

## Parameter estimation of heart, valve and vasculature

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### SUMMARY

The purpose of this project is to obtain clinically relevant patient specific information on valvular lesions by estimating the coefficients of a lumped model, which describes the heart, valves and arterial network, in an attempt to aid clinical diagnosis.

**Key Words:** *Optimisation, Stenosis, Heart valves, Lumped model, Arterial Network*

## 1 INTRODUCTION

A mathematical lumped model is proposed to investigate the entangled effects of valvular lesions in patients, using coefficients defining the heart, valve and vasculature. Patient data is characterised through the optimisation of the model coefficients. This is performed by minimising the error produced from the output of the governing equations when compared to patient specific input information, and so finding the coefficients that reproduce the original data best. This information is then used for understanding the interactions of combined valvular lesions.

Past research has examined singularly the aspects involved in this project, however, the purpose here is to explore the combining of heart, valve and vasculature models, when subject to valvular diseases. From this viewpoint, pressures of the left ventricle and aorta are used as the outputs for the 0D lumped model proposed.

## 2 METHODS

The proposed lumped model currently includes the equations for a (stenotic) aortic valve, a heart and the vasculature, and describes the corresponding left ventricular and aortic pressures.

These calculated pressures are used in the objective function of the Modified Cuckoo Search optimisation method, which minimises the error between the input (real or simulated) and the 0D lumped model results, so when the error is minimal, the 0D lumped model pressure curves recreate the input pressure data, and consequently the coefficients that create the input pressures.

**1) Heart** To capture the relation between the left ventricular pressure and volume, a standard elastance equation is used [1], while the elastance curve is described in [2]. The elastance of the ventricle can be seen to be the left ventricular pressure divided by the ventricular volume (minus the theoretical unstressed volume ( $V_0$ )), which can be seen in Figure 1, where  $E_{max}$  is estimated from the pressures and volumes at end systole (end of ejection).  $V_0$  and  $E_{max}$  represent coefficients of the heart, however, by using the aforementioned elastance curve [2], further heart coefficients, namely  $m_1$ ,  $m_2$ ,  $\tau_1$  and  $\tau_2$  representing the contraction rate constant, relaxation rate constant, and systolic time and diastolic time constants, respectively, are also introduced.

**2) Valve** Figure 2 and Equation 1 show that, net transvalvular pressure gradient ( $TPG_{net}$ ) is the net difference of the recovered static pressure of blood when travelling from the left ventricle to the reattachment point of the ascending aorta, having passed through the aortic valve. The maximum  $TPG$  is located at the vena contracta (VC), defined as the location where the cross sectional area of the ejecting blood jet from the aortic valve is minimal.

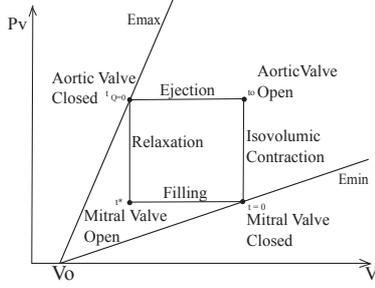


Figure 1: Pressure Volume representation showing peak and minimum elastance and valve states

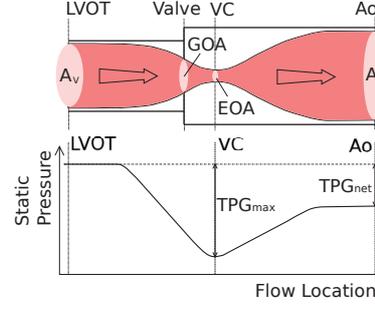


Figure 2: (top) Representation of blood flow from left ventricular outflow tract (LVOT), through Aortic Valve to ascending Aorta, (Bottom) Transvalvular Pressure Gradient

$TPG_{net}$  (eq. (1)), uses the Energy loss Coefficient ( $ELCo$ ) of the aortic valve (AV), which provides information on the health state of the AV.  $ELCo$  is a function of effective orifice area (EOA) and the sinotubular junction area ( $A_{stj}$ ) of the ascending aorta (Eq. (2)), and so is of significant use in a clinical setting.

$$TPG_{net}(t) = P_V(t) - P_A(t) = \frac{2\pi\rho}{\sqrt{ELCo}} \frac{\partial Q(t)}{\partial t} + \frac{\rho}{2} \frac{Q^2(t)}{ELCo^2} \quad (1)$$

$$ELCo = \frac{EOA \cdot A_{stj}}{A_{stj} - EOA} \quad (2)$$

Considering the range of  $A_{stj}$  [3], and the clinical ranges for EOA set by the British Heart Foundation shown in Table 1, the range for  $ELCo$  for aortic valves are shown in Figure 3, which can be used in diagnoses.

Table 1: British Heart Foundation (BHF) EOA ranges for levels of Aortic Stenosis

	Normal	Mild	Moderate	Severe
EOA( $cm^2$ )	>2	2-1.5	1.5-1.0	<1.0

**3) Vasculature** The 3 element Windkessel model detailed in Equation 3, can be represented as an electrical circuit, and is used in combination with Equation 1 and the standard elastance equation used to calculate the aortic pressures for the 0D lumped model. By using the 3 element model instead of the 4 element, the number of optimised coefficients are limited to three, where  $C$ ,  $R$  and  $Z_0$  are total arterial compliance, total vascular resistance and characteristic impedance.

$$\frac{\partial P_A(t)}{\partial t} + \frac{P_A(t)}{RC} = \frac{Z_0 + R}{RC} Q(t) + Z_0 \frac{\partial Q(t)}{\partial t} + \frac{P_{VE}}{RC} \quad (3)$$

**4) Optimisation (Modified Cuckoo Search (MCS))** To calculate the patient specific coefficients that recreate the original patient data inputs, a gradient free optimisation method i.e. Modified Cuckoo Search (MCS)[4], is used. This gradient free optimisation method is part of the family of genetic algorithm methods, and has been shown to be quite effective because it passes information forward to the following iterations, and due to the strong non-linearity of the problem, the gradient free nature of the optimisation method helps ensure that the solution does not end in local minima.

The coefficients to be optimised are, the representatives of the heart,  $E_{max}$ ,  $V_0$ ,  $m_1$ ,  $m_2$ ,  $\tau_1$  and  $\tau_2$ ; the representation of valve state,  $ELCo$  and the vasculature representations  $R$ ,  $C$  and  $Z_0$ . With this number of parameter estimations, different combinations could provide satisfactory error fits, but provide incorrect final coefficient values, and so the optimisation objective function is used with restrictions to ensure the results are correct.

The convergence of the method is demonstrated in Figure 4, in which the upper graph shows all of the value combinations for two of the coefficients being run, and at the bottom, how the error reduces as the iterations proceed.

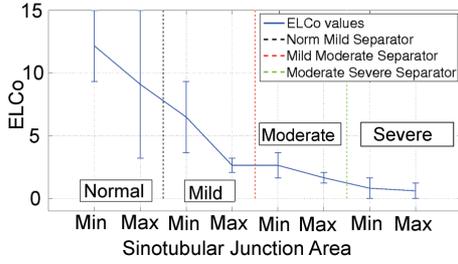


Figure 3: Energy Loss Coefficient ( $ELCo$ ) Ranges calculated using max and min Sinotubular Junction Area and EOA Areas for stenoses

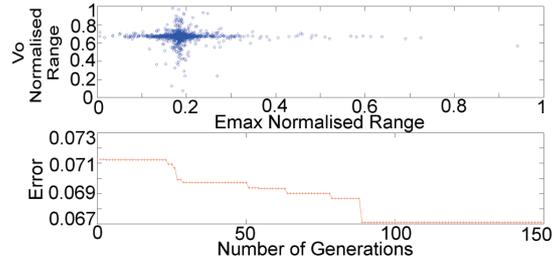


Figure 4: Modified Cuckoo Search - Search Space for 2 parameters and Reducing Error

**5) Project Data** The model requires verification of its accuracy and reproducibility, however, such that 1) the optimised coefficients of the model represent the actual measured information (representing physiology) and 2) the measurements are reproducible for different initialisations. As a first approach, optimisation of a forward run problem was performed with the coefficients taken from literature [5], which demonstrated that the optimisation method functioned with the 0D model well. Secondly, data from a 1D arterial network computer model [6](ANM) is used as a substitute for the measurement data. The ANM can be easily adapted to simulate valvular and vascular diseases which makes it ideally suited for this task.

For the verification analysis, the 1D ANM is run using initial conditions set by the user, and its output "measurements" are used in the objective function. The MCS optimisation then uses a number of restrictions and an objective function which minimises the 0D lumped output wave towards the real "measurements". These restrictions to the simulations decide whether the 0D outputs are "worthy" to go through the objective function, which adds to the computational cost. If the restrictions such as stroke volume tolerance and ejection duration are not similar to the input data, the objective function is bypassed, and a maximum error is passed back to the optimisation.

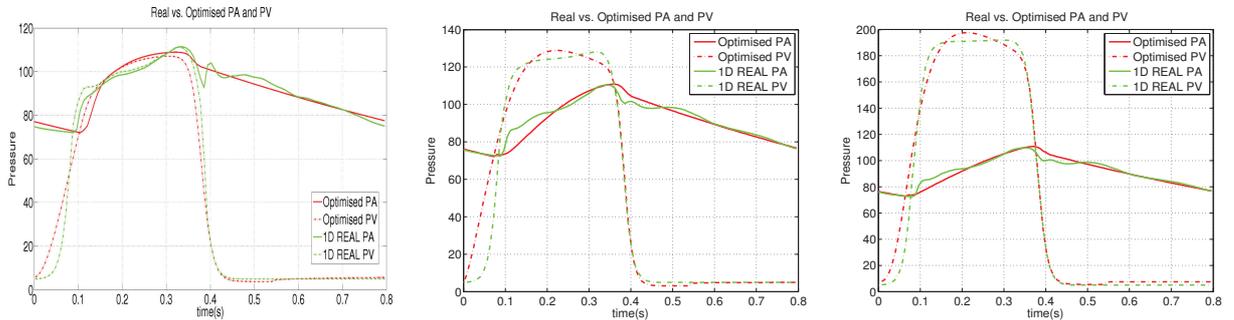


Figure 5: Pressure Comparisons for (a) Non-Stenosis ( $M_{st}=1$ ) (b) Moderate-Stenosis ( $M_{st}=0.2$ ) (c) Severe-Stenosis ( $M_{st}=0.1$ )

### 3 RESULTS & CONCLUSIONS

The 1D arterial network model has been run for varying cases of aortic valve stenosis, using a coefficient to restrict the maximum valve area ( $M_{st}$ ). By changing ( $M_{st}$ ), this alters the  $GOA$  (geometric orifice area), which highly affects  $EOA$ , because  $EOA = GOA * Cc$ , where  $Cc$  is the contraction coefficient (although this  $Cc$  is affected by shape of the orifice, for this research  $Cc \approx 0.7$  [7]). As  $EOA$  changes, so does  $ELCo$ , changing the transvalvular pressure gradient (difference).

By running different stenosis levels of the AV, it has been determined that the 0D model is highly affected by the permitted ranges of the coefficients, especially  $Zo$  and  $ELCo$ , because increasing  $Zo$  increases the ventricular pressure. If the acceptable range is too large for  $Zo$  and  $ELCo$ , viable fitting results of the pressure plots are obtained, however produce incorrect values of  $ELCo$ , by increasing  $Zo$ . When several simulation runs of the

same case were completed, a correlation coefficient analysis was performed on the results, and a relatively linear relationship was found between some of the coefficients. Because of this relationship, it was decided to estimate the total arterial compliance of the system [8], ensuring that the other coefficients which are linearly linked, would fluctuate less.

The ANM results have been used for the 0D lumped optimisation model and as can be seen in Figure 5, the overall fits for the normal and severely stenotic cases are acceptable given the simplicity of the lumped model.

The reproducibility of the coefficients for the normal and severely stenotic cases show that for repeated simulations, there is little fluctuation in the estimated coefficients (see Figure 6), have reducing  $ELCo$  values for more severe stenoses, and the optimised results show good agreement with the "measured" data, having a relatively small error tolerance. However, the mild and moderate stenosis cases require more additions to the model to ensure accuracy and consistency.

When the mild and moderate cases are completely accurate and consistent in calculating the correct coefficient values, the next step in the project is to run multiple compliance cases of the 1D ANM to validate the current 0D optimisation model completely, and when verified, mitral regurgitation can be added into the lumped model. When validation for the next stage is finalised, transcatheter aortic valve implantation (TAVI) patient data sets will be used as the model inputs and verified. The coefficients produced from the interactions between these valvular lesions will then be studied and better understood and will be able to provide improved information on timescales and diagnoses for medical intervention.

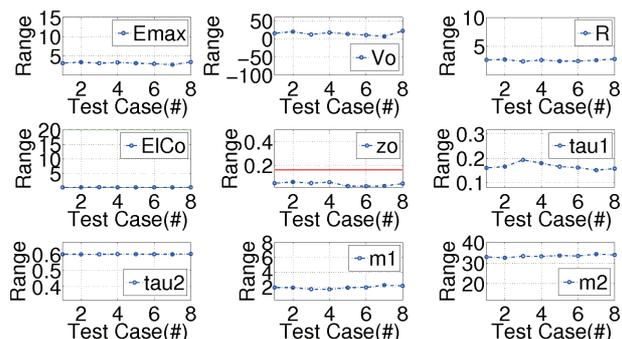


Figure 6: Coefficient Comparisons for Severe-Stenosis Case ( $M_{st}=0.1$ ), when re-testing using different initialization nest locations

### Acknowledgment

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