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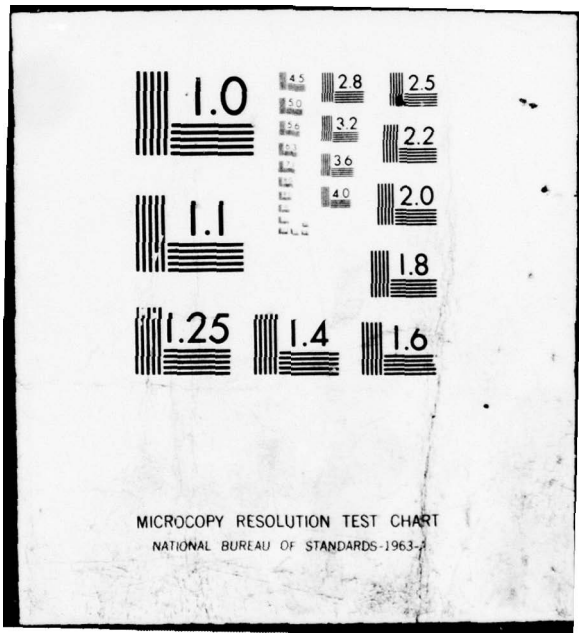
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Report SAM-TR-78-24

GAS EXCHANGE UNDER ENVIRONMENTAL STRESS

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July 1978

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Prepared for

USAF SCHOOL OF AEROSPACE MEDICINE
Aerospace Medical Division (AFSC)
Brooks Air Force Base, Texas 78235

NOTICES

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This report has been reviewed by the Information Office (OI) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

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The purpose of this project was threefold: (1) to assemble available information concerning the effects of various environmental factors such as altitude, acceleration, and breathing gas composition on gas exchange, (2) to initiate a mathematical simulation of gas exchange between atmosphere and tissues that would predict the effects of these factors on gas exchange at rest and during exercise, and (3) to identify areas for future experimental investigation.

A computer model which includes a multi-compartment lung and lumped tissue beds representing brain, heart, muscle, and the remaining tissues was

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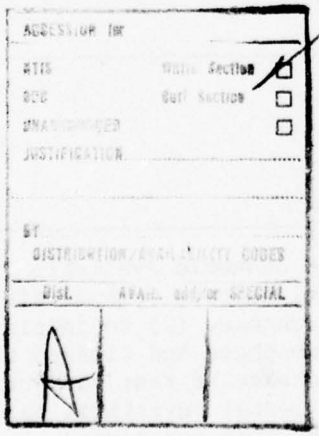
20. ABSTRACT (Continued)
developed. Inputs are barometric pressure, inspired oxygen and carbon dioxide concentrations, carboxyhemoglobin concentration, acceleration in the z vector, and oxygen consumption. Steady state values are calculated for gas exchange parameters in the lungs and in the four tissue compartments. The simulation is designed in a modular fashion to enhance the ability to modify it as additional experimental data become available. The model provides qualitatively accurate predictions of experimental data showing responses to a single stress. Extensive experimental data of responses to multiple stresses with which to compare model predictions are not available. Results with multiple stresses indicate that experimental work aimed at better definition of minute to minute control of ventilation is necessary. Other areas identified for further investigation include effects of acceleration and anti-G protective measures on pulmonary ventilation-perfusion relationships and gas exchange.



GAS EXCHANGE UNDER ENVIRONMENTAL STRESS

INTRODUCTION

Effective performance under altered environmental conditions depends on oxygen supply to critical tissues. This supply may be compromised by any number of variables affecting efficiency of gas exchange between the atmosphere and alveoli, efficiency of gas transfer in the lung, gas transport by blood, and the cardiovascular system's ability to provide adequate perfusion to the tissues. Environmental conditions may have profound effects on each link in the gas transport chain. For example, exchange of oxygen within the lung may be impaired significantly at low barometric pressures or when hypoxic gas mixtures are breathed. Mild hypoxia, when combined with significant levels of inspired carbon monoxide or carbon dioxide, results in decreased blood oxygen content and hence decreased oxygen delivery (50). Acceleration is another stress that influences gas transport. Zechman and coworkers (69) have shown a decrease in tidal volume, an increase in respiratory rate, and an increase in minute volume with exposure to increased gravitational forces. Watson and his colleagues (62) have shown decrements in total lung capacity and vital capacity of 20%-30% at relatively low levels of G exposure. Although these changes might not be expected to impair gas transport per se, they are accompanied by an increase in the total work of breathing (62). Arterial oxyhemoglobin saturation has been shown to decrease during acceleration secondary to changes in the distributions of ventilation and pulmonary perfusion (59). Although studies which have focused on the effects of environmental factors on gas exchange appear in the literature, no comprehensive analyses have been performed which include interrelated effects of altitude, acceleration, and inspired concentrations of oxygen, carbon dioxide, and carbon monoxide on oxygen delivery.

The purpose of this effort was threefold: 1) to assemble available information concerning the effects of the aforementioned environmental variables on gas exchange, 2) to initiate a mathematical simulation of gas exchange between atmosphere and tissues that would provide a vehicle for predicting the effects of these environmental factors at rest and during exercise, and 3) to identify areas for future experimental investigation.

GENERAL MODEL DESCRIPTION

Because this model was a first attempt to incorporate a large volume of information into a complete gas exchange system designed to be modified as new data become available, it was decided that only the steady state would be considered initially and that the final simulation should consist of a series of "stand-alone" building blocks. The model includes a lung and lumped tissue beds representing brain, heart, skeletal muscle, and the remaining tissues. Figure 1 is a flow diagram

of the model showing its major features. Inputs are barometric pressure, inspired oxygen and carbon dioxide concentrations, carboxyhemoglobin concentration, acceleration in the z vector, and oxygen consumption. Initial values are chosen for heart rate, stroke volume, respiratory frequency, and tidal volume. The cardiac output and alveolar ventilation are then distributed within a nine-segment vertical lung taking into account gravitational effects on these distributions. Regional ventilation-perfusion ratios are then calculated, and, using this information along with inspired gas tensions and initially assumed mixed venous gas tensions, gas exchange within each lung segment is calculated. Regional ventilation, perfusion, gas tensions, and blood oxygen and carbon dioxide contents are used to calculate mixed alveolar gas tensions and mixed arterial blood gas values. Alveolar and arterial gas tensions are then used as input information to the respiratory controller to determine minute ventilation. Cardiac output is distributed to the lumped tissue compartments, oxygen consumption is partitioned among these compartments, and venous blood gas composition from each is determined. Using flows through each tissue compartment and blood gas content from each, mixed venous blood gas values are calculated, thereby completing the iteration. The model continues to iterate until calculated values for two iterations are within preset tolerance limits (minute ventilation within 25 ml/min).

SPECIFIC MODEL DESCRIPTION

Utility Block

The utility block of the model (block 1 in Figure 1) handles the input-output functions and determines cardiac output and alveolar ventilation from oxygen consumption and minute ventilation, respectively. It further divides cardiac output into stroke volume and heart rate and divides alveolar ventilation into alveolar tidal volume and respiratory frequency.

It is well established that cardiovascular response to upright exercise is related to maximal oxygen consumption rather than the absolute work load (8, 54). Cardiac output is therefore related to oxygen consumption expressed as percent maximal oxygen consumption. Maximal oxygen consumption in the model is assumed to be 3.5 L/min. Heart rate and stroke volume are determined from the relationship reported by Astrand and his associates (1).

Milic-Emili and Cajani (34) determined the tidal volume-frequency relationship over a wide range of minute ventilations. Assuming an anatomical dead space of 150 ml, we used Milic-Emili and Cajani's data to obtain alveolar tidal volume-frequency relationships over a wide range of alveolar ventilation (see Table 1).

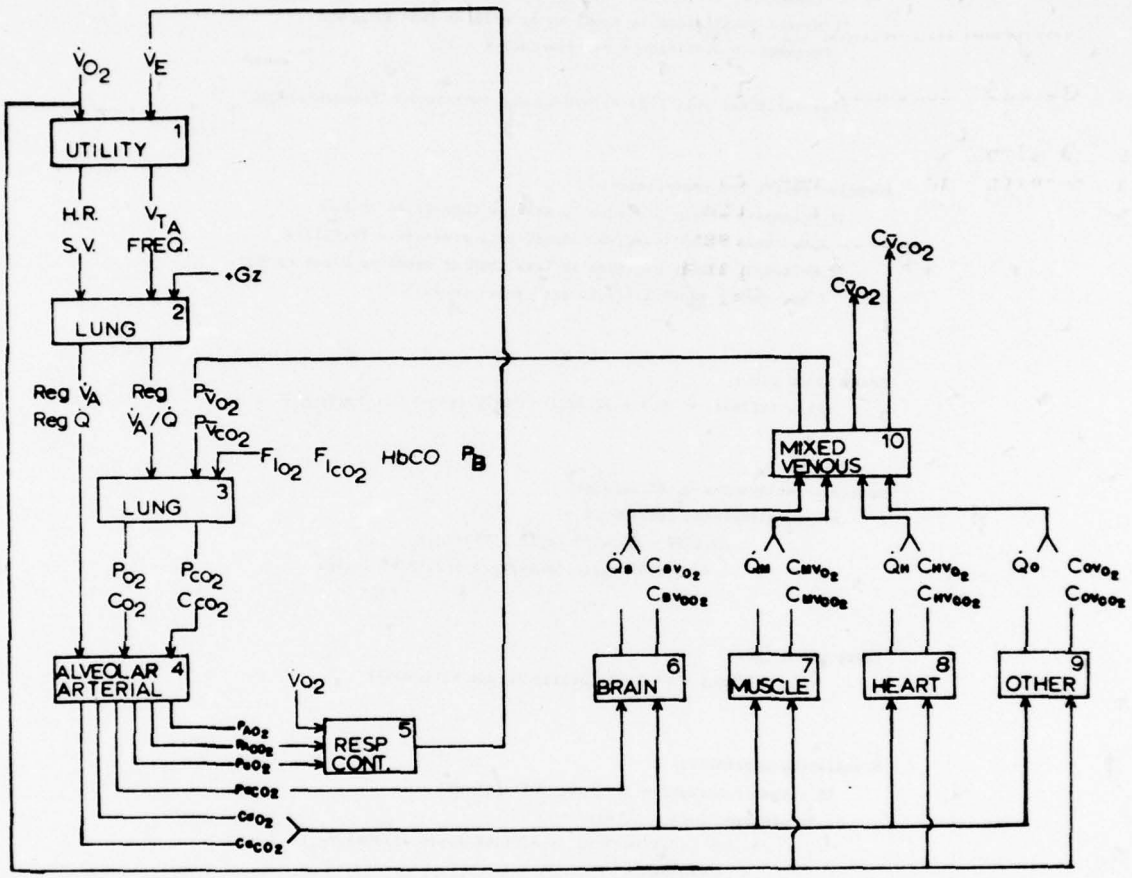


Figure 1. Schematic representation of the model.

TABLE 1. KEY EQUATIONS USED IN MODEL

Ventilation - breathing frequency relationships:

If minute ventilation is less than 67 L/min

$$\text{Frequency} = 6.25(\text{minute ventilation})^{0.34}$$

If minute ventilation is equal to or greater than 67 L/min

$$\text{Frequency} = 0.35(\text{minute ventilation}) + 1.14$$

$$\text{Alveolar tidal vol. (ml)} = 1000(\text{minute ventilation/frequency}) - 150$$

Alveolar vessel bed conductance:

If pulmonary artery pressure is greater than 27.44 cm H_2O

$$\%\text{ bed open} = 100(1-\exp(-0.46(\text{pul. art. pressure} - 24.817)))$$

If pulmonary artery pressure is less than or equal to 27.44 cm H_2O

$$\%\text{ bed open} = \exp(0.131(\text{pul. art. pressure} + 5))$$

Brain blood flow:

$$\text{Flow (ml/min)} = 20.9 + 92.8/(1 + 10570 \exp(-5.251 \log Pa_{CO_2})$$

Muscle arteriovenous O_2 difference:

$$\text{a-v } O_2 \text{ difference (ml/100ml)} = 29.0799 - 36.4279 \exp(1.07786/\dot{V}_{O_2}) + 10.0393 \exp(1.58099/\dot{V}_{O_2}) + 2.95798 \log \dot{V}_{O_2}$$

Heart blood flow:

$$\text{Flow (ml/min)} = 3(11.46 \text{ cardiac output} + 11.9039)$$

Ventilatory controller:

If oxygen consumption is above 50% maximum

$$\text{Minute ventilation (L/min)} = 16.1887 - 0.266675\ \dot{V}_{O_2} + 8.04466 \exp(0.0273085\ \dot{V}_{O_2}) + 50000/(Pa_{O_2})^3$$

If oxygen consumption is equal to or less than 50% maximum

$$\text{Minute ventilation (L/min)} = 3.8(P_{CO_2}-37.24)(1 + 13.6/(P_{O_2}-25)) + 50000/(P_{O_2}-25)^3$$

Oxygen dissociation curve:

$$\text{Saturation} = (1 - \exp(-2.3\ A\ P_{O_2}))^2$$

where $A = 0.02272 \exp((30 - P_{CO_2})/115)$

CO_2 dissociation curve:

$$CO_2 \text{ content (ml/100ml)} = (14.9 - 1.65\ S_{O_2})\ P_{CO_2}^{0.35}$$

Lung Mechanics

The lung (blocks 2 and 3 in Figure 1) is considered to be 27 cm in height and is divided into nine horizontal segments of equal depth. Each segment contains a pulmonary artery component, an alveolar vessel bed which behaves as a group of Starling resistors (2, 43, 66), and a pulmonary vein component. At 1 G conditions, a pleural pressure gradient of 6.75 cm H_2O is assumed to exist from lung apex to base (35). Regional total lung capacity was determined by assuming a total lung capacity of 6 liters and distributing this volume among the nine segments according to the data of West and Dollery (64). Lung volume in the model is expressed as percent regional total lung capacity. Since the lung is considered homogeneous in its mechanical properties, each segment is assumed to rest on a common pressure-volume curve (23, 36). The pressure-volume relationship used is shown in Figure 2. Note that airway closure occurs at a regional lung volume of approximately 20% (36).

The distribution of ventilation is affected significantly by gravity (23) and, hence, by additional acceleration imposed (5, 13). Before the distribution of tidal volume is determined in the model, functional residual capacity is calculated. Bryan and his associates (5) examined the effects of positive acceleration on distribution of ventilation and determined that a point exists approximately 13 cm from the top of the lung where regional volume remains constant regardless of acceleration (iso-volume point). If this is the case, an iso-pressure (transpulmonary pressure) point must also exist at the same level regardless of the acceleration. It is assumed that this point occurs in the 5th lung segment in our model and that transpulmonary pressure at this point is 8.45 cm H_2O at FRC. Since the intrapleural pressure gradient is assumed to be .25 cm H_2O/cm/G (23, 35), the transpulmonary pressure at each segment can be calculated at each G level, and, using the pressure-volume diagram shown in Figure 2, FRC may be calculated. After calculating FRC and alveolar tidal volume, regional ventilation is calculated through an iterative process. Total end-tidal volume is calculated, and the corresponding transpulmonary pressure is determined. Lung compliance in the tidal volume region is then calculated using the FRC and end-tidal values. An initial guess is made for the transpulmonary pressure at end-inspiration at the top of the lung. Regional volume changes are calculated and compared with the "true" alveolar tidal volume. If the calculated tidal volume is not within 2 ml of the required tidal volume, a new guess is obtained from the error signal and the calculated compliance using a secant method of approximation. The loop repeats until the tolerance is met. Regional tidal volume is then multiplied by respiratory frequency to obtain regional ventilation. If any region of the lung is below its respective closing volume, it receives no ventilation.

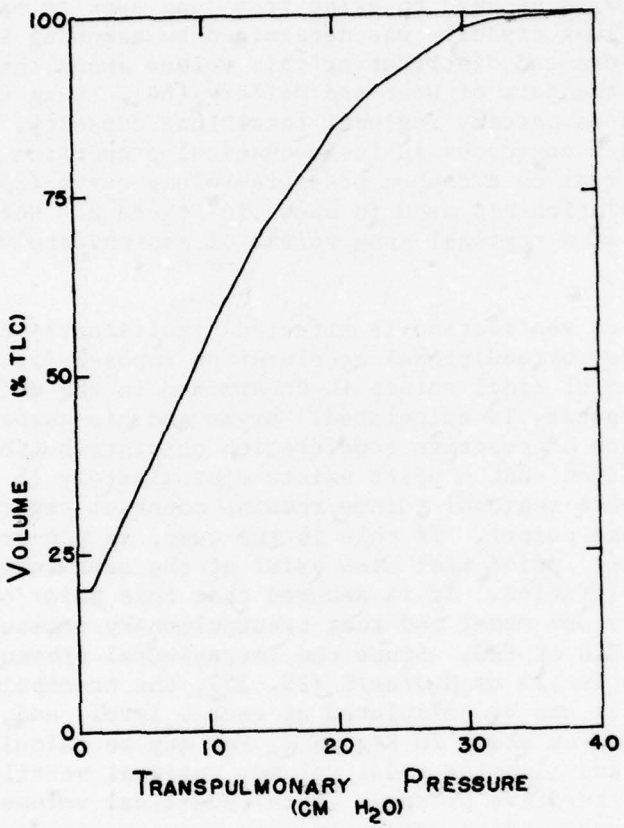


Figure 2. Pressure-volume curve used in the model.

Pulmonary Circulation

The pulmonary circulation is represented by a pulmonary artery compartment, alveolar vessel bed, and a pulmonary vein. The pulmonary artery is treated as a distensible compartment. Neglecting the compressibility of blood, arterial volume is dependent upon an initial volume and the integral of the difference between inflow and outflow. The transmural pressure of the compartment is given by the equation

$$Ptm = (1/C)\ (Q - Qu)$$

where C is the compliance and Qu is the unstressed volume (i.e., the volume at which Ptm is zero). Flow into the pulmonary artery is treated as a rectified sine wave with appropriate amplitude and period to provide the necessary stroke volume and heart rate. The unstressed volume of the pulmonary artery is assumed to be 37.1 ml (37), and the pulmonary artery compliance is assumed to be 2.286 ml/cm H_2O (37). The intrapleural pressure assumed to be acting on the pulmonary artery is the arithmetic mean of the intrapleural pressures of segments 6,7, and 8 at FRC. By using this information, pressure in the pulmonary artery at the entrance to the lung is calculated. Pulmonary artery pressure at the level of each segment is then calculated by correcting the main pulmonary artery pressure for the hydrostatic effects of gravity.

The alveolar vessel bed is considered to behave as a population of Starling resistors. The inlet pressure to this bed is the pulmonary artery pressure at the level of the respective segment. Pressure surrounding the vessels is alveolar pressure, and pressure at the outlet of the segment is pulmonary venous pressure corrected for hydrostatic forces acting at the level of the segment. Flow through a segment depends upon the relationship between these three pressures and a conductance term.

Since each segment of this bed contains a population of vessels, the conductance must reflect the effects of this population. Permutt et al. (44) have demonstrated that recruitment of vessels in the alveolar bed occurs as inlet pressure increases. Other investigators interpret this flow increase as distension of the bed (65, 66). Regardless of the exact mechanism, it is well established that conductance of the alveolar bed increases with increasing pulmonary artery pressure (2, 43, 44, 65, 66). In addition, Bruderman et al. (4) have shown that alveolar pressure is not completely transmitted to the alveolar vessels in air-filled lungs. In order to arrive at a conductance curve which reflects these observations, the following considerations were made. It was assumed that the entire alveolar bed is open during conditions of maximum flow through the lung at 1 G and that approximately 20% of the bed is open at resting cardiac output. Data are available in the literature which allow calculation of the mean transmural pressure of the alveolar bed under both of these conditions. Hence, two points may be obtained relating conductance through the alveolar bed to transmural

pressure of that bed. A third point may be obtained from the observation of Bruderman et al. (4) that flow ceases at a transmural pressure of -5 cm H_2O. For this model, these points were empirically fit to obtain an S-shaped curve relating conductance through the alveolar bed to its transmural pressure (see Table 1).

Pulmonary venous pressure at the level of the left atrium is assumed to be approximately 5 cm H_2O at all times. Pulmonary venous pressure at each segment of the lung is determined by correcting this value for hydrostatic effects due to gravitational force.

Flow through any segment is determined by the pulmonary artery-alveolar-pulmonary venous pressure relationships at that level. If alveolar pressure is greater than pulmonary artery pressure, no flow occurs through the segment. If pulmonary artery pressure is greater than alveolar pressure which is greater than pulmonary venous pressure, flow is determined by the pressure difference between pulmonary artery and alveolar pressures and the conductance which is also a function of that pressure difference. If pulmonary artery and pulmonary venous pressures are greater than alveolar pressure, the flow is determined by the difference in these two pressures and the conductance determined by the pulmonary artery-alveolar pressure difference.

Pulmonary Gas Exchange

To determine the extent of pulmonary gas exchange, mean alveolar ventilation and perfusion for each lung segment, calculated in the lung mechanics and pulmonary perfusion blocks, are used to calculate mean regional ventilation-perfusion ratios. The classic ventilation-perfusion line drawn on an O_2-CO_2 diagram (45) is the vehicle by which gas tensions in each lung segment are determined. An initial value for R is chosen, and blood and gas R lines are "drawn" from the mixed venous and inspired gas points for that value. When the intersection of the blood and gas R lines is encountered, the ventilation-perfusion ratio consistent with that point is calculated. This value is then compared to the ventilation-perfusion ratio for the respective segment. If these values are not within preset tolerance limits (0.02 $\dot{V}_A/\dot{Q}$), a new R value is chosen, and the process is repeated.

After gas tensions in each segment have been determined, mixed alveolar gas tensions and arterial blood gas status are calculated. The blood-gas routines used in conjunction with this block are described below.

Blood Gas Routines

Several mathematical descriptions of the oxyhemoglobin and CO_2 dissociation curves appropriate to this model are available in the

literature (11, 24, 31, 42, 56, 57). Since we viewed this model as an attempt to establish a framework around which future refinements could easily be made, we sought equations which incorporated the interactions of O_2 and CO_2 on blood gases and in which calculation of tensions from contents would be no more time consuming than calculating contents from tensions. Visser and Maas (57) described the oxyhemoglobin dissociation curve by a single equation of exponential form that included the influence of CO_2 on oxygen saturation. A form of this equation is used in this model to determine oxyhemoglobin saturation (see Table 1). The equation describing the CO_2 dissociation curve is based on that reported by Denison (11) and includes the influence of oxyhemoglobin saturation on CO_2 content (see Table 1). These equations conform to both of our criteria.

The influence of carbon monoxide on the oxyhemoglobin dissociation curve is also included in the model. To do this, a procedure similar to that described by Roughton (50) was incorporated into the blood-gas routines. In this procedure, the effect of CO on oxygen affinity by hemoglobin is determined by plotting the oxyhemoglobin dissociation curve of the hemoglobin not combined with CO. The resulting curves are shifted to the left reflecting the increased oxygen affinity.

Control of Ventilation

One difficulty encountered in developing this model was finding an appropriate means of simulating the control of ventilation. Numerous studies have been reported describing ventilatory response to a given set of circumstances such as inspired CO_2, exercise, and acid-base disturbances (9). There have been no studies, however, that provide sufficient information to develop a set of ventilatory controller equations that will predict minute ventilation under a wide variety of challenges. We assumed, for the purposes of this model, that if we could arrive at a set of controlling equations that would describe the ventilatory response to steady state dynamic exercise, it would suffice for the additional environmental challenges.

Several types of controllers were tested in an attempt to simulate steady state ventilatory response to exercise (10). Alveolar and arterial P_{CO_2} were taken into account as well as the metabolic acidosis resulting from lactate production at high levels of exercise. We were unable to simulate the overall response with a single equation relating these variables. We used two equations to describe minute ventilation (see Table 1). When oxygen consumption is less than or equal to 50% of maximum, an equation of the form described by Lloyd and Cunningham (30) with an additional term describing the response to low oxygen is used. Reference values for oxygen and CO_2 are those used by Milhorn and Brown (33). At oxygen consumption levels above 50% of maximum, minute ventilation is a function of oxygen consumption. This provides a good approximation to data reported by Dejours (10). Most experimental data

relate ventilation to alveolar P_{CO_2}. Hence, in the model, alveolar P_{CO_2} provides the controller error signal when oxygen consumption is in the lower range unless the arterial-alveolar P_{CO_2} difference is greater than 5 torr (e.g., as a result of marked ventilation-perfusion maldistribution) in which case arterial P_{CO_2} provides the error signal.

Lumped Tissue Compartments

The lumped tissue beds represent brain, heart, skeletal muscles, and the remainder of the tissues. The beds are treated from a gas exchange standpoint only, and hence, are each characterized by a flow, an oxygen consumption, and a CO_2 production. Venous gas tensions are assumed to reflect tissue gas tensions in the respective bed. Because of these limitations, the hydrostatic effects of acceleration on tissue bed flow is not considered in the present version of the model. It is assumed that flow in each case is maintained regardless of the level of acceleration. To correct for cardiac output changes in response to acceleration, it is assumed that a cardiac output corresponding to a heart rate of 155 beats per minute is achieved at +5 G and maintained at higher levels of G (7).

Blood flow to the brain compartment is regulated in response to arterial P_{CO_2} and oxygen delivery. Reivich (48) empirically fit a curve describing cerebral blood flow (ml/min/100 gm) as a function of arterial P_{CO_2}. For the model, the brain was assumed to weigh 1500 gm (21) and Reivich's equation was modified to provide total flow as a function of arterial P_{CO_2} (see Table 1). This equation serves as the primary control for brain blood flow. If venous (assumed to reflect tissue) P_{O_2} falls below approximately 10 Torr (corresponding to 2 ml oxygen/100 ml blood), flow is increased to increase oxygen delivery. It is generally accepted that brain metabolism remains fairly constant at approximately 3.5 ml oxygen/min/100 gm (19). Since we have assumed that brain weight is 1500 gm, the oxygen consumption of this bed is assumed to be 52.5 ml/min at all times. Glucose serves as the brain's primary nutrient. Hence, the respiratory quotient of the brain is assumed to equal 1 in the model.

An expression for myocardial flow as a function of cardiac output was derived as follows. Gregg and his associates (16, 17, 25, 46) and Wirthlin and Beck (68) studied coronary flow in dogs under a variety of conditions. In those studies, left circumflex arterial or left main coronary arterial flow was measured. Wirthlin and Beck also expressed their data in terms of flow/100 gm heart muscle. Using this data and the assumption that 85% of total coronary flow is through the left main coronary artery and 50% of the total is through the left circumflex artery (55), we related all the data from these studies to heart weight and derived an expression for total coronary flow/100 gm heart weight as a function of cardiac output. We then scaled this relationship to humans, and, assuming that the heart weighed 300 gm (21), we arrived at

an expression for myocardial blood flow as a function of cardiac output (see Table 1). As was the case with brain flow, if venous oxygen content from this compartment falls below 2 ml/100 ml blood, cardiac output is increased to increase oxygen delivery. It is assumed in the model that the heart extracts 75% of the oxygen delivered to it, although this value may be slightly high for man (19). According to Guyton (19), about 75% of the normal cardiac metabolism is derived from fatty acids. Van Citters (55) gives a figure of 60% from fatty acids and about 35% from carbohydrates. If this is the case, the respiratory quotient for the heart should range from approximately 0.78 to 0.81. We have assumed that the respiratory quotient for the heart remains at 0.8 under all circumstances.

Control of flow through the muscle compartment is handled somewhat differently from either brain or heart. Available data relating blood flow to muscle oxygen consumption do not extend to the metabolic ranges encountered in this model and do not provide adequate means of predicting flow in those ranges. Rather than controlling flow per se, we derived a relationship between muscle arteriovenous oxygen content difference and percent maximal oxygen consumption. Data were pooled from studies by Rowell (52), Reeves et al. (47), and Saltin et al. (53) in which femoral arteriovenous oxygen content differences were reported for a wide range of oxygen consumptions, and a least squares curve was fit to the data (see Table 1). By using the Fick equation with the calculated a-v oxygen difference and muscle oxygen consumption, flow through the bed is determined. Muscle oxygen consumption is assumed to equal the total body oxygen consumption minus the resting oxygen consumption of the remaining body tissues (assumed to be 240 ml/min). Data are not readily available relating the respiratory quotient of muscle to a wide range of oxygen consumptions. Issekutz and his associates (22) proposed a predictor of maximal oxygen consumption from submaximal exercise based on measurement of total body gas exchange ratio (R). We used percent maximal oxygen consumption as an input to this predictor and calculated corresponding R's. Assuming the major change in R resulted from muscle metabolism at increased levels of metabolism, we obtained a linear relationship between muscle R and muscle oxygen consumption. These relationships are used in the model to characterize gas exchange in the muscle compartment. As in the other beds, flow to the compartment is increased if venous oxygen content falls below 2 ml oxygen/100 ml blood.

Flow to the "other" tissue compartment is derived by subtracting the combined flows to brain, heart, and muscle from the total cardiac output. Similarly, oxygen consumption of this bed is equal to the total oxygen consumption minus the sums of brain, heart, and muscle oxygen consumption. The respiratory quotient of these tissues is assumed to equal 0.8 at all times.

Mixed Venous Blood Composition

Mixed venous blood-gas composition is a flow-weighted average of blood-gas compositions leaving the four tissue compartments. The calculated mixed venous point is then used in determining pulmonary gas exchange during the next iteration (block 3, Figure 1).

A complete listing of the model with accompanying symbol table and annotation may be found in Appendix A of this report.

RESULTS AND DISCUSSION

Comparison of model results with experimental data suggests that development of a simulation that is accurate under a wide variety of conditions requires more information than is presently available. Since this effort was designed to achieve a framework around which future refinements may be incorporated as new data are acquired, comparison with available data will stress qualitative rather than quantitative agreement.

Values obtained from the model for a resting individual at sea level breathing room air are presented in Table 2. Note that these values are consistent with normal resting values, and that the alveolar-arterial oxygen tension difference is approximately 10 Torr reflecting the normal ventilation-perfusion maldistribution.

TABLE 2. MODEL RESULTS FOR RESTING MAN

$\dot{V}_{O_2}$ = 0.3 L/min	$\dot{V}_{CO_2}$ = 0.26 L/min
$\dot{V}_E$ = 7.77 L/min	$\dot{V}_A$ = 5.73 L/min
$\dot{Q}$ = 4.99 L/min	
$P_{A_{O_2}}$ =105.8 Torr	$P_{A_{CO_2}}$ = 38.9 Torr
Pa_{O_2} = 96.2 Torr	Pa_{CO_2} = 41.3 Torr
Ca_{O_2} = 20 ml/100 ml	Ca_{CO_2} = 48.9 ml/100 ml
Sa_{O_2} = 97.9 %	
$P\bar{v}_{O_2}$ = 40.3 Torr	$P\bar{v}_{CO_2}$ = 49.9 Torr
$C\bar{v}_{O_2}$ = 14 ml/100 ml	$C\bar{v}_{CO_2}$ = 54.1 ml/100 ml
$S\bar{v}_{O_2}$ = 68.9 %	

Response to Exercise

Cardiopulmonary responses to steady-state exercise have been reviewed by Rowell (51) and Wasserman and Whipp (61). Mechanisms responsible for the ventilatory response to exercise have not been elucidated. Changes in minute ventilation depend not only on work load (i.e., metabolic level) but also on such variables as the type of exercise being performed (e.g., short stressful vs. prolonged dynamic exercise) and the muscle groups involved (e.g., leg vs. arm exercise) (61). In general, minute ventilation increases as oxygen consumption and CO_2 production increase. Arterial oxygen and carbon dioxide tension remain nearly constant until 50% to 60% of maximal oxygen consumption, when carbon dioxide tensions decrease from a disproportionate increase in minute ventilation (10, 61). Figure 3 shows a comparison of experimental data (10) and model results relating minute ventilation and arterial P_{CO_2} to oxygen consumption. In this respect the model provides a good prediction of experimental data.

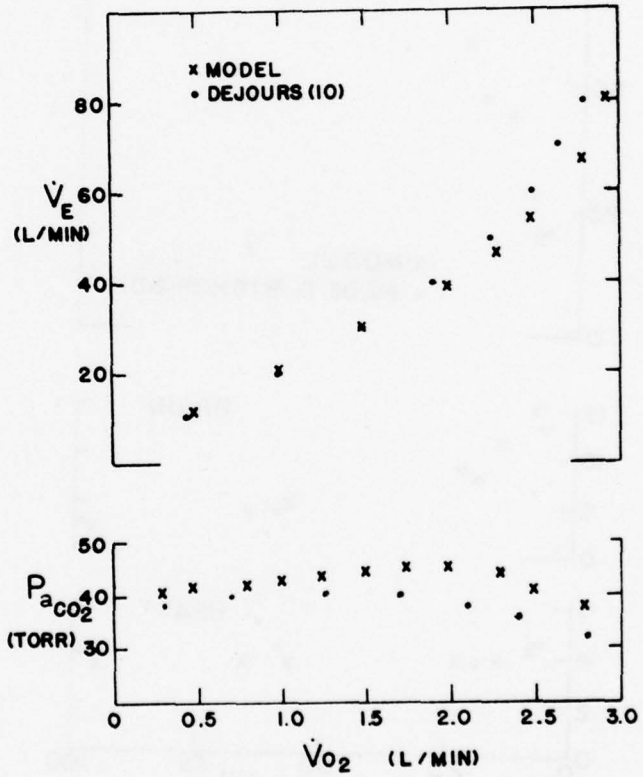


Figure 3. Comparison of model data with experimental data of Dejours (10).

The cardiovascular response to increased workload includes an increase in cardiac output and a redistribution of flow within the system. Splanchnic blood flow decreases to about 20% of its resting value and renal blood flow decreases to about 40% of its resting value as oxygen consumption increases from rest to the maximal level (18, 51). Flow is redistributed, increasing muscle blood flow, thereby providing increased oxygen delivery as muscle oxygen consumption increases. Data from Wade and Bishop (60) relating blood flow distribution to oxygen consumption are compared to results from the model in Figure 4. The model provides a good prediction of redistribution of blood flow during exercise. Note that, in relative terms, flow to the heart appears to remain constant or decrease slightly as oxygen consumption increases.

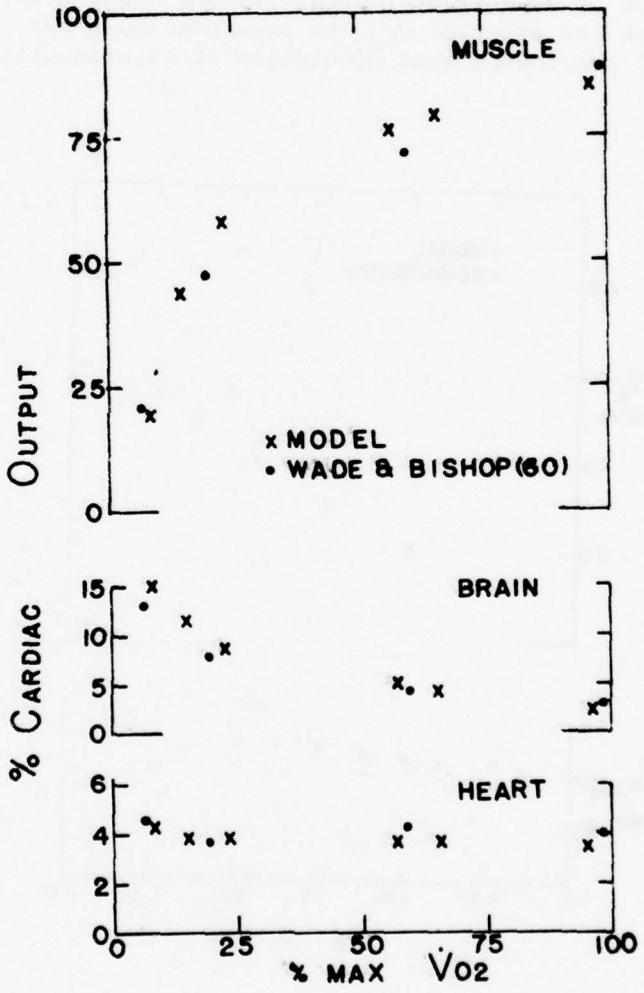


Figure 4. Comparison of model data with experimental data of Wade and Bishop (60).

Coronary blood flow has been shown to be related to myocardial oxygen consumption (3). Heart blood flow in the model is shown in absolute terms in Figure 5. As myocardial oxygen consumption increases, flow increases nearly linearly (39).

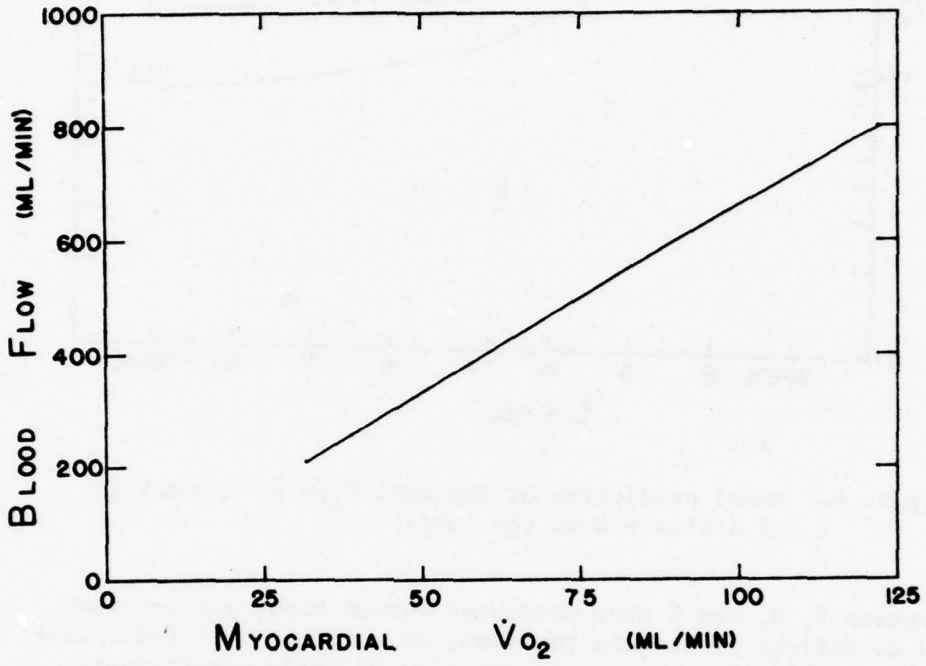


Figure 5. Model prediction of blood flow to the heart as a function of myocardial oxygen consumption.

Another model prediction that may be compared to experimental data is the distribution of pulmonary ventilation-perfusion relationships. Harf and his colleagues (20) have demonstrated with radioactive gas techniques that regional blood flow increases to the apices of the lung during exercise, thus yielding a better matching of ventilation and perfusion. Predictions of regional $\dot{V}_A/\dot{Q}$ at rest and at two levels of exercise are shown in Figure 6. These results are also consistent with data reported in the literature (20).

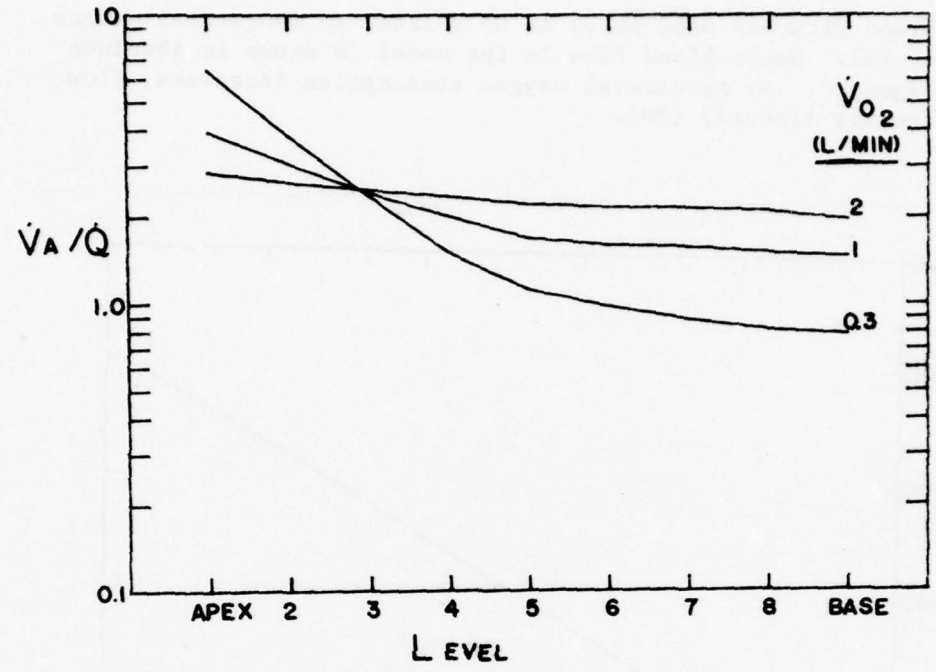


Figure 6. Model prediction of regional $\dot{V}_A/\dot{Q}$ as a function of distance down the lung.

Figures 7, 8, and 9 show predicted venous blood gas tensions, assumed to reflect tissue gas tensions, as a function of total body oxygen consumption for the muscle, heart, and brain compartments, respectively. Of particular interest in these plots is the venous P_{CO_2} as CO_2 production increases. As would be expected, the P_{CO_2} in each bed increases as metabolism increases until approximately 60% of maximal oxygen consumption. At this point, it begins to fall. The fall in P_{CO_2} corresponds to the disproportionate increase in minute ventilation seen at 50%-60% maximal oxygen consumption (see Fig. 3). Hence, at this point, arterial P_{CO_2} also begins to drop, and the tissue P_{CO_2} follows. The model predicts that brain P_{O_2} also begins to drop at this point (Fig. 9). The primary controller of brain blood flow in the model is arterial P_{CO_2}. Hence, as arterial P_{CO_2} falls, brain blood flow also decreases. Since brain metabolism is assumed to remain constant, oxygen extraction must increase, thus resulting in a lowered P_{O_2}.

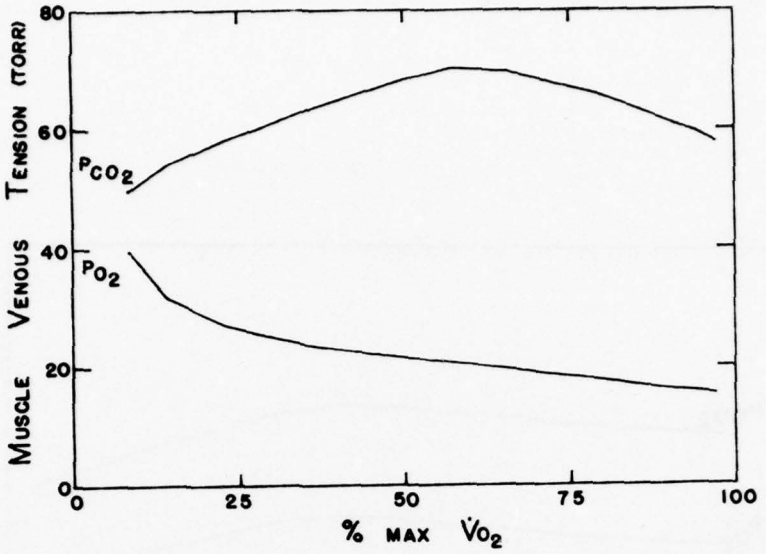


Figure 7. Model prediction of muscle venous blood gas tensions as a function of total body oxygen consumption.

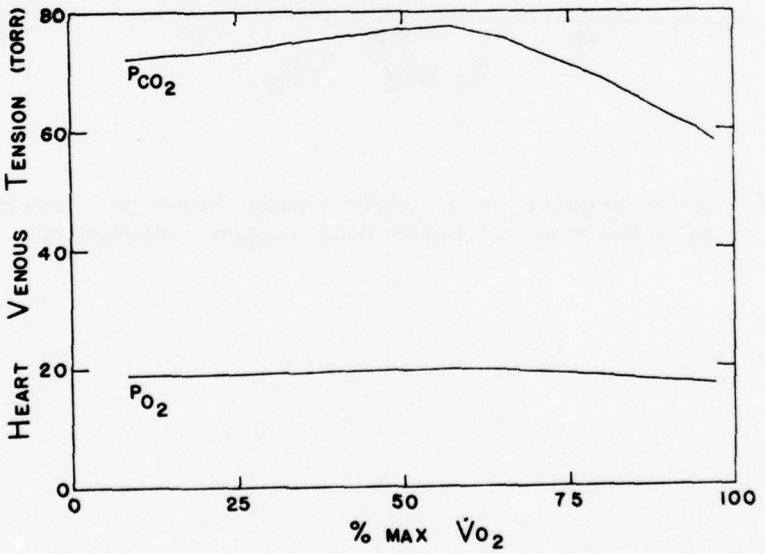


Figure 8. Model prediction of heart venous blood gas tensions as a function of total body oxygen consumption.

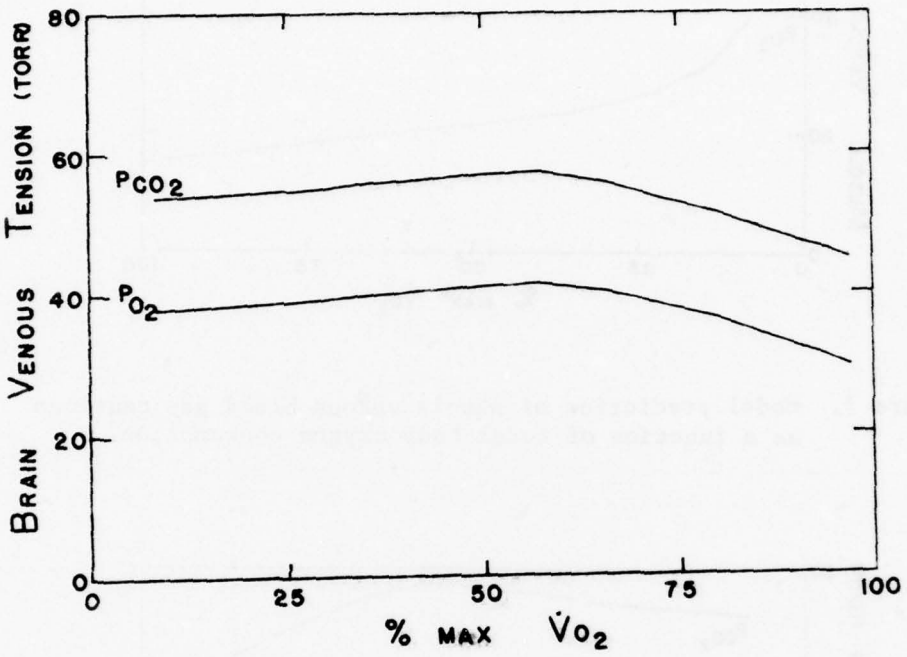


Figure 9. Model prediction of brain venous blood gas tensions as a function of total body oxygen consumption.

Response to CO_2

The response of the respiratory system to inspired CO_2 has been well documented (9). This response depends not only upon alveolar CO_2, but also upon the alveolar oxygen tension (40). Despite variability of the magnitude of the CO_2 response among subjects, the general shape of the response curve is similar (26). Figure 10 shows the model predicted response to inspired levels of CO_2 up to 5%. Lambertsen (27) summarized the respiratory response to increased CO_2 observed by a number of investigators. Results from the model far exceed the average response reported in this summary. However, when compared to data from Lambertsen's experimental studies (26) and from Nielsen and Smith (40), the response predicted by the model is of the same order of magnitude. The constants governing the ventilatory controller in this simulation were chosen in an attempt to simulate ventilatory changes seen during exercise. The comparison of responses to CO_2 breathing suggests that control of ventilation during exercise and CO_2 breathing is governed by more complex mechanisms.

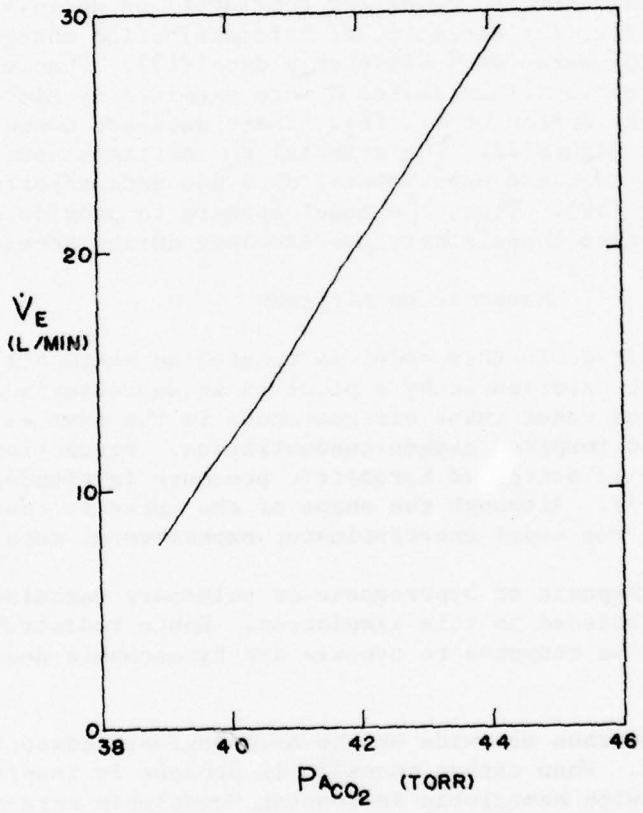


Figure 10. Model predicted ventilatory response to inspired carbon dioxide.

Response to Acceleration Stress

The effects of gravitational stress on cardiopulmonary function have been reviewed recently by Glaister (13, 14) and Burton et al. (6). During exposure to acceleration, increased hydrostatic forces result in pooling of blood in dependent regions of the cardiovascular system. To minimize these effects, a number of protective measures are commonly used. These include anti-G suits which restrict flow to the extremities and a voluntary straining maneuver (M-1) which performs the same function and increases intravascular pressure through an increase in intrathoracic pressure (6). Since this simulation does not include the systemic vasculature, effects of acceleration on the systemic circulation can not be examined.

Overall gas exchange detriment resulting from acceleration is due to decreased oxygen delivery secondary to both gravitational effects on the systemic circulation and decreased arterial P_{O_2}. The decreased arterial P_{O_2} results from an increased maldistribution of ventilation-perfusion ratios in the lung. Glaister (13) used radioactive gas techniques to examine the distribution of $\dot{V}_A/\dot{Q}$ as a function of acceleration up to accelerations of +3 G_z. $\dot{V}_A/\dot{Q}$ distributions obtained from the model for accelerations up to +9 G_z are shown in Figure 11. The direction of maldistribution changes predicted by the model agree with Glaister's data (13). Changes in arterial P_{O_2} as a function of increased G were examined by Michaelson (32) and summarized by Burton et al. (6). These data are compared to model predictions in Figure 12. The arterial P_{O_2} detriment predicted by the model is similar to these experimental data and data reported by von Nieding and Krekeler (59). Thus, the model appears to provide a good approximation to changes in pulmonary gas exchange during acceleration.

Response to Altitude

Response to altitude in this model is treated as acute altitude exposure such as that experienced by a pilot in an unpressurized aircraft. Ventilation under these circumstances is the same as during exposure to decreased inspired oxygen concentration. Prediction of ventilatory response to decreased barometric pressure (altitude) is presented in Figure 13. Although the shape of the curve is consistent with published data, the model underestimates experimental data (63).

The effects of hypoxia or hypercapnia on pulmonary vascular resistance are not included in this simulation. Hence redistribution of pulmonary blood flow in response to hypoxia and hypercapnia does not occur in the model.

The effects of carbon monoxide on the oxyhemoglobin dissociation curve are well known. When carbon monoxide is present in inspired gas, it readily combines with hemoglobin increasing hemoglobin oxygen affinity. The oxyhemoglobin dissociation curve is therefore shifted to the left, rendering hemoglobin less effective in the gas exchange process (50).

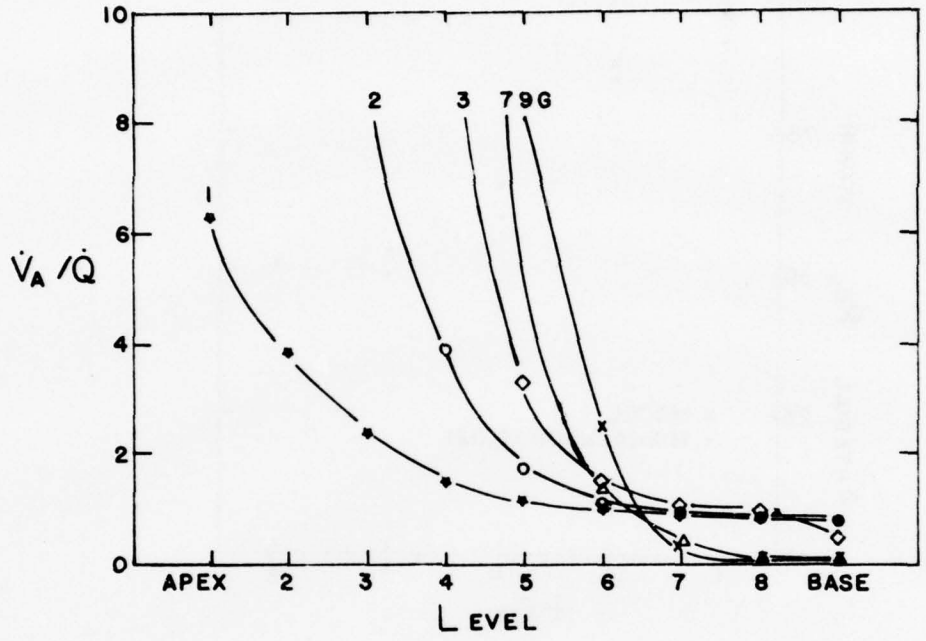


Figure 11. Model prediction of regional $\dot{V}_A/\dot{Q}$ as a function of vertical lung segment at various degrees of acceleration stress.

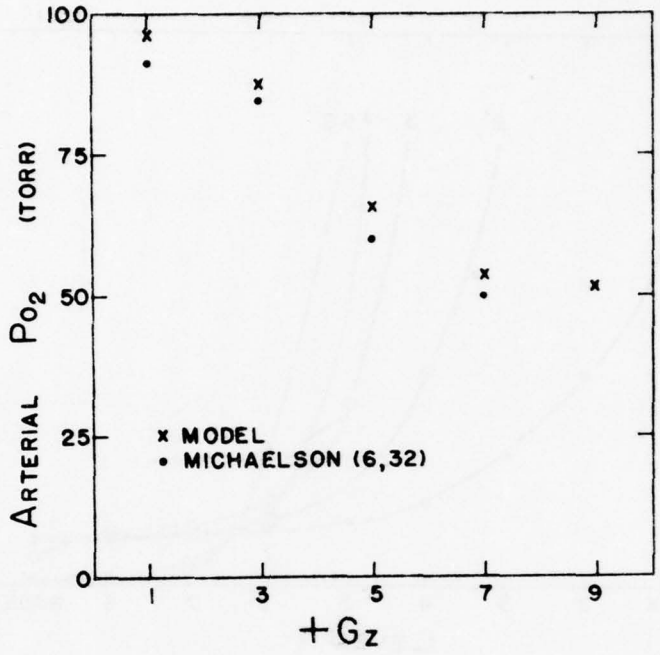


Figure 12. Comparison of model data with experimental data of Michaelson (6, 32).

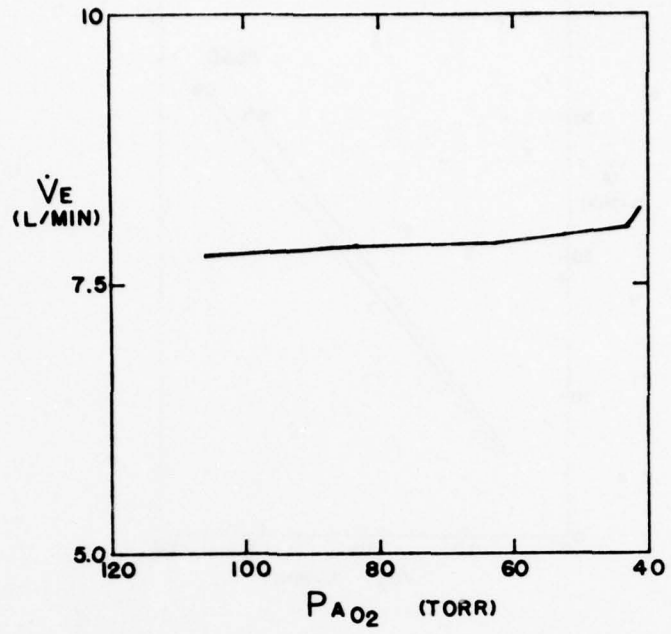


Figure 13. Model predicted ventilatory response to decreased inspired oxygen tension (altitude).

Multiple Stresses

The rationale for developing this simulation was to provide a means to examine the effects of combined environmental stress on the gas exchange process. The results presented in Figures 2 through 13 indicate that the model provides adequate predictions of single stresses. In this section, we will present representative predictions when two stresses are applied. In some cases, experimental data with which to compare these predictions are not available.

Vogel and Gleser (58) examined the influence of carbon monoxide in inspired gas on the response to dynamic exercise. Oxygen transport was studied in men at rest and during dynamic work while breathing air or an inspirate containing sufficient carbon monoxide to yield 18%-20% carboxyhemoglobin. These authors noted little change in arterial blood gases when work was performed with the added carbon monoxide stress. They did note, however, that ventilation increased when the subject was exposed to the carbon monoxide. Figure 14 shows the alveolar ventilation predicted by the model when levels of exercise and carboxyhemoglobin saturation similar to the Vogel and Gleser study were simulated. The magnitude of the ventilatory response was slightly larger than that reported by Vogel and Gleser, and, as a result, the model predicts that arterial P_{O_2} would rise slightly during the exercise.

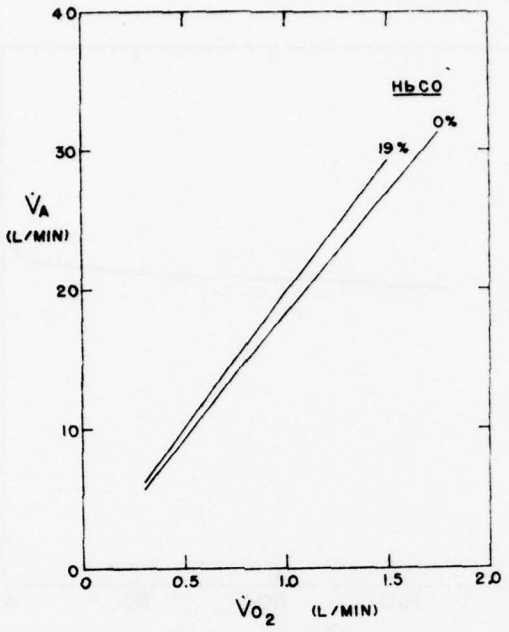


Figure 14. Model predicted ventilatory response to exercise with and without significant carboxyhemoglobin saturation.

Rosenhamer (49) and Nunneley (41) examined the response to exercise during increased gravitational stress. Rosenhamer compared cardiopulmonary parameters in men at rest and two levels of exercise at 1 G and +3 G_z. We compared predictions by our model to his data. Unfortunately, the maximal oxygen consumption of Rosenhamer's subjects was not included in his data. Hence it was difficult to compare the same levels of work. Results from the model are compared to the experimental data in Figure 15. The experimental data indicates a progressive drop in arterial P_{O_2} at +3 G_z, whereas the model predicts no change or a slight increase in arterial P_{O_2}. The difference appears to result from a difference in the ventilatory response to the stress, compared in Figure 16. Note that the response of the model exceeds the observed response. This suggests that the ventilatory controller overestimates ventilation during G stress. Nunneley's data (41) suggests that this is not the case, and when the model's ventilatory response to $+G_z$ alone is compared to Michaelson's data, summarized by Burton et al. (6), it underestimates the observed response. These comparisons indicate that factors governing ventilation during G stress require further examination. A second reason for the disagreement in arterial blood gases could be the lack of a systemic vasculature and hence blood pooling in the model.

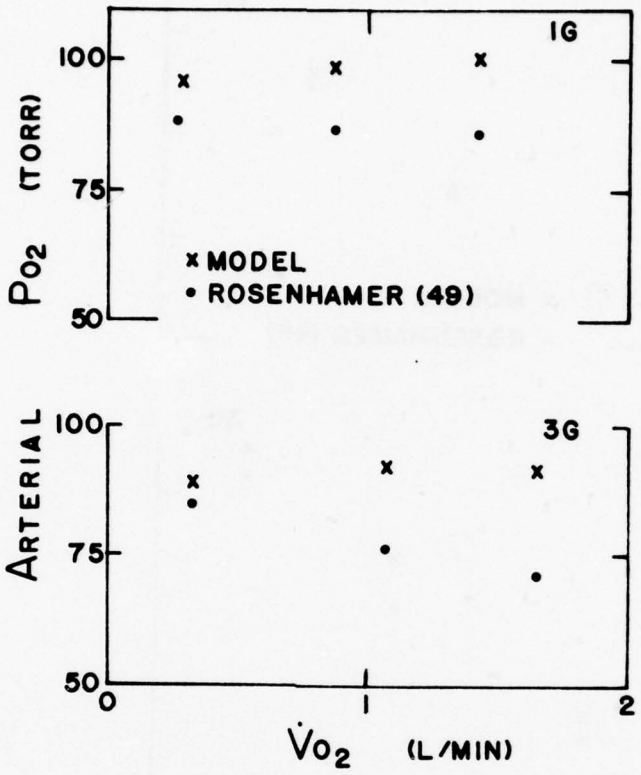


Figure 15. Comparison of model arterial oxygen data with experimental data of Rosenhamer (49).

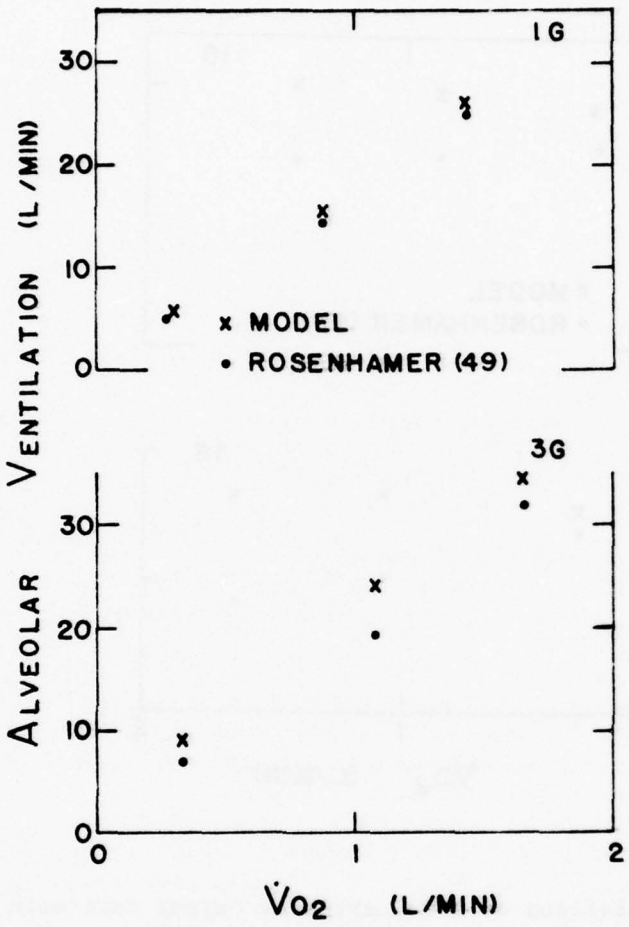


Figure 16. Comparison of model alveolar ventilation data with experimental data of Rosenhamer (49).

Addition of carbon dioxide to inspired gas has been considered a means of providing additional protection to high sustained G exposure (28). The rationale is that CO_2 inhalation increases systemic blood pressure. It is of interest to determine if the added CO_2 would cause a gas exchange detriment. Arterial blood gas tensions obtained from the model under conditions of increased G with and without the addition of 2% CO_2 to the inspired gas are presented in Figure 17. Note that with 2% inspired CO_2, arterial P_{CO_2} is maintained at a nearly constant level slightly above that predicted for room air breathing. The arterial P_{O_2}, however, is significantly higher when CO_2 is added to the inspired air. These results suggest that, if the subject is able to achieve the additional alveolar ventilation necessary to maintain arterial P_{CO_2} constant, addition of CO_2 may serve to improve oxygen delivery to the tissues. Experimental evidence confirming or refuting this prediction is not currently available.

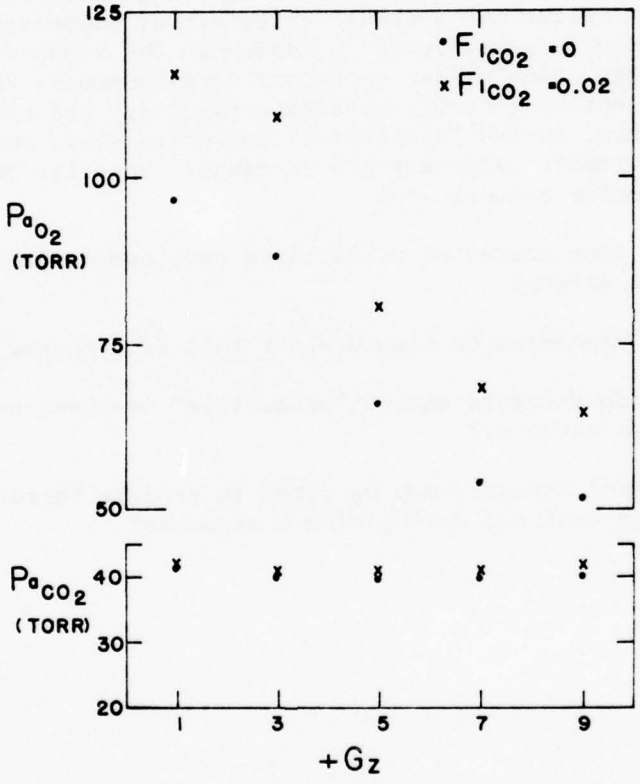


Figure 17. Model prediction of arterial blood gases as a function of acceleration stress with and without inspired carbon dioxide.

DIRECTIONS FOR FUTURE WORK

One goal of this project was to identify areas for future experimental investigation consistent with the mission of the Air Force. As a result of this effort, we have identified several areas in which crucial data are lacking. Sufficient data are not available to answer definitively, "What controls alveolar ventilation?" It is well known that alveolar ventilation increases in response to increased arterial P_{CO_2}, increased arterial hydrogen ion concentration, and decreased arterial P_{O_2}. These factors, however, can not account for the increase in ventilation seen during exercise at high work loads (10) or during isometric exercise (38, 67). Our model predictions indicate that they do not adequately account for the increase in ventilation seen during acceleration. To be able to predict the ventilatory response of pilots exposed to multiple environmental stresses, it is imperative to further delineate factors contributing to the regulation of alveolar ventilation and to determine the manner in which these factors interact.

As high-performance aircraft design becomes more sophisticated, pilots are required to withstand higher levels of longer duration acceleration stress. Unlike the systemic circulation, pulmonary hemodynamics are similarly sensitive to G forces in the x and z vectors (15). Thus tilting the pilot's seat to reduce cardiovascular effects of G_z exposure (7) will not necessarily alleviate pulmonary gas exchange detriment. Furthermore, anti-G "protective" measures (e.g., anti-G suits) may, in fact, impair pulmonary gas exchange. Specific questions in this area that require answers are:

1. What is the time course of atelectasis development during acceleration stress?

2. Do repeated exposures to high G alter this time course?

3. What effect do standard anti-G "protective" measures have on pulmonary gas exchange?

4. What additional measures may be taken to promote better pulmonary gas exchange during high G exposure?

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APPENDIX A

MODEL DETAILS

NOTES ON RUNNING THE MODEL

This program is written in BASIC for use on a PDP-11 computer using RT-11 software. To use the program, load and run it as any standard BASIC program. The program will ask for all input values the first time through. After all input values are assigned, the program repeats the description of conditions for that run. It then calculates the steady state values as described in this report. Two output formats are available. The short format presents only systemic data, whereas the long output also includes description of the tissue compartment and regional lung values.

After completion of the output, the program prints "CHANGE?". To change a variable value, answer "CHANGE?" with the appropriate abbreviation below. THE PROGRAM WILL THEN ASK FOR THE NEW VALUE.

PB = Barometric pressure
O2 = Percent inspired oxygen
CO2 = Percent inspired carbon dioxide
CO = Percent carboxyhemoglobin concentration
G = Acceleration in the z vector
VO2 = Oxygen consumption

After new value(s) have been entered, answer "CHANGE?" by typing GO for short output or GOC for complete output.

To terminate the program, answer "CHANGE?" by typing QUIT.

SYMBOL TABLE

Because of the modular nature of this model, the symbol table below is arranged according to module. In many cases, the same symbols are used for different variables in different modules. The variables A0(n) and A1(n) serve as storage for specific variable values and are defined at the end of this symbol list.

Module 1: input and initial conditions

A9	Acceleration in the z vector
C5(1)	Arterial oxygen content
F3	Minute ventilation
F5	Cardiac output
F8	Oxygen consumption (L/min)
F9	Oxygen consumption (% max)
G0	Inspired carbon dioxide tension
G9	Inspired carbon dioxide fraction
H0	Percent carboxyhemoglobin
I	Marker
I6	Iteration counter
M	Marker
N9	Switch defining first time through input
O0	Inspired oxygen tension
O4	Oxygen consumption of 'other' tissue beds
O9	Inspired oxygen fraction
P0	Barometric pressure minus water vapor
P1	Oxygen tension
P2	Mixed venous carbon dioxide tension
P8	Barometric pressure
Q4	Blood flow to 'other' tissue beds
R	Heart rate
R1	Respiratory frequency
V1	Alveolar tidal volume
V5	Stroke volume
X	Dummy variable

Module 2: Regional ventilation, perfusion, and ventilation-perfusion ratios

A	Sine wave amplitude for blood flow
A9	Acceleration in the z vector
B(11,2)	Data for function generator
C9	Lung compliance in the tidal volume range
D(1,n)	Regional total lung capacity
D(2,n)	Regional lung volume
D(3,n)	Regional volume expressed as % total volume

D0	Pulmonary artery volume
D1	Difference between pulmonary artery inflow and outflow
F	Heart rate
F(2,n)	Regional alveolar ventilation
F(4,n)	Regional end capillary flow
F(9,n)	Regional blood flow
F0	Respiratory frequency
F4	Total end capillary flow
F5	Instantaneous flow
F9	Flow summer
K	Regional alveolar bed conductance
O	Percent of alveolar bed open
P1	Pleural pressure
P3	Last pleural pressure value
P4	Mean pleural pressure at levels 6,7 and 8
P5	Pulmonary artery pressure
P6	Regional pulmonary pressure
P7	Regional pulmonary venous pressure
P9	Pleural pressure at end tidal volume
Q0	Cardiac output
Q5	Pulmonary artery stressed volume
Q9	Regional blood flow
T0	Heart rate per second
T1	Integration step
T2	Time for sine wave
U(11,2)	Data for function generator
V0	Alveolar tidal volume
V(n)	Regional volume
V9	Tidal volume summer
X	Dummy variable
X0	Flow adjustment for sine wave
X3	Tidal volume summer
Y	Dummy variable
L	Last point (function generator)
N1	Point counter (function generator)
X1	X coordinate of last point (function generator)
X2	X coordinate of present point (function generator)
Y	Output value (function generator)
Y1	Y coordinate of last point (function generator)
Y2	Y coordinate of next point (function generator)
Z	Slope (function generator)

Module 3: Regional lung blood gas calculations

C(4,1)	Arterial oxygen content
C(4,2)	Arterial carbon dioxide content
C(6,1)	Mixed venous oxygen content
C(6,2)	Mixed venous carbon dioxide content

D	Difference between calculated and true ventilation-perfusion ratio
D1	Same as D
D3	Previous difference in carbon dioxide tensions
D4	Difference in carbon dioxide tensions
G0	Inspired carbon dioxide tension
G4	Oxygen tension
G5	Carbon dioxide tension
G(1,n)	Regional alveolar oxygen tension
G(2,n)	Regional alveolar carbon dioxide tension
G(4,1)	End capillary oxygen tension
G(4,2)	End capillary carbon dioxide tension
G(6,1)	Mixed venous oxygen tension
G(6,2)	Mixed venous carbon dioxide tension
H0	Percent carboxyhemoglobin
H9	Available hemoglobin
I	Marker
K1	Oxygen content (for blood gas routines)
K2	Carbon dioxide content (for blood gas routines)
M	Marker
M1	Marker
M9	Marker
O0	Inspired oxygen tension
P	Oxygen tension
P1	Carbon dioxide tension
P2	Carbon dioxide tension
R3	Gas exchange ratio
R4	Regional ventilation-perfusion ratio
T5	Calculated ventilation-perfusion ratio
X1	Previous gas exchange ratio
X2	Gas exchange ratio
X3	Previous oxygen tension
X4	Oxygen tension

Module 4: Calculate alveolar, arterial, tissue, and mixed venous blood gas values

C(1,n)	Regional end capillary oxygen content
C(2,n)	Regional end capillary carbon dioxide content
C1	Oxygen content summer
C2	Carbon dioxide content summer
C5(1)	Arterial oxygen content
C5(2)	Arterial carbon dioxide content
C6(1,1)	Brain oxygen content
C6(1,2)	Brain carbon dioxide content
C6(2,1)	Heart oxygen content
C6(2,2)	Heart carbon dioxide content
C6(3,1)	Muscle oxygen content

C6(3,2)	Muscle carbon dioxide content
C6(4,1)	'Other' tissue bed oxygen content
C6(4,2)	'Other' tissue bed carbon dioxide content
C7(1)	Mixed venous oxygen content
C7(2)	Mixed venous carbon dioxide content
D0	Muscle arteriovenous oxygen content difference
F5	Cardiac output
F8(1)	Oxygen consumption (L/min)
F9	Oxygen consumption (% max)
G(1,n)	Regional alveolar oxygen tension
G(2,n)	Regional alveolar carbon dioxide tension
G1	Oxygen tension summer
G2	Carbon dioxide summer
G4	Oxygen tension
G5	Carbon dioxide tension
K1	Oxygen content
K2	Carbon dioxide content
O4	'Other' tissue bed oxygen consumption
Q(n)	Regional blood flow
Q1	Brain blood flow
Q2	Muscle blood flow
Q3	Heart blood flow
Q4	'Other' tissue blood flow
R3	Muscle gas exchange ratio
R9	Total body gas exchange ratio
V(n)	Regional lung volume

Module 5: Determine alveolar ventilation

F2	Alveolar ventilation
F3	Minute ventilation
F8(1)	Oxygen consumption (L/min)
F9	Oxygen consumption (% max)
I6	Iteration counter
K	Constant for ventilatory controller
M	Marker
R1	Respiratory frequency
V1	Alveolar tidal volume
X	Previous minute ventilation
X1	Oxygen tension
X2	Carbon dioxide tension

Module 6: Blood gas routine

A	Influence of carbon dioxide on oxygen dissociation curve
D	Oxygen tension difference
D1	Previous D

D9	Oxygen tension difference
G4	Oxygen tension
G5	Carbon dioxide tension
H0	Percent carboxyhemoglobin
H9	Available hemoglobin
K1	Oxygen content
K2	Carbon dioxide content
M0	Marker
O0	Inspired oxygen tension
P3	Input oxygen tension
P4	Oxygen or carbon dioxide tension
P5	Oxygen tension
S	Saturation
S1	Saturation
S3	Saturation
T	Previous oxygen tension
T1	Previous oxygen tension

Module 7: Output

S1	Arterial saturation
S2	Mixed venous saturation

Stored variables (arrays A0 and A1):

Array A0(n)

1-9	Regional alveolar ventilation
10-18	Regional perfusion
19-27	Regional ventilation-perfusion ratio
28-36	Regional alveolar oxygen tension
37-45	Regional alveolar carbon dioxide tension
46-54	Regional end-capillary oxygen content
55-63	Regional end-capillary carbon dioxide content
64	Mixed alveolar oxygen tension
65	Mixed alveolar carbon dioxide tension
66	Arterial oxygen content
67	Arterial carbon dioxide content
68	Arterial oxygen tension
69	Arterial carbon dioxide tension
70	Mixed venous oxygen content
71	Mixed venous carbon dioxide content
72	Mixed venous oxygen tension
73	Mixed venous carbon dioxide tension
74	Brain blood flow
75	Muscle blood flow
76	Heart blood flow
77	'Other' tissue bed blood flow
78	Brain oxygen tension

79	Muscle oxygen tension
80	Heart oxygen tension
81	'Other' bed oxygen tension
82	Brain carbon dioxide tension
83	Muscle carbon dioxide tension
84	Heart carbon dioxide tension
85	'Other' bed carbon dioxide tension

Array Al(n)

1	Blank
2	Blank
3	Cardiac output
4	Heart rate
5	Stroke volume
6	Respiratory frequency
7	Alveolar tidal volume
8	Mixed venous oxygen tension
9	Mixed venous carbon dioxide tension
10	Oxygen consumption
11	Marker for ventilation controller
12	Blank
13	Alveolar ventilation

```
00010 REM -- CONTROL FOR AF PROGRAMS
00020 REM--H.  MODELL, DEPT PHYSIOLOGY, UNIV OF WASH.  98195
```

A0(N) and A1(n) are stored variables serving as a 'common' space

```
00030 DIM A0(100),A1(25)
00040 N9=0
```

From line 50 to line 610 is the input section. Variables are input and allowable limits are tested.

```
00050 PRINT "BAROMETRIC PRESS (TORR)";
00060 INPUT P8
00070 IF P8<=760 THEN 100
00080 PRINT "PB MAX=760 (SEA LEVEL), PB MIN=225 (30,000 FT)"
00090 GOTO 50
00100 IF P8<225 THEN 80
00110 IF N9<>0 THEN 1350
00120 PRINT "PER CENT INSPIRED O2";
00130 INPUT O9
00140 O9=O9/100
00150 IF N9<>0 THEN 1350
00160 PRINT "PER CENT INSPIRED CO2";
00170 INPUT G9
00180 IF G9<=5 THEN 210
00190 PRINT "PLEASE KEEP INSPIRED CO2 LESS THAN 5%"
00200 GOTO 160
00210 G9=G9/100
00220 IF N9<>0 THEN 1350
00230 PRINT "% HBCO";
00240 INPUT H0
00250 IF H0<=25 THEN 290
00260 PRINT "SUBJECT IS BREATHING IN EXCESS OF 250 PPM CO"
00270 PRINT "PLEASE USE A LOWER VALUE FOR % HBCO"
00280 GOTO 230
00290 IF N9<>0 THEN 1350
00300 PRINT "+GZ";
00310 INPUT A9
00320 IF A9<=9 THEN 350
00330 PRINT "MIN G=1,MAXG=9"
00340 GOTO 300
00350 IF A9<1 THEN 330
00360 IF N9<>0 THEN 1350
00370 PRINT "OXYGEN CONSUMPTION (L/MIN)";
00380 INPUT F8
00390 IF F8<=3.5 THEN 420
```

```
00400 PRINT "RESTING VO2=.3 L/MIN, VO2 MAX=3.5 L/MIN"
00410 GOTO 370
00420 IF F8<.3 THEN 400
00430 IF N9<>0 THEN 1350
00440 PRINT "DO YOU WANT A COMPLETE OUTPUT";
00450 INPUT B$
00460 IF SEG$(B$,1,1)="N" THEN 480
00470 B$="GOC"
00480 N9=1
00490 IF (G9+O9)<=1 THEN 530
00500 PRINT "THE GAS MIXTURE YOU HAVE CHOSEN IS GREATER THAN 100%"
00510 PRINT "INSP O2= ";O9*100;"INSP CO2= ";G9*100
00520 GOTO 1350
00530 P1=(F8*8.63)+60
00540 IF P1<((P8-47)*O9) THEN 580
00550 PRINT "INSPIRED PO2 WILL NOT PROVIDE ENOUGH O2 FOR VO2"
00560 PRINT "PB= ";P8;"% O2= ";O9*100;"PIO2= ";INT((P8-47)*O9)
00570 GOTO 1350
00580 IF ((P8-47)*O9)>83 THEN 620
00590 PRINT "YOUR COMBINED PB AND FIO2 HAS RESULTED IN A PIO2 LESS THAN
       83"
00600 PRINT "(14,000 FT BREATHING AIR)."
00610 GOTO 1350

                      Set initial values of mixed venous PO2 (P1),
                      PCO2 (P2), and minute ventilation (F3)

00620 P1=40
00630 P2=49
00640 F3=7.7

                      Repeat input conditions

00650 PRINT
00660 PRINT
00670 PRINT "CONDITIONS:"
00680 PRINT "PB=";INT(P8);" % O2 INSP=";INT(O9*1000+.5)/10;
00690 PRINT " %CO2 INSP=";INT(G9*1000+.5)/10;
00700 PRINT " % HBCO=";INT(H0*10+.5)/10
00710 PRINT " +GZ=";INT(A9*10+.5)/10;" VO2= ";INT(F8*100+.5)/100
00720 I6=50
00730 M=0
00740 Q6=0
00750 I=0
00760 T0=0

                      Calculate O2 consumption in terms of % maximal
                      O2 consumption
```

```
00770 F9=(F8/3.5)*100
00780 REM--------------VO2MAX=3.5 L/MIN
00790 IF Q6<>0 THEN 850
00800 IF A9<5 THEN 840
```

Stroke volume and heart rate calculation if G equals or is greater than 5

```
00810 V5=.124855
00820 R=155.682
00830 GOTO 890
00840 X=F9
```

Stroke volume and heart rate calculation if G<5

```
00850 V5=(.13*(97.3514-65.7675*EXP(-.05222*X)))/100
00860 R=1.299*X+58.257
00870 REM ---------HEART RATE
00880 Q6=0
00890 F5=V5*R
00900 REM----CARDIAC OUTPUT L/MIN
00910 IF F5>23.7257 THEN 6610
00920 P0=P8-47
00930 O0=O9*P0
00940 REM PIO2
00950 G0=C9*P0
00960 REM----PICO2
00970 IF I=0 THEN 990
00980 RETURN
00990 IF F3<67 THEN 1030
```

Calculate respiratory frequency if VE equals or is greater than 67 L/min

```
01000 R1=.35*F3+1.14
01010 REM ------RESP FREQ
01020 GO TO 1050
```

Calculate respiratory frequency if VE is less than 67 L/min

```
01030 R1=EXP(LOG(6.25)+.34*LOG(F3))
01040 REM -------RESP FREQ
```

Calculate alveolar tidal volume

```
01050 V1=(F3/R1)*1000-150
01060 REM VT TO ALV IN ML--D.S=150ML
```

```
                        Store values for this module

01070 A0(69)=40
01080 A1(3)=F5
01090 A1(4)=R
01100 A1(5)=V5
01110 A1(6)=R1
01120 A1(7)=V1
01130 A1(8)=P1
01140 A1(9)=P2
01150 A1(10)=F8
01160 A1(11)=M
01170 GO TO 1480
01180 M=A1(11)
01190 IF M=0 THEN 1490
01200 I=1

                        If flow to 'other' tissue bed is positive, go to
                        output

01210 IF Q4>0 THEN 1330

                        Readjust flow to other tissue bed, cardiac
                        output, stroke volume, and heart rate

01220 Q4=Q4/(C5(1)*.01-.02)
01230 F5=A1(3)+(Q4/1000)
01240 IF F5>23.7257 THEN 6610
01250 IF A1(3)<15.5 THEN 1280
01260 R=F5/A1(5)
01270 GOTO 1290
01280 R=5.4844*F5+40.8329

                        Store readjusted values

01290 A1(3)=F5
01300 A1(4)=R
01310 A1(5)=F5/R
01320 GOTO 1490

                        Go to output (5420)

01330 GOSUB 5420
01340 REM----------------------OUTPUT

                        Change input variable values

01350 PRINT "CHANGE";
```

```
01360 INPUT B$
01370 IF B$="GO" THEN 490
01380 IF B$="GOC" THEN 490
01390 IF B$="PB" THEN 50
01400 IF B$="O2" THEN 120
01410 IF B$="CO2" THEN 160
01420 IF B$="CO" THEN 230
01430 IF B$="G" THEN 300
01440 IF B$="VO2" THEN 370
01450 IF B$="QUIT" THEN 6630
01460 PRINT "I DIDN'T UNDERSTAND -- TRY AGAIN"
01470 GOTO 1350
01480 REM------------CONTINUE

                        Begin module 2 which calculates regional V̇A/Q̇

01490 REM------AF MODULE 2 --CALC V/Q(N)
01500 REM--OPEN VQ.DAT IF CHAINED
01510 DIM D(4,9),U(11,2),F(9,9),P(2,9)
01520 DIM V(9),Q(9),B(11,2)

                        Regional TLC in ml.

01530 DATA 402,510,594,678,720,756,768,786,786

                        Pressure-volume curve coordinates

01540 DATA -4,1,3.6,11.5,14.5,18.5,20,23.5,30,32,40
01550 DATA 0,.2,.3,.6,.7,.8,.84,.9,.98,.99,1
01560 T1=.07

                        Begin regional V̇A calculation

01570 REM---CALC V(N)

                        Read stored values from previous module

01580 Q0=A1(3)
01590 F=A1(4)
01600 F0=A1(6)
01610 V0=A1(7)
01620 T0=F/60
01630 I=1

                        Read regional TLC

01640 FOR J=1 TO 9
01650 READ D(I,J)
```

```
01660 NEXT J

                        Read P-V curve

01670 FOR I=1 TO 2
01680 FOR J=1 TO 11
01690 READ U(J,I)
01700 NEXT J
01710 NEXT I

                        Set "Ppl" at 3 cm above segment 1

01720 P1=8.45+5*.75*A9
01730 X3=0
01740 P4=0
01750 FOR N=1 TO 9

                        Calculate Ppl at segment N

01760 P1=P1-.75*A9

                        Calculate mean Ppl acting on pulmonary artery

01770 IF N<6 THEN 1800
01780 IF N>8 THEN 1800
01790 P4=P4+P1/3
01800 X=P1
01810 Y=1

                        Go to P-V curve and calculate regional % TLC

01820 GOSUB 2910

                        Calculate regional volume

01830 D(2,N)=Y*D(1,N)

                        Calculate tidal volume

01840 X3=X3+D(2,N)
01850 NEXT N
01860 Y=2

                        Calculate % TLC at end-tidal volume

01870 X=(V0+X3)/6000

                        Calculate Ppl at end-tidal volume
```

```
01880 GOSUB 2910
01890 P9=Y
```

Calculate compliance in tidal volume range

```
01900 C9=(B(N1,2)-B(L,2))/(B(N1,1)-B(L,1))
```

Calculate initial Ppl set point

```
01910 P1=P9*1.04+3.75*A9
01920 GOTO 1940
01930 P1=Y
01940 V9=0
01950 P3=P1
01960 FOR N=1 TO 9
```

Calculate regional Ppl

```
01970 P1=P1-.75*A9
01980 X=P1
01990 Y=1
```

Calculate regional volume (%TLC) from Ppl

```
02000 GOSUB 2910
02010 V(N)=Y
02020 IF V(N)<0 THEN 6610
```

Calculate regional tidal volume

```
02030 X=V(N)*D(1,N)-D(2,N)
02040 IF X>=0 THEN 2060
02050 X=0
```

Calculate test tidal volume

```
02060 V9=X+V9
02070 NEXT N
```

Compare test tidal volume to "true" tidal volume

```
02080 IF ABS(V0-V9)<2 THEN 2110
```

Calculate new trial Ppl set point

```
02090 Y=P3+(V0-V9)*C9/6000
02100 GOTO 1930
```

```
02110 FOR N=1 TO 9

                        Calculate regional V̇A (L/min)

02120 F(2,N)=(V(N)*D(1,N)-D(2,N))*F0

                        Calculate regional V̇A (% total)

02130 D(3,N)=F(2,N)/(F0*V0)
02140 V(N)=100*V(N)

                        Store regional V̇A

02150 A0(N)=D(3,N)
02160 NEXT N
02170 REM---CALC Q(N)

                        Regional alveolar vessel bed conductance

02180 DATA 1.9363,2.4565,2.8611,3.2657,3.468,3.6414,3.6992,3.7859,3.7859

                        Set amplitude of sine wave for blood flow

02190 X0=(Q0+10)*1000/F
02200 A=X0*3.14159*F/60
02210 F9=0

                        Read regional conductance

02220 FOR N=1 TO 9
02230 READ D(1,N)
02240 NEXT N
02250 F4=0

                        Determine flow for systole

02260 FOR T2=0 TO T0/2 STEP T1
02270 F5=A*SIN(6.28*F*T2/60)
02280 GOSUB 2410
02290 NEXT T2

                        Determine flow for diastole

02300 FOR T2=T0/2 TO T0 STEP T1
02310 F5=0
02320 GOSUB 2410
02330 NEXT T2
```

```
                                Sum regional flow

02340 FOR N=1 TO 9
02350 F9=F9+Q(N)*F
02360 NEXT N

                                Calculate true regional flow

02370 FOR N=1 TO 9
02380 F(9,N)=(Q(N)*F/F9)*Q0
02390 NEXT N
02400 GO TO 2730

                                Pulmonary artery inflow minus P.A. outflow

02410 D1=F5-F4
02420 IF T2>=T1 THEN 2450

                                Initial P.A. volume

02430 D0=91.3
02440 GO TO 2460

                                Calculate P.A. volume

02450 D0=D0+(D1*T1)

                                Calculate P.A. stressed volume

02460 Q5=D0-37.1

                                Calculate P.A. pressure

02470 P5=(.437*Q5)-P4

                                Sum regional flow

02480 FOR N=1 TO 9
02490 IF T2>=T1 THEN 2520
02500 Q(N)=0
02510 GO TO 2530
02520 Q(N)=Q(N)+(F(4,N)*T1)
02530 NEXT N
02540 F4=0
02550 FOR N=1 TO 9

                                Calculate regional P.A. pressure
```

```
02560 P6=P5-((21.5-N*3)*A9)

                        Calculate regional pulmonary venous pressure

02570 P7=5.44-((21.5-N*3)*A9)
02580 IF P6<=27.44 THEN 2610

                        Calculate regional alveolar bed conductance

02590 O=100*(1-EXP(-.46*(P6-24.817)))
02600 GO TO 2650

                        Calculate alveolar vessel bed flow (to line
                        2690)

02610 IF P6>0 THEN 2640
02620 F(4,N)=0
02630 GOTO 2700
02640 O=EXP(.131*(P6+5))
02650 K=(O/100)*D(1,N)
02660 IF P7>=0 THEN 2690
02670 F(4,N)=K*P6
02680 GO TO 2700
02690 F(4,N)=K*(P6-P7)

                        Sum flow

02700 F4=F4+F(4,N)
02710 NEXT N
02720 RETURN

                        Calculate regional V̇A/Q̇ (to line 2800)

02730 FOR N=1 TO 9
02740 IF F(9,N)>0 THEN 2770
02750 D(1,N)=1000
02760 GOTO 2800
02770 D(1,N)=F(2,N)/(1000*F(9,N))
02780 IF D(1,N)<=1000 THEN 2800
02790 D(1,N)=1000
02800 NEXT N
02810 FOR N=1 TO 9
02820 V(N)=INT(V(N)*10+.5)/10

                        Calculate % regional flow

02830 F(9,N)=F(9,N)/Q0
```

```
                                Store % regional flow

02840 A0(9+N)=F(9,N)
02850 NEXT N
02860 FOR N=1 TO 9

                                Store regional V̇A/Q̇

02870 A0(18+N)=D(1,N)
02880 NEXT N
02890 RESTORE
02900 GO TO 3290
02910 IF Y<>1 THEN 3030

                                Function generator for P-V curve to line 3270

02920 FOR J=1 TO 2
02930 FOR I=1 TO 11
02940 B(I,J)=U(I,J)
02950 NEXT I
02960 NEXT J
02970 IF X>1 THEN 3000
02980 Y=.2
02990 GOTO 3270
03000 IF X<40 THEN 3130
03010 Y=1
03020 GOTO 3270
03030 FOR I=1 TO 11
03040 B(I,1)=U(I,2)
03050 B(I,2)=U(I,1)
03060 NEXT I
03070 IF X>.2 THEN 3100
03080 Y=1
03090 GOTO 3270
03100 IF X<1 THEN 3130
03110 Y=40
03120 GO TO 3270
03130 N1=1
03140 IF B(N1,1)>=X THEN 3170
03150 N1=N1+1
03160 GO TO 3140
03170 IF B(N1,1)<>X THEN 3200
03180 Y=B(N1,2)
03190 GO TO 3270
03200 L=N1-1
03210 X1=B(L,1)
03220 Y1=B(L,2)
03230 X2=B(N1,1)
```

```
03240 Y2=B(N1,2)
03250 Z=(X-X1)/(X2-X1)
03260 Y=Y1+(Z*(Y2-Y1))
03270 RETURN
03280 STOP
```

Begin module 3 which calculates regional lung blood gases

```
03290 REM---------AF MODULE 3 ----CALC BLOOD GASES OF V/Q(N)
03300 M9=0
03310 DIM G(6,9),C(6,9)
```

Calculate available hemoglobin concentration

```
03320 H9=15*(1-(H0/100))
03330 J=0
```

Recall mixed venous point and regional $\dot{V}A/\dot{Q}$ (to line 3360)

```
03340 G(6,1)=A1(8)
03350 G(6,2)=A1(9)
03360 R4=A0(19+J)
03370 J=J+1
03380 IF R4<100 THEN 3440
```

Blood gas status if $\dot{V}A/\dot{Q}>100$

```
03390 G(4,1)=O0
03400 G(4,2)=G0
03410 C(4,1)=0
03420 C(4,2)=0
03430 GOTO 3570
```

PO2,PCO2 for blood gas routines (mixed venous point)

```
03440 G4=G(6,1)
03450 G5=G(6,2)
03460 GOSUB 6640
```

Mixed venous O2 and CO2 contents

```
03470 C(6,1)=K1
03480 C(6,2)=K2
03490 IF R4>.001 THEN 3550
```

```
                                Blood gas status if V̇A/Q̇<.001

03500 G(4,1)=G(6,1)
03510 G(4,2)=G(6,2)
03520 C(4,1)=C(6,1)
03530 C(4,2)=C(6,2)
03540 GOTO 3570
03550 GOSUB 3640

                                Iteration counter

03560 IF I=100 THEN 3610

                                End-capillary O2 and CO2 tensions and contents
                                (to line 3600)

03570 D(1,J)=G(4,1)
03580 D(2,J)=G(4,2)
03590 D(3,J)=C(4,1)
03600 D(4,J)=C(4,2)
03610 REM
03620 IF J<9 THEN 3360
03630 GO TO 4270
03640 M=0
03650 I=0

                                Calculate first initial R value for Secant
                                method

03660 R3=(G(6,2)-G0)/(O0-G(6,1))
03670 IF R3<1 THEN 3720
03680 R3=5*R3
03690 GOTO 3720

                                Calculate second initial R for Secant method

03700 R3=7*R3
03710 M=1
03720 M1=0

                                Calculate first PO2 for Secant method

03730 P=O0-5
03740 I=0
03750 GO TO 3780
03760 M1=1

                                Calculate second PO2 for Secant method
```

```
03770 P=O0-20
```

Calculate PCO2 by alveolar gas equation (to line 3790)

```
03780 P1=(R3*O0+G0)-((R3+(1-R3)*G9)*P)
03790 P1=P1/(1-(1-R3)*O9)
03800 G4=P
03810 G5=P1
03820 GOSUB 6640
```

Calculate O2 content

```
03830 C(4,1)=K1
```

Calculate CO2 content from R and mass balance

```
03840 C(4,2)=C(6,2)-(R3*(C(4,1)-C(6,1)))
```

Insure that CO2 content is positive

```
03850 IF C(4,2)>=0 THEN 3870
03860 C(4,2)=C(6,2)/5
```

Calculate PCO2 from CO2 content

```
03870 P2=EXP(2.86*LOG(C(4,2)/(14.9-1.65*S)))
```

Compare PCO2's--if close enough (.03) go on to $\dot{V}A/\dot{Q}$ iteration

```
03880 D4=P2-P1
03890 IF ABS(P1-P2)<.03 THEN 4100
```

Iteration counter

```
03900 I=I+1
03910 IF I<100 THEN 3940
03920 PRINT "*";
03930 GO TO 4260
03940 IF M1<>0 THEN 3980
```

Calculate new trial PO2 (to line 4090)

```
03950 X3=P
03960 D3=D4
03970 GO TO 3760
03980 X4=P
```

```
03990 IF D4<>D3 THEN 4020
04000 R3=(R3+X2)/2
04010 GO TO 3720
04020 P=X4-D4*((X4-X3)/(D4-D3))
04030 IF P>=0 THEN 4050
04040 P=G(6,1)+((X4-G(6,1))/3)
04050 IF P<00 THEN 4070
04060 P=X4+((00-X4)/5)
04070 X3=X4
04080 D3=D4
04090 GO TO 3780
04100 IF P1<>0 THEN 4120
04110 P1=.1
```

Calculate $\dot{V}A/\dot{Q}$ at trial R

```
04120 T5=(8.63*R3*(C(4,1)-C(6,1)))/(P1-G0)
04130 IF M<>0 THEN 4170
04140 D=T5-R4
04150 X1=R3
04160 GO TO 3700
04170 D1=T5-R4
```

Compare trial $\dot{V}A/\dot{Q}$ with test $\dot{V}A/\dot{Q}$ -- if close enough (($\dot{V}A/\dot{Q}$)/50), go to next lung region

```
04180 IF ABS(T5-R4)<(R4/50) THEN 4240
04190 X2=R3
```

Calculate new trial R

```
04200 R3=X2-D1*((X2-X1)/(D1-D))
04210 X1=X2
04220 D=D1
04230 GO TO 3720
```

PO2 and PCO2 of lung region

```
04240 G(4,1)=P
04250 G(4,2)=P1
04260 RETURN
```

Store regional PO2

```
04270 FOR J=1 TO 9
04280 A0(27+J)=D(1,J)
04290 NEXT J
```

```
                        Store regional PCO2

04300 FOR J=1 TO 9
04310 A0(36+J)=D(2,J)
04320 NEXT J

                        Store O2 content

04330 FOR J=1 TO 9
04340 A0(45+J)=D(3,J)
04350 NEXT J

                        Store regional CO2 content

04360 FOR J=1 TO 9
04370 A0(54+J)=D(4,J)
04380 NEXT J

                        Begin module 4 which calculates mixed alveolar,
                        arterial, tissue bed and venous blood gases

04390 REM---------AF MODULE 4---CALC ART,VEN,TISSUE BED BLOOD GASES
04400 DIM C6(4,2)
04410 REM--OLD DIM STMNT AND C6(4,2)=VENOUS CONTENTS

                        Recall regional V̇A,Q̇,PO2,PCO2,O2 content, and
                        CO2 content (to line 4590)

04420 FOR N=1 TO 9
04430 V(N)=A0(N)
04440 NEXT N
04450 FOR N=1 TO 9
04460 Q(N)=A0(9+N)
04470 NEXT N
04480 FOR J=1 TO 9
04490 G(1,J)=A0(27+J)
04500 NEXT J
04510 FOR J=1 TO 9
04520 G(2,J)=A0(36+J)
04530 NEXT J
04540 FOR J=1 TO 9
04550 C(1,J)=A0(45+J)
04560 NEXT J
04570 FOR J=1 TO 9
04580 C(2,J)=A0(54+J)
04590 NEXT J

                        Calculate alveolar PO2 and PCO2 and arterial O2
```

```
                        and CO2 contents (to line 4690)

04600 G1=0
04610 G2=0
04620 C1=0
04630 C2=0
04640 FOR N=1 TO 9
04650 G1=G1+V(N)*G(1,N)
04660 G2=G2+V(N)*G(2,N)
04670 C1=C1+Q(N)*C(1,N)
04680 C2=C2+Q(N)*C(2,N)
04690 NEXT N

                        Store alveolar gas tensions and arterial
                        contents

04700 A0(64)=G1
04710 A0(65)=G2
04720 A0(66)=C1
04730 A0(67)=C2

                        Calculate and store arterial gas tensions

04740 C5(1)=C1
04750 C5(2)=C2
04760 K1=C1
04770 K2=C2
04780 GOSUB 6800
04790 A0(68)=G4
04800 A0(69)=G5

                        Recall cardiac output and V̇O2 and calculate %
                        max V̇O2

04810 F5=A1(3)
04820 F8(1)=A1(10)
04830 F9=(F8(1)/3.5)*100
04840 REM---% VO2MAX

                        Calculate brain blood flow

04850 Q1=(20.9+92.8/(1+10570*EXP(-5.251*.43429*LOG(A0(69)))))*15

                        Calculate brain venous O2 content

04860 C6(1,1)=C5(1)*.01-(52.5/Q1)
04870 REM ML/ML
```

```
                        Local O2 regulation

04880 IF C6(1,1)>=.02 THEN 4910
04890 Q1=52.5/(C5(1)*.01-.02)
04900 GOTO 4860

                        Calculate brain venous CO2 content

04910 C6(1,2)=C5(2)*.01+(52.5/Q1)
04920 REM R=1, ML/MIN

                        Calculate arteriovenous O2 difference of muscle
                        bed

04930 D0=29.0799-36.4279*EXP(1.07786/F9)+10.0393*EXP(1.58099/F9)
04940 D0=D0+2.95798*LOG(F9)
04950 REM--VOL%

                        Calculate muscle venous O2 content

04960 C6(2,1)=(C5(1)-D0)*.01
04970 REM ML/ML

                        Local O2 regulation

04980 IF C6(2,1)>=.02 THEN 5010
04990 D0=C5(1)-2
05000 GOTO 4960

                        Calculate muscle blood flow

05010 Q2=((F8(1)*1000-240)/D0)*100
05020 REM ML/MIN

                        Calculate muscle R

05030 R3=.837375+.059917*(F8(1)-.24)
05040 REM MUSC R

                        Calculate muscle venous CO2 content

05050 C6(2,2)=(C5(2)+R3*D0)*.01
05060 REM ML/ML

                        Calculate heart blood flow

05070 Q3=3*(.01146*A1(3)*1000+11.9039)
```

```
                        Calculate heart venous O2 content

05080 C6(3,1)=C5(1)*.25*.01
05090 REM-CORONARY EXTRACTION =.75---ML/ML

                        Local O2 regulation

05100 IF C6(3,1)>=.02 THEN 5120
05110 C6(3,1)=.02

                        Calculate heart venous CO2 content

05120 C6(3,2)=(C5(2)+.8*(C5(1)-C6(3,1)))*.01
05130 REM ML/ML

                        Calculate flow to 'other' beds

05140 Q4=A1(3)*1000-(Q1+Q2+Q3)
05150 IF Q4>0 THEN 5170
05160 Q4=0

                        Calculate O2 consumption of 'other' tissues

05170 O4=F8(1)*1000-(52.5+Q2*D0*.01+Q3*(C5(1)*.01-C6(3,1)))
05180 IF Q4>0 THEN 5210
05190 C6(4,1)=0
05200 GOTO 5230

                        Calculate 'other' bed venous O2 content

05210 C6(4,1)=C5(1)*.01-(O4/Q4)
05220 REM ML/ML

                        Calculate 'other' bed CO2 content

05230 C6(4,2)=.8*(C5(1)*.01-C6(4,1))+C5(2)*.01
05240 REM ML/ML

                        Store tissue bed flows (to line 5280)

05250 A0(74)=Q1
05260 A0(75)=Q2
05270 A0(76)=Q3
05280 A0(77)=Q4

                        Calculate mixed venous contents

05290 C7(1)=(Q1*C6(1,1)+Q2*C6(2,1)+Q3*C6(3,1)+Q4*C6(4,1))/(A1(3)*10)
```

```
05300 C7(2)=(Q1*C6(1,2)+Q2*C6(2,2)+Q3*C6(3,2)+Q4*C6(4,2))/(A1(3)*10)
05310 REM---C7(1) &(2) ARE VOL %
```

Calculate total body R

```
05320 R9=(C7(2)-C5(2))/(C5(1)-C7(1))
```

Store mixed venous contents, calculate mixed venous gas tensions and store mixed venous gas tensions (to line 5390)

```
05330 K1=C7(1)
05340 K2=C7(2)
05350 A0(70)=K1
05360 A0(71)=K2
05370 GOSUB 6800
05380 A0(72)=G4
05390 A0(73)=G5
05400 GO TO 5900
```

Lines 5420 to 5890 constitute the output section of the program

```
05410 REM----------AF OUTPUT SECTION
05420 PRINT
05430 PRINT "VCO2= ";INT(A1(10)*R9*100+.5)/100;"R= ";INT(R9*100+.5)/100
05440 PRINT
05450 PRINT "TOTAL SYSTEM: Q= ";INT(A1(3)*100+.5)/100;"L/MIN ";
05460 PRINT "VA= ";INT(A1(13)*100+.5)/100;"L/MIN"
05470 PRINT
05480 PRINT TAB(19);"OXYGEN";TAB(46);"CO2"
05490 PRINT TAB(14);"ALV ART VEN";TAB(41);"ALV ART VEN"
05500 PRINT
05510 PRINT "TENSION:";TAB(13);INT(A0(64)*10+.5)/10;TAB(20);
05520 PRINT INT(A0(68)*10+.5)/10;TAB(27);
05530 PRINT INT(A0(72)*10+.5)/10;TAB(40);INT(A0(65)*10+.5)/10;TAB(47);
05540 PRINT INT(A0(69)*10+.5)/10;TAB(54);INT(A0(73)*10+.5)/10
05550 PRINT "CONTENT:";TAB(20);INT(A0(66)*10+.5)/10;TAB(27);
05560 PRINT INT(A0(70)*10+.5)/10;
05570 PRINT TAB(47);INT(A0(67)*10+.5)/10;TAB(54);INT(A0(71)*10+.5)/10
05580 S1=(A0(66)-.0031*A0(68))/(H9*1.34)
05590 IF S1<1 THEN 5610
05600 S1=1
05610 S2=(A0(70)-.0031*A0(72))/(H9*1.34)
05620 IF S2<1 THEN 5640
05630 S2=1
05640 PRINT "SATURATION:";TAB(20);INT(S1*1000+.5)/10;TAB(27);
05650 PRINT INT(S2*1000+.5)/10
```

```
05660 IF B$<>"GOC" THEN 5870
05670 PRINT
05680 PRINT " BRAIN HEART MUSCLE OTHER"
05690 PRINT "PO2:";TAB(8);INT(A0(78)*10+.5)/10;TAB(16);
05700 PRINT INT(A0(80)*10+.5)/10;
05710 PRINT TAB(25);INT(A0(79)*10+.5)/10;TAB(32);INT(A0(81)*10+.5)/10
05720 PRINT "PCO2:";TAB(8);INT(A0(82)*10+.5)/10;TAB(16);
05730 PRINT INT(A0(84)*10+.5)/10;
05740 PRINT TAB(25);INT(A0(83)*10+.5)/10;TAB(32);INT(A0(85)*10+.5)/10
05750 PRINT "FLOW"
05760 PRINT "L/MIN";TAB(8);INT((A0(74)/10)+.5)/100;TAB(16);
05770 PRINT INT((A0(76)/10)+.5)/100;
05780 PRINT TAB(25);INT((A0(75)/10)+.5)/100;TAB(32);
05790 PRINT INT((A0(77)/10)+.5)/100
05800 PRINT
05810 PRINT "LUNG: SEGMENT V/Q % VENT % PERF"
05820 FOR N=1 TO 9
05830 PRINT TAB(10);N;TAB(18);INT(A0(18+N)*100+.5)/100;TAB(27);
05840 PRINT INT(A0(N)*1000+.5)/10;
05850 PRINT TAB(38);INT(A0(9+N)*1000+.5)/10
05860 NEXT N
05870 PRINT
05880 PRINT
05890 RETURN
```

Store mixed venous tensions

```
05900 A1(8)=G4
05910 A1(9)=G5
```

Calculate and store brain venous tensions (to line 5960)

```
05920 K1=C6(1,1)*100
05930 K2=C6(1,2)*100
05940 GOSUB 6800
05950 A0(78)=G4
05960 A0(82)=G5
```

Calculate and store muscle venous tensions (to line 6010)

```
05970 K1=C6(2,1)*100
05980 K2=C6(2,2)*100
05990 GOSUB 6800
06000 A0(79)=G4
06010 A0(83)=G5
```

```
                        Calculate and store heart venous tensions (to
                        line 6060)

06020 K1=C6(3,1)*100
06030 K2=C6(3,2)*100
06040 GOSUB 6800
06050 A0(80)=G4
06060 A0(84)=G5

                        Calculate and store 'other' tissue bed venous
                        tensions (to line 6110)

06070 K1=C6(4,1)*100
06080 K2=C6(4,2)*100
06090 GOSUB 6800
06100 A0(81)=G4
06110 A0(85)=G5

                        Begin module 5 which determines alveolar
                        ventilation

06120 REM-------AF MODULE 5----DETERMINE VA
06130 REM--OPEN "VQ.DAT" AS FILE A0(100)
06140 REM--OPEN "TEST.DAT" AS FILE A1(25)

                        Calculate O2 consumption as % max VO2

06150 F9=(F8(1)/3.5)*100
06160 REM-----%VO2 MAX
06170 IF F9<=50 THEN 6200

                        Calculate minute ventilation if O2 consumption
                        is greater than 50% max

06180 F3=16.1887-.266675*F9+8.04466*EXP(.0273085*F9)+50000/(A0(68)-25)^3
06190 GO TO 6280
06200 K=3.8
06210 IF ABS(A0(69)-A0(65))<5 THEN 6250

                        Set controller to use arterial PCO2 if
                        (a-A)DCO2 is equal to or greater than 5 torr

06220 X1=A0(69)
06230 X2=A0(68)
06240 GOTO 6270

                        Set controller to use alveolar PCO2 if
                        (a-A)DCO2 <5
```

```
06250 X1=A0(65)
06260 X2=A0(64)

                        Calculate new minute ventilation

06270 F3=K*(X1-37.24)*(1+13.6/(X2-25))+50000/(X2-25)^3

                        Calculate old minute ventilation

06280 X=A1(6)*(A1(7)+150)/1000
06290 I6=I6-1
06300 PRINT "-";
06310 IF I6<0 THEN 6590

                        Compare new to old minute ventilation -- if
                        within 25 ml/min, go to output

06320 IF ABS(X-F3)<=.025 THEN 6500

                        Calculate new minute ventilation, respiratory
                        frequency and alveolar ventilation (to line
                        6480)

06330 IF F9<=50 THEN 6370
06340 F3=X+(F3-X)/3
06350 IF F3>=.5 THEN 6400
06360 GO TO 6390
06370 F3=X+(F3-X)/(.1*A0(73))
06380 IF F3>=.5 THEN 6400
06390 F3=2*X/3
06400 IF F3<67 THEN 6430
06410 R1=1.14+.35*F3
06420 GO TO 6450
06430 REM
06440 R1=EXP(LOG(6.25)+.34*LOG(F3))
06450 V1=(F3/R1)*1000-150
06460 IF V1>0 THEN 6480
06470 V1=10
06480 F2=V1*R1/1000
06490 GO TO 6520
06500 M=1
06510 GO TO 6560
06520 M=0
06530 A1(6)=R1
06540 A1(7)=V1
06550 A1(13)=F2
06560 A1(11)=M
06570 REM---CLOSE FILE IF CHAINED*
```

```
06580 GOTO 1180
06590 PRINT "ITERATION LIMIT"
06600 GOTO 1350
06610 PRINT "CARDIAC OUTPUT LIMIT EXCEEDED"
06620 GOTO 1350
06630 STOP
```

Begin blood-gas routines
Lines 6640 to 6790 take tensions and determine contents

Trial PO2=input PO2

```
06640 P3=G4
```

Calculate PCO2 shift to O2 saturation curve (to line 6690)

```
06650 A=.02272*EXP((30-G5)/115)
06660 IF (A*G4)<38.8 THEN 6700
06670 G4=00
06680 G5=5
06690 GOTO 6650
```

Calculate O2 saturation

```
06700 S=(1-EXP(-2.3*A*P3))^2
```

Calculate %Hb bound to oxygen

```
06710 S1=S*(100-H0)
```

PO2 in equilibrium with H0% HbCO

```
06720 P4=P3/(1+(H0/S1))
```

Compare calculated PO2 to input PO2 -- if within 0.05 Torr, calculate content

```
06730 D9=P4-G4
06740 IF ABS(D9)<.05 THEN 6770
```

Pick new trial PO2

```
06750 P3=P3+((G4-P4)/3)
06760 GOTO 6700
```

Calculate O2 content

```
06770 K1=1.34*(15*(1-H0/100))*S+.0031*G4

                          Calculate CO2 content

06780 K2=(14.9-1.65*S)*EXP(.35*LOG(G5))
06790 RETURN

                          Lines 6800 to 7070 take contents and determine
                          tensions

06800 M0=0

                          Pick first trial PO2

06810 P3=O0-10

                          Calculate PO2,PCO2

06820 GOSUB 6940
06830 T=P3
06840 D1=D

                          Pick second trial PO2

06850 P3=(O0-10)/2

                          Calculate PO2 and PCO2

06860 GOSUB 6940
06870 T1=P3
06880 M0=1

                          Choose new trial PO2 (to line 6910)

06890 P3=T1-D*((T1-T)/(D-D1))
06900 IF P3>=0 THEN 6920
06910 P3=T1/3
06920 T=T1
06930 D1=D

                          Calculate saturation with trial PO2

06940 S3=(K1-.0031*P3)/(1.34*H9)

                          Calculate saturation without HbCO

06950 S=S3*(1-H0/100)+(H0/100)
```

```
                        Calculate PCO2

06960 P4=(K2/(14.9-1.65*S))^(1/.35)

                        Calculate saturation using PO2 and PCO2

06970 A=.02272*EXP((30-P4)/115)
06980 S1=(1-EXP(-2.3*A*P3))^2

                        Calculate PO2 from saturation

06990 P5=(K1-S1*(1.34*H9))/.0031

                        Compare PO2's--if within 0.1 Torr then finish
                        routine (to line 7020)

07000 D=P3-P5
07010 IF M0=0 THEN 7070
07020 IF ABS(D)>.1 THEN 6870

                        Recalculate saturation and PO2 in presence of
                        HbCO (to line 7040)

07030 S3=S*100-H0
07040 P5=P5/(1+H0/S3)

                        Return PO2, PCO2

07050 G4=P5
07060 G5=P4
07070 RETURN
07080 END
```