Seminar on Optimization and Control in Physiological systems

We ask you to write a code to implement the Kappel CVS model given below. We will provide the parameters and initial conditions. After the code is written, use simulations to answer the following questions.

1. Questions

1. For the basic parameters given, what are the steady state values of the system.
2. In this question we ask you to consider some changes in parameters and **interpret** the effect of these changes on the system.
   (a) What is the effect of increasing and decreasing the total blood volume V_0 by 30 % ?
   (b) What is the effect of increasing and decreasing A_{pesk} by 30 % ?
   (c) What is the effect of increasing and decreasing β_l β_r by 40 % ?
   (d) What is the effect of increasing t_d by 20 % ?
   (e) What is the effect of increasing and decreasing H by 50 % ?
3. Im this question we ask you to consider some changes in initial conditions and **interpret** the effect of these changes on the system.
   (a) What is the effect of increasing and decreasing the initial value for P_{as} by 25 % ?
   (b) What is the effect of increasing and decreasing the initial value for P_{vs} ?

2. CVS Model

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\begin{aligned}
c_{as}\dot{P}_{as}(t) &= Q_l(t) - F_s(t), && (1)\\
c_{vs}\dot{P}_{vs}(t) &= F_s(t) - Q_r(t), && (2)\\
c_{vp}\dot{P}_{vp}(t) &= F_p(t) - Q_l(t), && (3)\\
\dot{S}_l(t) &= \sigma_l(t), && (4)\\
\dot{S}_r(t) &= \sigma_r(t), && (5)\\
\dot{\sigma}_l(t) &= -\gamma_l\sigma_l(t) - \alpha_l S_l(t) + \beta_l H(t), && (6)\\
\dot{\sigma}_r(t) &= -\gamma_r\sigma_r(t) - \alpha_r S_r(t) + \beta_r H(t), && (7)
\end{aligned}
$$

These represent the state equations. We need to define Q_l and F_s, and Q_r and F_p. We also need an expression for P_{ap}. The following discussion shows how we do this. The equations to use for Q_l and Q_r are given by the expressions in (18). The equations to use for F_s and F_p are given by Equations (9) and (10). We also give a table of symbols (Table 1) and the block diagram for the cardiovascular-respiratory model (Figure 1). We are only modeling the CVS (cardiovascular) subsystem. Resistance R_s is given in Equation (19) and the expression for P_{ap} is given in Equation (8).

Mass balance equations for blood flowing through the systemic artery and vein components are given by equations (1) and (2) respectively. Equation (3) gives the mass balance equation for the pulmonary venous component. Under the assumption of a fixed blood volume V_0, the equation for the pulmonary arterial pressure can then be derived from the other cardiovascular compartment pressures:

$$P_{ap}(t) = \frac{1}{c_{ap}}(V_0 - c_{as}P_{as}(t) - c_{vs}P_{vs}(t) - c_{vp}P_{vp}(t)). \tag{8}$$

The Bowditch effect, which describes the observation that contractility S_l (respectively S_r) increases if heart rate increases, is introduced via Equations (4) through (7). This relation is essentially modeled via a second order differential equation.

Blood flow F, which appears in equations (1) through (3) is related to blood pressure via a form of Ohm's law

$$F_s(t) = \frac{P_{as}(t) - P_{vs}(t)}{R_s}, \tag{9}$$

$$F_p(t) = \frac{P_{ap}(t) - P_{vp}(t)}{R_p}, \tag{10}$$

where P_a is arterial blood pressure, P_v is venous pressure, and R is vascular resistance.

Table 1. Cardiovascular symbols

Symbol	Meaning	Unit
α	coefficient of S in the differential equation for σ	min^{-2}
A_{pesk}	$R_s = A_{\mathrm{pesk}} C_{v_{O_2}}$	$\mathrm{mmHg} \cdot \mathrm{min} \cdot \mathrm{l}^{-1}$
β	coefficient of H in the differential equation for σ	$\mathrm{mmHg} \cdot \mathrm{min}^{-1}$
c_a	arterial compliance	$\mathrm{l} \cdot \mathrm{mmHg}^{-1}$
c_v	venous compliance	$\mathrm{l} \cdot \mathrm{mmHg}^{-1}$
F	blood flow perfusing compartment	$\mathrm{l} \cdot \mathrm{min}^{-1}$
H	heart rate	min^{-1}
γ	coefficient of σ in the differential equation for σ	min^{-1}
P_{as}	mean blood pressure in systemic arterial region	mmHg
P_{vs}	mean blood pressure in systemic venous region	mmHg
P_{ap}	mean blood pressure in pulmonary arterial region	mmHg
P_{vp}	mean blood pressure in pulmonary venous region	mmHg
Q	cardiac output	$\mathrm{l} \cdot \mathrm{min}^{-1}$
R	resistance in the peripheral region of a circuit	$\mathrm{mmHg} \cdot \mathrm{min} \cdot \mathrm{l}^{-1}$
S	contractility of a ventricle	mmHg
σ	derivative of S	$\mathrm{mmHg} \cdot \mathrm{min}^{-1}$
u_1	control function, $u_1 = \dot{H}$	min^{-2}
V_{str}	stroke volume of a ventricle	l
V_0	total blood volume	l
l,r	left and right heart	-
p,s	pulmonary and systemic circuits	-

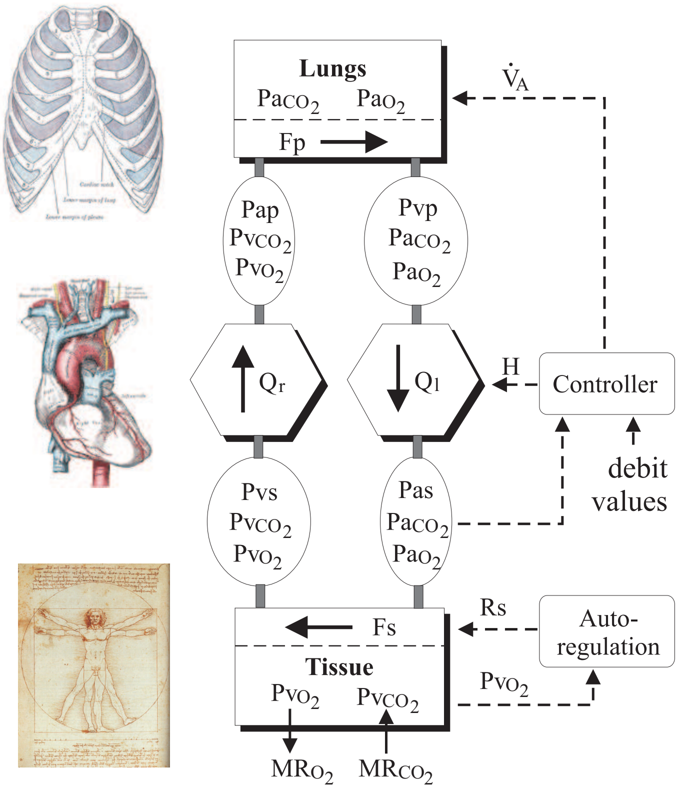

Fig. 1. Model block diagram

As mentioned above, cardiac output Q is defined as the mean blood flow over the length of a pulse,

$$Q(t) = H(t)V_{str}(t), \tag{11}$$

where H is the heart rate and V_{str} is the stroke volume. Subindices l and r are used to distinguish between left and right ventricle. Subindices s and p represent systemic and pulmonary circuits respectively. We will use a complex relationship between stroke volume and blood pressure given in Kappel and Peer [1] which reflects the Frank-Starling law and the basic relation

$$V_{str}(t) = S(t)\frac{cP_v(t)}{P_a(t)}. \tag{12}$$

Here S denotes the contractility, P_v is the venous filling pressure, P_a is the arterial blood pressure opposing the ejection of blood, and c denotes the compliance of the relaxed ventricle.

We need that

$$\frac{S}{P_a} \leq 1, \tag{13}$$

since otherwise more blood volume would be ejected than has been contained in the ventricle. To make (12) meaningful for all pairs of S and P_a, we replace S in (12) by $f(S, P_a)$,

$$V_{str} = f(S, P_a)\frac{cP_v}{P_a}, \tag{14}$$

where f is defined as (cf. Kappel et al. [1])

$$f(s, p) = 0.5(s + p) - 0.5((p - s)^2 + 0.01)^{1/2}. \tag{15}$$

This function is in principle equal to $\min(s, p)$. The term 0.01 is introcuced to smoothe $f(s, p)$ around $s = p$. To implement the basic relations for filling pressure of the ventricle and systolic and diastolic volume and other matters discussed in class we use the following complex formulas for Q:

We get the dependence of V_{str} upon P_v, P_a, and S,

$$V_{str} = \frac{cP_v f(S, P_a)(1 - e^{-\frac{t_d}{Rc}})}{P_a(1 - e^{-\frac{t_d}{Rc}}) + f(S, P_a)e^{-\frac{t_d}{Rc}}}. \tag{16}$$

For the duration of the diastole we assume

$$t_d = \tfrac{60}{H} - \kappa(\tfrac{60}{H})^{1/2}, \tag{17}$$

with the empirical factor $\kappa = 0.4$ (see Kappel and Peer [1]). We can now write the left and right cardiac output as

$$Q_l = H\frac{c_l P_{vp} f(S_l, P_{as})(1 - e^{-\frac{t_d}{R_l c_l}})}{P_{as}(1 - e^{-\frac{t_d}{R_l c_l}}) + f(S_l, P_{as})e^{-\frac{t_d}{R_l c_l}}}, \tag{18}$$

$$Q_r = H\frac{c_r P_{vs} f(S_r, P_{ap})(1 - e^{-\frac{t_d}{R_r c_r}})}{P_{ap}(1 - e^{-\frac{t_d}{R_r c_r}}) + f(S_r, P_{ap})e^{-\frac{t_d}{R_r c_r}}}.$$

The control for the system is heart rate H.

Local metabolic autoregulation of systemic resistance is modeled using the assumption that systemic resistance R_s depends on venous oxygen concentration $C_{v_{O_2}}$. Thus R_s is described by

$$R_s = A_{pesk}C_{v_{O_2}}, \tag{19}$$

where A_{pesk} is a parameter. This relationship was introduced by Peskin and is based on work on autoregulation by Huntsman.

Table 2. Optimal control parameters: normal adult sleep transition

Parameter	Awake
H	75.0
A_{pesk}	147.16
$C_{v_{O_2}}$	0.135
R_p	0.965
β_l	85.89
β_r	2.083
α_l	89.47
α_r	28.46
γ_l	37.33
γ_r	11.88
c_{ap}	0.03557
c_{as}	0.01002
c_{vp}	0.1394
c_{vs}	0.643
c_l	0.01289
c_r	0.06077
κ	0.4

Table 3. Initial states

Steady State	Awake
P_{as}	101.7
P_{vs}	3.619
P_{vp}	7.477
S_l	71.999
S_r	5.488
σ_l	0.0
σ_r	0.0

2.1. Parameters and initial values

The parameter values are given by:

The reference paper for this model is given in bibliography.

References

1. F. Kappel, R. O. Peer, *A mathematical model for fundamental regulation processes in the cardiovascular model*, J. Math. Biol., 1993, 31: 611-631.