École Polytechnique Fédérale de Lausanne

Chair of Modeling and Scientific Computing
CMCS

Semester Project - CSE II

Reduced order models for the simulation of pathological heart valves

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1 Introduction

Numerical modeling of the human cardiovascular system (CVS) represents an active branch of research which allows the medical specialists to advance in understanding of underlined processes inside the heart and blood vessels at any scale, moreover it helps to analyse the potential problems which can arise inside CVS by various modifications inside the models. Due to inability to capture in details the pressure and flow parameters without invasion into heart chambers, the process of diagnosing heart diseases can become very complicated, the limited data on atrial pressure and cardiogram results can give only overall representation of the heart condition and the exactness of the diagnosis is based mainly on experience of the doctor. Nevertheless the development of numerical models of CVS helps to get better understanding on processes which can cause particular disease (reverse flow leakage in heart chambers, improper contraction of heart muscles due to infarction of tissue). Mathematical model allows the analysis of all physical values of the system during the heart beat as well as possibility to adjust individual parameters specific to each patient. For example, introduction of pathology of valves in the model (regurgitation, stenosis) and pathology of tissue (ventricular hypotrophy), simulation of infarct by constraining the elastance of atriums and ventriculars produces the numerical results which can be matched with patient data and give more insight on potential malfunctioning. Therefore, developed models become an efficient tool for doctors to diagnose properly the heart disease and to assign necessary treatment and surgery (replacement of the valves and damaged tissue) as well as to predict the effect on blood circulation from implanting cardiac-assist devices.

1.1 Structure of the heart

Heart is a muscle which contains four chambers (two ventriculars and two atriums). Periodic contraction and relaxation of the chambers functions as a pump for blood circulation. Formally the heart can be split in two parts (left and right heart), each with own atrium-ventricular interaction. The left heart pumps the blood through systemic circulation (to deliver oxygen and nutrients to the organs) and the right heart pumps the blood from systemic veins to the pulmonary circulation, to the lungs, in order to oxygenate it for a new cycle. The four heart valves located at the exit of each chamber regulate the inflow and prevent the back-flow of the blood, thus constantly maintaining its right direction. For example, mitral and aortic valve separates the left ventricle from left atrium and aorta respectively, tricuspid and pulmonic valve divide the right ventricle from right atrium and pulmonary vein. Schematically the heart structure with flow direction is shown in Fig 1, in addition very detailed explanation of all the heart components

and vascular system up to muscle cells can be found in [9].

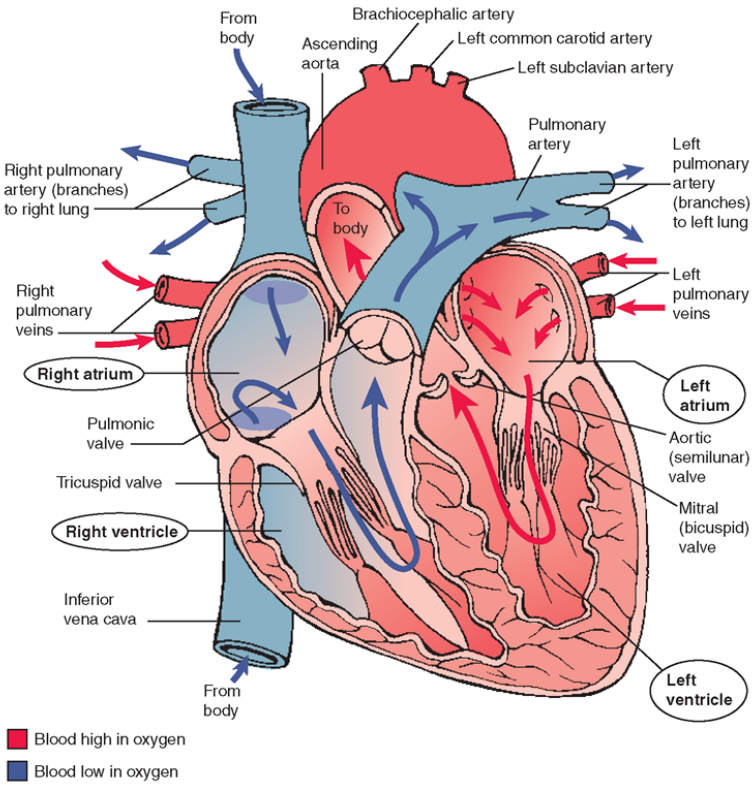


Figure 1: The interior structure of the heart [6]

The heart activity is regulated by autonomous nervous system with the parasympathetic and sympathetic nerves, which sends the neural impulses to myocardium and stimulates the heart contractions which pump the blood from the ventricles. These contractions compose the heart beat, which further drives the cardiac cycle with the whole pulmonary and systemic circulation.

The heart beat can be represented as a two stage pumping action with a duration of 1s. Systole phase is defined as the period between the closing of the mitral valve and subsequent closing of the aortic valve, during this phase the left ventricle is filled with blood and under the electric impulse from nervous system the myocardium contracts and pushes the blood out of the ventricle through aortic valve. Accordingly diastole phase is defined as the period between closing of aortic valve and subsequent closing of the mitral valve, the ejected blood from the left ventricular goes through aorta to systemic circulation, enters the right heart and pulmonary circulation, oxygenated it comes back from pulmonary veins to left atrium and after atrium contraction enters the left ventricular through the mitral

valve to begin the cycle again. The period constitutes approximately two thirds of the cardiac cycle, however due to the auto regulating nervous system, when the heart rate increases (during physical activities, adrenaline rise), diastole and systole phases can decrease to maintain necessary flow rates [8].

1.1.1 Heart working phases

The heart periodic contraction and relaxation can be decomposed in four main parts:

- **Contraction:** when the ventricle muscle receives the nerve impulse and starts contracting, it causes a strong increase of ventricular pressure, but at this moment the valve separating atrium and ventricle is closed and the volume is constant (iso-volumetric contraction).
- **Ejection:** the blood pressure on both sides of aortic (pulmonary) valve leaflets is equal and the pressure inside the ventricle is still increasing. The aortic (pulmonary) valve opens and the muscle contraction decreases the volume, as soon as the stroke volume is ejected and the reverse flow appears the valve closes.
- **Relaxation:** ventricle muscle relaxes, the atrium-ventricle valve is closed and the volume of the chamber does not change (iso-volumetric relaxation).
- **Filling:** when the blood pressure in the ventricle becomes lower than in atrium, the mitral (tricuspid) valve opens allowing the blood flow, and at the end of phase atrium contracts to push some blood further ("atrium kick").

The contraction and ejection phase compose together the systolic period, while the relaxation and filling phase form the diastolic period.

The condition of the heart is determined by the cardiac function, the most common indicators which are used by doctors to establish the diagnosis are the pressure-volume diagram (PV diagram) and cardiac output (CO). An example of PV diagram obtained from simulation is demonstrated in Fig 3.

The two main characteristics of the PV diagram are the End Systolic Pressure-Volume Relationship (ESPVR) and End Diastolic Pressure-Volume Relationship (ESPVR) which determine the upper and lower limits of the cardiac cycle. The EDPVR is used to measure the capacitance of the ventricle (due to elastic chamber walls) and ESPVR is used to define the strength of contraction. When the diastolic failure occurs, the compliance of the heart will decrease, as well as the contractility disfunction leads to the decrease of ESPVR slope.

The cardiac output characteristic is the main measure of the amount of blood pumped into the aorta from the left ventricle (ml/sec). It is defined as the product

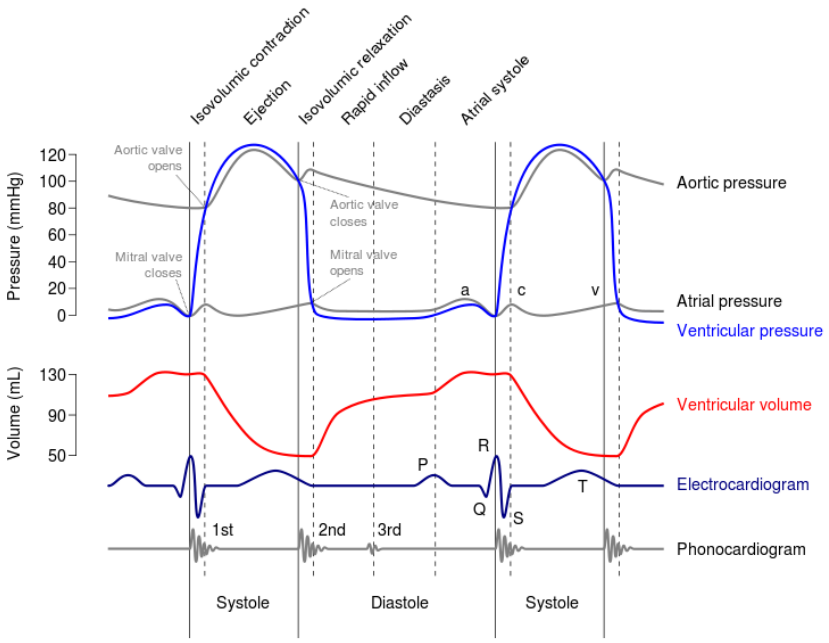


Figure 2: Wigger's diagram of typical healthy heart cycle [7]

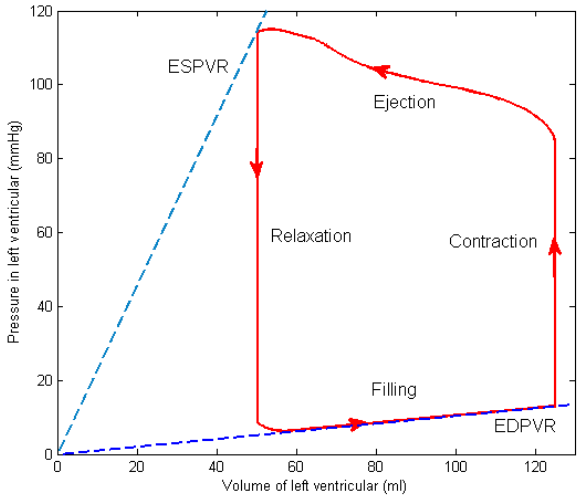


Figure 3: PV diagram, pumping mechanism of the ventricular

of the stroke volume (amount of blood ejected during one heart beat) SV and the heart rate HR:

$$CO = SV \times HR$$

It is an important measure which defines the ability of the heart to deliver necessary nutrients and oxygen to the body, and highly depends on the valves condition and the proper functioning of the sympathetic nervous system (healthy heart rate).

1.2 Lumped parameter models of the cardiovascular system (0D models)

0D models were developed as a simplification of the complex three dimensional distributed parameter models for CVS, since it is not necessary to simulate particular parts of CVS to the finest scale (capillaries, arterioles) to study bigger and more dynamic parts, such as heart chambers and valves. In addition it becomes unfeasible to run the full 3D model due to large computational time and costs involved, therefore instead of finding the distribution in space of all the physical values which characterize the flow, it is sufficient to operate with average values across the volume. It has been shown that less detailed models are still able to capture important features of the cardiac cycle and reproduce the response which matches the behavioral pattern of the real system. Furthermore, 0D models are computationally fast and flexible, there is a possibility to couple the advance dimensional model of particular local segment of interest with existing lumped model of the rest of the CVS (for example, complex heart coupled with the 0D model of the vascular system of blood vessels).

Derivation of the lumped model is based on the concept of a hydraulic-electrical analogue, since there have been found a lot of similarities between the pressure-flow and current-voltage dynamics. The most common concentrated parameter model is the Windkessel model, which is used to describe the relation between the blood pressure and the flow through the arterial and venous system using equations of typical RLC circuits (Ohm's and Kirchhof's laws), where the pressure corresponds to the voltage and the flow rate associates with the current, while the RLC components itself represent certain physical properties of the blood vessels. For example, the blood viscosity can be described by the resistance element R, the blood inertia by the inductance L and the wall compliance by the capacitance C. The more detailed description of the equations and variations in circuits for each part of the CVS is provided in section **??**. In general different combinations of the circuits with imposed parameters allow to model specific effects in vascular system up to any desired scale by adding more compartments and interacting them differently, but the major problem arises in imposing suitable constants for R, L, C elements in the whole system in order for simulation results to resemble the Wigger's diagram (Fig 2). Consequently, great consideration should be taken, when the model is designed, to prescribe the consistent values for each element, which are close to actual physical properties of the vessels. The model which

is described further is based on the work of Theodosis Korakianitis and Yubing Shi [3], where all the values for each compartment can be found as well as the detailed explanation of the governing equations.

1.3 Heart valves modeling

Study of mathematical models of the heart valves comprises an important and active part of CVS research as valve dynamics significantly influence the pressure and flow rates inside heart chambers, moreover the most common and potentially dangerous malfunctioning appears when the valves stop closing normally (regurgitation) or unable to fully open (stenosis). Consequently the blood can passively flow in the wrong direction and the auto regulation system in order to preserve necessary pressure and flow levels forces to contract the chambers more frequently and damages further the valve tissue, what in the end can lead to complete heart failure. Understanding in depth the underlying mechanism of opening and closure of the valves requires the analysis of the complex blood-leaflets interaction and in case of distributed parameter models heart valve dynamics is represented as a detailed 3D model which captures the vortices and the effects of turbulent flow on leaflet motion. However in order to decrease the computational cost and to determine the overall behavior of the valves in context of the full CVS model, the good approximation can be achieved by introducing simplified lumped parameter model. Particularly, several assumptions are made to facilitate the simulation: leaflet opening angle is considered as an averaged value among several possible angle configurations of real valve, the pressure, velocity and flow distributions are replaced by area-averaged values. At first approach, the valves are represented as diode elements in the circuit analog of CVS, thus there are only two possible states, when the valve is open to the maximum angle position and allows the direct flow, and when the valve is closed and no reverse flow is allowed. Secondly, more accurate model is considered, which involves second order differential equation for angle dynamics and takes into account the momentum produced from pressure differences and the frictional force.

2 Mathematical model

Hydraulic-electric analog of the model is used in order to simulate the pressure and the outflow of the parts of cardiovascular system. Capacitance C represents the elasticity property - storage capacity of the vessel and vascular compliance, resistance R represents the viscous resistance of the blood flow and inductance L is an inertia of the blood. Each part of the CVS can be substituted by analogous Graphically convenient circuit representation of the whole CVS double loop is

shown in Fig 4. The moment when the mitral valve closes is chosen as a start of the cardiac cycle. The detailed derivation of the equations of 0D model from averaging 1D and 3D models and taking into account the fundamental concept of conservation of mass and momentum is presented in [4] and [8].

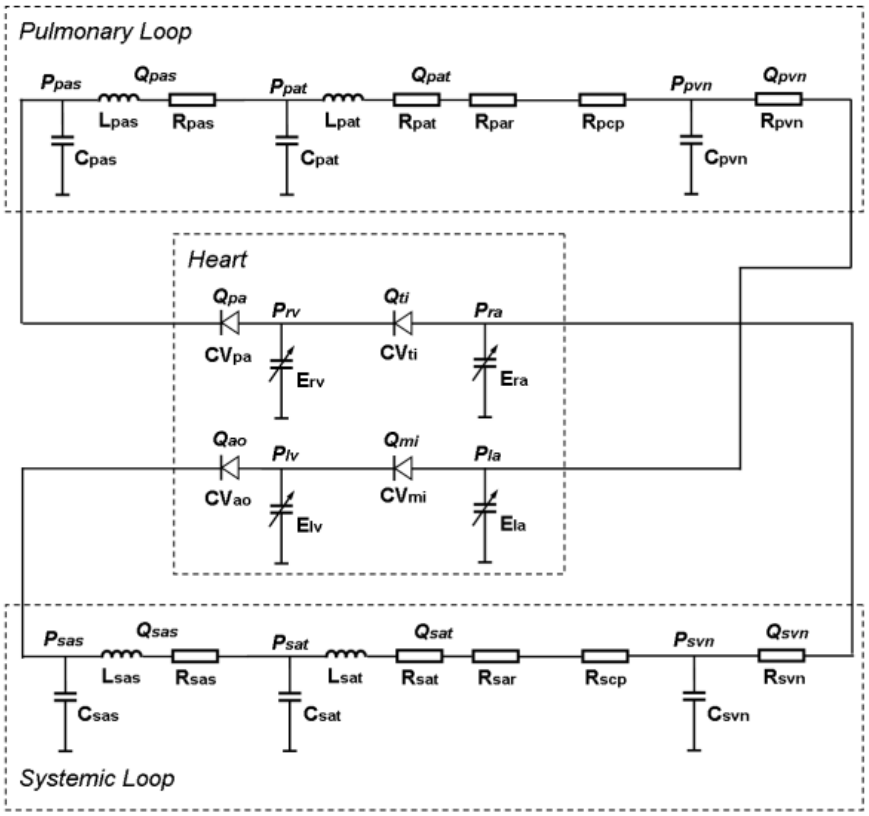


Figure 4: Schematic representation of the electric circuit analog of CVS [5]

2.1 Description of the heart

The pumping action of the heart is simulated by time-dependent functions of the left and right ventricular elastances.

2.1.1 Ventricles

The main characteristics of the heart chambers are described by the equation for the conservation of mass, when the instantaneous volume change is driven by the flow-rate change at the inlet and the outlet, by pressure-volume relation and

the variable in time elastance, which is a key function that simulates the action of the heart muscle.

The mass conservation law:

$$\frac{dV_v}{dt} = Q_{in} - Q_{out} \tag{1}$$

The ventricular elastance change:

$$e_v(t) = E_{dias} + \frac{E_{sys} - E_{dias}}{2} \cdot \tilde{e}_{activ}(t) \tag{2}$$

The values E_{dias} and E_{sys} represent the end-diastolic and end-systolic elastances of the ventricular respectively. The activation function $\tilde{e}_{activ}(t)$ is responsible for the contraction and relaxation dynamics of the ventricular muscle, the most commonly used type of the function is

$$\tilde{e}_{activ}(t) = \begin{cases} 1 - \cos(\frac{t}{T_s}\pi) & 0 \leqslant t < T_s \\ 1 + \cos(\frac{t-T_s}{T_s}2\pi) & T_s \leqslant t < \frac{3}{2}T_s \\ 0 & \frac{3}{2}T_s \leqslant t < T \end{cases} \tag{3}$$

Where the systolic time interval T_s is determined by Bazett formula as $T_s \approx 0.3\sqrt{T}$, and T represents the length of the cardiac cycle, which is $\approx 1s$. The shape of the elastance function is illustrated in Fig 5. Furthermore, the pressure-volume relationship is expressed as

$$P_v = P_{v,0} + e_v(t) \cdot (V_v - V_{v,0}) \tag{4}$$

which represents the linearized Voigt viscoelasticity model and simulates the pump activity of the ventricular. Both left and right ventriculars are described with the same type of equations, but with different constant parameters.

2.1.2 Atriums

The upper right and left atria which collects the blood from vena cava and pulmonary veins correspondingly are simulated similarly to contracting ventricular chambers. In the real heart, the atrium contraction also known as "atrium kick" leads to a rapid increase of the volume and pressure in the ventriculars, which can be observed from Wigger's diagram in Fig 2, right at the moment before the closure of the mitral valve. In order to observe the effect of atrium contraction on the overall system dynamics, firstly the simplified model with the constant elastance function $e_a(t) = E_{a,min}$ for both atriums is considered, and then it is

compared with the variable elastance model defined by activation function. The variable elastance of the atriums:

$$e_a(t) = E_{a,min} + \frac{E_{a,max} - E_{a,min}}{2} \cdot \tilde{e}_{a,activ}(t) \tag{5}$$

$$\tilde{e}_{a,activ}(t) = \begin{cases} 0 & 0 \leqslant t < T_b \\ 1 - \cos(\frac{t-T_b}{T-T_b} 2\pi) & T_b \leqslant t < T \end{cases} \tag{6}$$

Where the activation moment is set to $T_b = 0.92s$, the corresponding graph of the elastance change is presented in Fig 5. The remaining equations of mass conservation and pressure-volume dependence stay the same as in case of ventriculars (2), (4), but with different constant values for $P_{a,0}$ and $V_{a,0}$ in relaxed state, and the inflow and outflow rates correspond to systemic (pulmonary) vein inflow and mitral (tricuspid) valve outflow accordingly.

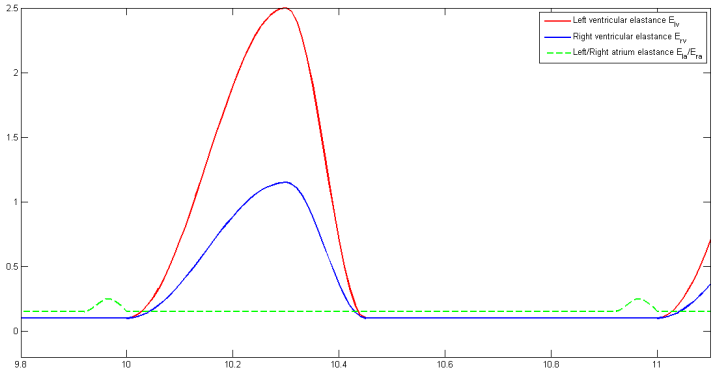


Figure 5: Elastance function of ventricles/atriums within one heart period

2.1.3 Diode model of the valves

The heart ejects blood in a short moment of heart beat, and in the rest of the cardiac cycle heart chambers relax, contract and fill. Therefore the valves open and close almost instantaneously, nevertheless the great care is taken to model properly all the processes which can affect the valve functioning, since small deviations in condition can lead to further serious complications up to complete tissue damage and abnormal volume and pressure rates in circulation. Most often the full 3D model of valves is developed which further is coupled with simplified 1D or lumped parameter model of the rest of CVS. However for the purpose of this modeling the

basic fluid mechanics orifice model is used to connect the flow through the valve and pressure rates on both sides of the leaflets. The following general pressure-flow relation is used:

$$Q_{valve} = C_D \cdot A_{valve} \cdot \sqrt{P_{in} - P_{out}} \cdot \text{sign}(P_{in} - P_{out}) \tag{7}$$

where C_D is a flow discharge coefficient, A_{valve} is the orifice passage area, P_{in} and P_{out} represent the input and output pressures in each of the compartment (heart chamber), for example, for the aortic valve the pressure in the left ventricular will be the input and the pressure in aortic sinus will be the output. The above equation takes into account that the reverse flow is possible in cases of leaflets angular motion and pathological valves. Further, there are two variations of the valve dynamics model are considered which affect only the variable A_{valve}. In case of diode model, the valve opening is simulated as an abrupt change of angle under pressure difference from 0 to maximum value and thus the state of the valve is either 0-closed or 1-open:

$$A_{valve} = \begin{cases} 1, & P_{in} \geqslant P_{out} \\ 0, & P_{in} < P_{out} \end{cases}$$

when the input pressure is lower than the output pressure, no flow is allowed. This model represents the basic concept of healthy valve "protection" function, when the blood flow is maintained in one direction and through the maximum passage area.

2.1.4 Dynamic model of the valves

More detailed description of the valve dynamics helps to capture particular features in cardiac cycle such as slight flow regurgitation during valve closure as well as allows to model valve pathologies (non-fully opening and closure of the leaflets). For this purpose the new state variable θ is introduced as an opening angle of the leaflets, thus the orifice passage area becomes a time-dependent parameter expressed as:

$$A_{valve} = \frac{(1 - \cos(\theta))^2}{(1 - \cos(\theta_{max}))^2} \tag{8}$$

Several factors affect the dynamics of the angle, the most important ones are the moment generated by pressure difference across the valve and the moment caused by frictional force:

$$M_{\Delta P} = k_P \cdot (P_{in} - P_{out}) \cdot \cos\theta \tag{9}$$

The resistance of the valve tissue is considered to be proportional to the angular velocity:

$$M_{fr} = -k_f \frac{d\theta}{dt} \tag{10}$$

Combining the two equations gives the angular momentum balance of the valve expressed as:

$$I\frac{d^2\theta}{dt^2} = M_{\Delta P} + M_{fr} \tag{11}$$

where I is the momentum of inertia of the valve. Introducing new coefficients as $K = k/I$ allows to simplify the notation and the final equation obtains the form:

$$\frac{d^2\theta}{dt^2} = K_P \cdot (P_{in} - P_{out}) \cdot \cos\theta - K_f \cdot \frac{d\theta}{dt} \tag{12}$$

In addition, in order to model the states when the valve is fully open and fully closed, threshold values $\theta_{max} \approx 75°$ and $\theta_{min} = 0°$ are imposed, thus when the angle reaches the maximum or the minimum value, it is further kept at constant level, the return to the differential equation is accomplished when the corresponding pressure difference across the valve reaches zero, meaning that the valve starts to close or to open and angular motion is active.

$$\theta = \begin{cases} \theta_{min}, & \theta < \theta_{min} \\ \theta_{max}, & \theta > \theta_{max} \end{cases} \tag{13}$$

As it will be later discussed, introduction of the functions with discontinuous derivatives leads to the problems in integration of the whole system and special mechanism of event tracking is used to indicate at which point to switch between equations.

2.2 Systemic and Pulmonary blood circulation

The blood circulation system consists of a pulmonary (through the lungs) and systemic (through the whole body) part. When under the high pressure blood is ejected from the left heart chamber, it flows trough aorta to the network of arteries and then to the smaller arterioles, capillaries and veins, delivering nutrients and oxygen to the organs and tissue. Consequently the desoxygenated blood is collected from systemic veins and under low pressure returns to the right heart chamber, where it is pumped again to the main pulmonary artery and further to the analogous pulmonary microcirculation. As a result the blood receives oxygen from the lungs and oxygen-rich is collected by pulmonary venous system back to the left heart to repeat the cycle. The bloodvessels which comprise the vascular system can be divided in three main groups: elastic arteries, resistant arterioles and capillaries, and compliant veins.

Arteries: when the left ventricular contracts, all the blood (SV - stroke volume) flows into the main systemic artery - aorta and further to smaller arteries. Some part of this volume will be conserved in vessels due to elastic stretching

walls, thus the electric analog for these compartments of the model consists of full RLC circuit. The following system of equations is adapted which is a result of averaging 1D model [8]:

$$C_{artery}\frac{dP_{out}}{dt} = Q_{out} - Q_{in} \tag{14}$$

$$L_{artery}\frac{dQ_{out}}{dt} = P_{in} - P_{out} - R_{artery}Q_{out} \tag{15}$$

In pulmonary circulation, the resistance values are significantly lower than in systemic part and thus the pressure rates differ notably. The normal systemic arterial pressure is considered to be 120/80 mmHg (end-diastolic, end-systolic), while the pulmonary pressure is 25/10 mmHg.

Arterioles and Capillaries: when the blood flows to the organs, the big arteries split into a large system of smaller vessels called capillaries, where the blood pressure and velocity becomes lower, it allows to transfer vital nutrients to the organs easily. Consequently the branched network joins back to form the veins. Both arterioles and capillaries are considered to be pure resistant units, thus the electric analog equation becomes:

$$P_{artel} = R_{artel}Q_{artel}P_{cap} = R_{cap}Q_{cap} \tag{16}$$

Veins: the blood vessels which collect the blood and carry it toward the heart. The resistance and pressure drops is small, taking into account the higher elasticity of the walls, the electric analogy of RC circuit is considered:

$$C_{vein}\frac{dP_{vein}}{dt} = Q_{in} - Q_{out} \tag{17}$$

$$R_{vein}\frac{dQ_{vein}}{dt} = P_{in} - P_{out} \tag{18}$$

All the equations are valid for both pulmonary and systemic circulation, but with adjusted parameters to model the actual physical values of pressure drop and flow rates.

3 Simulation

Combining all the equations for each compartment in blood circulation and the model for the left and right hearts, the system of differential-algebraic equations is obtained. Each compartment is coupled with the neighboring compartments as in scheme in Fig **??** via the input and output variables, thus the output parameter of one compartment ($P_{out},\ Q_{out}$) becomes an input parameter to the neighbor

(P_{in}, Q_{in}). In overall with dynamic model for the four heart valves, there are 38 unknowns which are indexed globally starting from input flow for the left atrium Q_{pvein}, then following the direction of circulation the rest of the unknowns are numbered. Each compartment is represented by its function which takes as an input the vector of unknowns related to its equations only and evaluates the residual, inside the body of the function local-indexing is used, thus the input parameters are at first, then the state variables and then the output parameters. The final system is constructed by merging the outputs of the local functions and by passing the appropriate parts of the global vector of unknowns. The presence of functions with discontinuous derivatives inside equations for heart chambers leads to the introduction of separate variable which reflects the current state of the whole system and helps to identify which equations should be active depending on the process of opening or closing of the valves, in more details the even-tracking concept is explained in chapter **??**.

3.1 Adaptive time-stepping integration

In order to integrate the resulted system of differential-algebraic equations (DAE) the built-in MatLab function **ode15i** is used, which is an advanced **fully implicit** integrator for stiff and DAE problems of index 1 (differentiation of an algebraic equation leads to solvable implicit system of ODEs). The main idea is to use the fixed leading coefficient BDF method (Backward Differentiation Formula) with adaptive time-stepping, however the main obstacle in treating this type of equations is to find consistent initial condition and to maintain exact equality in algebraic part of the system during integration. Therefore the additional MatLab function **decic** is used, which with the help of modified conjugate gradient method and Lagrange multipliers tries to find suitable initial configuration, but it does not eliminate the problem that in the full closed-loop CVS system the initial guess still has to be imposed in the close neighborhood of the desired x_0, otherwise the optimization method fails to converge. The detailed explanation of algorithmic routines behind these functions can be found in [10].

3.2 Event-functions

Due to specificity of the equations involved in modeling heart chambers and valves, the ordinary approach to integrate the DAE system with suitable integrator does not work, since the adaptive time-stepping is not capable to capture the jump in the function derivatives. Therefore special treatment of functions which are not of class C^1 is required, in proposed model the flow rates through the valves with changing sign depending on pressure difference and the angular dynamics of the valve with maximum and minimum constant values represent the pitfalls

for **ode15i** solver. To identify the moments when the system of equations should change special event tracking system is used, at each time step of the integration routine it checks whether the certain event occurred, for example, if the pressure difference $P_{in} - P_{out}$ across the valves reached zero value from above, it means that the valve starts to close, if it reached zero value from below, it indicates that valve starts to open, then the equations for the flow rates should change, if the angular position reached the maximum or minimum value, then the differential equation is replaced by constant value for the angle. The most important part in setting up the proper event tracking is to have the global parameter "state" which is responsible for the information which valves are currently open and which valves are at maximum and minimum angle positions. In order to avoid improper event firing, the events concerning the angular positions and the pressure differences are treated separately, thus depending on the current state either angular positions are tracked or the pressure differences across the valves. The direction in which the pressure difference or angular position event "fires" determines the modifications of the state variable. For example, by default, the system tracks the pressure differences, therefore for the four valves in four heart chambers there are 8 events (two events in each direction of $P_{in} - P_{out}$ for each valve), when one of this event fires, it indicates that the valve is closing or opening, thus the integration is stopped, in the variable state vector value "true" is set in corresponding valve if it starts to open and "false" if it starts to close, the equations of the flow are changed, the event function for the valve is changed to track the angular position. Furthermore, there are 8 events of angular positions (two events $\theta - \theta_{max}$ and $\theta - \theta_{min}$ for each valve), when one of this event fires, it indicates that the leaflets reached the maximum or minimum position, thus integration is stopped, the corresponding element in the state variable is set to "true" value and event function for this valve starts to track the pressure difference.

```
state = [0; 0; 0; 1; 0; 1; 0; 0; 0; 1; 0; 1];
%mitral valve (0−close, 1−opened), aortic valve,
%aortic_angle is max, aortic_angle is min,
%mitral_angle is max, mitral_angle is min,
%tricuspid valve, pulmonic valve,
%tricuspid angle is max, tricuspid angle min,
%pulmonic angle max, pulmonic angle min
```

Another problem which occurs while integrating equations with **ode15i** solver is that at the point when the pressure difference event fires, the integration is stopped and the equations of the flow are redefined, the square root function of the pressures involved in orifice model is non-differentiable, thus the solver is not capable to restart numerical integration, since it uses for optimization purposes

and error estimation the partial derivatives of the global system. In order to overcome this singularity, spline interpolation of the square root was introduced in a small neighborhood of the zero of the function, moreover as it appeared due to variable time step algorithm the integrator in order to estimate necessary step, tries to calculate the value of the equation in "forbidden" region below zero, thus introduction of the smooth approximation helps to avoid these particular problems. The plot of chosen cubic spline is presented in Fig 6.

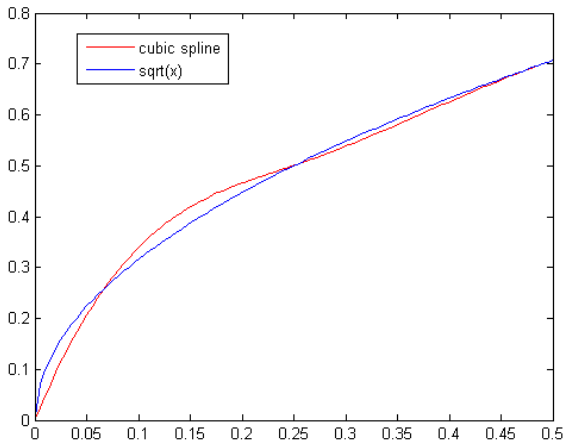


Figure 6: Smooth approximation in a small neighborhood of pressure difference

4 Results

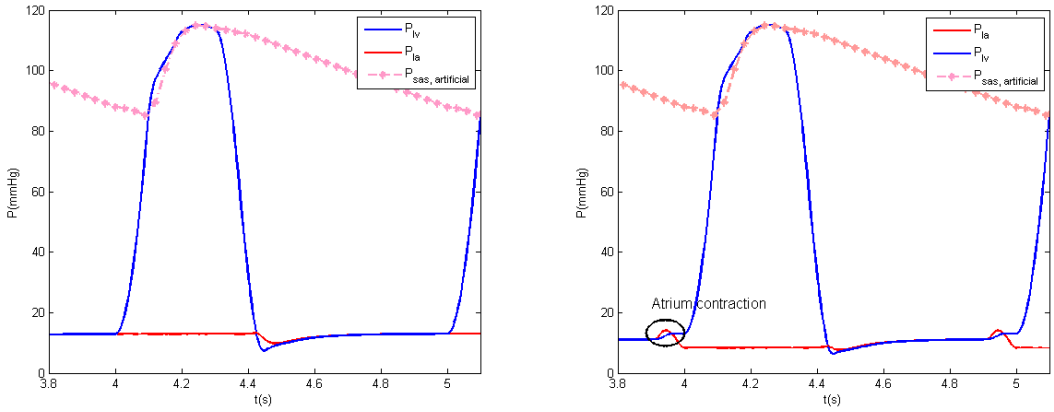
4.1 Modeling of the left heart alone

In order to test the model of the left heart only and to check if the results resemble the natural behavior during the cycle, the artificial input flow Q_{pvein} and output pressure P_{sas} were introduced as **smooth** (to fulfill the C^1 requirement) **periodic functions** interpolated from the data [3] using cubic Hermite splines. The plots are presented in Fig 7, Fig 8 along with the pressure-flow response of the system. The particular problems which occurred while trying to test the open system of one left heart only, is that the law of conservation of mass is not fulfilled, thus imposing constant rates for the input flow and output pressure led to inability for the solver to find consistent solution, further attempts to introduce close to physical values explicit expressions of smooth periodic functions resulted in non-realistic volume and pressure dynamics, thus the suitable interpolation function

was found to imitate the flow and pressure rates in closed double loop for the purpose of testing the main heart compartment.

4.1.1 Simplified model

At the beginning the valve model of the heart represents the diode concept, thus the leaflets can open and close to the full angle instantaneously. The elastance of the atrium is considered to be constant and then the system response is compared with introduced time-dependent elastance.



(a) Constant atrium elastance (b) Variable atrium elastance

Figure 7: Pressure rates in the left heart

Introducing the variable elastance of atrium allows to capture the 'a' wave of atrium pressure (Fig 7) which is present in Wigger's diagram (Fig 2).

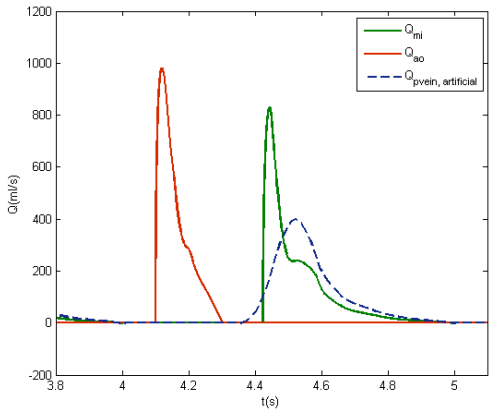
In the elastic model of the atrium, the A velocity peak is observed in mitral flow due to atrium contraction at the end of diastole (Fig 8), thus the ratio E/A (ratio of early to late ventricular filling velocity) can be evaluated.

From Fig 9 it can be seen that the volume in ventricle increases and in atrium decreases due to "atrium kick".

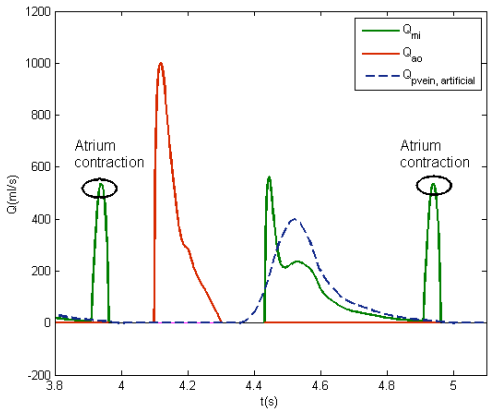
4.1.2 Full model

Time-dependent valve angle motion and variable atrium elastance is considered. The maximum opening angle is imposed to 75 degrees and the minimum angle is zero (since we first consider the healthy case).

In Fig 11 small regurgitation is observed due to time-dependent motion of the leaflets, thus when the pressure difference across the valve reaches zero and the

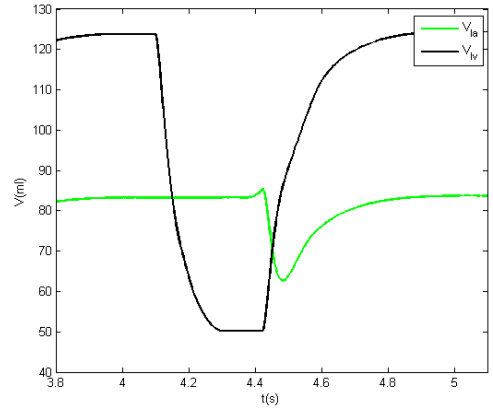


(a) Constant atrium elastance

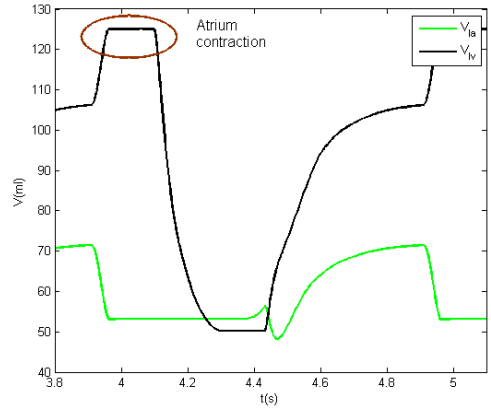


(b) Variable atrium elastance

Figure 8: Flow rates in the left heart



(a) Constant atrium elastance



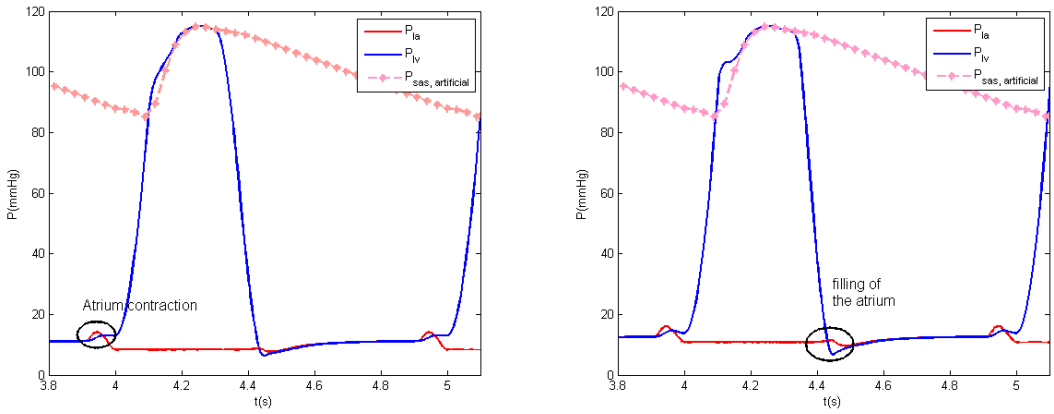
(b) Variable atrium elastance

Figure 9: Volume change in the left heart

valve starts to close, the reverse flow helps to close the valve as well as it enters the ventricle during small period of time.

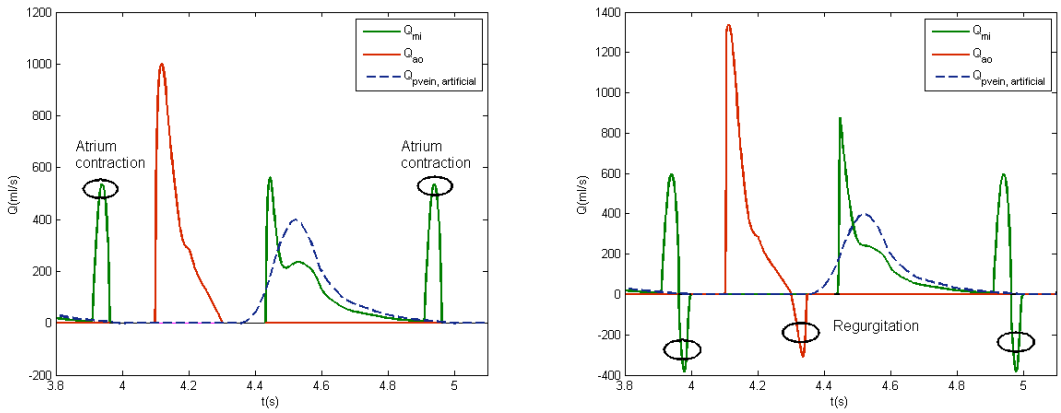
From Fig 12 it can be seen that the volume pick from atrial contraction quickly diminishes due to small regurgitant flow in mitral valve at the end of diastole.

The dynamics of the closure and opening of the valves is smoothed, even though the duration of this process is very short, it plays an important role in reproducing the features of the heart diagrams.



(a) Diode model (b) Dynamic model

Figure 10: Pressure rates in the left heart

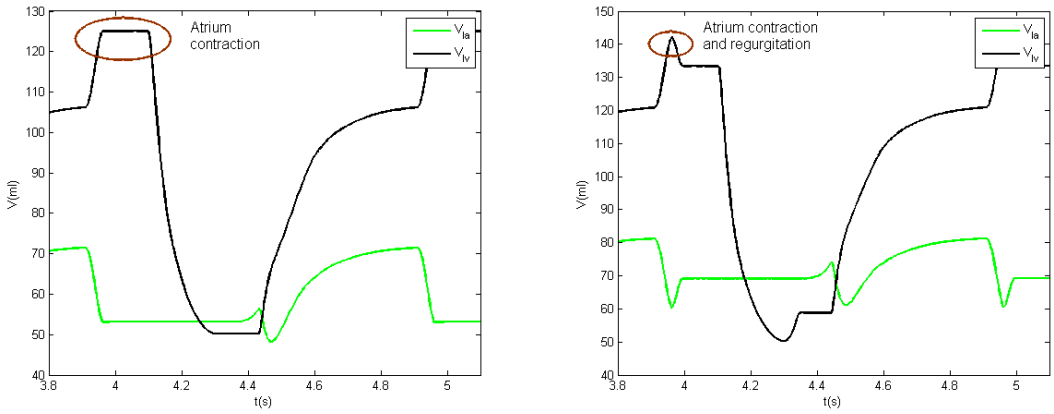


(a) Diode model (b) Dynamic model

Figure 11: Flow rates in the left heart

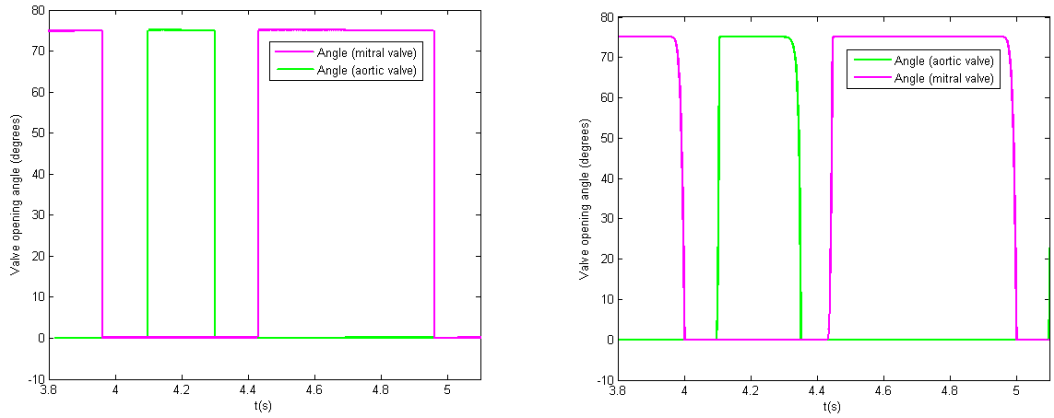
4.2 Modeling of the full heart in closed loop circulation

In order to fulfill the crucial law of mass conservation for the CVS system and thus to be able further to model the pathologies of the valves, the closed double-loop system is required, since it is not possible to impose the consistent input and output parameters suitable for each modification inside the heart model. Therefore, the right part of the heart was implemented with exact equations of the left, but with modified parameters to simulate lower intensity of pumping, and two sequence of circulation circuits were connected accordingly to non-linear heart compartments (Fig 4).



(a) Diode model (b) Dynamic model

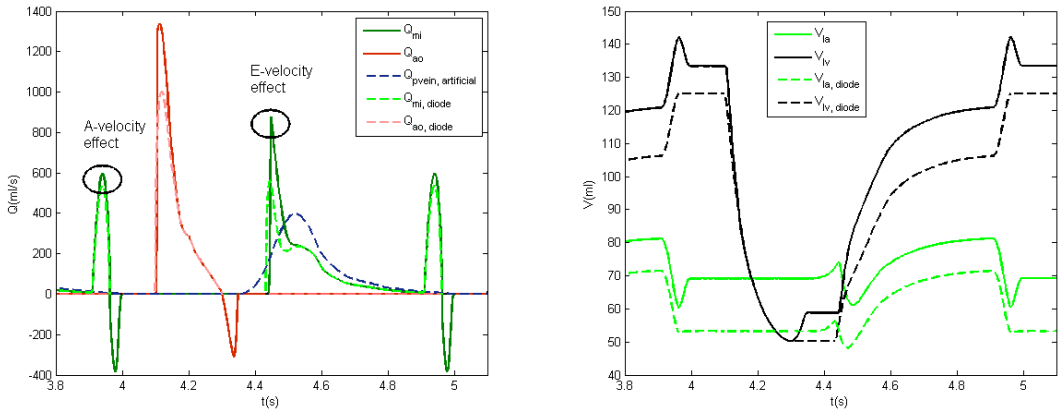
Figure 12: Volume change in the left heart



(a) Diode model (b) Dynamic model

Figure 13: Leaflets angular position of aortic and mitral valves

One of the challenging parts of running the full model is to find the consistent initial conditions and state, starting from which the system will converge to periodic solution, the initial values should be chosen close to physical values and coincide with the starting state of the system. At the beginning of simulation configuration is chosen in a way, that all four valves are closed (and in case of dynamic valves, they are also at minimum angle position) and there are zero flows in heart chambers. However without proper consideration of the pressure and flows in the rest of the system (systemic and pulmonary circulation), the solver is not capable to start integration, and optimization routine to find consistent initial parameters



(a) Flow rates comparison

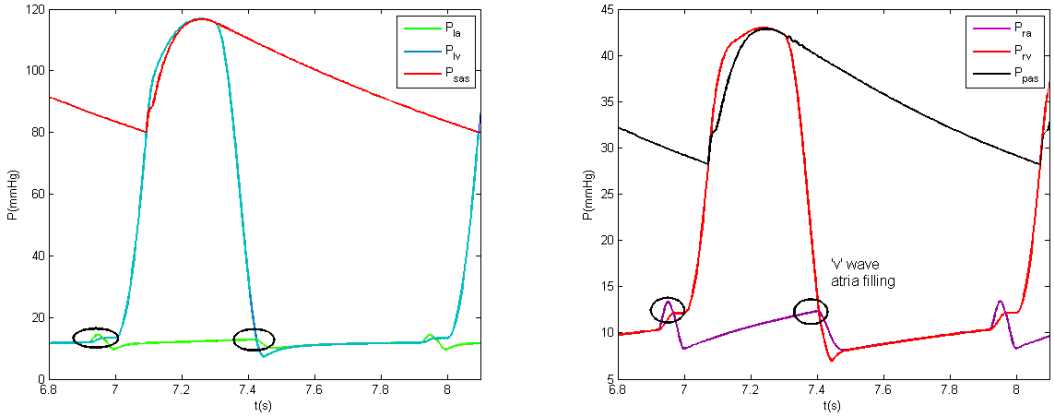
(b) Volume comparison

Figure 14: Comparison of left heart response for diode and dynamic valve model

does not converge. Moreover, it appeared that there is a possibility that even with manually calibrated initial values close to consistent ones, the whole system can converge to the wrong periodic solution, which does not represent proper range for physical values of volume, pressure and flows, thus the underlying behavior of non-linear dynamical system complicates the start of simulation. Due to the absence of information on a possible initial configuration compatible with this model, firstly the short-circuited model of the left heart only with systemic circulation is run until convergence to the stable periodic solution and its solution multiplied by two is taken as initial guess for the double loop simulation. Also in order to get realistic pressure response from the system, it is necessary to introduce the required amount of blood flow in peripheral circulation which will be conserved during the cardiac cycles, what appeared to be quite challenging since it is unpredictable to which area under the flow rates the system will converge starting from certain initial conditions, but the flow through the valves at initial moment is imposed to zero in case of the healthy heart. It has been seen that even twice smaller system with selected initial conditions very close to physical ones behaves very irregularly and close to instability blow up during the first five heart cycles, therefore the consistent initial values are very important while running the full system simulation and particularly in cases of modification of the model to the pathological one with non-fully closed or opened valves.

4.2.1 Simplified model

The model represents valves of the left and heart chambers as diodes, and the both atriums have the variable in time elastance. The results were compared with



(a) Left heart (b) Right heart

Figure 15: Pressure rates

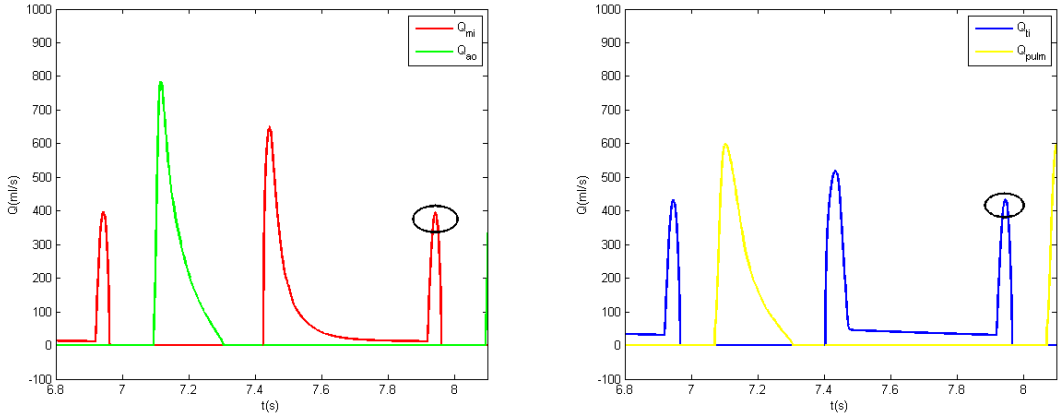
the original paper of Theodosis Korakianitis and Yubing Shi [3] as well as validated with the medical data and observations from Stanford School of Medicine [11]. The resulted range of physical values of pressures in atriums, arteries and ventriculars during systole and diastole periods agree very well with established healthy rates, also the shape and dynamics of obtained curves match very well those available experimental measurements at [11]. Even though, the diode model of the valves is a very simplified approximation, it allows to reproduce qualitatively the heart diagrams and make judgments on the cardiac function.

From the simulation results for the right heart in Fig 15 the 'v' wave of the atrial pressure can be more clearly observed, when the atrium is filling and the pressure increases.

4.2.2 Heart valves pathology

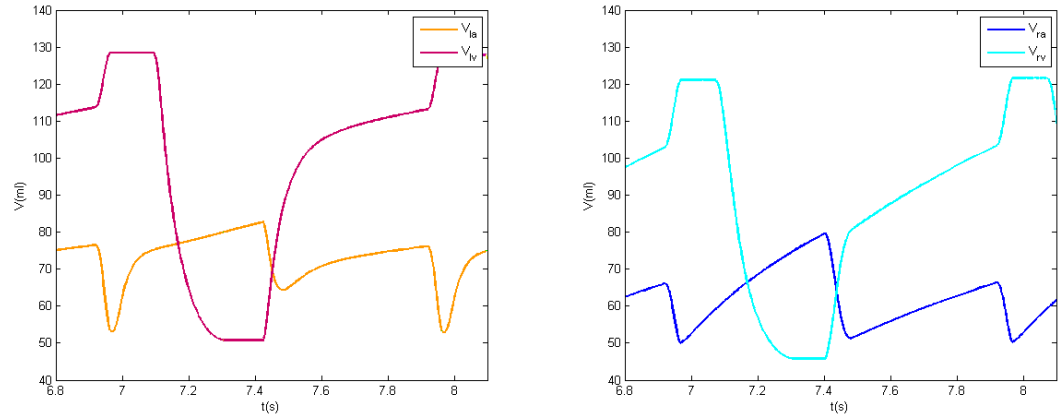
Diseases in the heart valves often occur on the side of systemic blood circulation, most common pathologies are mitral stenosis and aortic regurgitation. In case of mitral stenosis, the valve is not able to fully open (due to infarcted tissue or cholesterol deposits) and prevents the normal blood flow from left atrium to the left ventricular causing significant pressure drop in the left heart and increased pressure in the right heart. While in case of aortic regurgitation, the valve does not close properly and allows the back flow from aorta to the left ventricular, which causes the pressure drop in aorta and pressure increase in left atrium as well as the volume increase in the left ventricular.

Mitral stenosis: the maximum opening angle is imposed to 50° degrees, which corresponds to 24% of original orifice area of the mitral valve.



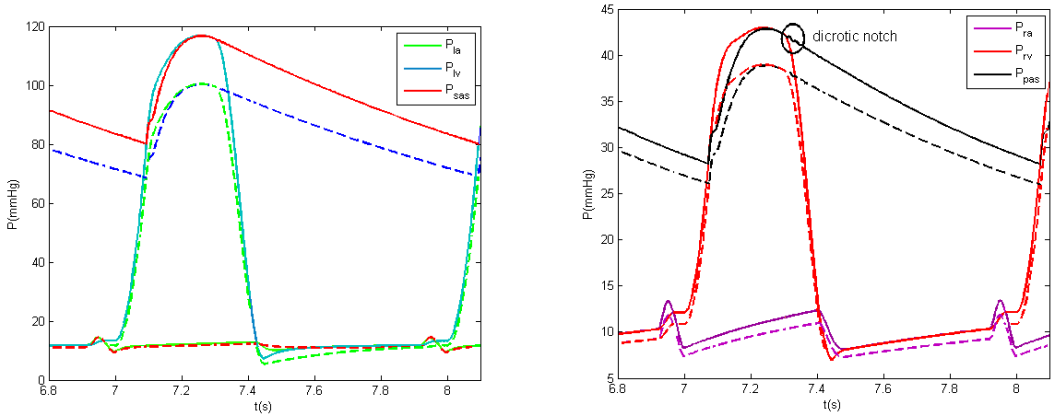
(a) Left heart (b) Right heart

Figure 16: Flow rates



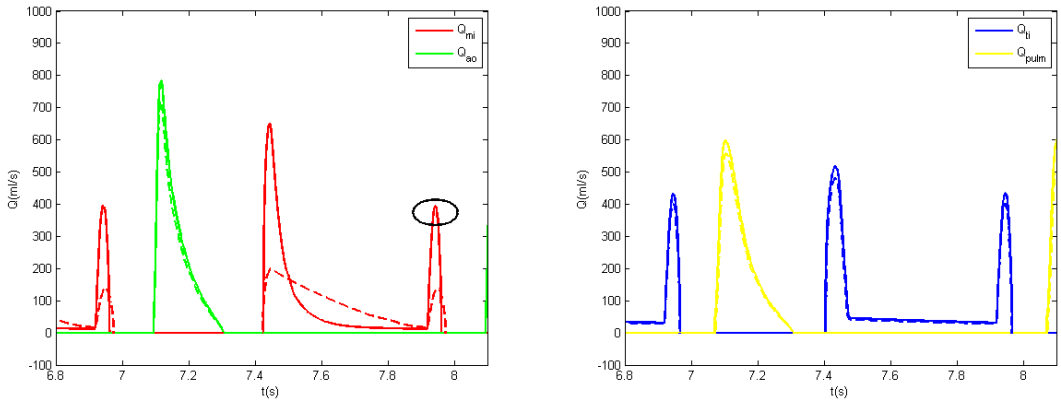
(a) Left heart (b) Right heart

Figure 17: Volume of chambers



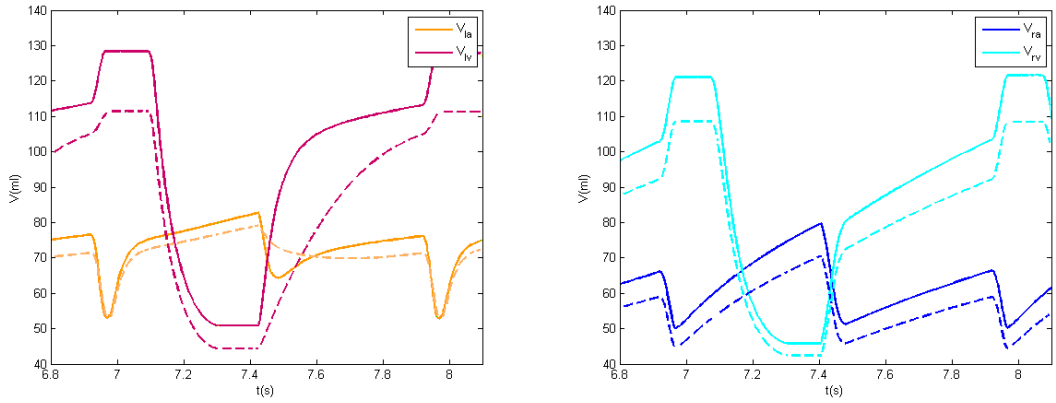
(a) Left heart (b) Right heart

Figure 18: Pressure rates, mitral stenosis, punctured lines are the response of unhealthy heart



(a) Left heart (b) Right heart

Figure 19: Flow rates, mitral stenosis

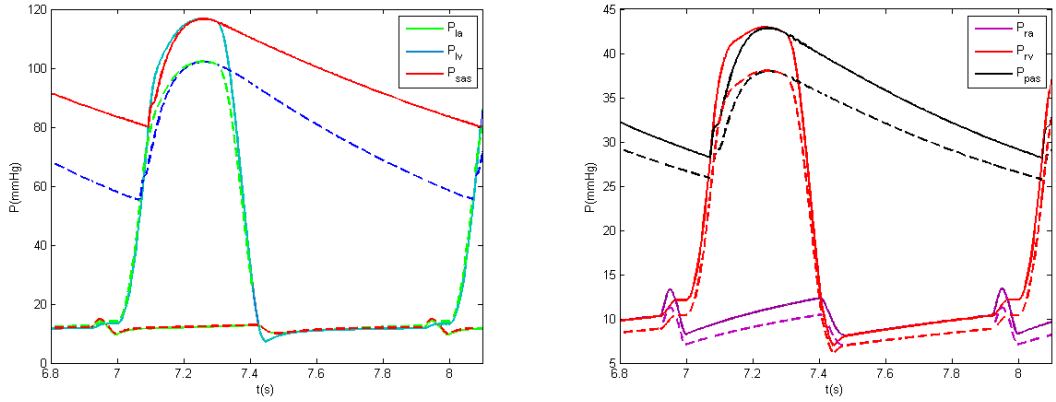


(a) Left heart (b) Right heart

Figure 20: Volume of chambers, mitral stenosis

In Fig 18, Fig 19 it can be seen that the flow pressure and flow rates in the left atrium significantly decrease due to non-fully opened mitral valve.

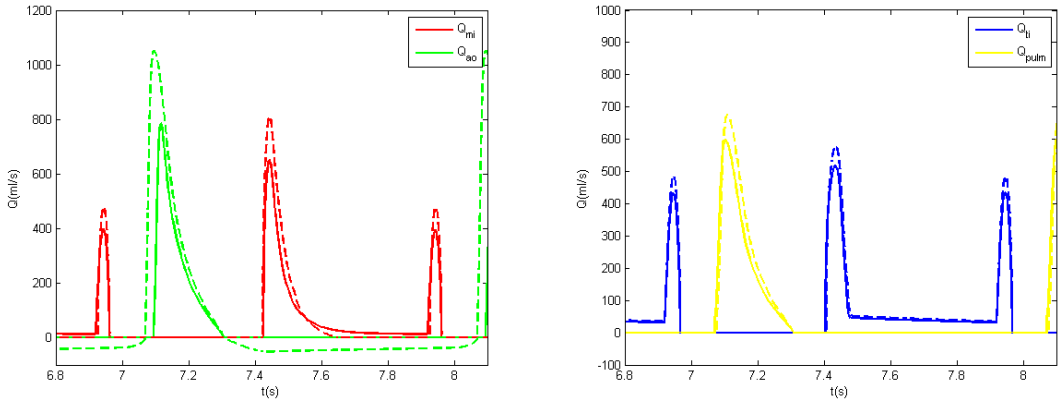
Aortic regurgitation: the minimum angle of closing the valve is set to 25° degrees allowing the leakage of flow during the diastole phase.



(a) Left heart (b) Right heart

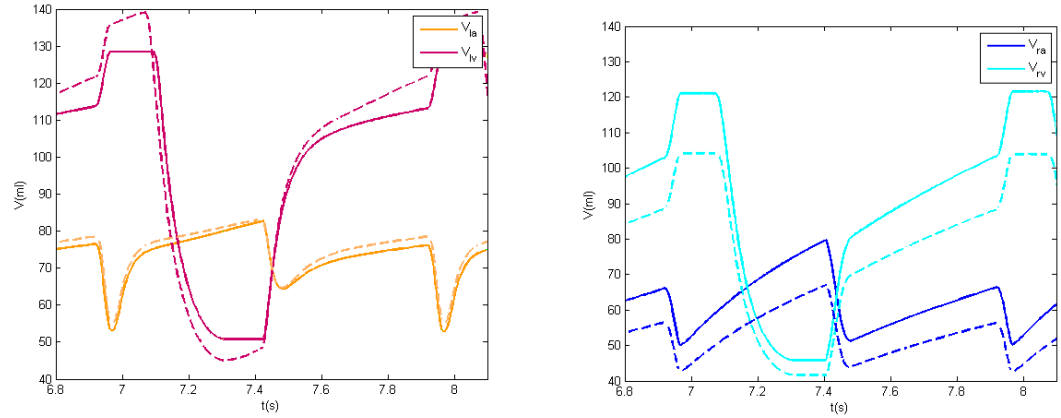
Figure 21: Pressure rates, aortic regurgitation, dashed lines indicate the response of unhealthy heart

Due to the passive filling of the left ventricle, from Fig 23 it can be observed how the volume of the left chambers increases while the right chambers reduce.



(a) Left heart (b) Right heart

Figure 22: Flow rates, aortic regurgitation



(a) Left heart (b) Right heart

Figure 23: Volume of chambers, aortic regurgitation

5 Conclusion

Concentrated parameter model used in simulation of CVS appeared to be an efficient and fast tool to get the global response of the system, and the results are in good agreement with available real measurements. Subsequent addition of new equations to represent the atrium contraction and angle motion allowed to capture physiologically important features in pressure and volume rates, which are observable through MRI measurements, and modifications of which may indicate a cardiovascular disease. Particularly, two pathologies were modeled, mitral stenosis and aortic regurgitation, and the results follow the expected changes in pressure and volumes of heart chambers, however further validation is required in comparison with the medical observations.

An important advancement of the model could be an incorporation of the central auto regulating neural system, which responds to the modified pressure and flow values in CVS due to appeared malfunctions inside the heart and adapts the parameters of the model as well as the relation between compartments. For example, it can regulate the contraction function and thus the intensity of blood pumping in order to preserve vital levels of blood flow and pressure in the organs. In addition more consideration can be taken in modeling elasticity of the heart chambers and valve tissue by adding possible interaction between the two atriums and ventriculars, since they are all connected with the same tissue and effect each other during contractions.

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