

## Matlab Design for Solving an Orthostatic Stress Optimal Control Problem of Cardiovascular-Respiratory System

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**Abstract:** *This paper deals with the resolution of an optimal control problem for cardiovascular-respiratory system in case of the orthostatic stress phenomenon where there is a fall in blood pressures with respect to the heart rate, alveolar ventilation and lower venous systemic capacitance which are changing extensively. It is applied to model the control action as an optimal control in terms of the cost functional by stabilizing the controlled values (arterial and venous systemic pressure, partial pressure of CO<sub>2</sub> and partial pressure of O<sub>2</sub> in arterial blood) such that they deviate as small as possible and preventing the Heart rate, alveolar ventilation and lower venous systemic capacitance from changing extensively. The Matlab routines are used for implementing this problem. The results show that there is a stabilization of blood pressures as responses of controls which are the solution of the optimal control problem for cardiovascular-respiratory system. They describe that there are orthostatic changes where the heart rate and contractility are generally higher and the venous systemic capacitance decreases in upright position while the blood pressures are maintained by an increase in heart rate, increase in contractility and a decrease in lower venous systemic capacitance.*

**Keywords:** *Orthostatic, stress, cardiovascular system, respiratory system, models, optimal control, autonomic nervous system.*

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### 1. INTRODUCTION

The appearance of issues has occurred in cardiovascular-respiratory systems of different people in the whole world. Among them, the orthostatic stress is included. Mathematical models have been previously applied to study several physiological situations in order to solve different problems arisen there [1], [2] and [3]. In our case, the optimal control is applied for solving the orthostatic stress issue. The human cardiovascular system is first of all a transport system [4] the oxygen, carbon dioxide and nutrients are carried by the blood from the various muscles and organs. In terms of control function in cardiovascular system; the autonomic nervous system controls and regulates all activities. The heart rate is controlled by both systems (sympathetic and parasympathetic nervous systems) [5], [6]. If the sympathetic nervous system excites a particular organ, often parasympathetic nervous system inhibits it [7].

The respiratory system is also a transport system of gases between the environment and the tissues [1], [8]. It acts to exchange oxygen ( $O_2$ ) which is very important as it is needed by various tissues in terms of metabolism with carbon dioxide produced by metabolic activities.

The orthostatic stress is an issue that exists in the cardiovascular-respiratory system, where it refers to the stress induced on the cardiovascular system due to gravitational effects produced by the upright position as compared to the supine position [6], [9]. When orthostatic stress happens the blood pressure must be counteracted by the baroreflex which senses its drop [10].

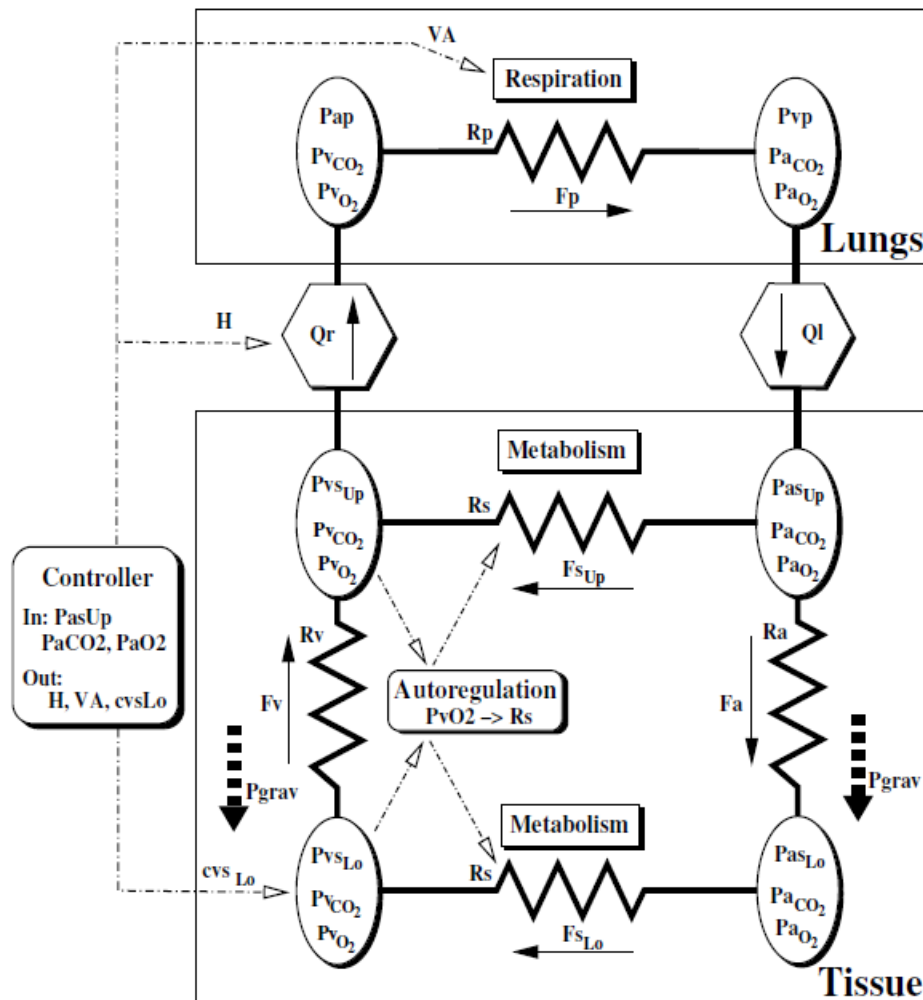
In this work, an optimal control allows us to know the behavior state of cardiovascular-respiratory system in the case of the orthostatic stress issue. The paper is organized as follows. The section 1 focuses on optimal control problem subject to model equations. The discretization of state

equations and optimal control problem are presented in section 2. The numerical approach is presented in the section 3 whereas the simulation results are discussed in the section 4. The section 5 deals with concluding remarks.

**2. MATHEMATICAL MODEL EQUATIONS AND SETTING OF AN OPTIMAL CONTROL PROBLEM**

**1.1 Model equations**

We deal with the presentation of the mathematical model equations for studying the orthostatic stress issue [Fink]. They consist of cardiovascular and respiratory components and include cardiovascular auto-regulation, ventilation control, and the baroreflex loop. The diagram for model equations is represented in the Fig. 1 [10] and the description of parameters and variables is given in the table 3-6 in appendix.



**Figure 1:** Orthostatic stress model diagram

For the nonlinear ordinary differential equations, we present the system of constraints for the optimal control problem that we have to solve. This system is composed by equations (1)-(16) where we consider some parts in this system such as; the mass balance for blood flow, the blood gases, the contractility as influenced by  $H$  and the control. Considering the mathematical model presented in [2] we have;

$$c_{asUp} \dot{P}_{asUp} = Q_l - F_a - F_{sUp}, \tag{1}$$

$$c_{asLo} \dot{P}_{asLo} = F_a - F_{sLo}, \tag{2}$$

$$c_{vsLo} \dot{P}_{vsLo} = F_{sLo} - F_v - \dot{c}_{vsLo} P_{vsLo}, \tag{3}$$

$$c_{vsUp} \dot{P}_{vsUp} = F_v - Q_r + F_{sUp}, \tag{4}$$

$$c_{vp} \dot{P}_{vp} = F_p - Q_l, \tag{5}$$

$$V_{ACO_2} \dot{P}_{aCO_2} = 863F_p (C_{vCO_2} - C_{aCO_2}) + \dot{V}_A (P_{iCO_2} - P_{aCO_2}), \tag{6}$$

$$V_{AO_2} \dot{P}_{aO_2} = 863F_p (C_{vO_2} - C_{aO_2}) + \dot{V}_A (P_{iO_2} - P_{aO_2}), \tag{7}$$

$$V_{Tco_2} \dot{C}_{vCO_2} = MR_{CO_2} + F_s (C_{aCO_2} - C_{vCO_2}), \tag{8}$$

$$V_{TO_2} \dot{C}_{vO_2} = -MR_{O_2} + F_s (C_{aO_2} - C_{vO_2}), \tag{9}$$

$$\dot{S}_l = \sigma_l, \tag{10}$$

$$\dot{S}_r = \sigma_r, \tag{11}$$

$$\dot{\sigma}_l = -\gamma_l \sigma_l - \alpha_l S_l + \beta_l H, \tag{12}$$

$$\dot{\sigma}_r = -\gamma_r \sigma_r - \alpha_r S_r + \beta_r H, \tag{13}$$

$$\dot{H} = u_1, \tag{14}$$

$$\ddot{V}_A = u_2, \tag{15}$$

$$\dot{c}_{vsLo} = u_3. \tag{16}$$

In the equations (2), (3) and (16), *Lo* refers to lower compartment while *Up* refers to upper compartment in the equations (1) and (4).

The model equations (1)-(5) represent the mass balance for blood flow while the model equations (6)-(9) represent the blood gases. The model equations (10)-(13) represent the contractility as influenced by *H* while the model equations (14)-(16) represent the control.

According to the model given in [10], we have the auxiliary model equations as follows:

$$P_{ap}(t) = \frac{1}{c_{ap}} (V_0 - c_{asUp} P_{asUp}(t) - c_{asLo} P_{asLo}(t) - c_{vsUp} P_{vsUp}(t) - c_{vsLo}(t) P_{vsLo}(t) - c_{vp} P_{vp}(t)), \tag{17}$$

$$Q_l(t) = H \frac{c_l P_{vp}(t) f(S_l(t), P_{asUp}(t)) (1 - k_l)}{P_{asUp}(t) (1 - k_l) + f(S_l(t), P_{asUp}(t)) k_l}, \tag{18}$$

$$Q_r(t) = H \frac{c_r P_{vsUp}(t) f(S_r(t), P_{ap}(t)) (1 - k_r)}{P_{ap}(t) (1 - k_r) + f(S_r(t), P_{ap}(t)) k_r}, \tag{19}$$

$$k_l = \exp(-t_d / (R_l c_l)) \quad \text{and} \quad k_r = \exp(-t_d / (R_r c_r)), \tag{20}$$

$$f(s, p) = 0.5(s + p) - 0.5((p - s)^2 + 0.01)^{\frac{1}{2}}, \tag{21}$$

$$t_d = \frac{60}{H} - k \left( \frac{60}{H} \right)^{\frac{1}{2}}, \tag{22}$$

$$C_{aO_2}(t) = K_1 (1 - e^{-k_2 P_{aO_2}(t)})^2, \tag{23}$$

$$C_{vO_2}(t) = K_1 (1 - e^{-k_2 P_{vO_2}(t)})^2, \tag{24}$$

$$C_{aCO_2}(t) = K_{CO_2} P_{aCO_2}(t) + k_{CO_2}, \tag{25}$$

$$C_{vCO_2}(t) = K_{CO_2} P_{vCO_2}(t) + k_{CO_2}, \tag{26}$$

$$\dot{V}_A = \dot{V}_E - \dot{V}_D, \tag{27}$$

$$F_v = \max(0, P_{vsLo} - P_{vsUp} + P_{grav}) / R_v, \tag{28}$$

$$F_a = (P_{asUp} - P_{asLo} + P_{grav}) / R_a, \tag{29}$$

$$F_{sUp} = (P_{asUp} - P_{vsUp}) / R_s, \tag{30}$$

$$F_{sLo} = (P_{asLo} - P_{vsLo}) / R_s, \tag{31}$$

$$F_p = (P_{ap} - P_{vp}) / R_p, \tag{32}$$

$$R_s = A_{pesk} C_{vO_2}, \tag{33}$$

$$F_s = F_{sUp} + F_{sLo}, \tag{34}$$

$$P_{grav} = c \rho g h \sin(\text{TiltingAngle}), \tag{35}$$

where  $\rho = 1.05 \text{mg/mm}^3 = 1050 \text{kg/m}^3$ ,  $c = 1/133.322 \text{mmHg/Pa}$ , and  $h = 0.6 \text{m}$  are the physical parameters for Hydrostatic pressure induced by gravity ( $P_{grav}$ ). The description of variables is presented in the table 3 in Appendix whereas the table 4-6 in Appendix describes the parameters.

The equations (17)-(22) represent the cardiovascular model equations. The pulmonary arterial pressure is described by the equation (17). The relation for  $Q$  is described in (18) and (19) [2], while the equation (21) implements a maximum condition so that stroke volume does not exceed the filling volume. In terms of  $H$ , the time of diastole  $t_d$  is described by the equation (22). The equations (23)-(27) represent the respiratory model equations as dissociation equations representing the partial pressures and concentrations of blood gases. The blood flow is represented by the model equations (28)-(35) where the max-function implements the action of the venous valves to avoid backflow while the  $P_{grav}$  represents the hydrostatic pressure induced on the lower compartments. These auxiliary equations with respect to pressure, flow and resistance are essentially the same as Ohm's law [2]. The effect of oxygen partial pressure on systemic resistance is described in the equation (33) while the flow through the tissue compartment is described in the equation (33). The equation (35) also describes the dependency of the gravitation effect on the degree of tilt.

We can summarize the model equations (1)-(16) in the following way. Let  $x(t) \in \mathbb{R}^{16}$  denote the state vector at time  $t$ ,

$$x(t) = \left( P_{asUp}, P_{asLo}, P_{vsLo}, P_{vsUp}, P_{vp}, P_{aCO_2}, P_{aO_2}, C_{vCO_2}, C_{vO_2}, S_l, S_r, \sigma_l, \sigma_r, H, \dot{V}_A, c_{vsLo} \right)^T$$

For clarity we have suppressed the dependence on time  $t$ . If convenient, the components of  $x$  will be also referred to as  $x_i$ ,  $i=1, \dots, 16$ . Similarly let  $u(t) \in \mathbb{R}^3$  denote the control vector

$$u(t) = (u_1(t), u_2(t), u_3(t))^T = (H, \dot{V}_A, c_{vsLo})^T$$

Let moreover  $u(t) \in \mathbb{R}^{16}$  denote the subset of physiologically meaningful state values. Since all states except  $\sigma_l$  and  $\sigma_r$  need to be positive, we have

$$U = \mathbb{R}_+^{11} \times \mathbb{R}^2 \times \mathbb{R}_+^3$$

We denote the right-hand side of (1)-(16) by  $f(x,u)$ . Obviously, the function  $f(x,u)$  is a smooth function with respect to  $x$ ,  $f(x;u) \in C^\infty(U, \mathbb{R}^{16})$  (Here  $C^\infty(U, \mathbb{R}^{16})$  denotes the vector space of all functions  $f: U \rightarrow \mathbb{R}^{16}$  with derivatives of arbitrary order).

Finally, we abbreviate  $\dot{x} = (x_1, \dots, x_{16})^T \in \mathbb{R}^{16}$  and then we can write (1)-(16) in the form

$$\dot{x} = f(x;u). \tag{36}$$

### 1.2 Optimal control problem

For the optimal control problem, let us consider the control functions  $u_1$ ,  $u_2$ , and  $u_3$  representing

variations in heart rate ( $H$ ), alveolar ventilation ( $\dot{V}_A$ ) and lower systemic venous capacitance  $C_{vsLo}$ . The control action is modeled as an optimal control via a cost functional where the transition from an initial steady state to the final steady state is optimal. Mathematically, we use the control functions such that the cost functional

$$\int_0^{T_{\max}} \left( q_a (P_{asUp} - P_{asUp}^f)^2 + q_v (P_{vsUp} - P_{vsUp}^f)^2 + q_{CO_2} (P_{aco_2} - P_{aco_2}^f)^2 + q_{O_2} (P_{ao_2} - P_{ao_2}^f)^2 + q_1 (u_1)^2 + q_2 (u_2)^2 + q_3 (u_3)^2 \right) dt. \quad (37)$$

is minimized subjected to the system of equations (1)-(16). The optimal control problem is formulated as follows.

Find  $u^* = (u_1^*, u_2^*, u_3^*) \in \mathbb{R}^3$  solution of

$$\min_{(u_1, u_2, u_3) \in \mathbb{R}^3} \int_0^{T_{\max}} \left( q_a (P_{asUp} - P_{asUp}^f)^2 + q_v (P_{vsUp} - P_{vsUp}^f)^2 + q_{CO_2} (P_{aco_2} - P_{aco_2}^f)^2 + q_{O_2} (P_{ao_2} - P_{ao_2}^f)^2 + q_1 (u_1)^2 + q_2 (u_2)^2 + q_3 (u_3)^2 \right) dt \quad (38)$$

subject to (36).

### 3. DIRECT APPROACH AND DISCRETIZATION OF OBJECTIVE FUNCTION

To approximate the system (36), let us consider

$$\mathcal{B}^N = \{\psi_j^N, j = 1, \dots, N\} \quad (39)$$

a linear B-splines basis functions on the uniform grid

$$\Omega_N = \left\{ t_k = \frac{kT_{\max}}{N}, k = 0, \dots, N \right\}, \quad (40)$$

such that

$$\psi_i^N(t_k) = \delta_{ik}.$$

Let us introduce the vector space  $W^N$  whose the basis is  $\mathcal{B}^N$ . We have

- 1)  $\dim W^N = N$
- 2)  $W^N \subset W^{N+1}$

Let us consider  $W = C^0(0, T_{\max})$  and let us take the interpolation operator

$$\begin{aligned} \Pi^N : W &\rightarrow W^N \\ \varphi &\mapsto \Pi^N \varphi \end{aligned} \quad (41)$$

satisfying

$$\Pi^N \varphi(t_k) = \varphi(t_k), \quad k = 1, \dots, N \quad (42)$$

We verify easily that

$$\|\Pi^N \varphi - \varphi\|_{E, N \rightarrow \infty} \rightarrow 0 \quad \forall \varphi \in E \quad (43)$$

$$\|\Pi^N\| = \sup_{\substack{\varphi \neq 0 \\ \varphi \in W}} \frac{\|\Pi^N \varphi\|_E}{\|\varphi\|_E} = 1 \quad (44)$$

Now, let us set

$$u^N = \Pi^N u = \sum_{k=0}^N u^k \psi_k^N, \quad (45)$$

With  $u^k = u(t_k)$ .

Therefore, the system (36) can be approached by the following form:

Find  $x^N \in (W^N)^{16}$  solution of the system

$$\frac{dx^N}{dt} = f(x^N; u^N) \quad (46)$$

$$x^N(0) = x^{N,0} \tag{47}$$

such that

$$\left| x^0 - x^{N,0} \right|_{N \rightarrow \infty} \rightarrow 0 \tag{48}$$

where  $x^0 = x(0)$ .

To approximate the objective function (38), let us set  $x^e$  the wanted equilibrium state vector and  $u^e = (H^e, \dot{V}_A^e)^T$  the equilibrium control vector;  $x_i^e$  and  $u_i^e$  designate the  $i^{th}$  components  $i^{th}$  of the vector  $x^e$  and  $u^e$ .

Therefore, the objective function (38) can take the following compact form

$$\min_{u \in Q} J^N(u) = \int_0^{T_{\max}} \left( \sum_{i=1}^{13} a_i (x_i^N(t) - x_i^e)^2 + \sum_{j=1}^3 b_j (u_j(t) - u_j^e)^2 \right) dt, \tag{49}$$

where  $x^N$  is solution of the approximated solution (36).

We must determine  $u^K = (u_1^K, u_2^K, u_3^K) \in Q^K$  an approximate solution of (49) in  $Q^K = (W^K)^3$ . It is necessary to note that we can write

$$u_j^K = \sum_{k=0}^K u_{j,k}^K \psi_k(t), \quad j = 1, 2, 3. \tag{50}$$

Therefore, we can approximate the objective function by

$$J^N(u^K) \approx \sum_{k=1}^K \left( \sum_{i=1}^{13} a_i (x_i^N(t_k) - x_i^e)^2 + \sum_{j=1}^3 b_j (u_{j,k}^K - u_j^e)^2 \right) \Delta t, \tag{51}$$

where  $\Delta t = \frac{T_{\max}}{N}$ .

Finally, the optimal control problem (38) subject to (36) is a minimisation problem with constraint. The discrete formulation of such problem can be written as follows.

Find  $u^{*,K} \in \mathbb{R}^{(K+1)} \times \mathbb{R}^{(K+1)}$  solution of

$$\min_{u^K \in \mathbb{R}^{(K+1)} \times \mathbb{R}^{(K+1)}} J^N(\underline{u}^K) \approx \Delta t \left( (Y^T R_1 Y) + (\underline{u}^K)^T R_2 \underline{u}^K \right), \tag{52}$$

subject to (46)-(47) where  $\underline{u}^K$  is a matrix  $(K+1) \times 3$  such that the components  $u_{j,k}^K$  are those function  $u_j^N$  in  $\mathcal{B}^N$  and  $Y$  is the matrix such that the  $(i,k)^{th}$  component is  $x_i^N(t_k) - x_i^e$ , where  $x^N$  is the solution of (36) associated to  $u = u^N$ .  $R_1 \in M_{13,13}(\mathbb{R})$  and  $R_2 \in M_{3,3}(\mathbb{R})$  are square matrices whose main diagonal is  $(a_1, a_2, \dots, a_{13})$  and  $(b_1, b_2, b_3)$  respectively that is  $R_1 = \text{diag}(a_1, a_2, \dots, a_{13})$  and  $R_2 = \text{diag}(b_1, b_2, b_3)$ . Here  $M_{n,m}(\mathbb{R})$  denotes the vector space of  $n \times m$  dimensional matrices with components in  $\mathbb{R}$ .

#### 4. NUMERICAL APPROACH

We use here a direct approach for minimizing the functional (52) subject to the state system (36). This approach consists in applying directly an optimization algorithm to the objective function, the solution of the state system being computed in each iteration of the algorithm. Two Matlab functions ode45 and fmincon will be used for solving the state system and the associated constrained optimization problem.

##### 4.1 The state system

Given a positive integer  $N$  we define a time grid points on the interval  $(0, T_{\max})$  using the following Matlab line

>> TT = 0 : Tmax/N : Tmax;

We first remark that the system (36) can be decomposed in three subsystems. In the first time one can solve the following system:

$$\begin{cases} \dot{x}_{14}(t) = u_1(t) \\ \dot{x}_{15}(t) = u_2(t) \\ \dot{x}_{16}(t) = u_3(t) \end{cases} \quad (53)$$

which represents equations (14)-(16). Let us consider the vector  $Q \in \mathbb{R}^{3(N+1)}$  whose components are defined by the vector  $(u_1(t_0), \dots, u_1(t_N); u_2(t_0), \dots, u_2(t_N), u_3(t_0), \dots, u_3(t_N))^T$  where  $t_i = iT_{\max} / N$ . Considering  $Q$  as a global variable, we implement the second hand side of the system (53) by the following code:

```
function S=qtild(t,X)
global Q N TT
u1t=interp1(TT,Q(1:N+1)',t);
u2t=interp1(TT,Q(N+2:2*(N+1))',t);
u3t=interp1(TT,Q(2*(N+1)+1:end))',t);
S=[u1t;u2t;u3t];
```

Then, the solution of the system (53) is computed via a single of Matlab line using the ode45 function. This is done by the command line:

```
>>[tt,xx]=ode45('qtild',TT,X0(14:16));
```

where X0 denotes the initial solution representing the cardiovascular - respiratory system at rest. Next, the solution of (53) is used for computing the sub-system of (1)-(13) composed of equations (10) to (13), the solution that will serve to compute the sub-system composed of equations (1) to (9). Following codes will be used for defining second hand sides of these considered sub systems. The second hand side of equations (10) to (13) is defined by the following function:

```
function Z=Stild(t,x)
global gammal alphas betal gammar alphas betar
global xx TT
S1=x(1);
Sr=x(2);
deltal=x(3);
deltar=x(4);
Ht=interp1(TT,xx(:,1))',t);
Z=[deltal;deltar;-gammal*deltal-alphas*S1+betal*Ht;...
-gammar*deltar-alphas*Sr+betar*Ht];
```

Similarly, using Matlab program ptild.m can be written for implementing right hand side of the sub-system (1)-(9). Finally, the solution of the global system (1)-(16) is obtained by the following code

```
function [tt,X]=solution(q)
global Q TT X0 xx xxx
Q=q;
X=zeros(length(TT),16);
[tt,xx]=ode45('qtild',TT,X0(14:16));
X(:,14:16)=xx;
[tt,xxx]=ode45('Stild',TT,X0(10:13));
X(:,10:13)=xxx;
[tt,xxx]=ode45('ptild',TT,X0(1:9));
X(:,1:9)=xxx;
```

Remark that all problem constants are defined as global variables. These constants should be introduced by a function which we have called pardef. We can also note that, splitting the system in three systems decreases considerably the CPU time for calculating the global system (1)-(16).

## 4.2 Control design

To compute the optimal control we first have to implement the objective function. Using Simpson's approximation one can write

$$J \approx \sum_{k=1}^N \left( \sum_{i=1}^{13} a_i (x_i(t_k) - x_i^e)^2 + b_1 u_{1_k}^2 + c u_{2_k}^2 + u_{3_k}^2 \right) \Delta t$$

where  $u_{1_k}$ ,  $u_{2_k}$  and  $u_{3_k}$  are the approximation of functions  $u_1$ ,  $u_2$  and  $u_3$  at the point  $t_k$ , and  $\Delta t = T_{\max} / N$ . The objective function is then implemented by the following code:

Having implemented the objective function, the optimal solution is derived using `fmincon` function. Finally, to design the optimal control problem we have implemented the following code:

```
function J=funobj(q)
global dt N R1 R2 Xe
[tt,X]=solution(q);
R1=getR1;
R2=getR2;
J=0;
for k=1:N
Y=X(k,1:13)-Xe;
qk=[q(k);q(N+k);q(2*N+k)];
J=J+dt*(Y*R1*Y'+qk'*R2*qk);
end
```

For a given experimental time  $T_{\max}$ , the above function main displays a time grid points  $tt$  and a matrix  $X$  whose component  $(j,k)$  represents  $x_k(t_j)$ ,  $t_j$  being the  $j^{\text{th}}$  component of the time grid  $tt$ .

As in many software environments, typical problems in Matlab are solved interactively and the results displayed graphically. Here is an example of Matlab command lines for plotting the problem solution.

```
>> pardef,[tt,X]=main(2);
>> plot(tt,x(:,1));
```



5. SIMULATIONS RESULTS

In solving the optimal control problem; the use of Matlab implementation is applied by considering the parameter values given in the table 4-6 in Appendix. The initial values are given in the table 1 whereas the table 2 gives final values.

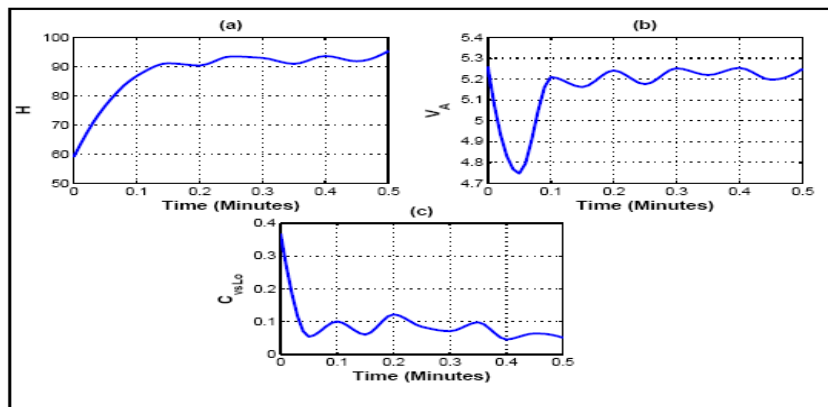
**Table 1:** The initial values for the variables presented in the orthostatic stress models and in the Matlab implementation.

Variables	Initial values	Variables	Initial values	Variables	Initial values
$C_{vsLo}$	0.368	$P_{vCO_2}$	48.14	$P_{vsLo}$	4.89
$P_{asUp}$	82.35	$P_{vO_2}$	34.39	$P_{vp}$	6.16
$C_{vCO_2}$	0.55691	$\dot{V}_A$	5.26	$S_l$	84.96
$C_{vO_2}$	0.16417	$H$	59	$S_r$	4.32
$P_{aCO_2}$	40.00	$P_{asLo}$	82.12	$\sigma_l$	0.00
$P_{aO_2}$	102.46	$P_{vsUp}$	4.66	$\sigma_r$	0.00

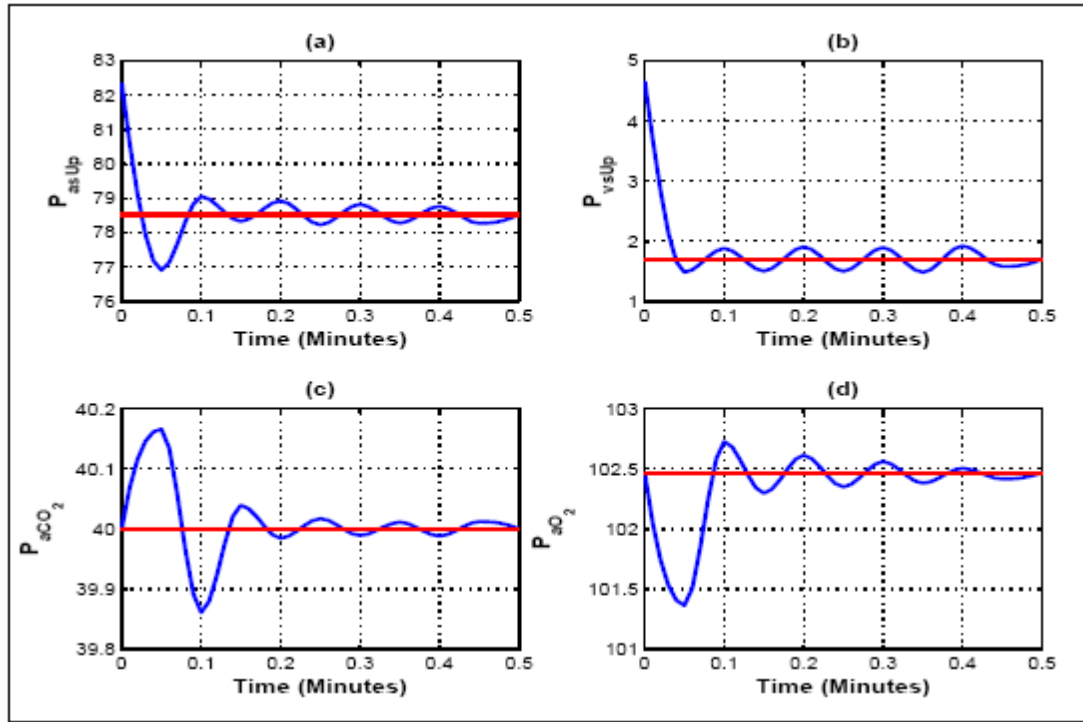
**Table 2:** The expected final values for the variables presented in the orthostatic stress model equations especially in the optimal control problem and in the Matlab implementation.

Variables	$P_{asUp}$	$P_{aCO_2}$	$P_{aO_2}$	$P_{vsUp}$
<b>Expected final values</b>	78.55	40.00	102.46	1.69

The results for the optimal control problem are obtained by considering the MaTlab implementation described in the Fig. 2 and 3.



**Figure 3:** The controls; Heart rate ((a)), alveolar ventilation ((b)) and the arterial systemic capacitance on the lower compartment ((c))



**Figure 4:** The arterial systemic pressure on upper compartment ( $P_{asUp}$ ) ((a)), the venous systemic pressure on upper compartment ( $P_{vsUp}$ ) ((b)), the partial pressure of  $CO_2$  in the arterial blood ((c)) and the partial pressure of  $O_2$  in the arterial blood ((d))

## 6. DISCUSSION

The discussion refers to figures plotted in the previous section where we consider the variation of variables according to the time of about 30 seconds.

In general, the results presented in the Fig.2 show us that for the Fig. 2(a), the heart rate is highly increased during the time lower than 10 seconds and it starts by gradually increasing until the end of time variation. The Fig. 2(b) demonstrates that the alveolar ventilation is highly decreased up to its minimum and then it starts by increasing in the time of about 10 seconds where after it also starts gradually increasing. The venous systemic capacitance on the lower compartment is highly decreasing in the time lower than 10 seconds, where it starts by gradually decreasing until the end of time as it is shown by the Fig. 2(c). In this case, the first amount of time lower than 10 seconds of which the controls are in high variation explains the orthostatic stress period.

The Fig. 3 shows that; there is a fall in blood pressures where the Fig. 3(a) indicates that the  $P_{asUp}$  is highly decreased towards its minimum and after a time of 6 seconds, the  $P_{asUp}$  has begun by being stabilized around its expected final value. In the Fig. 3(b), the venous systemic pressure on upper compartment is also decreased towards its minimum, where it starts by being stabilized after an amount of time of about 6 seconds as the  $P_{asUp}$ . The Fig. 3(c), and the Fig. 3(d) illustrate that the partial pressure of  $CO_2$  and the partial pressure of  $O_2$  in arterial blood are around the expected final values as their initial values coincide to their expected final ones and after a time around 10 seconds, the  $P_{acO_2}$  is also being stabilized with respect to its expected final value while after the time of about 6 seconds, the  $P_{aO_2}$  is being stabilized at its expected final value. In fact there is no orthostatic stress in the case that the blood pressures  $P_{asUp}$ ,  $P_{vsUp}$ ,  $P_{acO_2}$  and  $P_{aO_2}$  are stabilized thanks to controls  $H$ ,  $\dot{V}_A$  and  $C_{vsLo}$ .

## 7. CONCLUSION

In this work, the orthostatic stress has been studied in the resolution of an optimal control problem for cardiovascular-respiratory system. Using a Matlab implementation, we have got solutions to the optimal control problem where the blood pressures are stabilized by the actions of the controls  $H$ ,  $\dot{V}_A$  and  $C_{vsLo}$ . The solutions of an optimal control problem have well shown that the orthostatic stress has happened when the controls  $H$ ,  $\dot{V}_A$  and  $C_{vsLo}$  are in high variation while the stabilization of the blood pressures  $P_{asUp}$ ,  $P_{vsUp}$ ,  $P_{aCO_2}$  and  $P_{aO_2}$  leads us to the success in terms of the orthostatic stress issue.

## REFERENCES

- [1] Ellwein L. M., Cardiovascular and Respiratory Regulation, Modeling and Parameter Estimation, North Carolina State University, 2008
- [2] Kappel F., A. de Los Reyes V., A mathematical cardiovascular model with pulsatile and non-pulsatile components, Karl Franzens Universität Graz, SFB-report no. 2010 - 011, march 2010
- [3] Moberg N., Hemodynamic Model of the Cardiovascular System during Valsalva Maneuver and Orthostatic Changes, Umeå University, Department of Engineering Physics UMEÅ WEDEN, 2011
- [4] Ottesen J.T., Olufsen M.S., and Larsen J.K., Applied Mathematical Models in Human Physiology, Roskilde University Denmark, 2006.
- [5] Timischl S., A Global Model for the Cardiovascular and Respiratory System, Karl- Franzens Universität Graz, 1998
- [6] Valdessa A. A., Heart Rate Regulation: Modeling and Analysis, Raleigh, North Carolina University, 2009
- [7] Fishman A. P., editor, The respiratory system, volume 3:II:2 of Handbook of Physiology, American Physiological Society, Bethesda, MD, 1983.
- [8] Kaufman A., Development of a Fast Response Carbon Monoxide Sensor for Respiratory Gas Analysis, University College London, 2001.
- [9] Batzel J. J., Furtinger S., Bachar M., Fink M., Kappel F., Sensitivity identifiability of a baroreflex control system model, University of Graz, 2009.
- [10] Fink M. and Batzel J. J., An Optimal Control Approach to Modeling the Cardiovascular-Respiratory System: an Application to Orthostatic Stress, Karl- Franzens Universität Graz, 2004.

**Appendix**

**Table 3:** Description of variables of mathematical model presented in the section 2.

Variables	Meaning	Unit
$c_{vsLo}$	Lower venous systemic capacitance	$l.mmHg^{-1}$
$P_{asUp}$	Arterial systemic pressure on upper compartment	$mmHg$
$C_{aCO_2}$	Concentration of $CO_2$ in arterial blood	$ml/ml$
$C_{aO_2}$	Concentration of $O_2$ in arterial blood	$ml/ml$
$P_{aCO_2}$	Partial pressure of $CO_2$ in arterial blood	$mmHg$
$P_{aO_2}$	Partial pressure of $O_2$ in arterial blood	$mmHg$
$P_{vCO_2}$	Partial pressure of $CO_2$ in mixed venous blood	$mmHg$
$P_{vO_2}$	Partial pressure of $O_2$ in mixed venous blood	$mmHg$
$\dot{V}_A$	Alveolar ventilation	$l_{STPD}.min^{-1}$
$F_p$	Blood flow perfusing the lung compartment	$l.min^{-1}$
$F_s$	Blood flow perfusing the tissue compartment	$l.min^{-1}$
$H$	Heart rate	$min^{-1}$
$P_{as}$	Mean blood pressure in arterial region: systemic circuit	$mmHg$
$P_{ap}$	Mean blood pressure in arterial region: pulmonary circuit	$mmHg$
$P_{vs}$	Mean blood pressure in venous region: systemic circuit	$mmHg$
$P_{vp}$	Mean blood pressure in venous region: pulmonary circuit	$mmHg$
$Q$	Cardiac output	$l.min^{-1}$
$S$	Contractility of the ventricle	$mmHg$
$\sigma$	Derivative of $S$	$mmHg.min^{-1}$

**Table 4:** The meaning and value of parameters that are used in presenting different model equations (First part)

Parameters	Descriptions	Value	Unit
$C_{asUp}$	Arterial systemic capacitance on upper compartment	$0.01002 * frac$	$l.mmHg \times min^{-1}$
$C_{asLo}$	Arterial systemic capacitance on lower compartment	$0.01002 * (1 - frac)$	$l.mmHg \times min^{-1}$
$C_{vsUp}$	Venous systemic capacitance on upper compartment	$0.70 * frac$	$l.mmHg \times min^{-1}$
$C_{ap}$	Capacitance of the arterial ; the pulmonary circuit	0.03557	$l.mmHg \times min^{-1}$
$C_{vp}$	Capacitance of the venous; the pulmonary circuit	0.1394	$l.mmHg$
$MR_{CO_2}$	Metabolic $CO_2$ production rate	0.244	$l_{STPD}.min^{-1}$
$MR_{O_2}$	Metabolic $O_2$ consumption rate	0.290	$l_{STPD}.min^{-1}$
$V_{ACO_2}$	Effective $CO_2$ storage volume of the lung compartment	3.200	$l_{BTPS}$
$V_{AO_2}$	Effective $O_2$ storage volume of the lung compartment	2.5	$l_{BTPS}$
$V_{TCO_2}$	Effective tissue storage volume for $CO_2$	15.000	$l$
$V_{TO_2}$	Effective tissue storage volume for $O_2$	6.000	$l$
$K_1$	Constant for the $O_2$ dissociation curve	0.2	$l_{STPD}.l^{-1}$
$K_2$	Constant for the $O_2$ dissociation curve	0.05	$mmHg^{-1}$
$K_{CO_2}$	Slope of the physiological $CO_2$ dissociation curve	0.0065	$l_{STPD} \times (l.mmHg)^{-1}$
$k_{CO_2}$	Constant for physiological $CO_2$ dissociation curve	0.244	$l_{STPD}.l^{-1}$
$k$	(kappa): Duration of the systole	0.4	$sec^{1/2}$
$f_{rac}$	Upper fraction of basic total prone systemic volume	0.3	$l$
$\rho$	Physical parameter: volumic mass	1050	$kg/m^3$

**Table 5:** The meaning and value of parameters that are used in presenting different model equations (Second part)

Parameter	Description	Value	Unit
$c$	Physical parameter for hydrostatic pressure	1/133.322	$mmHg/Pa$
$g$	Physical parameter: earth acceleration	9.8	$m/s^2$
$h$	Physical parameter for hydrostatic pressure: height	0.6	$m$
$c_l$	Compliance of the relaxed left ventricle	0.01289	$l.mmHg^{-1}$
$c_r$	Compliance of the relaxed right ventricle	0.06077	$l.mmHg^{-1}$
$\alpha_l$	Coefficient of $S_l$ in the differential equation for $\sigma_l$	89.47	$min^{-2}$
$\alpha_r$	Coefficient of $S_r$ in the differential equation for $\sigma_r$	28.46	$min^{-2}$
$\beta_l$	Coefficient of $H$ in the differential equation for $\sigma_l$	128.83	$mmHg.min^{-1}$
$\beta_r$	Coefficient of $H$ in the differential equation for $\sigma_r$	2.08	$mmHg.min^{-1}$
$\gamma_l$	Coefficient of $\sigma_l$ in the differential equation for $\sigma_l$	37.33	$min^{-1}$
$\gamma_r$	Coefficient of $\sigma_r$ in the differential equation for $\sigma_r$	11.88	$min^{-1}$
$V_0$	Total blood volume	5.0	$l$
$q_a$	Weighting factor of $P_{asUp}$ in the cost functional	0.015	$mmHg^{-2}$
$q_v$	Weighting factor of $P_{vsUp}$ in the cost functional	6.49	$mmHg^{-2}$
$q_{CO_2}$	Weighting factor of $P_{aCO_2}$ in the cost functional	1.07	$mmHg^{-2}$

**Table 6:** The meaning and value of parameters that are used in presenting different model equations (Third part)

Parameter	Description	Value	Unit
$q_{o_2}$	Weighting factor of $P_{aO_2}$ in the cost functional	0.006	$mmHg^{-2}$
$q_1$	Weighting factor of $u_1$ in the cost functional	0.0002	$min^4$
$q_2$	Weighting factor of $u_2$ in the cost functional	0.0105	$min^4.l^{-2}BTPS$
$q_3$	Weighting factor of $u_3$ in the cost functional	8.3500	$l.min^{-1}$
$R_p$	Resistance in the region of the pulmonary circuit	1.965	$mmHg.min.l^{-1}$
$R_l$	Total viscous resistance of the left ventricle	11.35	$mmHg.min.l^{-1}$
$R_r$	Total viscous resistance of the right ventricle	4.158	$mmHg.min.l^{-1}$
$R_s$	Peripheral resistance in the systemic circuit	16.79	$mmHg.min.l^{-1}$
$A_{pesk}$	$R_s = A_{pesk}C_{vO_2}$	124.60	$mmHg.min.l^{-1}$

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