A mathematical model that allows the representation of the regurgitation flow of a prosthetic cardiac valve^{*}

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Abstract: This work proposes a lumped parameter model (0D) for biological prosthetic heart valves which represents the flow regurgitation. This model is used to obtain a more precise model of a pulsatile pediatric ventricular assist device (pVAD). The 0D model consists of the cannula-valve inlet and cannula-valve outlet configurations, which represent the discrete transfer functions related to the conduction and non-conduction states of the input and output valves, respectively. The flow and pressure curves in the inlet and outlet cannulas of the heart valves are measured from a hydraulic simulator connected to a pVAD. To find this model, a sequence of steps is performed, which includes the data pre-processing, the structure model choice and the refinement of model parameters. From the simulation of the refined model, the regurgitation phenomenon was represented with fidelity of 90 % of the value measured in the nominal condition test. The great importance of pVAD modeling is the possibility of coupling to the 0D model of the human cardiovascular system so that its interactions can be studied and automatic control strategies developed.

Keywords: Heart valves, Ventricular assist device, Mathematical model, System identification.

1. INTRODUCTION

Ventricular assist devices (VADs) are mechanical blood pumps that assist the ventricular work of patients who are waiting for a heart transplant, by keeping the hemodynamic variables at acceptable levels (Bacal et al. (2009)). An important part of the pulsatile-type VADs are biological prosthetic heart valves which establish an unidirectional flow in the blood pumping.

Mathematical models have been studied to explain the behavior of the prosthetic heart valves, which present several advantages, such as diagnostics, development of new prostheses and control of VADs. The main techniques used to model heart valves are finite elements, isogeometric or lumped parameters (Kolar (2016)). The lumped parameter modeling (0D) is an approach with less complex and require fewer computational resources than other methods.

Cardiovascular system models that include heart valves representation are based on Bernoulli equation (Aboelkassem et al. (2015); Mynard et al. (2012)), hydraulic valve equation (Korakianitis and Shi (2006)) and analogy to an electrical circuit with passive elements (Casas et al. (2017)). In relation to biological prosthetic heart valves used in pVADs, Sousa et al. (2018) and Hunsberger (2005)

characterized the valves as ideal diodes. The main disadvantage of the ideal diode model is the inability for representing pathological conditions like regurgitation, in which reverse flow occurs. This phenomenon happens when there is an inability of the leaflets contacts to seal themselves, increasing the work of the heart. Considering VADs, the modeling of this condition may help the design of more robust controllers.

Thus, this work aims at the development of a biological prosthetic heart valve model based on lumped parameters for a pulsatile pVAD, that allows the reverse flow to be characterized. The organization of the paper is as follows. The hydraulic test platform used in experimental tests is presented in Section 2. The problem statement and methodology applied to model the heart valves are described in Section 3 and 4. In Section 5, the flow measurements of the hydraulic test platform are compared with the estimated 0D model. Concluding remarks are presented in Section 6, and future works are suggested.

2. HYDRAULIC TEST PLATFORM

To evaluate the flow dynamics associated with a heart valve operation, a hydraulic test platform is used, as shown in Fig. 1.

This system is constituted by two acrylic reservoirs, which represent aortic and atrial chambers, a pulsatile pVAD,

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cannulas to link the components and a pneumatic actuation driver to provide a periodical pressure that drives the system.

Figure 1. The hydraulic test platform coupled with the pVAD and pneumatic actuator driver.

The pulsatile pVAD has 15 mL of ejection volume, and it is composed of air and a blood chamber with a membrane to separate them. It provides a one-way flow liquid through the system utilizing two biological valves on the inlet and outlet of the pVAD.

Specifically, the pressure signals are measured in mmHg using pressure sensors based on a strain gauge (Edwards Lifesciences LLC Irvine (2018)), and the flow signals are acquired using one SonoTT Clamp-On ultrasonic flow transducer (em-tec GmbH (2018)), which gives the measurements in L/min. The signals measured by the pressure and flow sensors were collected employing a data acquisition system connected to a computer via USB cable. Besides, these signals were monitored and stored using a human-machine interface (HMI) implemented on the LabVIEW platform.

3. PROBLEM STATEMENT

To model properly the valves, the variables of interest in the hydraulic test platform are the left atrial pressure p_{la} , blood chamber pressure p_{bc} at the blood chamber of the pVAD, aortic pressure p_{ao} , the flow q_i at the inlet cannula and the flow q_o at the outlet cannula (See Fig. 3). A 0D model of this pVAD proposed by Sousa et al. (2018) is shown in Fig. 2.

In this model, the heart valves were represented by ideal diodes. Besides, these pressure and flow signals were used for the estimation of RL circuits, considering the values estimated only belonging to the cannula, due to there are not sensors present on the hydraulic test platform that allows the measurement of the pressure differential in the valves.

With the flow sensor connected at a time on the inlet and outlet cannulas (shown in Fig. 1), the opening and closing states of the heart valve prostheses on the flow dynamics can be observed in Fig. 3. This 0D model has not shown a good approximation for flow signals, because with the ideal diodes is not possible to reproduce the regurgitation phenomenon, which are the oscillations that occur in the measured signal when the flow value of the ideal diode is 0.

Based on these curves and comparing the model response against the data collected, confirms that the heart valves

Figure 2. Representation of the 0D model of pDAV connected to the hydraulic test platform.

Figure 3. Flow and differential pressure curves through the (a) input and (b) output pVAD valves, considering the raw signal and original model response.

representation employing an ideal diode is not very suitable, thus evidencing the need to search for a new modeling approach for these prostheses.

4. METHODOLOGY

Since the influence of the cannulas cannot be ignored, then what is effectively estimated and analyzed is the valve-cannula configuration, as shown in Fig. 4. The new 0D model is composed by *inlet cannula-valve configuration*, which represents the discrete transfer functions related to the conduction and non-conduction states of input valve; and *outlet cannula-valve configuration*, which represents the discrete time transfer functions for the conduction and non-conduction states of output valve.

Figure 4. Representation of the new 0D model of pDAV to be connected to the hydraulic test platform. The single pole changeover switches (spdt) are controlled by the signs pressure differentials, $p_{la} - p_{bc}$ and $p_{bc} - p_{ao}$, respectively.

In this work, each model is determined considering the p_{la} , p_{bc} and p_{ao} signals as pressure sources, to directly extract the characteristics of the flows signals from the measured pressure signals in hydraulic test platform, without incorporating the defects present in the previous 0D model.

Thus, the proposed methodology for the modeling of biological prosthetic heart valves is presented by a flowchart, as follows in Fig. 5.

4.1 Data pre-processing

In the characterization procedure of the pVAD valves, a set of tests is done to define the operation range of the hydraulic test platform, according to the dataflow in step (A) shown in Fig. 5. For each test, the p_{ao} signal can be maintained at pediatric levels (around 85/55 mmHg). From the results obtained in these tests, several analyzes can be performed and hypotheses are taken for the parameter estimation.

Collect data Considering the existence of only one sensor, each test condition must be maintained so that the flow in the inlet and outlet cannulas near the valves is collected. This means that, in each test, two p_{ao} curves, two p_{bc} curves, and one q_i and one q_o curves are collected.

The ejection pressure p_{ej} in the pneumatic driver can be set in values between 0 and 300 mmHg and the heart rate HR can range from 20 to 150 beats per minute (bpm). The ejection time can be set between 100 and 600 ms and

it has been set to be 40 % of the HR value in the whole experiment. According to the trials, it is not possible to maintain p_{ao} signal at pediatric levels for HR values less than 70 and p_{ej} values lower than 140 mmHg (Bacal et al. (2009)).

All the tests are listed in table 1, in which the curves obtained in the test T_{or8} were chosen for the parameter estimation since it is located in the central part of the table, which facilitates the application of the proposed methodology.

Table 1. Experiment configuration to valves operation range.

p_{ej} HR	140	150	200	250	300
70	T_{or1}	T_{or2}	T_{or3}	T_{or4}	T_{or5}
90	T_{or6}	T_{or7}	T_{or8}	T_{or9}	T_{or10}
120	T_{or11}	T_{or12}	T_{or13}	T_{or14}	T_{or15}
150	T_{or16}	T_{or17}	T_{or18}	T_{or19}	T_{or20}

Flow signal filtering Although this sensor is able to identify the flow dynamics, its sampling is still not sufficient to obtain a signal without noise. Thus, to minimize the effects of noise and deformation on the flow signals, digital filtering is performed. The strategy chosen is the spectral subtraction given by

$$\hat{X}_q(f) = |Q(f)| - \hat{N}_q(f), \quad (1)$$

in which: $\hat{X}_q(f)$ is a spectral estimation of the raw signal of flow; $Q(f)$ is the spectra of the raw signal of flow; $\hat{N}_q(f)$ is a spectral estimation of the flow noise.

Data separation Considering that the valve dynamics is distinct in the opening and closing states, then the pressure and flow data collected under test are separated based on the valve state. In this case, the pressure differential in the valve-cannula set and the flow signal define the change of state.

Thus, in accordance with the circuit shown in Fig. 4, the condition for the begin of the conduction state is $p_{la} \geq p_{bc}$ for the input valve, and $p_{bc} \geq p_{ao}$ for the output valve; and the instant that the flow value changes to the positive for negative represents the begin of the non-conduction mode in the pVAD valves.

4.2 Structure model choice

According to the dataflow in step (B) shown in Fig. 5, from the conduction and non-conduction data, it is obtained at the end of this step a full structure of valve model, composed by subsystem models of each valve state.

Parameter estimation The cost function to each valve state is defined as

$$V_s(\theta_i, Z_i^{N_E}) = \frac{1}{N_E} \sum_{k=1}^{N_E} [q_i(k) - \hat{q}_i(k|\theta_i)]^2, i \in \{c, nc\}, \quad (2)$$

in which: $V_s(\theta_i, Z_i^{N_E})$ is the cost function calculated during structure model choice; N_E is the number of data points

Figure 5. Methodology flowchart: A) data pre-processing; B) structure model choice; C) model refinement.

selected in the estimation data set $Z_i^{N_E}$ and $k = 1, \dots, N_E$; q_i is the flow measured in each valve-cannula; $\hat{q}_i$ is the estimated model flow; i denotes the conduction (c) or non-conduction (nc) discrete-time subsystem model.

Thus, the parameter estimation for each subsystem model is found with a numerical algorithm designed to solve (Ljung (1987))

$$\hat{\theta}_i = \underset{\theta_i}{\operatorname{argmin}} V_s(\theta_i, Z_i^{N_E}), i \in \{c, nc\}. \quad (3)$$

To verify the quality of the estimated model, the normalized root mean square error (NRMSE) criterion is calculated, which represents the output variations percentage that are reproduced by the model in relation to the actual output. A larger number evidences a better model and its precise definition is calculated as:

$$\Omega_s(\hat{\theta}_i, Z_i^{N_V}) = \left(1 - \frac{\|q_i - \hat{q}_i\|_2}{\|q_i - \bar{q}_i\|_2}\right) \times 100\%, i \in \{c, nc\} \quad (4)$$

in which: $\Omega_s(\hat{\theta}_i, Z_i^{N_V})$ is the NRMSE criterion calculated during the structure model choice; N_V is the number of values in the validation data set $Z_i^{N_V}$; q_i is the flow measured in each valve-cannula, which can be in conduction (c) or non-conduction (nc) state; $\hat{q}_i$ is the estimated model flow; $\bar{q}_i$ is the mean flow; $\|_2$ indicates the 2-norm of a vector.

Conduction and non-conduction model choice Each subsystem is defined by a generic discrete transfer function on the form

$$G(z) = \frac{Y(z)}{U(z)} = \frac{b_1 z^{-1} + \dots + b_{n_b} z^{-n_b}}{1 + a_1 z^{-1} + \dots + a_{n_a} z^{-n_a}}, \quad (5)$$

in which: $Y(z) = Q_i(z)$ represents the $\mathcal{Z}$ transform of flow signal as the output model; $U(z) = \Delta P_i(z)$ represents the $\mathcal{Z}$ transform of differential pressure signal as the input model, with i denotes the conduction (c) or non-conduction (nc) states of valves; n_b and n_a are the polynomial orders of the numerator and denominator of transfer function, respectively. For example, the discrete transfer function in conduction state ($i = c$) for the input valve (I) is

$$G_{s_c}^I(z) = \frac{Q_c^I(z)}{\Delta P_c^I(z)} = \frac{Q_c^I(z)}{P_{la}(z) - P_{bc}(z)} \quad (6)$$

and for the output valve (O) is

$$G_{s_c}^O(z) = \frac{Q_c^O(z)}{\Delta P_c^O(z)} = \frac{Q_c^O(z)}{P_{bc}(z) - P_{ao}(z)}. \quad (7)$$

Thus, the discrete transfer function in non-conduction state ($i = nc$) for input and output valves are $G_{s_{nc}}^I(z) = -G_{s_c}^I(z)$ and $G_{s_{nc}}^O(z) = -G_{s_c}^O(z)$, respectively.

The number of poles p and zeros z starts with unit value and this quantity is incremented m times until a maximum order n of the transfer function is reached. On each interaction j , the $V_s(\theta_i, Z_i^{N_E})$ and $\Omega_s(\hat{\theta}_i, Z_i^{N_V})$ metrics are calculated, generating a data stack $\Gamma_{s_i} = [V_s(\theta_i, Z_i^{N_E}), \Omega_s(\hat{\theta}_i, Z_i^{N_V})]$ for conduction ($i = c$) and non-conduction ($i = nc$) data.

At last, the choice of conduction model $G_{s_c}(z)$ and non-conduction model $G_{s_{nc}}(z)$ is done for the input and output valves, considering the best values obtained in each Γ_{s_i} for both metrics.

Valve model composition From the conduction and non-conduction models chosen, a full structure model is de-

finied for valve-cannula configuration, both in the inlet and outlet of pVAD. In total, four discrete transfer functions are used for behavior description of valve-cannula configuration, in which the switching between the $G_{sc}^I(z)$ and $G_{snc}^I(z)$ transfer functions describes the operation of inlet valve-cannula configuration, and the $G_{sc}^O(z)$ and $G_{snc}^O(z)$ transfer functions describes the operation of outlet valve-cannula configuration.

4.3 Model refinement

According to the flowchart in step (C) shown in Fig. 5, the parameters obtained in the structure model chosen are used as initial values for an optimization code. The best cost function and the best NRMSE criterion calculated during the refinement ($V_r(\theta, Z^{NE})$ and $\Omega_r(\hat{\theta}, Z^{NV})$) result in a refined conduction model $G_{rc}(z)$ and refined non-conduction model $G_{rnc}(z)$ for the input and output valves, which will be used as the new 0D model of pVAD in the valve-cannula configuration.

4.4 Model simulation

To properly simulate the full dynamics of the input valve, one must follow the steps described in Algorithm 1. This algorithm can be applied for the outlet valve as well as by considering $p_{bc}(i) \geq p_{ao}(i)$.

Algorithm 1 Valve simulation

procedure INPUT VALVE

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 $q_{in}(0) \leftarrow 0$                                 ▷ initial flow
 $state(0) \leftarrow 0$                             ▷ valve state
 $state_{aux} \leftarrow 0$ 
 $aux \leftarrow 0$  ▷ to not enter on else if on first interaction
 $tsim \leftarrow n$                                 ▷ time simulation
for  $i = 1 \rightarrow n - 1$  do
    if  $p_{la}(i) \geq p_{bc}(i)$  then
         $state_{aux} \leftarrow 1$ 
         $aux \leftarrow 1$ 
    else if  $aux == 1$  and  $q_{in}(i - 1) \geq 0$  and  $q_{in}(i) < 0$  then
         $state_{aux} \leftarrow 0$ 
    end if
     $state(i) \leftarrow state_{aux}$ 
    if  $state(i) > 0$  then
         $q_{in}(i + 1) \leftarrow -a_1 q_{in}(i) - a_2 q_{in}(i - 1) + b_1(p_{la}(i) - p_{bc}(i))$ 
    else
         $q_{in}(i + 1) \leftarrow -c_1 q_{in}(i) - c_2 q_{in}(i - 1) - c_3 q_{in}(i - 2) + d_1(p_{la}(i) - p_{bc}(i)) + d_1(p_{la}(i - 1) - p_{bc}(i - 1)) + d_2(p_{la}(i - 2) - p_{bc}(i - 2))$ 
    end if
end for
end procedure

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5. RESULTS AND DISCUSSION

The least squares algorithm was applied to both valves in the conduction and non-conduction states. Using $n = 3$, different orders of the numerator and denominator polynomials were tested for $G_{sc}^I(z)$, $G_{sc}^O(z)$, $G_{snc}^I(z)$ and $G_{snc}^O(z)$, considering the complexity and data adherence.

The best estimation results for cost function and NRMSE criterion for initial conditions are shown on table 2.

Table 2. The cost function and NRMSE criterion results for structure model choice.

Conduction model $G_{sc}(z)$		Non-conduction model $G_{s_{nc}}(z)$	
$n_b = 1$ and $n_a = 2$		$n_b = 3$ and $n_a = 3$	
Input valve			
$G_{sc}^I(z)$		$G_{s_{nc}}^I(z)$	
$V_s(\theta_c, Z_c^{NE})$	$\Omega_s(\hat{\theta}_c, Z_c^{NV})$	$V_s(\theta_{nc}, Z_{nc}^{NE})$	$\Omega_s(\hat{\theta}_{nc}, Z_{nc}^{NV})$
(mL/s)	(%)	(mL/s)	(%)
1.2397	92.2985	15.3159	82.2725
Output valve			
$G_{sc}^O(z)$		$G_{s_{nc}}^O(z)$	
$V_s(\theta_c, Z_c^{NE})$	$\Omega_s(\hat{\theta}_c, Z_c^{NV})$	$V_s(\theta_{nc}, Z_{nc}^{NE})$	$\Omega_s(\hat{\theta}_{nc}, Z_{nc}^{NV})$
(mL/s)	(%)	(mL/s)	(%)
23.2259	92.2460	14.4797	82.4845

The nonlinear least squares use these transfer functions as initial conditions in order to refine the chosen model. The results obtained are shown in table 3.

With refined transfer functions, computational simulations are performed to verify the operation of this model. The integration method used was the 4th order Runge-Kutta, with fixed integration step 0.001. As described in Section 4, the proposed methodology is applied to the data obtained in the test T_{or8} . The final result is shown in Fig. 6.

Figure 6. Heart valve model proposed flow response in the input and output valves, compared with data collected in the T_{or8} test and original model response.

It is observed that the model has good adherence to the experimental data. To verifies if the structure model is valid through all the pVAD operation range for pediatric conditions, the proposed methodology is applied to the data from T_{or1} until T_{or20} tests. The results are resumed at table 4 and the values are considered acceptable for this work.

6. CONCLUSIONS

A 0D model of biological prosthetic heart valves was proposed, in which both conduction and non-conduction

Table 3. Transfer functions obtained for each valve in conduction and non-conduction states.

Initial values	Values after non-linear estimation
Input valve - Conduction	
$G_{sc}^I(z) = \frac{0,0028z^{-1}}{1 - 1,9110z^{-1} + 0,9116z^{-2}}$	$G_{rc}^I(z) = \frac{0,0029z^{-1}}{1 - 1,9107z^{-1} + 0,9113z^{-2}}$
Input valve - Non-conduction	
$G_{sc}^I(z) = \frac{-0,0206z^{-1} + 0,0448z^{-2} - 0,0242z^{-3}}{1 - 2,8648z^{-1} + 2,7521z^{-2} - 0,8856z^{-3}}$	$G_{rc}^I(z) = \frac{-0,0803z^{-1} + 0,1680z^{-2} - 0,0876z^{-3}}{1 - 2,9018z^{-1} + 2,8229z^{-2} - 0,9201z^{-3}}$
Output valve - Conduction	
$G_{sc}^O(z) = \frac{0,0008z^{-1}}{1 - 1,9900z^{-1} + 0,9906z^{-2}}$	$G_{rc}^O(z) = \frac{0,0006z^{-1}}{1 - 1,9953z^{-1} + 0,9959z^{-2}}$
Output valve - Non-conduction	
$G_{sc}^O(z) = \frac{-0,0196z^{-1} + 0,0341z^{-2} - 0,0144z^{-3}}{1 - 2,8849z^{-1} + 2,7856z^{-2} - 0,8998z^{-3}}$	$G_{rc}^O(z) = \frac{0,0382z^{-1} - 0,1073z^{-2} + 0,0691z^{-3}}{1 - 2,8762z^{-1} + 2,7717z^{-2} - 0,8943z^{-3}}$

Table 4. Model result for experimental test. For each test T_{or} , the top values of $V_r(\theta)$ and $\Omega_r(\hat{\theta})$ are for input valve and the bottom values are for output valve.

Test	$V_r(\theta, Z^{NE})$ (mL/s)	$\Omega_r(\hat{\theta}, Z^{NV})$ (%)	Test	$V_r(\theta, Z^{NE})$ (mL/s)	$\Omega_r(\hat{\theta}, Z^{NV})$ (%)
T_{or1}	48.6818	71.2994	T_{or11}	14.2069	79.9624
	61.7340	78.1821		38.1865	78.2097
T_{or2}	27.4176	79.7893	T_{or12}	45.4715	68.3938
	23.5239	90.3017		47.7138	80.1972
T_{or3}	50.2779	72.6048	T_{or13}	23.7901	85.3767
	23.8331	91.9579		45.9903	88.7453
T_{or4}	137.1844	65.4189	T_{or14}	14.8854	87.0816
	67.3933	89.0495		16.7359	93.3863
T_{or5}	72.6544	72.8276	T_{or15}	17.8715	85.8744
	48.6550	90.9399		94.5968	86.0230
T_{or6}	17.7984	79.8784	T_{or16}	30.2966	64.4180
	32.3097	83.8376		79.6496	55.7850
T_{or7}	20.9329	80.2563	T_{or17}	36.7028	69.9597
	65.1157	79.6461		83.4547	55.5276
T_{or8}	11.8146	89.6951	T_{or18}	24.5239	83.7437
	33.1216	91.9358		31.9358	88.3759
T_{or9}	54.0684	78.5325	T_{or19}	27.7253	86.9058
	251.2073	78.8843		24.1375	93.0684
T_{or10}	121.8763	60.9681	T_{or20}	69.6157	78.8351
	73.4334	88.1877		27.6108	93.1813

states were adequately represented. With the new model, the flow regurgitation phenomenon in the pulsatile pVAD was faithfully reproduced in simulation (fidelity of 90% of the measured value in T_{or8} test). This work proposes a consistent methodology that can be applied to different types of valves (for example, mechanical valves) and at different operating points of the hydraulic test platform.

From these results, it is possible to improve the control algorithms that processes the coupled models between this device with the human cardiovascular system. These computational simulations contribute to the evaluation of the interaction of this coupled system before the application of pVAD *in vivo* tests.

In future works, we intend to find the analog electric circuit from the transfer functions chosen that represent the valve-cannula configuration; evaluate the possibility of measuring the pressure differential in the valve, since in this way the estimation can generate a decoupled model of the cannula; to use the proposed methodology to model the pVAD blood chamber and to obtain a new improved version of the complete hydraulic test platform model.

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REFERENCES

- Aboelkassem, Y., Savic, D., and Campbell, S.G. (2015). Mathematical modeling of aortic valve dynamics during systole. *Journal of theoretical biology*, 365, 280–288.
- Bacal, F., Souza-Neto, J.D., Fiorelli, A.I., Mejia, J., Marcondes-Braga, F.G., Mangini, S., and Oliveira Jr, J.L. (2009). Sociedade brasileira de cardiologia. II Diretriz brasileira de transplante cardíaco.
- Casas, B., Lantz, J., Viola, F., Cedersund, G., Bolger, A.F., Carlhäll, C.J., Karlsson, M., and Ebbens, T. (2017). Bridging the gap between measurements and modelling: a cardiovascular functional avatar. *Scientific reports*, 7(1), 6214.
- Edwards Lifesciences LLC Irvine, California, U. (2018). Truwave disposable pressure transducer.
- em-tec GmbH, Berlin, G. (2018). Experts in non-invasive flow measurement.
- Hunsberger, A.Z. (2005). *Modeling and analysis of interactions between a pulsatile pneumatic ventricular assist device and the left ventricle*. University of Pittsburghs. Thesis (Master of Science in Bioengineering).
- Kolar, P. (2016). *Heart Valve Mathematical Models*. Rochester Institute of Technology. Thesis (Master of Science in Applied and Computational Mathematics).
- Korakianitis, T. and Shi, Y. (2006). A concentrated parameter model for the human cardiovascular system including heart valve dynamics and atrioventricular interaction. *Medical engineering & physics*, 28(7), 613–628.
- Ljung, L. (1987). *System Identification: Theory for the User*. Prentice Hall.
- Mynard, J., Davidson, M., Penny, D., and Smolich, J. (2012). A simple, versatile valve model for use in lumped parameter and one-dimensional cardiovascular models. *International Journal for Numerical Methods in Biomedical Engineering*, 28(6-7), 626–641.
- Sousa, D.L., Cordeiro, T.D., Melo, T.R., Da Rocha Neto, J.S., Cestari, I.A., and Lima, A.M.N. (2018). Modeling, characterization and test of a pediatric ventricular assist device. *IOP Conf. Series: Journal of Physics*, 1044, 1–6. DOI 10.1088/1742-6596/1044/1/012047.