen as: a = 2.36kPa, b = 1.75, a_f = 0.49kPa, and b_f = 9.01. Active stress was generated by using a model of active stress proposed in [7], with a maximum active stress of T_{max} = 125kPa. All fibers are triggered simultaneously. Results Peak systolic pressure in the left and right ventricles were 146mmHg and 19mmHg respectively (Fig. 3a). Multiple cycles were required to obtain a periodic solution, and in the fourth cycle, a left-ventricular ejection fraction of 19% was obtained. Moreover, Fig. 3b demonstrates that the pericardial constraint limits the motion of the apex and gradually allows more motion toward the base.

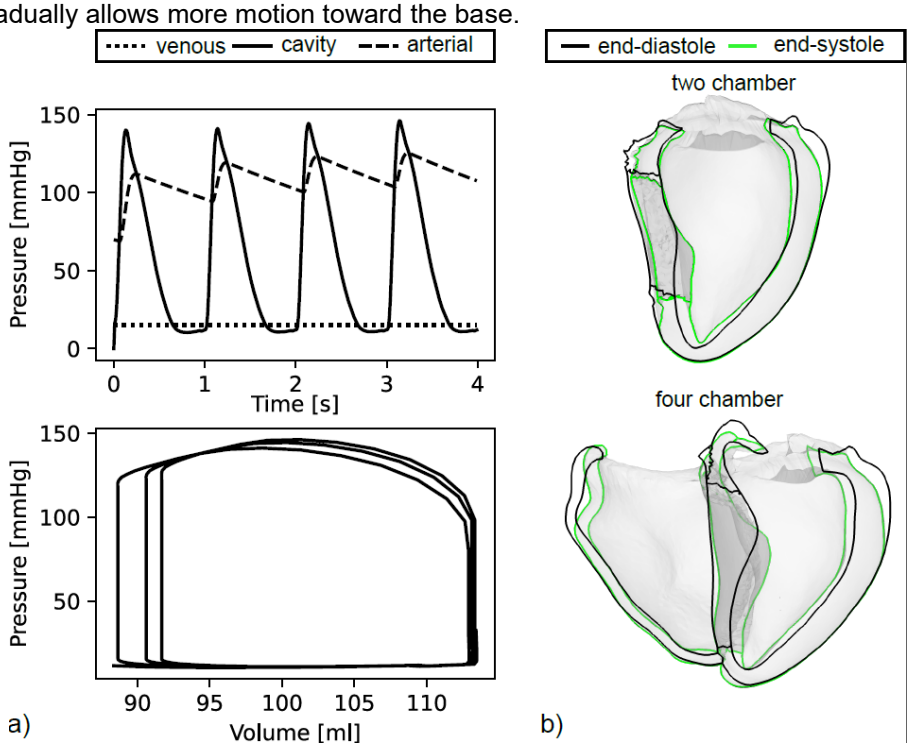

Fig.3: Flow chart demonstrating the preprocessor and simulator modules. The preprocessor is used to instantiate a model of a certain geometric type. Consequently, this instantiated model can be used to instantiate a simulator class that defines the physics of interest.

4 Discussion

In this manuscript we present a python library to create LS-DYNA heart models. This python library was developed in a modular fashion, that enables a user to create heart models of various levels of complexity through a python interface. Two example models were created: a full-heart electrophysiology model, and a bi-ventricular model of cardiac mechanics. Both models are able to represent typical electrophysiology and mechanical behavior with parameters and model constants from literature. Even though these models are patient-specific with respect to geometry, calibration with clinical data is necessary. For instance, total activation times observed in Durrer et al. [6] are lower than those obtained with the presented model, conductivity would need to be optimized to reach proper activation times. Hence, methods are being developed to optimize conduction velocity given patients' ECG signals, or based on desired conduction velocities. For the mechanical model, passive material parameters may be personalized by ensuring that the end-diastolic pressure-volume relationship corresponds to empirical relationships found in [11]. To address this need, a calibration module, in line with the framework proposed by [12], would be required for further personalizing these models, and is currently being developed.

5 Conclusion

In this manuscript we presented a python library to generate LS-DYNA based heart simulations. We adopted a modular approach, where the geometry of interest and physics of interest are exposed in an abstract way. Consequently, with just a few lines of python code a user can generate example models

of different levels of complexity. Hence, we believe this library will facilitate the democratization of cardiac simulation for realistic geometries.

6 Literature

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