Automated Parameter Tuning for Living Heart Human Model using Machine Leaning and Multiscale Simulations

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1. Introduction

Living Heart Human Model is a finite element model with realistic three dimensional geometries of four heart chambers, the overall heart responses are driven by sequentially coupled electrical conduction and structural contraction analyses, with blood flow modelled as a closed loop lumped parameter model [1]. It provides a virtual environment to help test medical devices or surgical treatments before they are utilized in human. It is critical to tune the model to a patient or disease state, however this is extremely difficult using traditional varying-one-parameter-a-time approach, as there are a large number of parameters with complex interactions between parameters, and large number of CPU time to perform each analysis. Another popular type of model in cardiovascular research is the Lumped Parameter Network (LPN) model that can approximate the pressure-volume relationship and fluid flow properties. This type of model can be solved in real-time, but it requires some pre-knowledge for the cardiac driving functions, i.e., the time varying pressure and volume relationship of the active chambers [2].

It will be highly beneficial if we could establish a model that can link physical parameters and cardiac driving function. Machine learning opens a new path to science and discovery by finding insights and strategies that we as humans may never be able to find out. The **objective** of this study is to use Machine learning and LHHM to train a model to characterize the relationship between realistic physical parameters and time varying pressure and volume relationship for active chambers, and then use ML trained model to guide the LPN model to quickly tune the model to a particular patient or disease state.

2. Method

LHHM

LHHM includes realistic geometry, material properties and boundary condition. The geometries of atria and ventricles are from a 50% healthy male, the material properties consider passive material during diastole and contractile materials during systole of the four active chambers, and boundary conditions include the outlet of each cardiac chambers connected to the inlet of the other, with peripheral elastance and resistances, capturing dynamics of pulmonary and systemic circulations.

Of all the parameters in LHHM, the active tissue behaviour is what drives the contractile behaviour of the active chambers [3]:

$$T_0 = T_{max}\frac{Ca_0^2}{Ca_0^2+ECa_{50}^2}C_t \qquad (1)$$

where T_{max} is the isometric tension at the largest sarcomere length and highest calcium concentration, Ca_0 is the peak intracellular calcium concentration, and

$C_t = \frac{1}{2}(1 - cos\omega)$,

$$\omega = \begin{cases} \pi\dfrac{t}{t_0} \text{ when } 0 \le t \le t_0 \\ \pi\dfrac{t - t_0 + t_r}{t_r} \text{ when } t_0 \le t \le t_0 + t_r \\ 0 \text{ when } t \ge t_0 + t_r \end{cases}$$

$t_r = ml + b$

m, b are constants that specify the shape of the linear relaxation duration and sarcomere length relaxation, and $t_0$is the time to reach peak tension after the initiation of active tension. In addition, $ECa_{50} = \frac{(Ca_0)_{max}}{\sqrt{\exp[B(l-l_0)]-1}}$, $l = l_R\sqrt{2E_{ff}+1}$, where:

E_{ff} = Lagrangian strain in the fiber direction,

B is a constant that specifies the shape of the peak isometric tension-sarcomere length relation,

l_0 is the sarcomere length that does not produce active stress,

l_R is the sarcomere length with the stress-free condition,

and $(Ca_0)_{max}$ is the maximum peak intracellular calcium concentration.

Machine Learning

The structure of the ML-FE surrogate model is a supervised learning regression problem. We use a tree ensemble learning approach whereby "xgboost" package in python programming language was used to predict the time varying pressure and volume curves based on material properties and time. "xgboost" stands for eXtreme Gradient Boostings, it is a machine learning technique for regression and classification, which produces a prediction model [4].

Latin hypercube design of experiments (DOE) method was used to sample features as follows: 0.0015μm $<l_0<$0.0028μm, 0.075s$< t_0<$0.25s, 0.65MPa$< t_{max}<$1.9MPa for both left and right ventricles. The number of LHHM simulation provides 77 training sets and 11 test sets. After the model was trained using the training set, predicted time varying elastance was calculated for the test sets.

LPN model

The system level LPN circulatory model is developed in Dymola using Modelica standard libraries. This model is decomposed into several distinct components which compute output volume, pressure and flow, based on inputs of elastance, flow and pressure.

Active chambers of atria and ventricles are modelled as elastance generators, input from the Machine Learning model. **Elastic compartment** is used to model systemic arteries, veins and pulmonary circuit, it characterizes the relation between increase in volume and pressure. **Resistor** is modelled between arteries and veins, veins and right atrium, and pulmonary circuit and left atrium, it defines the relation between flow rate and pressure gradient. **Valves**, including aortic, mitral, pulmonary and tricuspid valves, are characterized by the direction where the flow is allowed and a resistor. Previous efforts indicate that by using consistent elastance, resistance and compliance parameters, LHHM and Dymola model can predict highly similar pressure and volume for all

chambers.

Optimization

An optimization workflow is developed in Isight, a process automation and design optimization tool, show in Figure 1. The optimization parameters include the 6 material parameters of LHHM model, hemodynamic parameters of the LPN circulatory model, the objective function is to reach target volumes and pressures. Based on the material parameters, machine learning predicts active chamber elastance, which is then used to drive the LPN circulatory model to predict all chambers pressure and volume. Pointer2 technique, a powerful exploration approach that combines multiple optimization approaches, is used because it is ideal for complicated unknown design space with potentially multiple optimums.

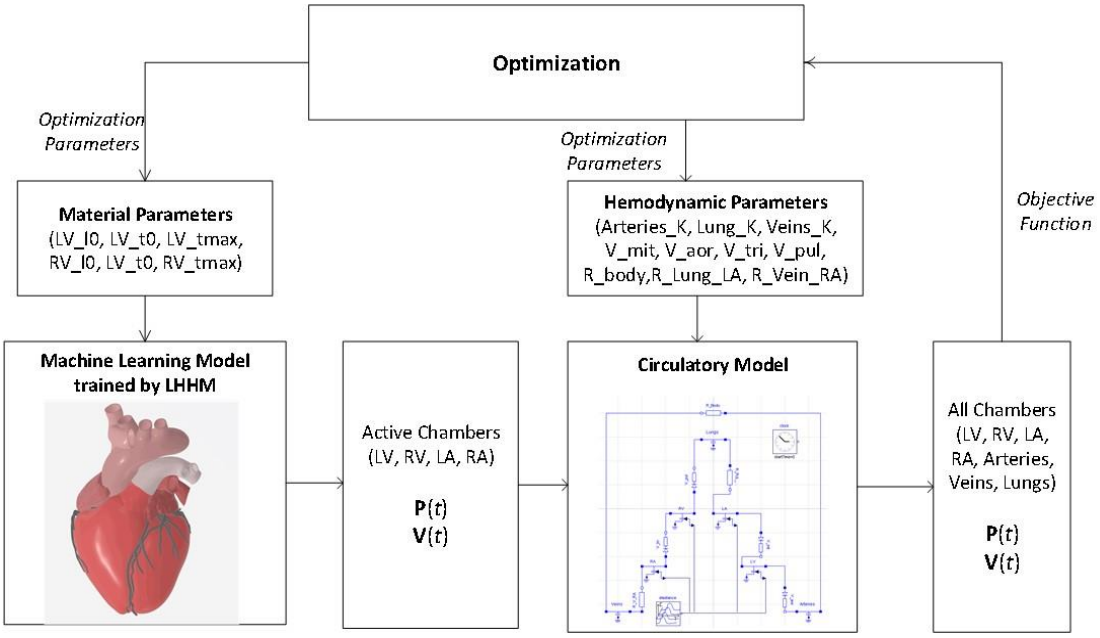

Figure 1 Flowchart of the automated tuning process

3. Results

Machine Learning model is trained by the pressure and volume responses of 77 LHHM simulations of varying active material parameters, and this ML model is used to predict the pressure and volume response based on three LHHM simulations with randomly selected material parameters that were not used in the training set. The ML-predicted LV pressure and volume were in good agreement with LHHM simulation with average error of 6% in pressure and 2% in volume (Figure 2). Similarly, the errors in ML predicted RV pressure and volume are 10% and 1% respectively.

Automated parameter tuning process was able to adjust the active material parameters and hemodynamic parameters to reach target responses of maximal LV/RV pressures, diastolic blood pressure and LV/RV ejection fractions (Table 1).

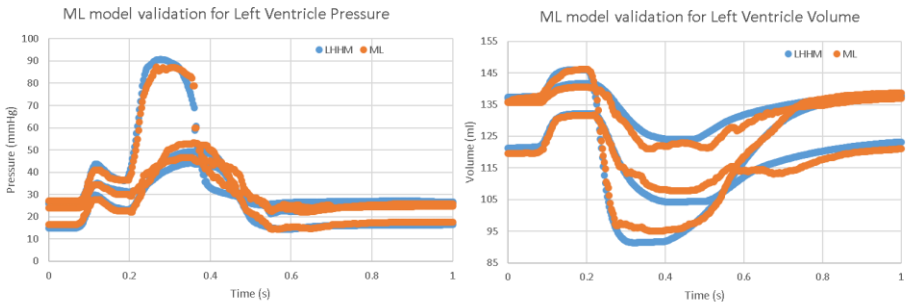

Figure 2 LHHM-calculated and ML-predicted LV pressure and volume for three instances based on random selection of active mechanical properties.

Output variables	target	before optimization	after optimization
Max pressure in LV (mmHg)	100-140	**92**	121
Max pressure in RV (mmHg)	15-30	22	30
Diastolic Arterial Blood Pressure	60-90	**28**	65
LV Ejection fraction	≥50%	**40**	50
RV Ejection fraction	≥40%	40	40

Table 1. Objective function values

4. Conclusion

We developed a workflow to automated tune the material and hemodynamic parameters for the Living Heart Human model using machine learning and multiscale simulations, including three dimensional finite element simulation and LPN circulatory simulation. We used ML to predict elastance for active chambers in matter of seconds, the results of ML model were in close agreement with FE models. LPN circulatory model with optimization allow explore the additional contribution of the hemodynamic parameters to the model behaviour. Future study will use similar method to tune LHHM into disease states.

Reference

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