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# Mathematical model of Mobile Circulatory Module for ex-vivo lungs perfusion

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Abstract: The article deals with mathematical modelling of a system for ex-vivo lung perfusion. The system which is modelled here is named Mobile Circulatory Module and is designed for transport of live lungs namely porcine or human lungs. Transported lungs should be used for various research or even for transplantation. The article describes mathematical model of thermal circuit and hydraulic circuit which are vital parts of the MCM to secure living conditions of the transported organ. Mathematical model is simulated with MATLAB Simulink and shows good qualitative correspondence with real behavior of the system. Based on math model there is designed control algorithm for temperature control and there is discussed control of perfusion liquid as well.



*Keywords:* ex-vivo lungs perfusion, isolated organ, MCM, Matlab model, control of flow, temperature control

## 1. INTRODUCTION

Mobile Circulatory Module (MCM) is a system which is designed for transport and short time preservation of live lungs (namely porcine or human lungs) for transplantation or ex-vivo experiments. Systems of this type are object of concurrent research in the field of live organs transplantation (Aigner et al., 2012)

Organs from cadaver donor, especially lungs, must be carefully treated before transplantation to prevent irreversible functional changes which can occur during transport from the donor to the recipient. The same is valid when we want to perform some ex-vivo experiments (Wallinder, 2014),(Okamoto et al., 2010).

MCM is in fact designed to provide sterile and reliable ex-vivo perfusion of lungs. Basic part of the MCM is a reservoir of the perfusion liquid which is connected via a pump and tubes with lungs. The liquid is pumped from the reservoir by the peristaltic pump to the lung artery and returns back from lung vein to the reservoir. The lungs are placed in a sterile and airtight box (Organ Chamber). Control system of the MCM must secure required flow and temperature of the perfusion liquid.

Intensity of flow is given by the speed of the peristaltic pump. Temperature of the perfusion liquid is secured by electrical heating of the reservoir. Because of heat losses the temperature must be controlled via feedback control. To this end there can be used several temperature sensors. One temperature sensor is placed in the reservoir, other two are placed at the lung artery and at the lung vein. All the temperature sensors can be used in the feedback control if the need be. Other sensors namely flow sensor and pressure sensors can be used for the flow control. For safety and service reasons MCM uses several shut-off valves and also level sensor in the liquid reservoir. Detailed construction of the MCM is described in (Eschli, 2013)

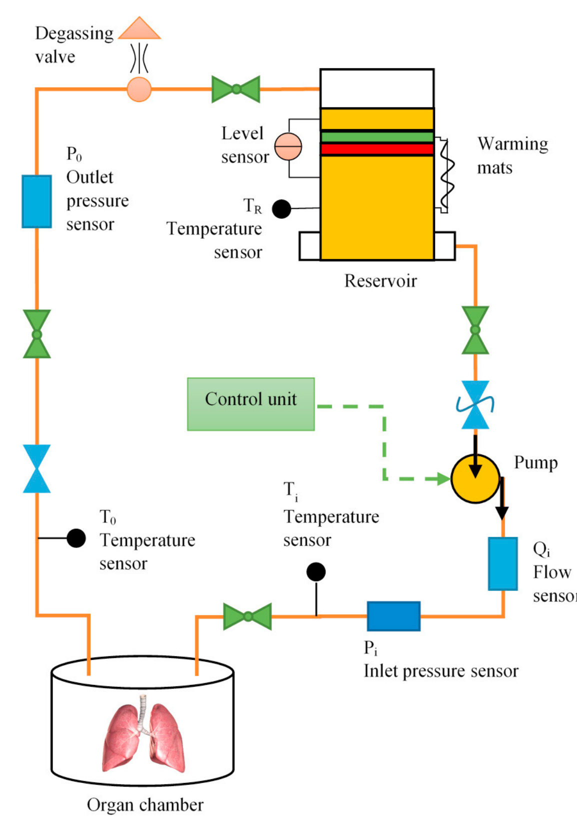


Fig. 1 Scheme of the MCM

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The goal of the paper is to show development of a mathematical model of thermal and hydraulic behavior of the MCM. The mathematical model should enable study of the MCM behavior and design of the control law especially for control of the temperature of the perfusion liquid. Mathematical models are verified via MATLAB Simulink simulation. The paper also describes control laws for temperature and flow control and discusses MCM behavior. Standard textbooks (Dean C. Karnopp, Donald L. Margolis, 1990), (Noskievič Petr, 1999)were used for construction of the math model.
Scheme of the MCM is depicted on Fig.1. We presume that mathematical model of the MCM can be developed as a thermal and hydraulic model separately.

## 2. MATHEMATICAL MODEL OF THE THERMAL CIRCUIT

We suppose that the thermal part of the MCM can be described as a system of vessels shown on Fig.2.

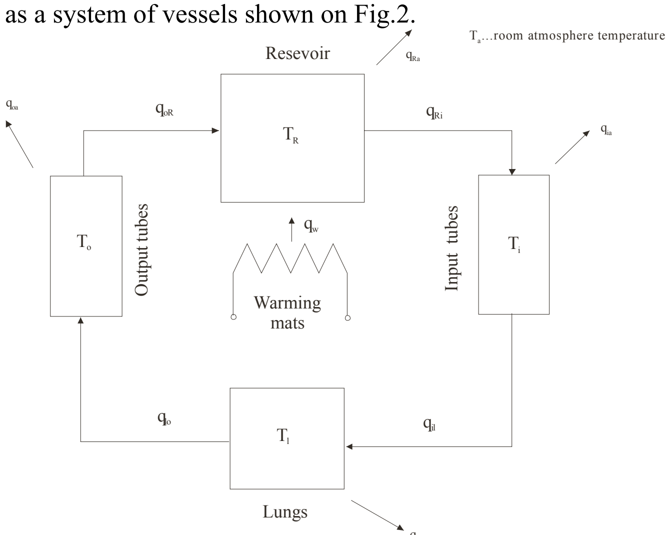


Fig. 2 Principial scheme of the thermal model

Perfusion liquid transfers heat from reservoir through input tubes to lungs and from lungs through output tubes to reservoir. Also warming mats transfer heat to reservoir. Heat transfer is harcterised by heat flux q. The following equations characterize heat transfer

$$cm_R \frac{dT_R}{dt} = q_w + c\rho Q(T_0 - T_R) - \left(\frac{T_R - T_a}{R_R}\right) \qquad (2.1)$$

$$cm_i \frac{dT_i}{dt} = c\rho Q(T_R - T_i) - \left(\frac{T_i - T_a}{R_i}\right) \qquad (2.2)$$

$$cm_l \frac{dT_l}{dt} = c\rho Q(T_i - T_l) - \left(\frac{T_l - T_a}{R_l}\right) \qquad (2.3)$$

$$cm_o \frac{dT_o}{dt} = c\rho Q(T_l - T_o) - \left(\frac{T_o - T_a}{R_o}\right) \qquad (2.4)$$

where denotes
$c$… specific heat capacity of the perfusion liquid [Jkg$^{-1}$K$^{-1}$]
$q$…heat flux [W]
$m$…mass of nutrittion liquid in the specific vessel [kg]
$\varrho$…density of perfusion liquid [kgm$^{-3}$]
$Q$…volumetric flow of perfusion liquid [m$^3$s$^{-1}$]
$T$…temperature [K]
$R$…thermal wall resistance of the specific vessel [KW$^{-1}$]

Equations (2.1)-(2.4) can be rewritten into state variable form

$$\begin{aligned}
\frac{dT_R}{dt} &= \left(\frac{\rho Q}{m_R} + \frac{1}{cm_R R_R}\right) T_R + \frac{\rho Q}{m_R} T_o + \frac{1}{cm_R R_R} T_a + q_w \\
\frac{dT_i}{dt} &= \left(\frac{\rho Q}{m_i} + \frac{1}{cm_i R_i}\right) T_i + \frac{\rho Q}{m_i} T_R + \frac{1}{cm_i R_i} T_a \\
\frac{dT_l}{dt} &= \left(\frac{\rho Q}{m_l} + \frac{1}{cm_l R_l}\right) T_l + \frac{\rho Q}{m_l} T_i + \frac{1}{cm_l R_l} T_a \\
\frac{dT_o}{dt} &= \left(\frac{\rho Q}{m_o} + \frac{1}{cm_o R_o}\right) T_o + \frac{\rho Q}{m_o} T_l + \frac{1}{cm_o R_o} T_a
\end{aligned} \qquad (2.5)$$

where we denoted

*input variables:*
$q_w$… control variable…heat flux from warming matts
$T_a$…disturbance…ambient temperature

*output variables (see Fig.1):*
$T_R$…temperature inside reservoir (measured)
$T_i$…temperature in input tubing (measured)
$T_l$…temperature inside lungs (not measured)
$T_o$…temperature in output tubing (measured)

Equations (2.5) can be written in more compact form

$$\dot{\mathbf{x}} = \mathbf{A}\mathbf{x} + \mathbf{B}\mathbf{u} \qquad (2.6)$$

Where

$$\mathbf{x} = [T_R \quad T_i \quad T_l \quad T_o]^T \quad \mathbf{u} = [q_w \quad T_a]^T$$

$$\mathbf{A} = \begin{bmatrix} -\left(\frac{\rho Q}{m_R} + \frac{1}{cm_R R_R}\right) & 0 & 0 & \frac{\rho Q}{m_R} \\ \frac{\rho Q}{m_i} & -\left(\frac{\rho Q}{m_i} + \frac{1}{cm_i R_i}\right) & 0 & 0 \\ 0 & \frac{\rho Q}{m_l} & -\left(\frac{\rho Q}{m_l} + \frac{1}{cm_l R_l}\right) & 0 \\ 0 & 0 & \frac{\rho Q}{m_o} & -\left(\frac{\rho Q}{m_o} + \frac{1}{cm_o R_o}\right) \end{bmatrix}$$

$$\mathbf{B} = \begin{bmatrix} \frac{1}{cm_R} & \frac{1}{cm_R R_R} \\ 0 & \frac{1}{cm_i R_i} \\ 0 & \frac{1}{cm_l R_l} \\ 0 & \frac{1}{cm_o R_o} \end{bmatrix}$$

Matrix form can be used for calculation of equilibrium steady state where **x**=**x**$_0$=**const** and **u**=**u**$_0$=**const.**

$$\mathbf{x}_0 = -\mathbf{A}^{-1}\mathbf{B}\mathbf{u}_0 \qquad (2.7)$$

which can be used for calculation of necessary power of heating matts.
E.g with parameters that are given bellow with power of heating matts to be 100W at ambient temperature 20ºC equation (2.7) yields steady state temperatures **x**=[23.41 22.65 22.58 22.50]$^T$ .

Equations (2.5) are calculated in Matlab Simulink according to the following figure

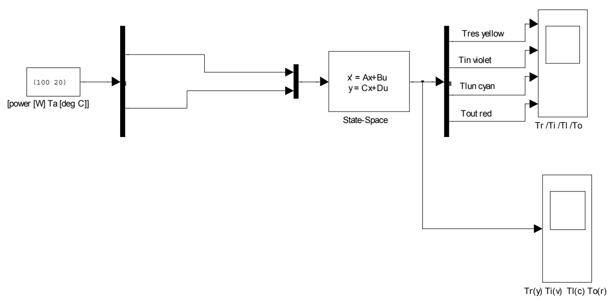


Fig. 3 Simulation scheme of the thermal system

Table 1. Parameters of the thermal model

| Parameters | Description |
|---|---|
| c=4183 | Specific heat of water [J/kgK] |
| ro=998.3 | Density of water [kg/m^3] |
| **Parameters of tubes** | |
| Lin= 2 | Length of input tube [m] |
| Lout= 2 | Length of output tube [m] |
| Din= 1/100 | Diameter of input tube [cm]/100->[m] |
| Dout= 1/100 | Diameter of output tube [cm]/100->[m] |
| | |
| Q=0.5/1000/60 | Volume flow rate of liquid [l/min]/1000/60->[m^3/sec] |
| Rres=1/20 | Thermal resistance of reservoir [Ks/J]=[K/W] |
| Rin =1/10 | Thermal resistance of input tube [Ks/J]=[K/W] |
| Rlun=1/1 | Thermal resistance of lung [Ks/J]=[K/W] |
| Rout=1/1 | Thermal resistance of output tube [Ks/J]=[K/W] |
| Vres=3/1000 | Volume of reservoir [l]/1000->[m^3] |
| Vin= pi*(Din/2)^2*Lin | Volume of input tube [m^3] |
| Vlun=2/1000 | Volume of lung [L]->[m^3] |
| Vout= pi*(Dout/2)^2*Lout | Volume of output tube [m^3] |
| mres=ro*Vres | Mass of liquid in reservoir [kg] |
| min=ro*Vin | Mass of liquid in input tube [kg] |
| mlun=ro*Vlun | Mass of liquid in lungtissue [kg] |
| mout=ro*Vout | Mass of liquid in output tube [kg] |

The figures (Fig.4, Fig. 6.) show some simulation results.

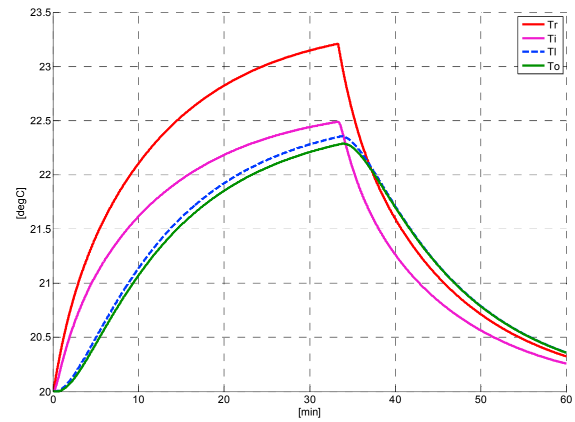


Fig. 4 Response of the system to impulse of power 100W to heating mats. Duration of the impulse is 33.3 min. Ambient temperature 20°C.

Mathematical model of the thermal circuit represents relatively simple linear system with one actuating signal (power of the electrical heating) and several output variables (temperatures).
We assumed that controlled variable will be temperature of the perfusion liquid from the lungs vein. Simulation experiments showed that simple on-off controller should control the temperature with reasonable precision.

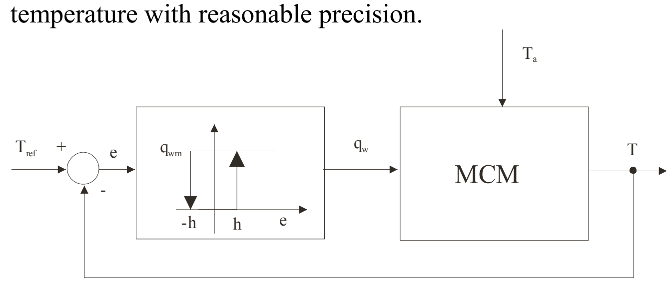


Fig. 5 On-off temperature control

The figure 6 show results of control of the output temperature $T_o$ which should be close to temperature of lungs.

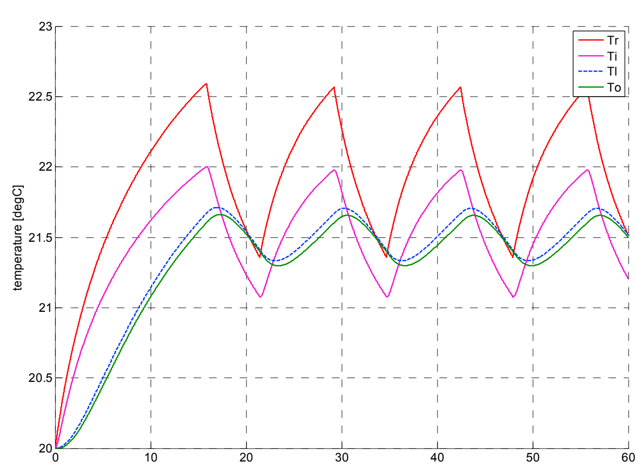


Fig. 6 Control of output temperature $T_o$ with on-off controller. Parameters $T_{oref}$=21.5°, h=0.1°C, $q_{wm}$=100W, $T_a$=20°C. Other parameters as in Tab.1.

Results of simulation should be taken with care. Model itself is rather simple, nevertheless it shows basic principal behaviour of the system. Problem is in parameters of the model. They should be estimated according to measurement on the real system. Especially vital is estimation of thermal resistances. They are important especially for correct design of supply power. E.g. our simulation shows that with 100W power supply to heating matts we can reach temperatures only around 22ºC at ambient temperature 20ºC.

## 3. MATHEMATICAL MODEL OF THE HYDRAULIC CIRCUIT

Volume flow of the perfusion liquid is dictated by the speed (rpm) of the peristaltic pump. This speed is the only actuating signal in the hydraulic circuit of the MCM. Pressure in the circuit will be dictated by the volume flow and hydraulic resistance of the tubes, the valves and the lungs itself. We suppose that hydraulic resistances of the tubes and valves will be constant. On the other side hydraulic resistance of the lung tissue can change. Though the total hydraulic resistance of the lungs will be significant the changes themselves will have no effect on the pressure in the circuit.

We presume that the hydraulic section of the MCM can be described as a system of rigid pipes representing tubes of the perfusion system and an air bladder representing the lungs as shown inFig.7. The pipes represent hydraulic resistors and the air bladder represents hydraulic capacitor. Peristaltic pump is a source of hydraulic volume flow $Q_i$.

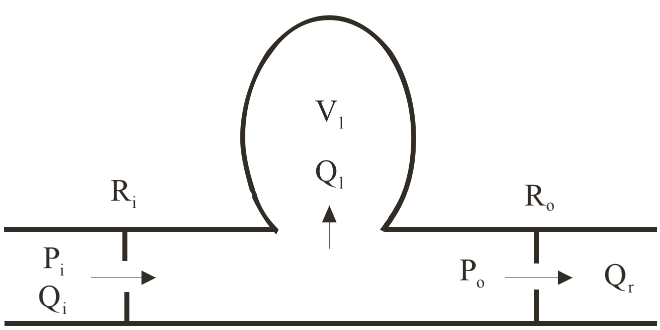

Fig. 7 Principial scheme of the hydraulic model.

The following equations describe the hydraulic system.

$$Q_i = Q_l + Q_r \tag{3.1}$$

$$Q_l = \frac{dV_l}{dt} \tag{3.2}$$

$$V_l = f(P_0) = CP_0 \tag{3.3}$$

$$Q_i = \frac{P_i - P_0}{R_i} \tag{3.4}$$

$$Q_r = \frac{P_0}{R_0} \tag{3.5}$$

where denotes

$Q_i$…volumetric flow delivered by the peristaltic pump [$m^3s^{-1}$]
$Q_r$…output volumetric flow to reservoir [$m^3s^{-1}$]
$Q_l$…volumetric flow of perfusion liquid to lung tissue [$m^3s^{-1}$]
$V_l$…volume of perfusion liquid stored in the lung tissue [$m^3$]
$P_i$…pressure developed by the peristaltic pump
$P_o$…pressure of perfusion liquid in the lung tissue [$Nm^{-2}$]
$R_i$…hydraulic resistance in the input piping [$Nsm^{-5}$]
$R_o$…hydraulic resistance in the output piping [$Nsm^{-5}$]
$f(P_o)$…represents nonlinear lung tissue compliance
$C$… lung tissue compliance [$m^5N^{-1}$]

For simplicity we shall assume linear compliance or stiffness of the lung tissue and express the mathematical model in state variable form. From (3.1)-(3.5) we see that we have only one input variable namely $Q_i$. Other variables $Q_l$ , $Q_r$ , $V_l$ , $P_o$ , $P_i$ are unknown, among them $V_l$ is state variable. Now we shall construct state variable equation

$$\frac{dV_l}{dt} = Q_i - Q_r = Q_i - \frac{P_0}{R_0} = Q_i - \frac{V_l}{C_l R_0} \tag{3.6}$$

and output equations for measured values $P_o$ $P_i$

$$\begin{aligned} P_0 &= \frac{V_l}{C_l} \\ P_i &= Q_i R_i + \frac{V_l}{C_l} \end{aligned} \tag{3.7}$$

We are also interested in other variables which are not measured namely $V_l$ , $Q_r$ and $Q_l$

$$\begin{aligned} Q_r &= \frac{V_l}{R_0 C_l} \\ Q_l &= Q_i - Q_r = Q_i - \frac{V_l}{R_0 C_l} \end{aligned} \tag{3.8}$$

Let us investigate steady state equilibrium of the system for $V_l=V_{l0}=const.$ and $Q_i=Q_{i0}=const.$

We come to the following values

$$\begin{aligned} V_{l0} &= R_0 C_l Q_{i0} \\ \mathrm{P}_0 &= \frac{V_{l0}}{C_l} = R_0 Q_{i0} \\ P_{i0} &= R_i Q_{i0} + P_0 = (R_0 + R_i) Q_{i0} \\ Q_{r0} &= \frac{V_{l0}}{R_0 C_l} = Q_{i0} \\ Q_{l0} &= Q_{i0} - Q_{r0} = 0 \end{aligned} \tag{3.9}$$

From these equations we can deduce that in equilibrium the following will be true

a) lung tissue will be "swelled" proportionally to output hydraulic resistance, lung compliance and input volumetric flow
b) pressure in lungs will be proportional to output resistance
c) pressure developed by the peristaltic pump will be proportional to input volumetric flow and total hydraulic resistance of the system
d) output volumetric flow will be equal to input volumetric flow
e) "swelling" of lung tissue will not increase

Steady state equilibrium values of the system with parameters given in the following table are $Q_{i0}$ =5 $dm^3/min$, $V_{l0}$=0.013 $dm^3$, $P_{io}$=10.19 $mmHg$, $P_o$=5.09 $mmHg$.

Model of hydraulic circuit is calculated in Matlab Simulink according to the following scheme.

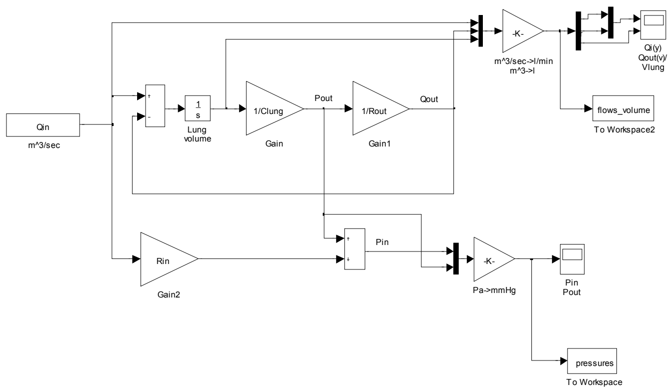


Fig. 8 Simulation scheme of the hydraulic system

Table 2. Parameters of the hydraulic model

| Parameters | Description |
|---|---|
| mi= 0.001 | Dynamic viscosity of water [Ns/m$^2$] |
| **Parameters of tubes** | |
| Lin= 2 | Length of input tube [m] |
| Lout= 2 | Length of output tube [m] |
| Din= 1/100 | Diameter of input tube [cm]/100->[m] |
| Dout= 1/100 | Diameter of output tube [cm]/100->[m] |
| **Hydraulic resistance according to Hagen-Poiseuill** | |
| Rin= 128*Lin*mi/pi/Din^4 | input hydraulic resistance [Nsec/m$^5$] |
| Rout=128*Lout*mi/pi/Dout^4 | output hydraulicresistance [Nsec/m$^5$] |
| **The estimation of lung tissue compliance** | |
| Psystolic=120*133.322 | Systolic pressure [mmHg]*133,322->[Pa] |
| Pdiastolic=80*133.322 | Systolic pressure [mmHg]*133,322->[Pa] |
| Clung=0.1*0.001/(Psystolic-Pdiastolic) | Lung capacity [dm$^3$/Pa]*0.001->[m$^3$/Pa] |
| | |
| Qimax=5/1000/60 | The peak of input flow [l/min]/1000/60->[m$^3$/s] |
| Hrate=60 | Heartrate ranges from 60–100 [beats/min] |
| Hfreq=pi/60*Hrate | Freqency of generator |
| **Steady state equilibrium** | |
| Qi0=5*0.001/60 | [dm$^3$/min]*0.001/60->[m$^3$/s] |
| Vl0=Rout*Clung*Qi0 | [m$^3$] |
| P0=Rout*Qi0 | [N/m$^3$] |

| Parameters | Description |
|---|---|
| Pi0=(Rout+Rin)*Qi0 | [N/m$^3$] |
| Vl_0=Vl0*1000 | [dm$^3$] |
| P_0=P0/133.322 | [mmHg] |
| P_i0=Pi0/133.322 | [mmHg] |

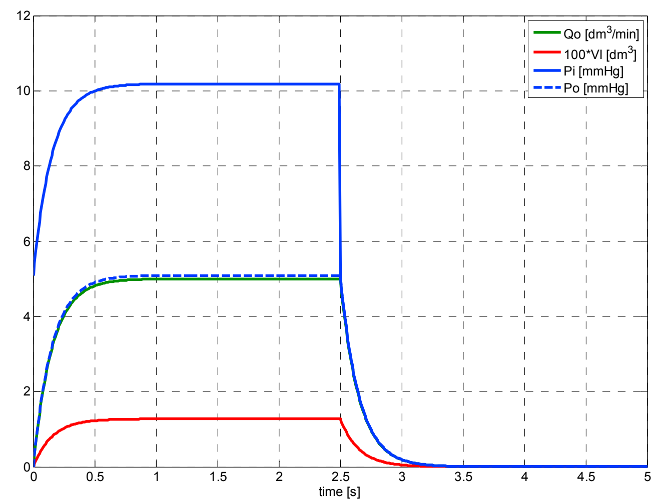


Fig. 9 Response of hydraulic system to pulse of $Q_i$=5 $dm^3/min$.

The same warning as in the case of thermal model is valid here. Very important parameters here are hydraulic resistances and of course lung tissue compliance. We suppose that no feedback control of pressures is necessary here as we do not presume any substantial disturbances. User of MCM simply sets rpm of the peristaltic pump according to desired pressure in the circuit. Simple P or PI controller should do the job if the need be.

## 4. CONCLUSION

The article discussed mathematical model of the Mobile Circulatory Module which was developed in frame of the international research programme AlveoPic between Austria and Czech Republic. MCM should serve for further medical research on lungs or even for transport of lungs for transplantation. Two basic subsystems of the MCM are modelled, namely thermal subsystem and hydraulic subsystem. Parameters of the model are calculated form the technical data of the MCM and will be made more precise after final completion of the MCM. Anyhow simulation results show good accordance with common knowledge of physics. As for control of hydraulic pressure and flow we presume open loop control by setting rpm of the peristaltic pump accordingly.

## 5. ACKNOWLEDGEMENT

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