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Computers in Biology and Medicine 31 (2001) 59–72

Computers in Biology
and Medicine

www.elsevier.com/locate/combiomed

Multiple modeling in the study of interaction of hemodynamics and gas exchange

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Received 23 March 2000; accepted 10 July 2000

Abstract

Circulation plays an important role in gas exchange. Therefore, there is an interaction between circulation and gas exchange. To understand the dynamic effect of these two physiological systems, a computer simulation model of hemodynamics and gas exchange is established in this work. This model includes two physiological systems, namely the respiratory and circulatory systems. It consists of five parts: the model of gas transport, exchange and storage within the body, the multi-element nonlinear mathematical model of human circulatory system, an alveolar ventilation controller, a cardiac output controller, and a controller of breathing frequency. Model simulations provide results consistent with both dynamic and steady-state responses under hypoxia. Simulation results can reflect the interaction of hemodynamics and gas exchange. Using this model, the changes of pulmonary arterial pressure and right ventricular pressure in high altitude are studied. The optimal mode of breathing extra oxygen using nasal prongs or a facial mask is studied. This model may provide a useful tool to study reaction of hypoxia and the oxygen inhalation mode under hypoxia environments. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Hemodynamics; Circulatory system; Respiratory system; Hypoxia; Pulmonary hypertension; Oxygen inhalation; Computer simulation; Physiological model

1. Introduction

Grodins [1] presented the first mathematical dynamic model of the respiratory system in 1954. Horgan, Grodins, Milhorn, Fincham, and Lorenzo followed this work [2–7]. Many comprehensive

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Nomenclature

C	gas volume concentration
P	gas partial pressure
MR	metabolic rate
V	gas volume
f	frequency of breathing
Q	blood flow
HF	ventricular contractility index
$\overline{P_{rv}}$	right ventricle mean pressure
$\overline{P_{lv}}$	left ventricle mean pressure
$\overline{P_{pula}}$	pulmonary arterial mean pressure
<i>Subscripts</i>	
a	artery
v	vein
A	alveolar
Ae	end-capillary of lung
I	air
B	brain
vB	brain vein
T	body tissues
vT	tissue vein
E	external ventilation

mathematical models of the human respiratory system as well as cardiovascular system were published in the past years. Many of these models are dealing only with either gas exchange process or hemodynamics. Only a few works represent the comprehensive functions of both ventilatory and circulatory hemodynamics. Further understanding of the mechanism of the interaction of respiration and circulation may play an important role in the protection technique development for some special environment, such as flight conditions of hypobaric hypoxia and hypobaric oxygen inhalation.

The purpose of this paper is to develop an integrated model of cardio-pulmonary system and to study the interaction of hemodynamics and gas exchange. To be able to present the systemic interaction of the two physiological systems, an integrated model is developed. It consists of two human physiological systems: respiratory and circulatory systems. This model can be depicted as follows: (1) the process of gas transport, exchange and storage; (2) a pressure-flow model; (3) an alveolar ventilation controller; (4) a cardiac output controller; and (5) a controller of frequency of breathing.

Using the model presented in this paper, normal and hypoxic physiological conditions are simulated. Results referring to steady-state and transient conditions are presented and compared with the data previously reported.

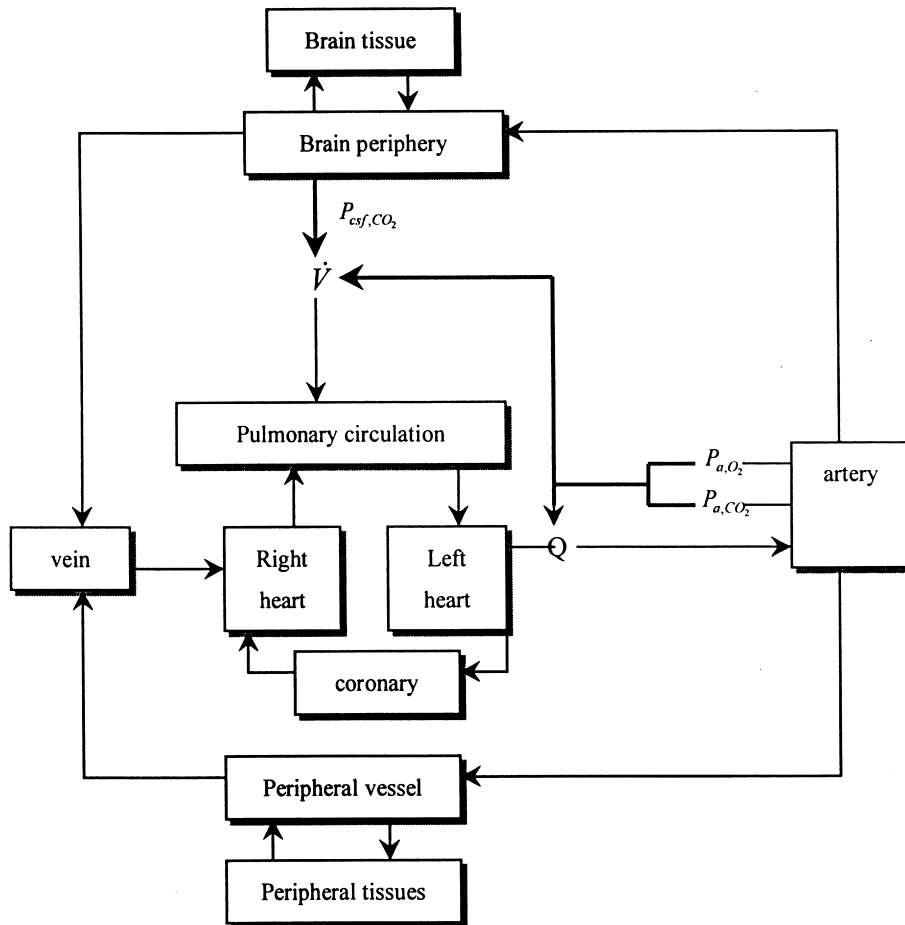


Fig. 1. Model diagram: (—) O_2, CO_2 and blood circulation; (---) controllers.

2. Model description

Fig. 1 shows a schematic diagram of the model of hemodynamics and gas exchange. This model consists of five parts: the multi-element, nonlinear mathematical model of human circulatory system, the model of oxygen (O_2) and carbon dioxide (CO_2) exchange, transport and storage, the model of respiratory frequency and the controllers that adjust cardiac output (Q) and alveolar ventilation (\dot{V}). Each part of the model is depicted in this section. A full list of the symbol used is given in the nomenclature.

2.1. Circulatory system

The model of the circulatory system developed is based on the multi-element, nonlinear mathematical model of human circulatory system by Jaron et al. [9–11]. This model is modeled by a

multi-blood vessel segments network that includes the four chamber heart model, pulmonary circulation model, coronary circulation model and arterial, venous and peripheral tree model. The four chamber heart model is a time-varying elastance model; the pulmonary circulation model is only a single connection between the right and left heart; the coronary circulation model is a connection between the left ventricle and the right atrium; the arterial, venous and peripheral tree models, each of them consists of 30 connected segments. In terms of the properties of each arterial or venous or peripheral vessel using the equivalent circuit elements (i.e. resistance, capacity and inductance) describe the vessel resistance, inertance and compliance.

2.2. Oxygen and carbon dioxide transport, exchange and storage in the human

This part of the model is based on the work of Fincham [5] and Lorenzo [6]. The subscript i stands for O_2 or CO_2 . When i is O_2 , every following equation is the equation of oxygen (O_2) transport in the human, but when i is CO_2 , every following equation is the equation of carbon dioxide (CO_2) transport in the human.

Lung:

The diffusion equation for alveolar CO_2 partial pressure (P_{A,CO_2}) is taken to be [6]

$$V_A \frac{dP_{A,CO_2}}{dt} = \dot{V}(P_{I,CO_2} - P_{A,CO_2}) + kQ(1 - \delta)(C_{v,CO_2} - C_{Ae,CO_2}), \quad (1)$$

where V_A is an equivalent volume in alveolar gas and lung tissue, \dot{V} is the alveolar ventilation, P_{I,CO_2} stands for the air CO_2 partial pressure, C_{v,CO_2} and C_{Ae,CO_2} are venous and end-capillary CO_2 concentrations at the standard temperature and pressure dry (STPD) and Q is the cardiac output. Also, k is a constant parameter that converts gas concentrations in the blood into alveolar gas partial pressures and δ is a pulmonary shunt fraction in order to describe not all blood flows through the lung.

Similar to Eq. (1), the diffusion equation for alveolar O_2 partial pressure (P_{A,O_2}) is taken to be

$$V_A \frac{dP_{A,O_2}}{dt} = \dot{V}(P_{in,O_2} - P_{A,O_2}) + kQ(1 - \delta)(C_{v,O_2} - C_{Ae,O_2}), \quad (2)$$

$$P_{in,O_2} = \begin{cases} P_{I,O_2} & \dot{V} \leq \dot{V}_{in,O_2}, \\ \left(1 + 4 \frac{\dot{V}_{in,O_2}}{\dot{V}}\right) P_{I,O_2} & \dot{V} \geq \dot{V}_{in,O_2}, \end{cases} \quad (3)$$

where P_{in,O_2} is the practical inspired O_2 partial pressure. \dot{V}_{in,O_2} is the volume of breathing extra oxygen per minute. In Eq. (3), we assume that P_{in,O_2} is equal to 149 mm Hg if P_{in,O_2} is higher than 149 mm Hg. For normal respiration, \dot{V}_{in,O_2} is equal to zero. In this case, the value of P_{in,O_2} is the same as P_{I,O_2} .

Artery:

O_2 or CO_2 concentration in artery $C_{a,i}$ is given by [6]

$$C_{a,i} = (1 - \delta)C_{Ae,i} + \delta C_{v,i}. \quad (4)$$

Brain and body tissues:

O₂ or CO₂ concentrations in brain and body tissues ($C_{B,i}$, $C_{T,i}$) are given by [6]

$$V_B \frac{dC_{B,i}}{dt} = Q_B(C_{a,i} - C_{vB,i}) \pm MR_{B,i} \tag{5}$$

$$V_T \frac{dC_{T,i}}{dt} = Q_T(C_{a,i} - C_{vT,i}) \pm MR_{T,i} \tag{6}$$

where V_B and V_T are the volumes in the brain and body tissues, respectively. $C_{vB,i}$ and $C_{vT,i}$ are brain and body tissue venous gas concentrations. Q_B and Q_T stand for the cerebral blood flow and body tissue blood flow. $MR_{B,i}$ and $MR_{T,i}$ are metabolic rates of O₂ and CO₂ in brain and body tissues. When i is O₂, $MR_{B,i}$ and $MR_{T,i}$ are negative, but when i is CO₂, $MR_{B,i}$ and $MR_{T,i}$ are positive.

Vein:

O₂ or CO₂ concentration in vein ($C_{v,i}$) is given by [6]

$$QC_{v,i} = Q_B C_{vB,i} + Q_T C_{vT,i}, \tag{7}$$

where $Q = Q_B + Q_T$.

Alveolar volume (V_A) increases during inspiration, but during expiration V_A decreases. V_D stands for the dead space volume in lung. These equations are given by [5]

$$V_A = \bar{V}_A + \varepsilon \dot{V} \cos(2\pi ft), \tag{8}$$

$$V_D = 0.1587 + 0.1698 \dot{V}, \tag{9}$$

$$V_E = \dot{V} + fV_D \tag{10}$$

where \bar{V}_A represents the alveolar mean volume, f is the respiration frequency, and V_E enables comparison to be made between experimental and model results.

Hemo-oxygen saturation curve:

The relationship of oxygen concentration (C_{O_2}) and partial pressure (P_{O_2}) in brain and tissues is given by [6]

$$C_{O_2} = \alpha_{O_2} P_{O_2} \tag{11}$$

where α_{O_2} is the solubility of oxygen in tissues.

The relationship of oxygen concentration (C_{O_2}) and partial pressure (P_{O_2}) in artery and vein is defined by hemo-oxygen saturation S . S is given as [12]

$$S = \frac{a_1 P_{O_2} + 2a_2 P_{O_2}^2 + 3a_3 P_{O_2}^3 + 4a_4 P_{O_2}^4}{4(1 + a_1 P_{O_2} + 2a_2 P_{O_2}^2 + 3a_3 P_{O_2}^3 + 4a_4 P_{O_2}^4)}, \tag{12}$$

$$C_{O_2} = \lambda_1 C_{Hb} S + \lambda_2 P_{O_2}, \tag{13}$$

where C_{Hb} stands for hemoglobin concentration. λ_1 and λ_2 are constant.

2.3. Dissociation curve of carbon dioxide

The relationship of carbon dioxide concentration (C_{CO_2}) and partial pressure (P_{CO_2}) whether in blood or in tissues is given by [5]

$$C_{CO_2} = \alpha_{CO_2} P_{CO_2}, \quad (14)$$

where α_{CO_2} is the solubility of carbon dioxide in brain and tissues.

Providing $P_{B,i} = P_{VB,i}$; $P_{T,i} = P_{VT,i}$; $P_{A,i} = P_{Ae,i}$ [6], Eqs. (11)–(14) are used to calculate $C_{VB,i}$, $C_{VT,i}$, $C_{Ae,i}$. Eqs. (1)–(10) constitute the model of oxygen and carbon dioxide transport, exchange and storage in the body.

2.4. Frequency of breathing

By assuming a sinusoidal flow waveform, the frequency of breathing f is influenced by the lung elastance R_1 , airway viscous resistance R_2 and airway turbulent resistance R_3 as follows [13]:

$$4R_3(\varepsilon V_D)^2 f^3 + \varepsilon^2 V_D(R_2 + 4R_3 \dot{V}) f^2 + R_1 V_D f - R_1 \dot{V} = 0. \quad (15)$$

2.5. An alveolar ventilation controller

The controller that adjusts alveolar ventilation is complicated. The alveolar ventilation \dot{V} integrates stimuli coming from the peripheral and central chemoreceptors. \dot{V} is adjusted in order to keep the arterial and cerebrospinal fluid (CSF) gas levels close to their normal values during changes of external conditions [6].

2.6. A cardiac output controller

Cardiac output Q is a sharing parameter in circulatory and respiratory systems. In this study, cardiac output Q is the bridge that connects a circulatory system with a respiratory system. Blood carries O_2 and CO_2 everywhere in the body. Cardiac output deviation from the normal value depends on the shifting arterial O_2 and CO_2 partial pressures from the normal range. Because, how much blood the left ventricle pumps is determined by a working load for the heart, the influence of gas partial pressures in a respiratory system on blood flow is reflected by reducing or increasing a working load for the heart. A gain factor (HF), named as the ventricular contractility index, is introduced into the model. During systolic period the left ventricular pressure (Plv) is divided by HF; during diastolic period Plv is multiplied by HF [11]. The relationship of HF and cardiac output Q is given by

$$\Delta HF = K \Delta Q, \quad (16)$$

$$\Delta Q = Q_1 + Q_2, \quad (17)$$

where K is constant. Q_1 is the variable of Q when arterial O_2 partial pressure P_{a,O_2} changes [14].

$$Q_1 = \begin{cases} 0, & P_{a,O_2} \geq 95 \text{ mm Hg} \\ 10^{-5} \times 60[2445.1T_0(X) - 3233.3T_1(X), & 25 \text{ mm Hg} \leq P_{a,O_2} \leq 95 \text{ mm Hg} \\ +1050.4T_2(X) - 143.5T_3(X)], & \end{cases} \quad (18)$$

Table 1
Relevant parameters

Symbol	Definition	Unit	Value
	Volume	l	
\bar{V}_A	Alveolar mean volume	l	3.28
V_B	Brain volume	l	0.90
V_T	Tissues volume	l	38.74
k	Conversion coefficient	mm Hg	863
δ	Pulmonary shunt fraction	—	0.024
MR_{B,O_2}	Metabolic rate of oxygen in brain	l/min	0.05
MR_{B,CO_2}	Metabolic rate of carbon dioxide in brain	—	0.05
MR_{T,O_2}	Metabolic rate of oxygen in tissues	—	0.192
MR_{T,CO_2}	Metabolic rate of carbon dioxide in tissues	l/min	0.15
α_{O_2}	Solubility of oxygen	l mm Hg/l	$3.17e-5$
α_{CO_2}	Solubility of carbon dioxide	l mm Hg/l	0.016
C_{Hb}	Hemoglobin concentration	g/l	150
a_1	Adair coefficient	—	0.01524
a_2	Adair coefficient	—	$7.1e-5$
a_3	Adair coefficient	—	0
a_4	Adair coefficient	—	$2.7e-6$
R_1	Lung elastance	m/l	0.0855
R_2	Airway viscous resistance	m min/l	$5.17e-4$
R_3	Airway turbulent resistance	m min ² /l ²	$3.57e-6$
λ_1	—	l/g	$1.312e-3$
λ_2	—	mm/Hg	$3.03e-5$
K	—	min/l	0.111

where $X = (2P_{a,O_2} - 115)/65$.

Q_2 is the variable of Q when CO_2 arterial partial pressure P_{a,CO_2} changes [14].

$$Q_2 = \begin{cases} 10^{-5} \times 60[3600T_0(X) + 3600T_1(X)] & 58 \text{ mm Hg} \geq P_{a,CO_2} \geq 42 \text{ mm Hg,} \\ 0 & P_{a,CO_2} < 42 \text{ mm Hg,} \end{cases} \quad (19)$$

where $X = (2P_{a,CO_2} - 100)/16$.

$T_i(X)$ is a Chebyshev polynomial. The equations for polynomials of the first kind of degree i with X are given by

$$T_0(X) = 1, \quad T_1(X) = X, \quad T_2(X) = 2X^2 - 1, \quad T_3(X) = 4X^3 - 3X.$$

3. Simulation results

This model was implemented using an IBM compatible personal computer. Relevant parameters in this model are given in Table 1 in terms of Refs. [5,6,9–12]. The model was adjusted to present a subject with a resting heart rate of 72 beats per second. It was assumed that oxygen metabolic rates in body tissues and brain tissue are constant. A comprehensive set of simulations was performed

Table 2

Steady-state values under the normal and hypoxia physiological conditions (units: P , $\overline{P_{rv}}$, $\overline{P_{lv}}$, $\overline{P_{pula}}$ are in mm Hg; Q , \dot{V} are in l/min; f is in 1/min)

	P_I		P_a		P_T		P_B		V	Q	f	$\overline{P_{rv}}$	$\overline{P_{lv}}$	$\overline{P_{pula}}$
	O ₂	CO ₂	O ₂	CO ₂	O ₂	CO ₂	O ₂	CO ₂						
Normal	149	0	95.1	40.5	40.5	42.9	34.2	45.0	4.20	5.0	12.9	12.4	55.0	14.2
hypoxia	120	0	75.7	40.0	39.3	42.8	33.7	44.3	4.81	5.31	14.0	13.0	58.0	14.7
	80	0	51.1	37.8	34.9	41.3	30.9	41.5	7.06	6.27	17.2	13.8	68.8	16.1
	64	0	41.7	36.1	31.2	40.1	28.2	39.5	9.08	6.95	19.4	14.2	76.6	16.7

in order to test the model under the normal and hypoxic physiological conditions. Steady-state simulation data under above physiological conditions were given in Table 2.

Dynamic simulation process under hypoxia was performed. The simulation can be divided into three periods as follows:

- (1) from 0 to 5 min, simulation of the normal state;
- (2) from 5 to 20 min, simulation of hypoxia;
- (3) from 20 to 30 min, simulation of recovery period.

Figs. 2 and 3 show the dynamic behavior simulated by this model. In this case, after 5 min normal state, the simulated subject undergoes hypoxia of $P_{I,O_2} = 64$ mm Hg for 15 min and then has a subsequent recovery. At the fifth minute, P_{I,O_2} decreased from 149 mm Hg to 64 mm Hg. From Eqs. (2) and (3), we can deduce that P_{A,O_2} would decrease when P_{I,O_2} decreases. It can lead to the fact that P_{a,O_2} would be lower than the normal value. From curve 1 in Fig. 2(b), we can see this response. P_{B,O_2} and P_{T,O_2} , shown by curves 2 and 3 in Fig. 2(b), decrease due to the fall of P_{a,O_2} .

The rapid fall of P_{a,O_2} affects alveolar ventilation \dot{V} and the working load of the heart. When P_{a,O_2} decreases, the peripheral chemoreceptors adjust an alveolar ventilation controller and produce the rise of \dot{V} . Usually, the increase of \dot{V} is reflected by f (Fig. 2(e)), and the rise of V_D concurs with Fig. 2(d). From Eq. (18), it can be deduced that Q_1 is higher than zero and HF increases. The heart can pump more blood and cardiac output Q rises (Fig. 2(f)). Curves 1 and 3 in Fig. 3 show that diastolic pressure of the left ventricle under hypoxia is higher than in the normal physiological condition. The rise of Q and \dot{V} supports O₂ required by the tissues. In turn, it causes the decrease of CO₂ partial pressures (Fig. 2(a)). As decreasing P_{a,CO_2} , the central chemoreceptors produce an antagonistic effect that the increase of \dot{V} would be limited by the central chemoreceptors. Afterwards, the new equilibrium state is approached. Here, both O₂ and CO₂ partial pressures in the human body are lower than the normal values; Q and \dot{V} are higher. The changes of gas exchange can cause the changes in hemodynamics. The pulmonary arterial pressure P_{pula} and the left ventricular pressure P_{lv} are higher (Fig. 3). The above responses are compensations for the temporary decrease of P_{I,O_2} . When P_{I,O_2} returns to the normal value, the various responses recover toward initial condition (Figs. 2 and 3).

Fig. 4 compares the changes in P_{a,O_2} , Q and V_E predicted by this model with other simulated responses [5,6] and experimental data [8] for different P_{I,O_2} . The results shown in Fig. 4(c) indicate that this model can provide results that match the experimental data better than other models.

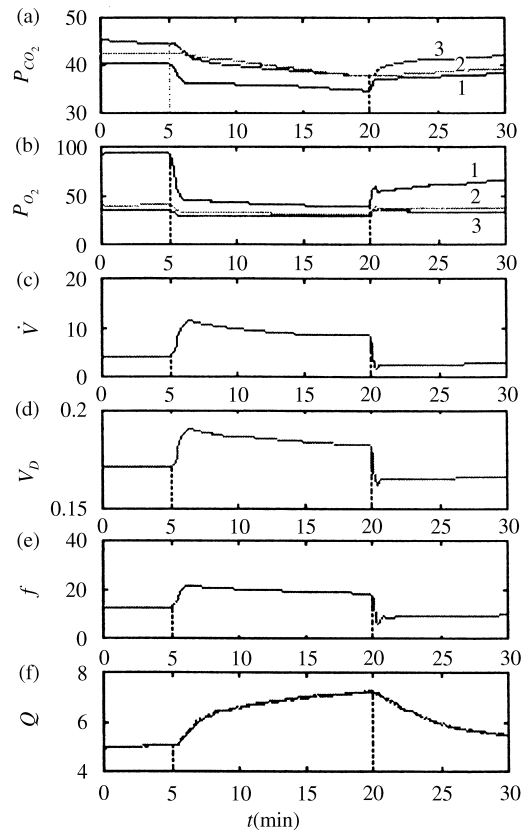


Fig. 2. Hypoxia ($P_{1,O_2} = 64$ mm Hg): simulated the dynamic behaviors of the main variables. (a) Carbon dioxide partial pressures P_{CO_2} ; (b) oxygen partial pressures P_{O_2} ; (c) alveolar ventilation \dot{V} ; (d) dead space volume V_D ; (e) frequency of breathing f ; (f) blood flow Q : 1, artery; 2, tissues; 3, brain.

4. Discussion

Responses in the respiratory and circulatory systems to hypoxia are given. Figs. 2 and 3 describe their mutual interactions during 15 min hypoxia ($P_{1,O_2} = 64$ mm Hg) and subsequent recovery. The ratio of alveolar ventilation to cardiac output \dot{V}/Q decides whether gas pump can accord with blood pump. Its normal range is from 0.7 to 1. Fig. 5 shows that it is higher than the normal range during hypoxia. This result illustrates that there is not enough Q that all gas in the lung can exchange with, \dot{V} exceeds the normal value during hypoxia. Gas and blood pumps do not work normally. If hypoxia lasts for a long time, it can cause disease of circulatory and respiratory systems.

It is evident that people are under hypoxia when they go into high altitude. Physiological pulmonary hypertension and increasing frequency of breathing are the most symptoms that are called acute mountain sickness [15,16]. Their causes are unclear. Using the model presented in this paper, the reaction of high altitude can be studied in terms of the interaction of hemodynamics and gas exchange. The simulated data can be compared with experimental data [15] (Fig. 6). These experimental data were statistic data by examining eight healthy subjects that migrated to 3950-m high

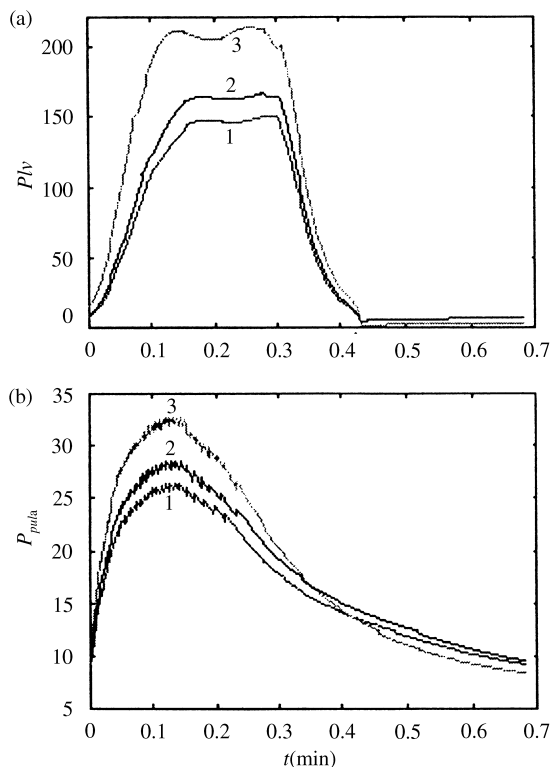


Fig. 3. Hypoxia ($P_{I,O_2} = 64$ mm Hg): simulated the dynamic behaviors of the main variables. (a) The left ventricular pressure P_{lv} ; (b) the pulmonary arterial pressure P_{pula} : 1, normal physiological condition; 2, recovery; 3, hypoxia.

altitude ($P_{I,O_2} = 86$ mm Hg). Fig. 6 shows that $\overline{P_{pula}}$ and $\overline{P_{lv}}$ are higher during hypoxia. Increasing cardiac output caused by the fall of arterial O_2 partial pressure results in increasing $\overline{P_{pula}}$ and $\overline{P_{lv}}$. These symptoms in high altitude are the compensatory response to adapting to hypoxia. Suitable pulmonary hypertension can improve \dot{V}/Q and enable tissues obtain more oxygen. But excessive pulmonary hypertension can lead to increasing the right ventricular pressure P_{rv} (Fig. 6(b)) and the working load of the right heart. Consequently, it can lead to some diseases, such as chronic mountain sickness, pulmonary edema and cerebral edema. Then, physiological pulmonary hypertension will become pathological pulmonary hypertension. P_{pula} and P_{lv} are the indicators by which pathological pulmonary hypertension is diagnosed. From Fig. 6, we can see that this model can simulate the reaction of high altitude and predict sickness of high altitude.

The reason that results in above symptoms of acute mountain sickness is the decrease of atmospheric O_2 partial pressure, or hypoxia. This brings about decreasing arterial O_2 partial pressure. Nasal prongs or a facial mask is a simple treatment to increase the arterial O_2 partial pressure [17]. In Eq. (3), \dot{V}_{in,O_2} is the effective volume of breathing extra oxygen every minute via nasal prongs. We assure that this extra oxygen is inspired. The results for different \dot{V}_{in,O_2} are presented in Table 3. From Table 3, we can see that P_{a,O_2} is increased when the subject breathes extra oxygen. At the same time $\overline{P_{rv}}$, $\overline{P_{pula}}$ as well as f are decreased. Breathing extra oxygen brings rapid relief.

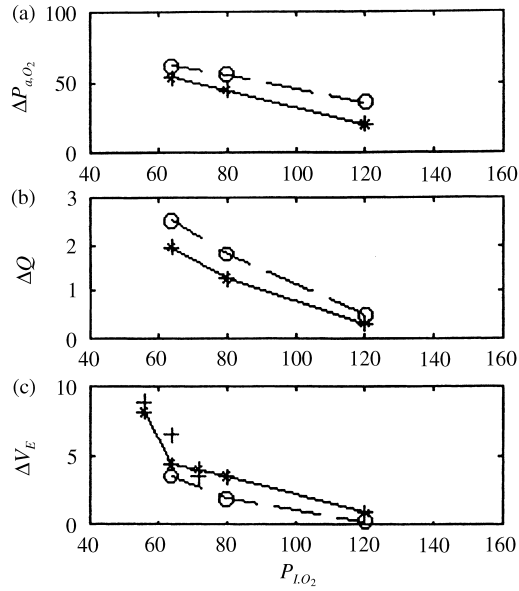


Fig. 4. Hypoxia ($P_{I,O_2} = 64$ mm Hg): changes between the new steady state and normal values of P_{a,O_2} , Q and V_E for different P_{I,O_2} : (*) present model; (o) Fincham and Tehrani's [5] simulated results; (+) experimental results [8].

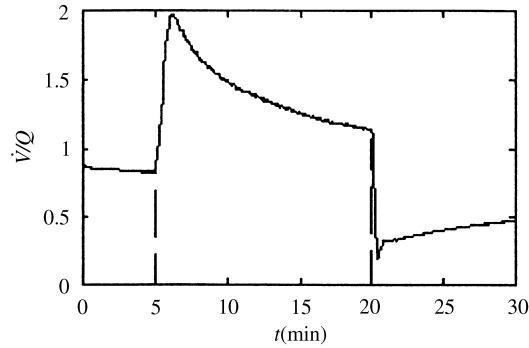


Fig. 5. Hypoxia ($P_{I,O_2} = 64$ mm Hg): simulated the dynamic behaviors of pulmonary ventilation to blood flow \dot{V}/Q .

Table 3

The results for different \dot{V}_{in,O_2} in 3950-m high altitude (units: \dot{V}_{in,O_2} is in l/min; P_{a,O_2} , \overline{Prv} , \overline{Ppula} are in mm Hg; f is in l/min)

\dot{V}_{in,O_2}	P_{a,O_2}	\overline{Prv}	\overline{Ppula}	f
0	57.0	13.6	15.2	17.2
0.2	58.0	13.2	14.3	14.3
0.5	73.2	13.1	13.6	12.6
0.8	90.0	12.7	13.5	12.2

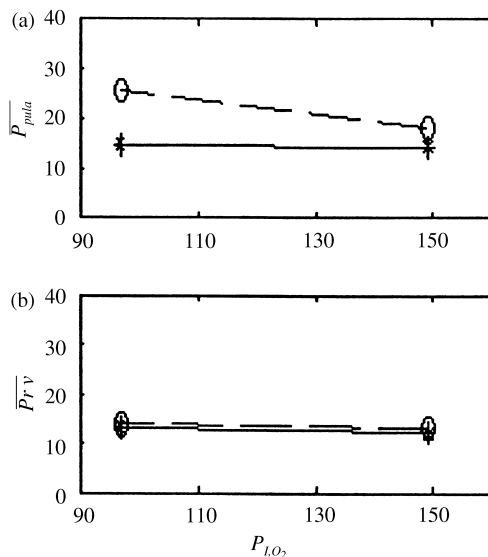


Fig. 6. The reaction of high altitude. (a) mean pulmonary arterial pressure $\overline{P_{pulva}}$ for different P_{1,O_2} ; (b) mean right ventricle pressure $\overline{P_{rv}}$ for different P_{1,O_2} : (*) present model; (o) statistic data [15].

Simulation results suggest that in 3950-m high altitude, the optimal rate of breathing extra oxygen be about 0.75 l/min when P_{in,O_2} is equal to 149 mm Hg. This value is the minimum value needed by the subject at high altitude while all of this extra oxygen can exchange with blood in lung is assumed.

When we established this model, we made use of some assumptions and simplifications. The first concerns controllers of Q and \dot{V} . We ignored effects of H^+ and HCO_3^- in blood on Q and \dot{V} . The second concerns that the heart rate is constant. The third is concerned with the metabolic rate of oxygen in brain and body tissues. We assumed that they are constant during hypoxia. In fact, they will change during hypoxia or other physiological conditions. Adding the model of oxygen metabolism may become necessary in future works, if we intend to use this model to study the response of metabolic rate of oxygen in the human.

Based on the above discussion, we can see that the model developed in this work may have two potential applications. Firstly, this model can be used to study the reaction of high altitude. It can predict the reaction of respiratory and circulatory systems when healthy people go into high altitude. Up to now, physiological mechanism of reaction of high altitude is not explained. Secondly, this model may provide a framework for investigation of the oxygen metabolism in the body.

5. Summary

The interaction of hemodynamics and gas exchange is studied with the model presented in this paper. It consists of both respiratory and circulatory systems. Model simulations provide results of both dynamic and steady-state responses for different P_{1,O_2} . Steady-state results agree with the data reported in the literature. Dynamic results reflect the interaction of hemodynamics and gas exchange.

Using this model, the changes of pulmonary arterial pressure P_{pula} and left ventricular pressure P_{lv} in high altitude are simulated. P_{pula} and P_{lv} are the indicators by which pathological pulmonary hypertension is diagnosed. Nasal prongs or a facial mask helps people adapt to hypoxia. This model can be used to study the reaction of high altitude and predict mountain sickness. It is also useful for study of the dynamic interaction of respiration and circulation. If the model of oxygen metabolism is added to the model presented in this paper, this model can be used to study the response of metabolic rate of oxygen in the body.

Acknowledgements

The Chinese National Natural Science Foundation and The Ministry of Science and Technology supported this work.

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