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# EVALUATION OF EXERCISE-RESPIRATORY SYSTEM MODIFICATIONS AND PRELIMINARY RESPIRATORY-CIRCULATORY SYSTEM INTEGRATION SCHEME

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# I. INTRODUCTION

Both the circulatory and respiratory control systems are excellent examples which illustrate the influence of exercise upon physiological systems' responses. Certainly the magnitude and length of the exercise stimulus as well as the physical condition of the subject play an integral role in determination of the circulatory and respiratory systems' responses. Two major aspects of exercise simulation are discussed in the following report. The respiratory control system, functioning as an independent system, is presented with modifications of the exercise subroutine. These modifications illustrate an improved control of ventilation rates and arterial and compartmental gas tensions. A very elementary approach to describing the interactions of the respiratory and circulatory system is presented. This is the first step in developing a realistic interface between the simulations of these two major physiological systems.

## II. RESPIRATORY CONTROL SYSTEM SIMULATION MODIFICATIONS

For implementation and evaluation of exercise subroutine modifications for the respiratory control system simulations a spectrum of exercise levels were simulated (1). Appropriate magnitudes and lengths of exercise levels were implemented. These ranged from the resting state to a submaximal exercise level of 250 watts. After careful examination of the system's responses to each exercise level a level of 200 watts was chosen as the base run from which exercise subroutine modifications were evaluated. Although the simulation provides approximately 60 physiologically oriented output variables the following variables were closely monitored so as to determine the exercise simulation deficiencies.

(a) inspired ventilation rate ($V_I$, l/min)

(b) cerebrospinal fluid $H^+$ concentration ($C_{CSF(H^+)}$, nanomoles/l CSF)

(c) arterial $O_2$ tension ($P_{a(CO_2)}$, mm Hg)

(d) arterial $CO_2$ tension ($P_{a(O_2)}$, mm Hg)

(e) tissue $O_2$ metabolic rate ($MR_{T(O_2)}$, l/min)

(f) tissue $CO_2$ metabolic rate ($MR_{T(CO_2)}$, l/min)

(g) alveolar respiratory quotient (Alv RQ)

(h) cardiac output (Q, l/min)

(i) brain blood flow ($Q_B$, l/min)

Figure 1 illustrates the type of response generated by the system before the modifications were introduced. Inspired ventilation, $V_I$, contains a reasonable neurological component as illustrated by the immediate on-set of ventilation when exercise is initiated.

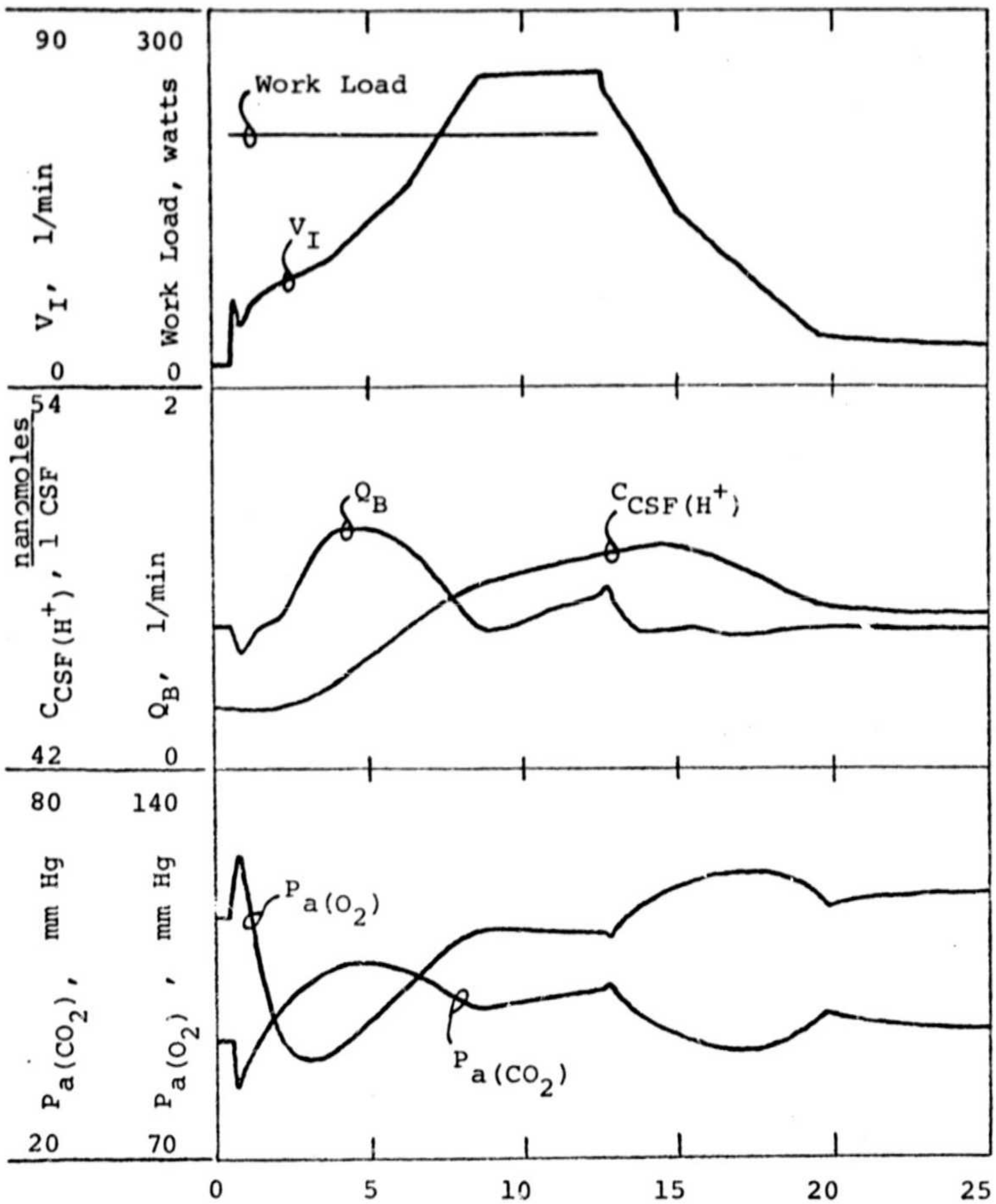



Figure 1. Selected variables from the respiratory system simulation of an exercise (work load) excitation prior to exercise subroutine modifications.

Then there is a slowly rising $V_I$ response, humoral component, which doesn't allow for sufficient ventilation in order to regulate the arterial $O_2$ and $CO_2$ tensions. This effect is also demonstrated in the tissue $O_2$ and $CO_2$ tension responses. The inadequate blow-off of $CO_2$ is reflected in the increased concentration of the $H^+$ ion in the CSF compartment. Since the CSF compartment's $H^+$ ion is an important regulator of ventilation one would expect to see an increase in the ventilation rate; however, this regulatory component is of minor importance in exercise simulations with normal environmental conditions, i.e. physiologically compatible atmospheric gaseous mixtures. Also evidenced from Figure 1 is the poor regulation of brain blood flow which correlates with an insufficient ventilation rate.

Similar observations can be made with regard to the off-transient exercise phenomenon. In addition, the piece-wise linear off-transient $V_I$ response is not physiologically justifiable.

Two basic modifications were implemented. These modifications yielded more satisfying results. In compliance with Åstrand and Rodahl (2) a change in the functional relationship between steady-state $O_2$ requirement and exercise level (SSO2W(WORK)) was made. All functional discontinuities were removed giving the relationship

$$\begin{aligned} SSO2W(X) &= (X/75.) + .215*(75.-X)/75., \quad 0 \leq X < 75 \\ &= -.072 + X/70., \quad 75 \leq X \leq 250 \\ &= 3.5, \; X > 250 \quad \text{for } X = \text{WORK} \end{aligned}$$

For a 200-watt exercise level this increased the steady-state $O_2$ requirement by 4.5% to 2.785 l/min and correspondingly increased steady-state ventilation approximately 6.4% (1). One should remember that these changes are reflected in the system responses for the respiratory control system independent of a circulatory system simulation. This type of simulation will be discussed later.

The other major modification which improved the ventilation response and consequently the regulatory aspects of the system involved the exponential functional expression that describes the on- and off-transient ventilation responses. VTIME is an expression in subroutine RC12 which indirectly describes the dependency of ventilation upon magnitude and duration of exercise levels. By altering the expression for VTIME a satisfactory on- and off-transient response for ventilation was achieved. VTIME for the on-transient response was expressed as

VTIME = 1.1 - 1.1*EXP(-TCT*(CXT-TIMEON)/1.92)

and for off-transient as

VTIME = 1.1 - 1.1*EXP(-TCT*(CXT-TIMEON)/3.84)

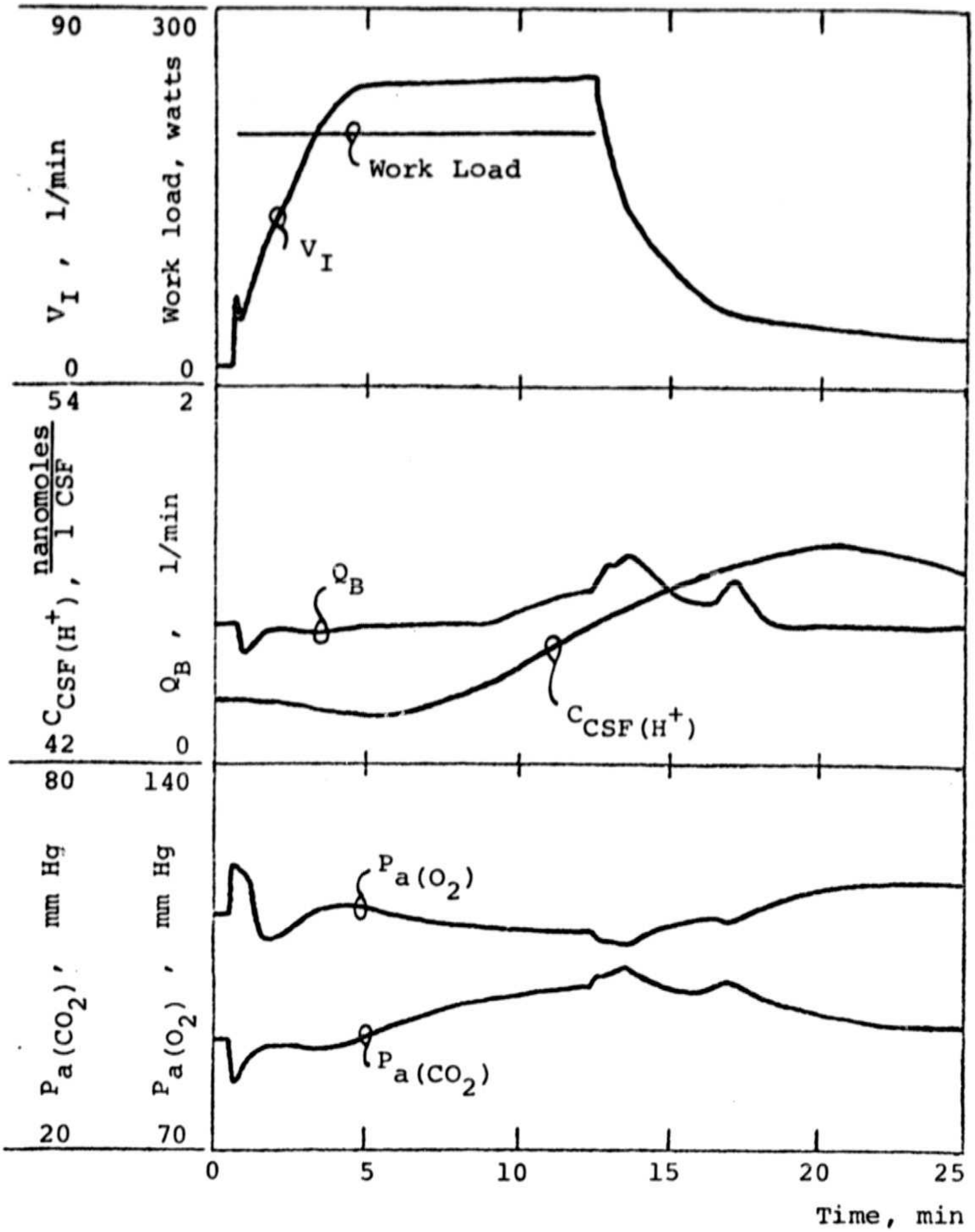
where

1/TCT = time constant associated with the exponential functions related to exercise levels.

CXT = simulated time, and

TIMEON = time for initialization of new exercise level.

Figure 2 illustrates the responses utilizing the forementioned modifications. The neurological component of the $V_I$ response is still present. Steady-state ventilation is approached much more swiftly with a slight upward trend in ventilation prevailing until exercise is terminated. The faster response in ventilation rate, which is more acceptable physiologically speaking, provides a better regulation of the arterial $O_2$ and $CO_2$ tensions during the initial portion of the exercise stimulus. Also, better regulation of cerebral blood flow is observed. There still seems to be an apparent




Figue 2. Selected variables from the respiratory system simulation of an exercise (work load) excitation utilizing exercise subroutine modifications.

misrepresentation of the system in the off-transient mode.

To further illustrate the capabilities of the system to respond to a variety of exercise levels a 40-minute simulation involving the following series of exercise levels was run.

| Exercise level (Work load, watts) | Duration (min) |
|---|---|
| 0 | 0.5 |
| 40 | 2.0 |
| 100 | 3.0 |
| 150 | 5.0 |
| 0 | 7.0 |
| 150 | 5.0 |
| 250 | 5.0 |
| 0 | 12.5 |

The system variables, $V_I$ (l/min), $C_{CSF(H^+)}$ (nanomoles/lCSF), $Q_B$ (l/min), $P_{a(CO_2)}$ (mm Hg), and $P_{a(O_2)}$ (mm Hg) are shown in Figure 3. Justifiable regulation of $P_{a(CO_2)}$ and $P_{a(O_2)}$ was achieved. $Q_B$ is regulated during on-transient periods and for low to medium exercise levels; however, the off-transient of $Q_B$ corresponding to sub-maximal exercise levels exhibits poor control which is supportive of the statements made in the previous paragraphs.

Perhaps, observations of the integrated respiratory-circulatory system will provide an insight to the metabolic requirements of $O_2$ during the off-transient mode and thus allow for a more realiable independently simulating respiratory system.

Another modification has been implemented without appreciable sacrifice in the simulation's fidelity. This modification involves the differential equation subroutine RC13. Since the system's variables are not rapidly varying as a function of time the thesis is the following. There is no real requirement for a differential

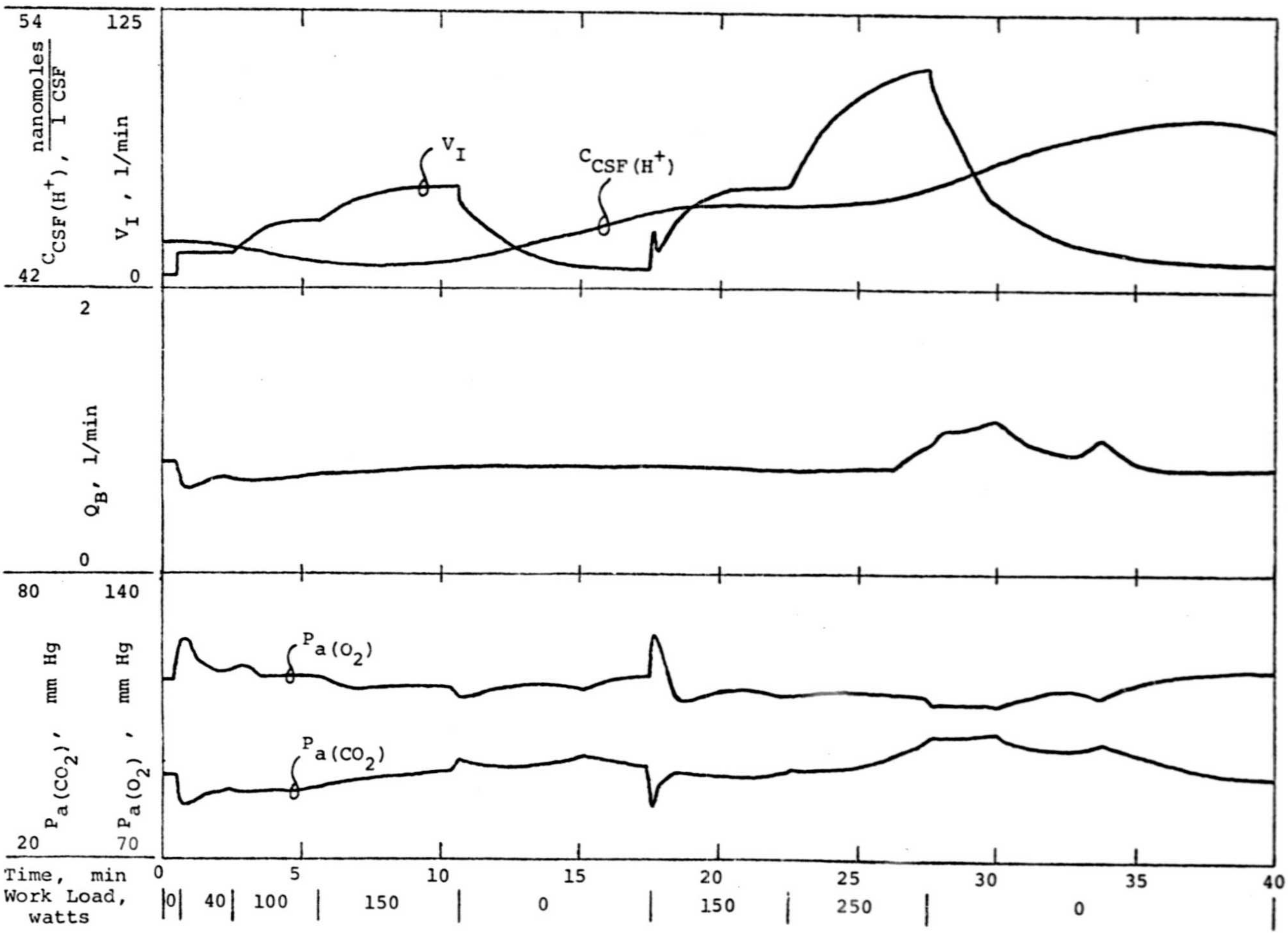



Figure 3. Selected variables from the respiratory system simulation of several exercise (work load) excitations utilizing exercise subroutine modifications.

equation subroutine having the capabilities of a 4th order Runge-Kutta method and an Adams-Moutlon predictor-corrector scheme. Using this criterion the following subroutine may be substituted for the forementioned method.

```
      C(35) = C(35) + C(36)
      CALL RC14
      DO 1350 I = 1, M
1350  C(I) = C(I) + C(36)*DC(I)
      RETURN
      END
```

Here C(35) = time,

C(36) = time increment,

C(I) = system variable, and

DC(I) = derivative of system variable.

In the initial portion of the variables' transient responses there is a small variation in comparison of the responses of the simulations using the two differential equation routines. This variation would be expected during this particular portion of the response if it occurred at all since the variables are changing most rapidly here. Although not as yet evaluated, it appears that this modification would present the most difficulties when simulating extreme variations in environmental gaseous concentrations.

## III. ELEMENTARY RESPIRATORY-CIRCULATORY SYSTEM INTERFACE

There are several approaches that can be taken in the process of combining the two simulations of the respiratory and circulatory systems. The one discussed here entails a minimum amount of alteration of the existing systems and yet provides an interface that improves or supplements the simulation responses of each system. The basic structure of the interfacing scheme that has been implemented is illustrated in Figure 4.

Descriptions of the two basic control systems are only referenced here (1, 3-6). Exercise simulations are of prime importance; thus it is included as one of the major stimuli. Other stimuli include the option of changing system parameters or properties. Not all parameters are common to both systems as further explained in the following paragraphs. Another stimulus which directly affects the respiratory system is the gaseous make-up of the environment. Under the existing formulation of the circulatory system the responses to environmental variations are not simulated.

Additional comments regarding the effects of these stimuli follow. With regard to the exercise phenomenon it is important to consider aerobic and anerobic oxygen deficits and debts. As an improvement upon the formulation of the $O_2$ metabolic rate of the tissue compartment in the respiratory system simulation the following interface was established. $MR_{T(O_2)}$ is obtained from a weighted conversion on the rate of $O_2$ delivery by the blood to the muscle tissue (RMO) and the rate of $O_2$ delivery by the blood to the non-muscle tissue (DOB). The total $O_2$ metabolic rate of the body is

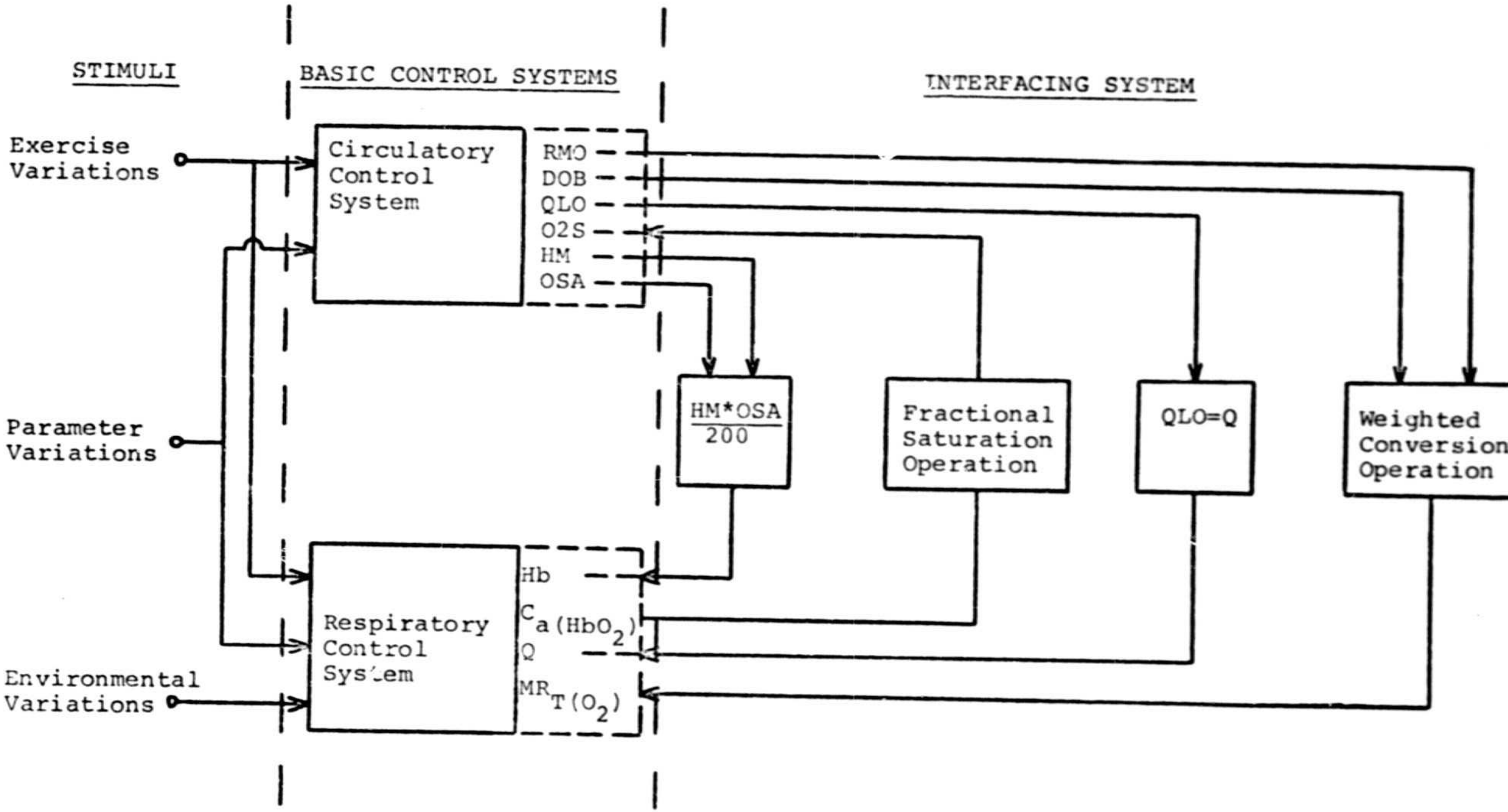



Figure 4. Proposed integration scheme for respiratory and circulatory control systems.

given as

$$\frac{(RMO + DOB)}{1000} = RMT(2) + C(26) = MR_{T(O_2)} + MR_{B(O_2)}.$$

Thus, $MR_{T(O_2)}$ is obtained from the circulatory system simulation which provides a more reasonable description of the variable. The calculation of the metabolic production rate of $CO_2$ in the tissue compartment is retained in the respiratory system simulation. Also, direct neurological control of ventilation related to exercise levels is retained in the respiratory model.

The total cardiac output is an important component of both systems. The circulatory system simulation describes cardiac output as a weighted expression of several physiological attributes. In the respiratory system it is functionally dependent upon specific levels of $O_2$ and $CO_2$. Based upon the comparisons of these two foundations and the complexity of altering each, the decision was made to allow the respiratory system to receive cardiac output from the circulatory system. The formulation of cerebral blood flow is retained in the respiratory system.

Another interfacing component involves the blood oxygen capacity. In the respiratory system this term is a constant (Hb = C(17)) alterable by an input data card. Once again this term is continuously calculated in the circulatory system as $\frac{HM \cdot OSA}{200}$ where HM = hematocrit and OSA = arterial oxygen saturation. Thus, the circulatory system provides this term. In turn the oxygen volume attached to hemoglobin in the aortic blood is provided by the respiratory system. The circulatory system uses this term in the expression OVA = 1000* CHBA where CHBA = $C_{a(HbO_2)}$. It is hoped that this interaction will be of particular importance when the inspired gas concentrations are altered since $C_{a(HbO_2)}$ changes under those conditions. It is postulated that this particular pathway would provide an environmental stimulus to the circulatory system model. Since the venous blood in the respiratory model is not correlated with any particular venous site in the circulatory model the calculations of tissue venous hemoglobin concentration ($C_{vT(HbO_2)}$) is retained in the individual models.

## IV. EVALUATION OF RESPIRATORY-CIRCULATORY SYSTEM INTERFACE

Preliminary runs have been made with the proposed respiratory-circulatory system interface. In order to establish a base run, appropriate initial conditions had to be obtained for the respiratory system component. Basically, cardiac output and metabolic rates had to be made compatible between the two systems. The input data as shown in Appendix 6.1, Table 2 of the reference by Gallagher (4) was utilized with the following modifications.

| Input Data Card No. | Variable | New Value |
|---|---|---|
| 10 | Q | 5.1200 |
| 25 | MRB(CO2) | .0450 |
| 26 | MRB(O2) | .0450 |
| 31 | FI(CO2) | .0004 |
| 32 | FI(O2) | .2096 |
| 33 | FI(N2) | .7900 |
| 39 | PRINT AL TIM | .2000 |
| 45 | RMT(CO2) | .1716 |
| 46 | RMT(O2) | .1950 |

Table 1. Input data cards reflecting changes in cardiac output and metabolic changes under normal environmental gaseous conditions.

This simulation was allowed to run until steady-state conditions were reached, i.e. changes in C(1) - C(14) were minimal. These values for C(1) - C(14) were then established as the input data for normal environmental conditions. The variable values obtained for the steady-state conditions are tabulated below.

| Input Data Card No. | Variable | Value |
|---|---|---|
| 1 | FA(CO2) | .1767 |
| 2 | FA(O2) | .5338 |
| 3 | FA(N2) | .2895 |
| 4 | CB(CO2) | .6345 |
| 5 | CB(O2) | .0012 |
| 6 | CB(N2) | .0011 |
| 7 | CT(CO2) | .6142 |
| 8 | CT(O2) | .0014 |
| 9 | CT(N2) | .0013 |
| 10 | Q | 5.1554* |
| 11 | QB | .7391 |
| 12 | PCSF(CO2) | 46.3498 |
| 13 | PCSF(O2) | 38.4441 |
| 14 | PCSF(N2) | 70.6931 |

*Perhaps Q = 5.12 should be used for complete compatibility with the circulatory system.

Table 2. Initial conditions for physiological variables under normal environmental conditions.

Several exercise simulations were then performed utilizing the integrated system. Both on- and off-transient exercise conditions were simulated using the above inital conditions. An example of a run which correlated very well with a previously performed respiratory system exercise simulation is listed here.

| Exercise level (Work Load, watts) | Duration (min) |
|---|---|
| 0 | 0.5 |
| 40 | 3.0 |
| 100 | 3.0 |
| 150 | 5.0 |
| 0 | 9.0 |

For a general evaluation of the integrated system performance as compared to the performance of the respiratory system functioning alone the following comments are made. The integrated system, for any of the exercise levels, provides increased cardiac output, inspired and expired ventilation rates, alveolar RQ, tissue $P_{O_2}$, and decreased arterial and tissue $P_{CO_2}$, arterial $P_{O_2}$, and brain blood flow. Other physiological variables are altered accordingly. Although no definite trend can be established, the VI-VE difference is changed when the integrated system is performing as compared to the independently functioning respiratory system. A closer evaluation should be in order before any firmer statements are made with regard to the system's performance under these conditions.

Similar types of simulations were performed under altered environmental conditions. As previously described the establishment of initial conditions was necessary. To evaluate these initial conditions the input data as shown in Appendix 6.1, Table 2 of the reference by Gallagher (4) was used with the following modifications.

| Input Data Card No. | Variable | New Value |
|---|---|---|
| 10 | Q | 5.1200 |
| 25 | MRB(CO2) | .0450 |
| 26 | MRB(O2) | .0450 |
| 30 | B | 260.0000 |
| 31 | FI(CO2) | .0192 |
| 32 | FI(O2) | .7000 |
| 33 | FI(N2) | .2808 |
| 39 | PRINT AL TIM | .2000 |
| 45 | RMT(CO2) | .1716 |
| 46 | RMT(O2) | .1950 |

Table 3. Input data cards reflecting changes in cardiac output and metabolic changes under altered environmental conditions.

As before, this simulation was allowed to run until steady-state conditions were established. Input data cards C(1) - C(14) shown below correspond to steady-state conditions for the altered environmental conditions.

| Input Data Card No. | Variable | Value |
|---|---|---|
| 1 | FA(CO2) | .1767 |
| 2 | FA(O2) | .5338 |
| 3 | FA(N2) | .2895 |
| 4 | CB(CO2) | .6345 |
| 5 | CB(O2) | .0012 |
| 6 | CB(N2) | .0011 |
| 7 | CT(CO2) | .6142 |
| 8 | CT(O2) | .0014 |
| 9 | CT(N2) | .0014 |
| 10 | Q | 5.1554 |
| 11 | QB | .7391 |
| 12 | PCSF(CO2) | 46.3498 |
| 13 | PCSF(O2) | 38.4441 |
| 14 | PCSF(N2) | 70.6931 |

Table 4. Initial conditions for physiological variables under altered environmental conditions.

As illustrated by the values of Table 4 the combination of barometric pressure and volumetric gas fractions of the altered environment provides a physiological condition similar to that at sea level. One of the interesting experiments involves implementing the conditions as illustrated in Tables 3 and 4 and observing the effects of exercise upon the system. On-and off-transient exercise conditions were simulated for levels of 50, 100, 150, and 200 watts. Each level was of a duration that allowed for the physiological variables to attain or approach their steady-state conditions. Results similar to those described for the normal environmental conditions were observed.

As previously mentioned one of the goals of the interfacing system was that of providing the circulatory system with an environmental stimulus via the respiratory system. At present, this type of simulation has not been realized. Further investigation is necessary and will be pursued. It appears that an additional forcing variable described as a function of $CO_2$ will be required in the formulation of cardiac output in the circulatory system component of the integrated system. The lone tie, $C_{a(HbO_2)}$, does not supply enough stimulus to encompass the total interaction required.

## V. SUMMARY AND PROJECTED RESEARCH ENDEAVORS

With respect to the circulatory-respiratory integrated system the immediate thrust is its utilization in demonstrating the dependency of the ventilation rate upon abnormal functioning of the circulatory system. Under normal or physiologically compatible environmental conditions the circulatory system is stressed and then the integrated system is exercised. Respiratory system responses under these conditions should be most enlightening. The simulations will be implemented in the following manner. Steady-state conditions will be obtained for the circulatory system under the given stress condition. A multitude of conditions could be categorized as stressful situations. Examples could include any malfunctioing of the renal system, large degree of fluid intake, unilateral or bilateral heart failure, regional volume loading, anemia, or hematocrit level variations.

Once the steady-state has been established for the circulatory system the integrated system is made operative and steady-state conditions are realized for the respiratory system. Then the exercise stimulus is introduced. As planned now the outputs of the simulation are put on magnetic tape with a graphical display made available by calling the output variables off of tape and plotting on the Calcomp plotter. Several variables from both subsystems are desired. The variables from the respiratory system component are included in Table 5.

| Physiological Variable | Computer Variable | Range |
|---|---|---|
| VI | VI | 0-90 |
| VE | VE | 0-90 |
| $P_{a(CO_2)}$ | F(7) | 20-60 |
| $P_{a(O_2)}$ | F(1) | 70-140 |
| $P_{T(CO_2)}$ | CPT | 20-90 |
| $P_{T(O_2)}$ | PTO2 | 20-70 |
| $C_{CSF(H^+)}$ | CH(4) | 42-54 |
| Q | Q* | 0-30 |
| $Q_B$ | QB | 0-2 |
| Work Load | Work 2 | 0-300 |
| $MRCO_2$ | RMT(1) | 0-6 |
| $MRO_2$ | RMT(2) | 0-4 |
| Alveolar RQ | RQ | 0-4 |

*Q = QLO in circulatory system

Table 5. Output variables from respiratory system component of integrated system that are needed for plotting routine.

It is anticipated that the ranges indicated in Table 5 will allow for direct comparison of results for exercise levels of 0-200 watts. Specific exercise levels of 50, 100, and 150 watts are planned. Results of these simulations are forthcoming. Continued efforts in the development of a more thoroughly integrated system for the respiratory and circulatory systems will be made.

Initial steps are under way to develop another integrated system using a pulsatile cardiovascular system model and the respiratory system model. The two models must be made compatible for the resting steady-state case. To allow for this compatibility to exist it is necessary to establish the empirical a-v $O_2$ difference curve for a range of exercise levels as formulated by the present respiratory program. In the integrated system cardiac output will be supplied by the cardiovascular system component. One variable that is of importance as a forcing function to the cardiovascular system is respiratory frequency. Respiratory frequency is now available in the respiratory system; however, a more physiologically based expression is required. This expression should include neurological and humoral control and should be valid for both resting and exercising subjects in altered environments.

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