A MATHEMATICAL MODEL OF THE HUMAN RESPIRATORY CONTROL SYSTEM DURING EXERCISE

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ABSTRACT
This paper describes a respiratory control system model and the associated computer simulations for human subjects during incremental exercise, involving work rates from zero up to the highest level in the heavy exercise domain. Modelling the respiratory control system for conditions above lactate threshold has rarely been attempted because many subsystems begin to lose proportionality in their responses. Our model is built on the basis of putative mechanisms and is based on information identified from a large body of published work. Simulation results are presented and validated using experimental results from published sources. The model confirms that the human body employs an open-loop control strategy for ventilation during exercise, which contrasts with the negative feedback control mode employed for the rest condition. It is suggested that control of ventilation simultaneously involves at least two variables, one being proportional to the pulmonary CO_2 output and another being proportional to blood acidity.

KEY WORDS
Biomedical modelling, respiratory control system, exercise, simulation

1. Introduction

The human body has a large number of control systems. These include neural and mechanical systems, such as those involved in the control of erect posture and body movement, as well as many chemical systems, such as those controlling the level of blood glucose and the regulation of arterial blood pressure. Most of these systems are negative feedback control systems where we can identify control actions that tend to reduce or eliminate deviations of the system output from normal levels. For example, a high concentration of blood carbon dioxide stimulates pulmonary ventilation in an attempt to restore the concentration back to normal levels. Some systems, however, contain elements of feedforward operation, as has been proposed by some investigators in modelling the respiratory control system during exercise.

Due to their complexity, the systems of the human body have become a focal point for much activity involving computer-based modelling and simulation. Traditional linear control theory also provides a useful framework within which to discuss physiological control mechanisms, but detailed quantitative investigation of most of these systems requires the use of computer-based methods. Engineering control systems usually operate in a more or less linear fashion under normal conditions and have identifiable and known set point values. Physiological systems, on the other hand, rarely have any identifiable set points and the normal steady-state operating condition results from nonlinear interactions between elements arranged in series and, in some cases, multiple closed loops. Among the objectives of modelling work of this kind is the testing of hypotheses about physiological systems, the analysis of dysfunctions of various kinds or the investigation of diseased conditions.

Interest in modelling in the case of exercise physiology includes, for example, gaining a more complete understanding of the mechanisms involved in the relevant physiological systems, evaluation of different strategies for training in sports and rehabilitation and assessment of levels of medication and other forms of treatment. Simulation and experimentation, used together, can often provide valuable insight that is difficult to obtain using experimental methods alone.

Although computer simulation techniques have been widely used in modelling some aspects of the respiratory system in humans and in other mammals, little progress appears to have been made in using these techniques successfully in the study of the dynamic response of the respiratory system to exercise, especially for higher exercise intensities when subsystem responses typically begin to lose their original proportionality against the rise of exercise work rate and associated functions. The

application of computer simulation techniques and control system methods of analysis to respiratory control dynamics in exercise has been confined largely to statistical modelling of experimental data sets, but with considerable success [1,2,3]. However, there has been less work on the application of such experimental modelling methods to structural dynamic models based on putative physiological control mechanisms. We therefore attempt to create a comprehensive dynamic model which is applicable to cycle ergometry exercise in the upright posture.

2. Model Development

The respiratory system can be defined as a group of organs involved in drawing oxygen into and removing carbon dioxide out of the body or cells. Oxygen is required to enable living cells to conduct aerobic metabolism (or respiration) to obtain energy and carbon dioxide is the waste product of the metabolism.

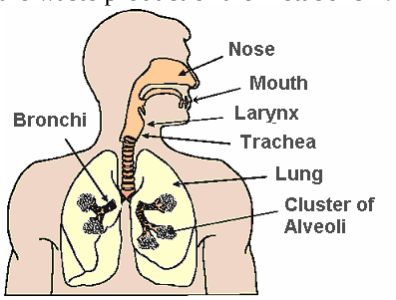

Figure 1 The human respiratory system

In humans, the respiratory system consists of several organs. The nose or mouth, the trachea and the bronchi serve as the air passage (**Figure 1**). The lung with its alveoli facilitates oxygenation of the blood with a concomitant removal of carbon dioxide. The system extends further to involve body tissues because respiration, which utilizes oxygen and produces carbon dioxide, takes place in the body tissues. Within this context, the heart plays a part in the respiratory system because it drives the blood, which transports O_2 and CO_2 through the lungs and the body tissues (**Figure 2**). The body tissues are particularly important when considering the respiratory control system during exercise because tissue respiration changes considerably in exercise.

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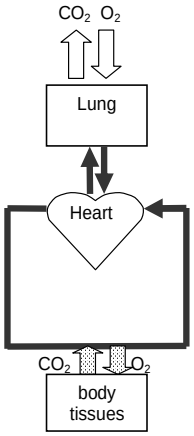

Figure 2. Conceptual model of the human respiratory system

2.1 Model Structure

The structure of a model of the respiratory control system during exercise is depicted in **Figure 3**. In the model, blocks represent body compartments, thick lines represent blood flow, thin lines represent controller stimuli to the corresponding compartments, and dashed lines indicate which compartments are directly influenced by the changes in work rates. Gas flows between the lung compartment and the air are depicted using block arrows, where O_2 has a net flow into the lung and CO_2 has a net flow out of the lung. It should be noted that within this structure the representation for the blood flow between the lung and the heart has been simplified with blood being shown as flowing from the mixed venous compartment to the lung and the heart.

Blocks with the letter D represents time delay elements. Venous blood is assumed to have delay elements but arterial blood has none.

The muscle compartment represents the muscles that perform the exercise. Hence muscles that do not participate in the exercise, and all body tissues other than muscle, are lumped together as the other tissues compartment.

A change in exercise work rate will directly affect the muscle, other tissues, cardiac controller and ventilation controller. An increase in work rate will raise the muscle O_2 extraction and its lactate production. At the onset of exercise, by the time O_2 extraction reaches a steady state level, the energetic (or ATP) requirement is fulfilled anaerobically so lactate production at this period is high. The increase of work rate, as well as the increase in blood lactate concentration, raises the lactate consumption of other tissues. The work rate also has a positive impact on ventilation and on the cardiac controller, whereby the

lung will increase ventilation and the heart will increase cardiac output.

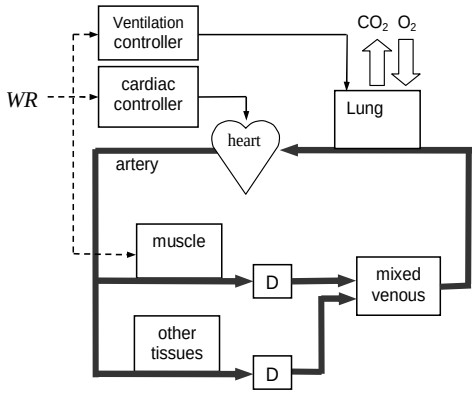

Figure 3 Structure of the Respiratory System Model

As illustrated in **Figure 3**, work rate is the only stimulus included within this representation of the human respiratory system during exercise. The behaviour of certain variables from compartments that are directly affected by work rate has to be pre-defined. Those variables include the muscle oxygen consumption ($\dot{V}O_2$), ventilation ($\dot{V}E$), and cardiac output ($\dot{Q}$).

2.2 Model Equations

2.2.1. Arterial partial pressure

In the artery, the partial pressures of oxygen and carbon dioxide are calculated using the following equations [4,5]:

$$PaCO_2 = \frac{863 \cdot \dot{V}CO_2}{\dot{V}E \cdot (1 - VD/VT)} \quad \textbf{(1)}$$

$$PaO_2 = 147 - \frac{863 \cdot \dot{V}O_2}{\dot{V}E \cdot (1 - VD/VT)} \quad \textbf{(2)}$$

where $PaCO_2$ and PaO_2 are the arterial partial pressures of CO_2 and O_2, respectively, $\dot{V}CO_2$ is pulmonary CO_2 output, $\dot{V}O_2$ is pulmonary O_2 uptake, $\dot{V}E$ is the ventilation, and VD/VT is the ratio of dead space volume to tidal volume. The ratio VD/VT is assumed to change hyperbolically in accordance with the equation:

$$VD/VT = \frac{0.5578}{\dot{V}E} + 0.1482 \quad \textbf{(3)}$$

which represents an approximation based on the graphical analysis of an experimental result presented in [6].

2.2.2. Blood gas storage

The relationship between blood O_2 partial pressure and content follows Kelman's equation [7] and the relationship between CO_2 partial pressure and content follows the algorithm described in [8].

2.2.3. Blood pH

The arterial and mixed-venous pH is calculated using Siggaard-Andersen nomogram [9] which has been adapted into a computer algorithm by researches from the University of Prague [10].

2.2.4. Blood flow

The response of cardiac output ($\dot{Q}$) to an increase in exercise load has two phases [11,12,13]. The first initial phase (denoted as phase 1) is short and fast representing the vascular vasodilation and the pumping effect of muscular contraction and relaxation. The fundamental (or phase 2) component represents the response of the vascular system to fulfil the increasing demand in terms of energy during exercise. The characteristics of both the fundamental and initial component have been assumed to be of first-order exponential form. Therefore, the cardiac output response has been modelled as a sub-system consisting of two linear ordinary differential equations and an algebraic equation and is described mathematically as:

$$\begin{aligned} \tau_i \frac{\dot{Q}_i(t)}{dt} + \dot{Q}_i(t) &= 0.05 \cdot \mu \cdot WR \\ \tau_f \frac{\dot{Q}_f(t)}{dt} + \dot{Q}_f(t) &= 0.05 \cdot (1-\mu) \cdot WR \cdot e^{TDf} \\ \dot{Q}(t) &= \dot{Q}_{bl} + \dot{Q}_i(t) + \dot{Q}_f(t) \end{aligned} \quad \textbf{(4)}$$

where $\dot{Q}_{bl}$ is the base line value of cardiac output, (i.e. the cardiac output before the exercise work load is applied), WR is the work rate (W), TD_f and τ are the time delay (s) and time constant (s) of the response components respectively, and subscripts i and f denote that the corresponding variables are for the initial and fundamental components respectively. The initial component in the system response relates to the fast changes within the first few seconds (typically 20 s) which occurs immediately after the onset of exercise. The constant μ represents the relative magnitude of the initial component compared to the magnitude of the fundamental component.

It is assumed that all increase of cardiac output during exercise goes to the muscle and therefore blood flow to the other tissues is constant.

2.2.5. Oxygen consumption

The pulmonary oxygen uptake ($\dot{V}O_2$) exhibits a three-phase response against a step increase of exercise. The initial response component (or phase 1) during the first seconds of exercise is "cardiodynamic" which means that it is due to the rapid increase of cardiac output [14]. The fundamental component (or phase 2) is first-order exponential. The late slow component (or phase 3) is

observable during exercise in the heavy intensity domain [15].

The fundamental and slow component of $\dot{V}O_2$ are assumed to originate from the exercising muscle. The change in oxygen extraction of the muscle ($\Delta\dot{Q}O_2$) has been modelled using two ordinary differential equations together with an algebraic equation. One of the differential equations represents the fundamental component while the other describes the slow component:

$$\begin{aligned}
&\tau_f \frac{d(\Delta\dot{Q}O_2)_f}{dt} + (\Delta\dot{Q}O_2)_f = G_f \cdot WR \\
&\tau_s \frac{d(\Delta\dot{Q}O_2)_s}{dt} + (\Delta\dot{Q}O_2)_s = G_s \cdot WR \cdot \lambda \cdot e^{TD_s} \\
&\Delta\dot{Q}O_2 = (\Delta\dot{Q}O_2)_f + (\Delta\dot{Q}O_2)_s
\end{aligned} \qquad \textbf{(5)}$$

where WR is the work rate (W), G, TD and τ are the gain, time delay (s) and time constant (s) of the $\Delta\dot{Q}O_2$ components respectively, and subscripts f and s represent variables for fundamental and slow component respectively. The constant λ is defined as:
$\lambda = 0$ for WR(t) <= LT
$\lambda = 1$ for WR(t) > LT
where LT is lactate threshold. The actual value of $\dot{Q}O_2$ is obtained by adding the base line value $\dot{Q}O_{2,bl}$ to the variable $\Delta\dot{Q}O_2$ in Equation (5). The increase of $\dot{Q}O_2$ is subject to limitation so that the muscle venous O_2 content does not drop below zero (or below a certain level which effectively limits muscle O_2 extraction). The slow component emerges after a delay of about 2 – 3 minutes after the lactate threshold is passed.

Note that lactate threshold defines the exercise work rate beyond which exercise would cause lactate ions to start to accumulate in the blood. This accumulation may settle down at a steady state level above the value at rest or may continue to increase until the subject suffers exhaustion. Lactate threshold is also the marker to partition exercise intensity into the moderate and heavy domains. It is in the heavy domain that the slow component of oxygen consumption starts to emerge.

2.2.6. Lactate metabolism

Lactate production and utilization takes place in the muscle compartment and in the other tissues compartment and the circulatory system serves purely as the transport agent. The following equation applies for the muscle compartment:

$$V_M \frac{dCMLa}{dt} = PMLa - UMLa + \dot{Q}M \cdot (CaLa - \sigma_{La} \cdot CMLa) \qquad \textbf{(6)}$$

where V_M is the effective volume of the muscle compartment, CMLa and CaLa are lactate concentrations in the muscle compartment and in the blood artery respectively, PMLa and UMLa are the production and utilization of lactate in the muscle compartment respectively, $\dot{Q}M$ is muscle blood flow. A similar equation applies for the other tissues compartment.

The derivation of Equation **(6)** is based upon the mass balance principle [16]. Lactate transport into and out of the body tissues depends on a mechanism called proton-lactate co-transport and is represented as the third term on the right hand side of the equation. The quantity σ_{La} in the equation is the blood tissue partition coefficient for lactate. This partition coefficient represents how much lactate can be transported between the blood capillary and the relevant compartment and, in this case, is equal to CvMLa/CMLa where CvMLa is the lactate concentration in the muscle venous blood.

In the muscle compartment, lactate production rate is dependent on the discrepancy between the energy requirement represented by the work rate and the energy provided by aerobic catabolism. In the muscle and other tissues compartment, lactate utilization is dependent on lactate concentration in the corresponding compartment.

2.2.7. CO_2 production and storage

Carbon dioxide production in the steady state condition is often expressed for the whole body as the respiratory exchange ratio (RER) and for body tissues as the respiratory quotient (RQ). These quantities represent the molar ratio of CO_2 produced to the O_2 consumed by the body or tissue. In our model, both the RER and the RQ at rest are assumed equal to 0.75. During exercise, muscle RQ is set at 0.9.

Muscle has the capacity to store carbon dioxide and the amount of CO_2 stored has been assumed to increase linearly with muscle CO_2 production ($\dot{Q}CO_2$). However, this variable is reduced by a buffering mechanism when the muscle suffers acidosis. This reduction has been assumed to be linearly related to the muscle lactate increase. Therefore, the model for muscle CO_2 production has two algebraic terms, one that is caused by respiration and another that is produced by the buffering mechanism:

$$\begin{aligned}
&\rho \frac{d(\Delta\dot{Q}CO_2)_r}{dt} + (\Delta\dot{Q}CO_2)_r = \Delta\dot{Q}O_2 \cdot RQ \\
&(\Delta\dot{Q}CO_2)_b = \beta \frac{d(LaM)}{dt} \\
&\Delta\dot{Q}CO_2 = (\Delta\dot{Q}CO_2)_r + (\Delta\dot{Q}CO_2)_b
\end{aligned} \qquad \textbf{(7)}$$

where ρ represents the time constant of the linear CO_2 storage dynamics due to CO_2 production, β represents the amount of CO_2 released due to the buffering mechanism and subscript r and b indicate the respiratory CO_2 production and buffering components, respectively.

2.2.8. Mixed venous blood

The concentration of oxygen in the mixed-venous blood entering the lung is expressed in terms of concentrations in venous blood leaving the muscle and other tissue compartment after a fixed delay time:

$$CvO_2(t) = \frac{1}{\dot{Q}}(\dot{Q}M \cdot CvMO_2(t - TD) + \dot{Q}OT \cdot CvOTO_2(t - TD)) \quad \textbf{(8)}$$

where CvO_2 is the mixed-venous O_2 concentration, $\dot{Q}$ is the cardiac output, $\dot{Q}M$ and $\dot{Q}OT$ are the blood flow through muscle and other tissues, respectively, $CvMO_2$ and $CvOTO_2$ are the oxygen concentration in muscle and other tissue venous blood, respectively, and TD is the delay representing the time taken for blood to pass through the venous pathway.

Similar expressions apply for mixed venous CO_2 and mixed venous lactate concentration.

2.2.9. Control of ventilation

The steady state increase of ventilation in the model is related to the arterial lactate concentration as follows:

$$\Delta\dot{V}E_{ss} = \gamma \cdot WR + \varphi \cdot \Delta La \quad \textbf{(9)}$$

where WR and ΔLa are work rate and the change of arterial lactate concentration, respectively and γ and φ are proportionality constants. The temporal pattern of ventilation for a step increase of exercise is biphasic and is described by the following equations:

$$\begin{aligned} \tau_i \frac{\Delta\dot{V}E_i(t)}{dt} + \Delta\dot{V}E_i(t) &= \mu \cdot \Delta\dot{V}E_{ss} \\ \tau_f \frac{\Delta\dot{V}E_f(t)}{dt} + \Delta\dot{V}E_f(t) &= (1-\mu) \cdot \Delta\dot{V}E_{ss} \cdot e^{TDf} \\ \Delta\dot{V}E(t) &= \Delta\dot{V}E_i(t) + \Delta\dot{V}E_f(t) \end{aligned} \quad \textbf{(10)}$$

Equation (10) has a structure that is similar to the response for cardiac output (see section 0 for meaning of several symbols).

2.3. Model parameters

Table 1 displays parameter values as they are used in the model. Fundamental time constants for O_2 uptake and ventilation and the time constant of muscle CO2 storage are selected such that the time constants for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ are in ascending order, which corresponds with results found in many investigations [11,17,18,14].

Table 1. Parameter values that are used in the model. See text in Section 0 for meaning of symbols.

Parameter	Unit	Value
Blood flow		
τ_i	s	4
τ_f	s	15
μ	-	0.66
TD_f	s	21
Muscle oxygen consumption		
τ_f	s	32
τ_s	s	150
LT	Watt	125
G_f	-	10
G_s	-	4.5
TD_s	s	180
Muscle CO2 storage		
ρ	-	50
β	-	0.8
RQ	-	0.9
Lactate metabolism		
V_M	litre	8.1
σ_{La}	-	0.55
V_{OT}	litre	26.17
Mixed-venous blood		
TD	s	16
Ventilation		
γ	-	0.1575
φ	-	13
τ_i	s	4
τ_f	s	49
μ	-	0.17
TD_f	s	21
Other assumptions		
Body temperature (T)	^oC	37
Barometric pressure (PB)	mmHg	760

3. Simulation Results

The model has been tested using an incremental exercise stimulus of 30 W/minute from the base line of unloaded exercise. The simulation results are compared with the experimental results presented in [19] and both results are depicted in the figures below.

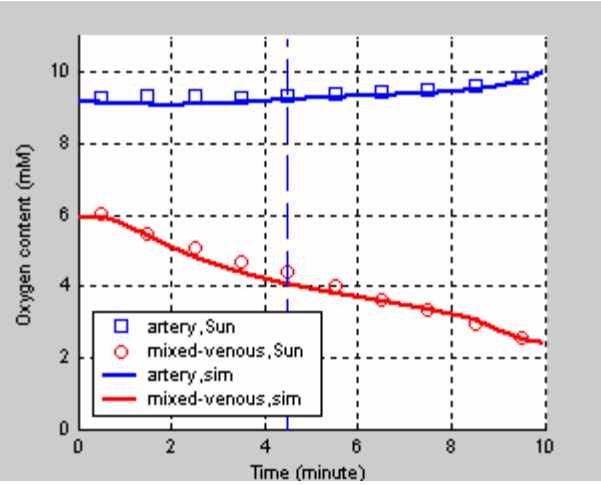

Figure 4. Simulation result for blood O_2 content in artery (blue line) and mixed-venous (red line); square and circle points are experimental results for O_2 content in artery and mixed-venous, respectively (as presented in [19]); dashed line denotes the time when lactate threshold (LT) is passed.

Figure 4 compares the time histories of blood O_2 content in the artery and mixed-venous pathway from simulation and experiment. The O_2 content difference of the two sites indicates how much O_2 is extracted and utilized in the exercise. **Figure 5** shows the blood CO_2 content in the artery and mixed-venous pathway and this indicates how much CO_2 is stored in blood. The CO_2 content difference also indicates how much CO_2 is produced and released during exercise. **Figure 6** shows the arterial and mixed venous CO_2 partial pressure. The CO_2 partial pressure and CO_2 content indicate the level of metabolic acidosis of the corresponding blood vessels.

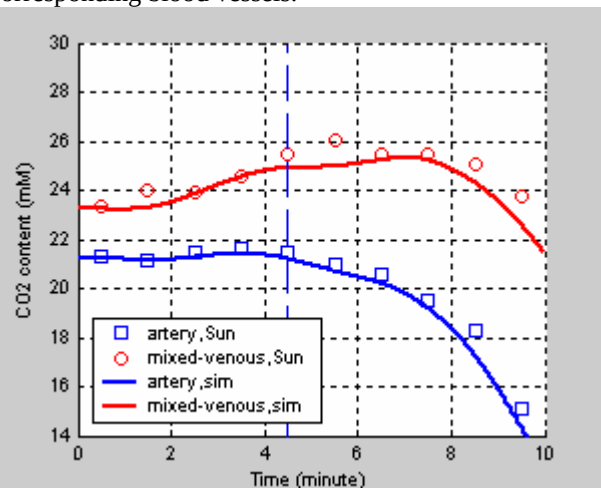

Figure 5. Simulation result for arterial (blue line) and mixed-venous (red line) blood CO_2 content

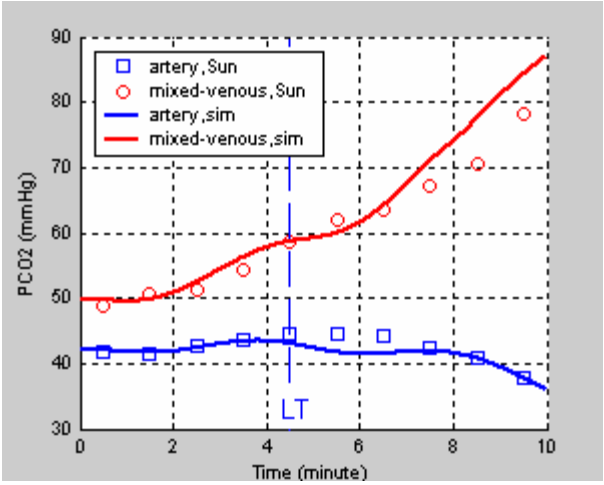

Figure 6. Changes in CO_2 partial pressure during incremental exercise.

4. Discussion

Under rest conditions, the control of breathing serves to maintain the arterial CO_2 and O_2 partial pressures within normal homeostatic levels, typically about 40 mmHg for $PaCO_2$ and 100 mmHg for PaO_2. Two groups of receptors are active within this feedback control system: central and peripheral chemoreceptors. Central chemoreceptors on the surface of the medulla are sensitive to the partial pressure of carbon dioxide (PCO_2) and the acidity (pH level). This group of sensors is responsible for driving 70 – 80% of the ventilation. When the subject inhales 100% oxygen, the respiratory controller produces a level of ventilation that exhibits linearity to $PaCO_2$ [20]. The peripheral chemoreceptors, which lie in the carotid bodies, are sensitive primarily to an increase in $PaCO_2$, a decrease in arterial pH or a decrease in PaO_2. This group of sensors is responsible for driving 20 – 30% of the steady state ventilation at rest.

It is clear that ventilation under rest conditions is controlled by a multiple input single output regulatory feedback control system. In exercise condition, however, there has been no general agreement on which receptors play a significant role in controlling ventilation [21]. During moderate exercise, arterial pH, PCO_2 and PO_2 are essentially unchanged so those quantities are not likely to cause the large changes of exercise ventilation observed experimentally. Extensive researches have been conducted to discover chemoreceptors in potential locations such as the exercising muscle and pulmonary blood vessel but these efforts have been largely unsuccessful.

Without a clear mechanism that can explain ventilatory control response during exercise, mathematical modelling of ventilation controller may only be conducted by introducing relationship between hyperpnoea (the increase of ventilation) and the changes of ventilatory

variables or biochemical quantities in the blood artery that have a high statistical correlation. These variables and quantities include the pulmonary CO_2 production ($\dot{V}CO_2$), arterial potassium concentration and lactate anion.

In the steady conditions of exercise below lactate threshold, ventilation was found to be linearly related to pulmonary CO_2 production [22]. Above lactate threshold, this relation still holds until a point of respiratory compensation where ventilation changes more remarkably [14,23]. Arterial potassium concentration (Ka+) has a very high correlation with ventilation so that Ka+ has been strongly suggested as an agent that stimulates exercise hyperpnoea [24,2], although the pattern of change of Ka+ cannot account for the phenomenon of ventilatory threshold [25].

Beside arterial potassium concentration, lactate anion level may have a role in control of ventilation during strenuous exercise [1] where arterial lactate concentration has a significant correlation with ventilation [2]. The second term of Equation **(9)** has been introduced on this basis and takes effect when the arterial lactate concentration is high, i.e. during strenuous exercise.

Another approach may also be considered, with ventilation being calculated on the basis of the change of work rate. This approach appears to be equally valid in the absence of a convincing hypothesis concerning the real control mechanism of exercise hyperpnoea. The first term of Equation **(9)** described in section 2.2.9 has been developed following this approach and the term will correspond to the magnitude of produced CO_2 if the system attains steady state. Equation **(9)** and **Figure 3** suggest that the ventilation during exercise is apparently regulated in an open loop fashion.

The model is able to reproduce the general behaviour of many variables of the system including the pulmonary oxygen uptake ($\dot{V}O_2$), pulmonary CO_2 output ($\dot{V}CO_2$) and blood O_2 and CO_2 partial pressures. Quantitative assessment of the model is carried out by comparing the system response in terms of output variables generated by simulation with the corresponding time histories of measurements obtained experimentally.

The simulation results appear broadly satisfactory in that several variables show similar trends with experimental results with a few variables showing deviations if examined on the basis of point by point values. The result for blood O_2 content (**Figure 4**) is very realistic suggesting that the model estimates muscle O_2 extraction (and $\dot{V}O_2$) very well. The simulation result for CO_2 content (**Figure 5**) is close to the experimental result except at a few points where isolated experimental values appear to be in error or the simulation has diverged. The results suggest that the model is able to predict that blood CO_2 storage will increase slightly during exercise below the LT but will decrease significantly above the LT. The model is, to some extent, able to estimate the pulmonary CO_2 output.

The simulation result for PCO_2 (**Figure 6**) is close to the experimental result at many points below the LT but it shows deviations at points above the LT. This result suggests that for moderate exercise (below the LT) the model mimics the behaviour of the real system but for heavy exercise, the model needs further improvement. This improvement may involve the respiratory system model, or the controller, or both. Simple functions and conventional forms of model may not be sufficient for an adequate description of the controller. It is possible that approaches based on fuzzy logic might show advantages in this application. For the respiratory model, further study and experimentation is needed to increase our understanding of the behaviour of the respiratory system above lactate threshold. For example, experiments are needed to obtain consistent sets of data relating work rate, arterial lactate concentration, blood gas contents and partial pressures and pulmonary exchange rate over the whole range of exercise conditions.

It is worth noting that the model has a large number of variables and parameters. The model formulation and parameters have been obtained from many published sources involving data obtained from many different subjects in different conditions and using different experimental methods. This poses problems because a model or a parameter value that is valid for one situation may not be valid in other conditions. Ideally, all the data should be acquired from a single set of experiments carried out using consistent conditions using different subjects. Although such data are currently not available, efforts are made to achieve this ideal or at least to provide experimental data sets that include more variables within a single experiment. It is also important to ensure that sufficient data are available to allow the data to be split into data sets used for model development and separate data sets used for external validation of the model. Until that final target is achieved, we may always expect to have imperfect respiratory system models where the simulated response shows significant inconsistencies with experimental results.

5. Conclusions

A model of the respiratory control system during incremental exercise has been described and the simulation results demonstrate interesting similarities with data obtained experimentally. Several variables of the simulation model show a very good response while some others have deviations. The model structure suggests that the control of ventilation is based on negative feedback for rest conditions but appears to be in open loop mode during exercise conditions. Control of ventilation in exercise is dependent on at least two

variables. One variable is proportional to the work rate or to the steady state of pulmonary CO_2 output and another variable is proportional to arterial lactate concentration which resembles blood acidity or the level of exercise metabolic acidosis.

To obtain a better model, improvement can be introduced to the controller or modifications can be made to the respiratory system plant model itself. For the controller it might well be useful to consider incorporating some form of fuzzy controller. For the respiratory model, more studies and experiments are needed in order to obtain a larger and more useful data set from a single form of experiment.

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