MODELLING OF FLOW AND PRESSURE PATTERNS. ESTIMATION OF BLOOD FLOW AND BLOOD PRESSURE MANNER IN DIFFERENT SIZED PATIENTS. NEW CHALLENGE FOR CARDIOLOGY AND CARDIAC SURGERY

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Abstract

“Modelling of flow and pressure patterns could help us to better understand real blood flow and blood pressure in the human body.” We use Modelica for modelling blood flow and blood pressure patterns in different size patients. Every patient has his/her unique systemic vascular bed size and pulmonary vascular bed size. We define the vascular bed parameters for describing the patient's vascular bed. We acquire vascular bed data by means of assessment and processing of flow and pressure biosignals. We are at the beginning of developing models of blood flow and blood pressure pattern in the human body, but we are aware of the importance of our efforts for cardiology and for cardiac surgery and for the development of new pumps - mechanical circulatory support devices. Modelling of blood flow and blood pressure pattern in the human body is going to become a very important tool for solution of cardiology and cardiac surgery problems in the case of patients supported by pumps worldwide. As the main medical aim of our contribution we present pressure and flow pattern change, when employing pump with stroke volume of 100 ml into the normal-sized patient (the patient adapted to the stroke volume of 65ml).

Keywords: Modelling, Blood flow, Blood pressure, Cardiology, Cardiac surgery

Presenting Author’s biography:

David Macku, MD, MSc works as the research fellow in the BioDat Research Group at the Gerstner laboratory. He graduated in chemical engineering at the Institute of Chemical Technology Prague in 1997. He is a medical doctor. He finished the 1st Medical Faculty of the Charles University in Prague in 2003.

His main research is focused on mechanical circulatory support devices, another research interests include modeling of blood flow and blood pressure patterns, fluid dispersion in branched systems.

1 Introduction

In these days we can see a fast progress in all medical specializations. New drugs and devices help patients with their illnesses to sustain alive for longer and longer time. Mechanical circulatory support devices represent pumps, which help to maintain circulation, when a heart fails. This new technology brings not only a lot of ethical and legal issues but also more responsibility for physicians. Physicians are forced to solve more technical problems in addition to their medical work. They take care not only about the patient, but also about the machine. The patient is still human but large part of him/her is replaced by a machine. There is not a small mechanical valve or pacemaker present, but a powerful pump, which generates artificial blood flow and blood pressure in the native vascular bed. Selection and implantation of an inappropriate pump and / or setting inappropriate parameters could create catastrophic insults for patients and even their death. For a sufficient care there is needed not only sufficient *medical* care, but more - interdisciplinary care provided by a multidisciplinary team of physicians, biomedical engineers, perfusiologists and others.

We choose modelling of complicated flow and pressure relationships in the human body because there are many advantages for doing that. Modelling is comparatively inexpensive solution for our research; it is presented as a very comfortable and friendly approach to real clinical problems. Experiments with models represent less ethical and legal impediment than experiments with experimental animals, or direct experimentation on human patients is ethically inadmissible. Design of our experiments is very easy to vary; it means changes in input setting are followed by changes in output results in very short time

2 Methods

We use Modelica for modelling blood flow and blood pressure patterns in different size patients. Every patient has his/her unique systemic vascular bed size and pulmonary vascular bed size. We define the vascular bed parameters for describing the patient's vascular bed. We acquire vascular bed data by means of assessment and processing of flow and pressure biosignals.

2.1 Hypothesis

I set up the medical hypothesis during the cardiovascular fellowship of five years in IKEM. I had been observing that many adverse events (bleeding, cerebro-vascular accidents) in the patients supported by pulsatile ventricular assist device were linked to their size. In my hypothesis I even claim, that some small-sized patients (I call them extremely small patients) can experience iatrogenic systemic and/or pulmonary arterial hypertension and vice versa extremely large patients, for example, can experience iatrogenic systemic hypotension in their systemic vascular beds. Some my statements could be supported by medical articles and case reports in the literature. It seems that for the reliable and safe function of a pulsatile VAD it is needed to adjust the stroke volume expelled into ascending aorta or pulmonary artery with regard to the requirements of vascular beds, with regard to the parameters of vascular beds. That is the main conclusion of my hypothesis.

Filip Ježek chose this issue as a topic of a Master Thesis [2]. His primary goal has been to interconnect the state of the art in the research area of mechanical circulatory support and modelling of flow and pressure pattern. His secondary goal has been to confirm my medical hypothesis. Hereby we present some of the results of his work.

2.2 Software and modelling consequences

Now we can present excellent tutorial software for medical specialists. By changing parameters of pulsatile pump on the one hand and by changing vascular bed parameters on the other hand we are able to anticipate the manner of systemic and pulmonary arterial pressure. If we enter the pulsatile pump parameters using at clinical practice and the vascular bed parameters of extremely small patient, the systolic pressure is reaching non physiological value above 140 mmHg. If this situation occurs in the hospital in the case of patients supported by pulsatile pump, the experts should be forced to change initial pump setting, in particular a decrease of stroke volume.

3 Model

The model is designed to substitute mock circulatory models of human vascular system by mathematic abstraction. We use model implemented in Modelica language, which allows us to keep it simple, flexible and lucid. Current model has been derived from the one proposed by Conlon et al [1]. One of the greatest advantage of this model was, that it included Matlab source codes for direct simulation, which helped debugging while converting model to Modelica environment. Its drawback however was, that authors did not work directly with pressure and flow units, but with volume ([cm3]) and fluid momentum ([N.s.cm-2]). So there had to be done some transformation to pressure ([N.cm-2]) and flow ([cm3.s-1]), which meant to completely rewrite the model in the end. Also, the model of the pump has been completely rewritten to meet our requirements.

Components in this model represent the major parts of the systemic HCS loop, with all component parameters based on physiological data available in the literature (adopted from [1]).

3.1 Simplifications and assumptions

Since living organism is usually very complex environment, a number of simplifications and abstractions had to be employed,

All vessels form closed system with no leakages, blood is homogenous and incompressible and none of the organs are elevated upon each other (no gravity effect). We do not consider the subject standing or moving anyway. The appropriate patient would be lying on its back with basal metabolism only.

Because modelling turbulent flow is extremely difficult, all flow is modeled as laminar. But as we are interested only in overall macroscopic circulation, it is enough to incorporate the effect of turbulent flow as a slightly higher resistance than it is usual for laminar flow (i.e. in outflow cannulla).

Also, the pulse wave propagation has been simplified. Originally, the pulse travels not only through the liquid, but also through the expansion of artery's walls. Instead we introduce just a few compliant vessels, which could change their volume in dependence on pressure and thus simulate the Windkessel effect. These compliant elements are assumed to have constant and instant compliance. Delay in which the pulse travels all over systemic circulation is not realistic as well, since the delays are disregarded. This is valid only when studying stable circulation, which is the case.

The pressure inside thoracic cavity is assumed to be constant zero, but it in fact it varies from – 2 to – 6 mmHg during breathing, which is disregarded.

We simulate the beginning of circulatory support, when the native heart is impaired, which was an indication for mechanical support. Thus, we assume not only zero aortic valve flow, but also zero ventricle contribution to pump filling. Secondly, the interaction would make the aortic waveforms unnecessarily complex.

As the pump in model works in fixed rate mode now, with enough time to fill, that it waits fully filled for an ejection, the native heart would just contribute to even faster filling and, when the VAD is full, to eject through aortic valve to possibly contribute to VADs ejection. That could in all cases just increase the aortic pressure. Therefore, by disregarding ventricle, the objective would not be easier to prove, thus such simplification is valid for current scope.

Since we are observing aortic flow and pressure patterns only, we decided to deal with left (systemic) circulation only. This approach is often used. Still, the pulmonary circulation could be introduced easily later.

Apart from hydraulics only, the circulation is not regulated. Human circulatory is regulated by a number of mechanisms, which keep together homeostasis. Some of the mechanism could help the body to adapt circulatory system to artificial pump, but this is not the current objective. We want to show instead, how the *unadapted* circulation would react to installation of a new pump.

Also, we disregard all transitional phenomena.

3.2 Overall structure

The model is structured for lucidity into a few main components, as could be seen in Fig. 1.

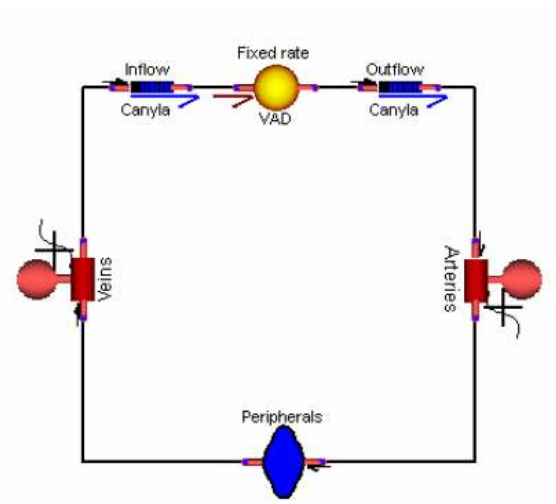

Fig. 1: Overall structure of the model

Vascular system could be characterized by a serio-parallel combination of three basic components – resistance, compliance and inertia. This approach is equivalent to electrical analogies method, used in most of other models, but with an advantage, that it is referred directly to pressure and flows fluid and not to abstract voltage and electrical flow. Thus, the model is closer to reality.

3.3 Basic components

Most of the blocks are made of basic components, which resemble basic electrical elements – resistor, capacitor (with the second pin grounded) and inductor, but they work with different physical quantities - instead of voltage and current they use pressure and flow. Following equations describe the behavior of resistance (eq 1), compliance (eq 2.) and inertia (eq 3):

$$\Delta p = R \times q \tag{1}$$

$$\begin{aligned} volume &= \int q_{in} + q_{out} dt \\ stressVol &= \max(volume - P0Vol, 0) \\ \Delta p &= \frac{stressVol}{C} \end{aligned} \tag{2}$$

(3) $$\Delta p = I \times \frac{dq}{dt}$$

, where Δp is pressure difference on element ([hPa]), *q* flow in *ml* (inflow is positive, whereas outflow negative), *volume* is accumulated volume also in *ml*, *P0Vol* is a volume, which generates no pressure, *C* is compliance and *I* inertance constants.

Note, that the compliance element is not limited, i.e. it could have unlimited as well as negative volume.

3.4 Arteries

Arteries block model in together all arteries, from large ones to small arterioles. In many mock circulatory systems, the arteries are modeled using the only one compliance, whereas in this model it is divided into two segments. The left compliance mimics large artery – aorta, whose compliance is of special significance and the other compliance models summed compliance of the other arteries. Between them is some inertia and aortic resistance, which damps oscillations.

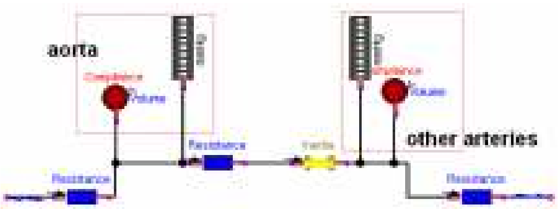

Fig. 2: Arteries component is formed of basic components. The Inlet is on the left side.

The whole component is shown on Fig. 2. Both outermost resistances are of very low values and are there for numerical stability only, components with caption mmHg are just converting the pressure in units of *hPa* to *torr*

3.5 Peripherals

Peripheral block models microarterioles, capillaries and microvenules and represents all of the microcirculation. The capillaries have very small diameter, but as there are many of them, extremely large total cross-sectional area. Thus they have significant resistance and inertia, while any compliance is neglected [1]. As peripheral resistance and inertance are not directly mentioned in literature, Conlon et al. based their values on compilations of data available.

3.6 Veins

Veins block is very similar to arteries block. It also incorporates dual compliances; one represents veins and the other vena cava, which volume-pressure relationship is non-linear. Between them is a resistance, which is able to collapse on low (negative) pressure and thus increase its resistance. For normal circulation it does not have any particular reason, but VAD could induce suction to the system, which makes it particularly important.

3.7 Cannullae

The pump is connected to body using inlet cannulla, which leads blood from ventricle to the paracorporeal pump, and the outlet cannulla, which connects the output of the pump with aorta.

They are both modeled as thin, flexible tubes with resistance and compliance. The resistance of the outlet cannulla could not be easily calculated though, because of the complex (semi-turbulent or turbulent) characteristics of the flow. Thus, the resistance is quite higher and adjusted so the model has appropriate response.

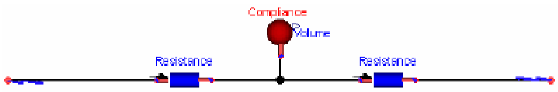

Fig. 3: Inner structure of cannullae

To the contrary of Conlon, the resistance here is divided to two elements - before and after the compliance (Fig. 3). This is to describe the reality in more detail and to add numerical security -- e.g. when connected directly to other component such as compliance, then there would be infinite flow due to zero resistance.

3.8 Pump

The model of pump was based on design of Thoratec PVAD device working in fixed rate mode. As could be seen in Fig. 4, the base is a blood sac with limited volume and with external pressure applied. Because the diaphragma is thin and flexible, I assume, that provided pressure equals pressure in sac inlet and outlet. This provided pressure matches that applied by pneumatic driving console.

Driving pressure mimics pneumatic driving as in Thoratec device. The pressure generated in real pneumatic console switches from filling to ejection and vice versa in a more or less ideal step function. However, as the inlet tube is of small diameter, it has significant resistance, which would delay the pressure rise during ejection. Some consoles do even provide a possibility to modify this resistance. Therefore, the driving pressure is simulated as step function with exponential rise in form of

$$\text{pressure} = 1 - \exp(-\frac{\text{time} - T_0}{alpha})$$

and then scale it to fit filling and ejection pressures. Here T_0 is time of starting current systole and alpha is a term controlling the exponential slope. Alpha was arbitrarily set to 0.025 to generate pretty output.

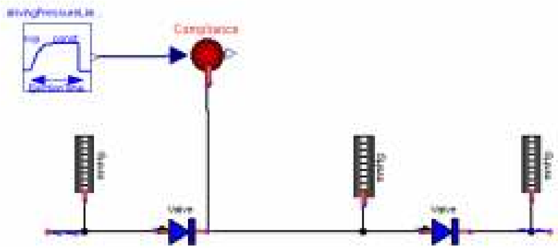

Fig. 4: Structure of the pump

Pumping sac originally developed from compliance element, which compliance parameter changed over time with ejection. That design is more similar to native heart, but the VAD works with provided external pressure. Assuming the pressure in blood sac is the same as provided pressure, we can directly change inner pressure by the *Driving pressure*.

One issue, which must be carefully addressed is the volume limiting. In physical component, the volume could not be negative or larger than its maximal vessel's volume. For numerical reasons, this is not easily done in Modelica, but after initial struggles we came with an elegant solution. The pressure function is divided into three parts - normal, empty and full:

$$p = provided\,\mathrm{Pr}essure + \left| \begin{array}{ll} \dfrac{(volume - \max Vol)}{microCompliance} & if\,(volume > \max Vol) \\ 0 & otherwise \\ \dfrac{(volume - \min Vol)}{microCompliance} & if\,(volume < \min Vol) \end{array} \right.$$

where the microCompliance is a small number to describe large changes of pressure on small changes in volume (as the sac is at limit).

Valves are another component, which induces nonlinearities and discontinuities. They provide some small resistance when opened and large resistance, when closed. Current state depends on pressure and flow direction. In the end, we decided to have them based on diode in Modelica.Electrical.Analog.Ideal.IdealDiode library.

In addition, the pump is computing actual outflow from outlet (aortic) valve. Integrated outflow during the whole period must equal stroke volume. If it is lower, then the pump was either not fully filled or fully emptied.

4 Implementation issues

Discussed model has been implemented in Modelica language, version 3.1. As the relations and equations are known and Modelica is a language of high abstraction, the implementation was easy. In fact, it is nearly a matter of just rewriting equations into appropriate blocks. As already mentioned above, we chose abstraction of major blocks, which consist of basic blocks. All blocks are connected using the PressureFlowConnector, which transfers pressure and flow according to Kirchhoff's laws. Some blocks (arteries and cannullae) use inheritance to inherit global icons.

Although this model is quite simple compared to other circulatory models, it is not as simple for Modelica. Having in together more than 200 equations, of which more than half are non-trivial (more elements than just $x = 1$), both time-continuous (e.g. pressure course) and discrete variables (ejection signal, current stroke volume) and discrete events (volume of the pump, valves), it makes the simulation particularly complex.

Proprietary Modelica environment Dymola has quite advanced simulation optimization and thus is able to simulate it rather quick (with time span 20s and 1800 intervals it takes around 1s), whereas open-source implementation of OpenModelica takes more than 13s to perform the same simulation. This was even optimalized from around 13 minutes in OpenModelica by removing inertias from cannullae (and other slight changes) and thus reducing many state events created by oscillations especially on valves.

It was an attempt to substitute the *if* clause by polynomial or exponential functions, but it led to very hard computation with unstable Jacobians reported and in effect the time needed was even a few folds higher. Thus, I do not recommend continuous time approximation of step functions.

5 Experiment

Default parameters of the model were adopted from [1] and slightly adjusted to adapt for different type of pump. For normal-sized patient, the stroke volume equals 65 ml. Now we observed, how the pressure and flow patterns would change, when employing pump with maximal stroke volume of 100 ml, which is fully filled and emptied in each cycle.

6 Results

Aortic pressure and flow waveforms, measured on the resistor between aortic and arterial compliances, are visualized in figure 5.

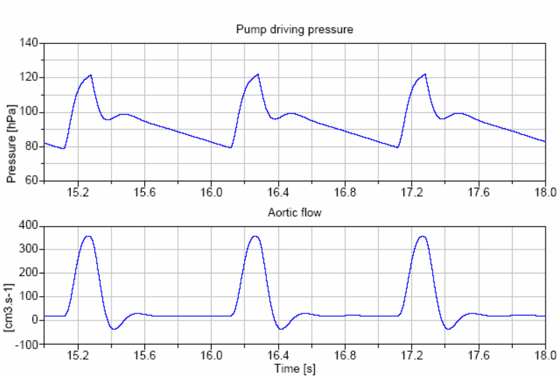

Fig. 5: Simulated aortic pressure (top) and flow (bottom) waveforms after transients in patient with appropriate stroke volume of 65 ml, rate 60 bpm and systole fraction of 30%.

Result of experiment is shown in Fig. 6. As the pressure curve exceeds the limit of hypertension (140 mmHg), this figure proves, that using pulsatile pump with full-fill-full-eject mode could be dangerous for patients with body size, which is used to lower stroke volumes.

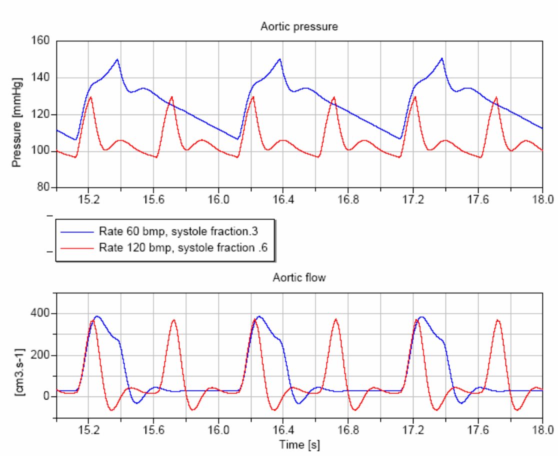

Fig. 6: Simulated aortic pressure (top) and flow (bottom) waveforms after transients using different rate, so the pump fills to its maximal stroke volume of 100 ml at 60 bpm, or to stroke volume of 40 ml at 120 bpm in a patient used to stroke volume of 65 ml

7 Future work

Current model is in very basic form and is intended to be extended as the Modelica environment offers us a comfortable way in modifications and add-ons.

For future usage, the heart could be easily added. It is enough to create a model of a ventricle and connect it in series to the inflow cannulla (disabling the aortic valve in model) to simulate initial phase of treatment (with zero aortic valve flow). Enabling the heart's aortic valve and connecting it to aorta (parallel to VAD pump) we could simulate stronger heart with VAD as a support and observe the interaction.

Extensive future work would be to add at least baroreflex regulation for vasoconstrictions, which is helping the body to acclimatize to a range of pressures by changing (peripheral) resistance.

8 Conclusion

We are at the beginning of developing models of the blood flow and blood pressure pattern in the human body, but we are aware of the importance of our efforts for cardiology and for cardiac surgery and for the development of new pumps - mechanical circulatory support devices. Modelling of blood flow and blood pressure pattern in the human body is going to become a very important tool for solution of cardiology and cardiac surgery problems in the case of patients supported by pumps worldwide.

Even the currently developed model gives us valuable results and proves the threat of too high stroke volume of the artificial pumps to the patient.

9 Acknowledgements

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10 References

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