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RESEARCH REPORT

EVALUATION OF EXERCISE-RESPIRATORY SYSTEM MODIFICATIONS AND INTEGRATION SCHEMES FOR PHYSIOLOGICAL SYSTEMS

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ABSTRACT

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Exercise subroutine modifications are implemented in an exercise-respiratory system model yielding improvement of system response to exercise forcings. A more physiologically desirable respiratory ventilation rate in addition to an improved regulation of arterial gas tensions and cerebral blood flow is observed. A respiratory frequency expression is proposed which would be appropriate as an interfacing element of the respiratory-pulsatile cardiovascular system.

Presentation of a circulatory-respiratory system integration scheme along with its computer program listing is given. The integrated system responds to exercise stimulation for both nonstressed and stressed physiological states. Other integration possibilities are discussed with respect to the respiratory, pulsatile cardiovascular, thermoregulatory, and the long-term circulatory systems.

EVALUATION OF EXERCISE-RESPIRATORY SYSTEM MODIFICATIONS AND INTEGRATION SCHEMES FOR PHYSIOLOGICAL SYSTEMS

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

1. INTRODUCTION

1.1 Overview of Modeling Effort

The major objectives and emphasis of the overall physiological system modeling effort focus on the development of an effective whole-body algorithm as being the most significant feature. (1) Utilizing system theory, mathematical descriptions of physiological functions, appropriate empirical interrelationships between variables, and a computer implementation and display system complex physiological systems have been realized.

Physiological systems that were deemed important to the project's overall goals included the respiratory, fluid-electrolyte balance circulatory, pulsatile cardiovascular, and thermoregulatory systems. Proper evaluation, modification, and adaptation of selected models (2-5) have been made with their implementation coordinated with the project's goals. The indicated references provide the necessary details of the models. Therefore, only specific modifications will be discussed in this report.

The computer program for the integrated circulatory and respiratory control systems which will be presented in more detail in later sections is included in the Appendix. This program is comment laden and provides an adequate description of the involvement of each subroutine within itself and also its relationship to other subroutines in the program. Many of the comments in the respiratory system component refer to Grodins' basic model. (2) Block diagrams and explanatory material for each of the two major systems (circulatory and respiratory) are given by White (6) and Gallagher (7).

Since the primary thrust of the modeling revolves around the effects on parameters that are influenced by the space environment, variations in gravitational forces, external body pressures, inspired gas composition, and thermal conditions are some of the inputs utilized in determining dynamic physiological responses and associated hypotheses. Implementation and coordination of the simulations with major Skylab experiments provide the research-application impetus. Such a research effort demands a well-defined set of tasks which are fulfilled in sequence and/or concert. Some of the major milestones which are detailed by numerous specific tasks include

(a) evaluation and modification of major physiological subsystems,

(b) development and evaluation of hypotheses regarding physiological systems responses' to stresses and altered environments,

(c) implementation of integrated system simulations and verification of responses, and

(d) implementation of supporting software systems for collecting, storing, and correlating simulated and experimental data.

With utilization of this complete whole-body simulation or its selected subsystems, revised techniques for remote medical care can be evaluated and implementation procedures established for future manned spaceflights. In addition, potential diagnostic and therapeutic capabilities may emerge from correlation of simulation and physiological testing during real time medical monitoring. In keeping with the spirit of the project one should not lose sight of the important contribution that simulation provides in understanding physiological processes under the influence of normal and altered environments.

1.2 Exercise and the Respiratory System Model

The respiratory control system is an excellent example of a physiological system that illustrates the influence of exercise upon its variables' responses. The magnitude and length of the exercise stimulus as well as the physical condition of the subject play integral roles in determination of the system's responses. One aspect of exercise simulation discussed in the following report involves the respiratory control system functioning as an independent system. Modifications of the exercise subroutine are evaluated illustrating improved control of ventilation rates and arte ial and compartmental gas tensions.

1.3 Integration of Physiological System Models

There are several approaches which can be taken in the process of integrating the simulations of the respiratory and circulatory systems. Since both systems' dynamic responses are influenced by exercise and with exercise variations and their associated physiological forcing roles being major components of the manned spaceflight medical experiments, the integration scheme revolves around the implementation of exercise simulations. As implied in Section 3 there are extensions in the utility of these models for nonspaceflight experiments. (8)

In the following report emphasis is placed upon the interface component of the integrated model. For details concerning other variable formulations in the individual modes one should refer to the references. (2, 3, 6, 7). The interface allows for a minimal amount of alteration of each existing system while improving or supplementing the simulation responses of each system.

The integrated system can be described in terms of three functional components; stimuli, basic control systems, and the interfacing system as illustrated in Figure 1. Major categories of stimuli include exercise, parameter, and environmental variations.

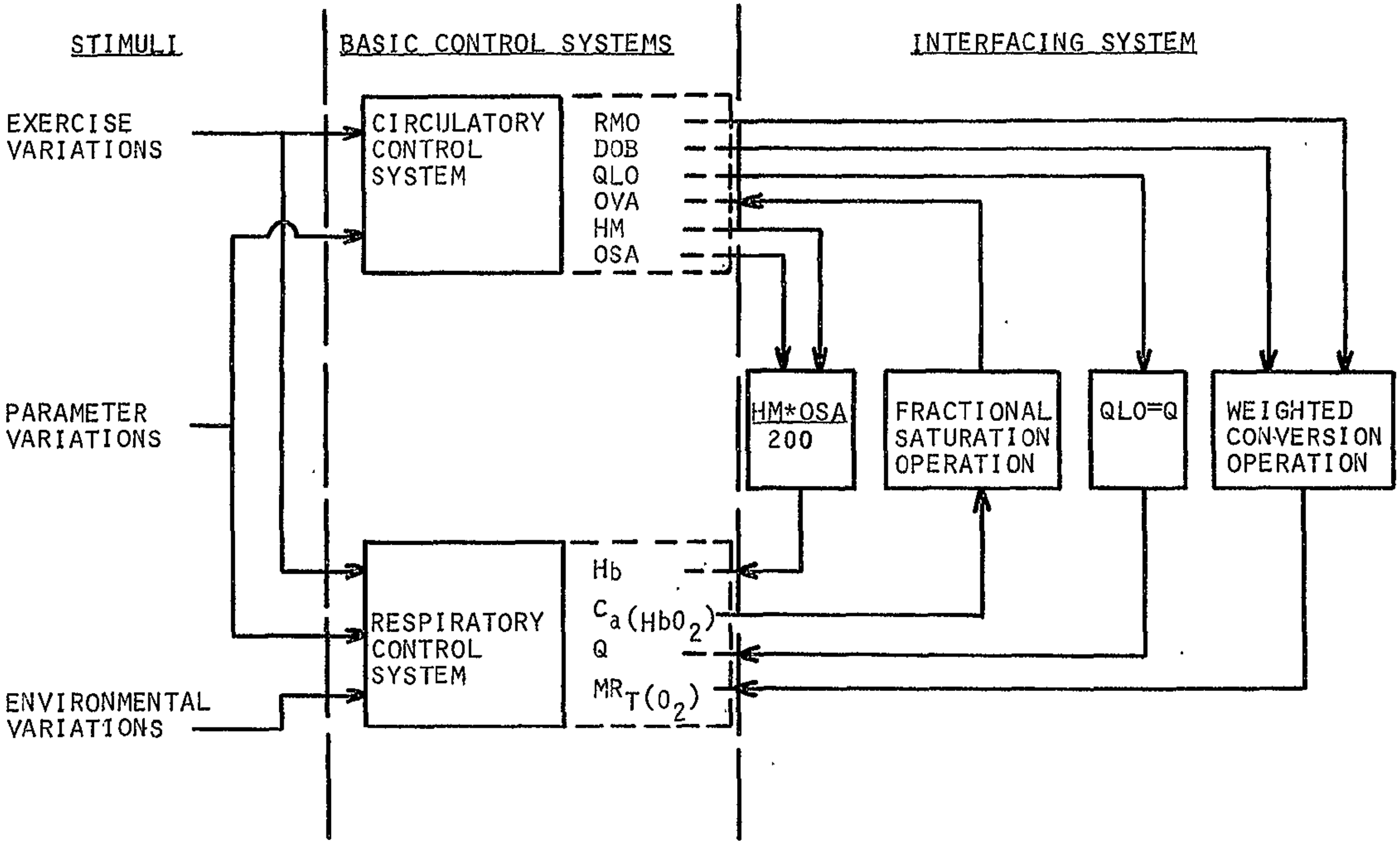

Figure 1. Integration scheme for respiratory and circulatory control systems.

As previously mentioned emphasis is placed upon the exercise stimulus since several manned spaceflight experiments stress man's physiological performance under various exercise levels in an altered environment.

Since all of the basic control system's parameters are not common to both subsystems another stimulus includes the option of changing subsystem parameters and properties. This allows for investigation of the response of one system to a particular physiological change when that response is only indirectly related to that change. Therefore, another dimension of complexity has been added to physiological system modeling which has been previously unavailable.

Another stimulus which directly affects the respiratory system model is the gaseous composition of the environment. Responses to these environmental variations are not available in the existing formulation of the circulatory system model. The implications of providing an indirect environmental stimulus to the circulatory system via the respiratory system enhances the capabilities of the integrated system. Preliminary simulations of this classification of experiemnts have indicated a need for additional modifications of the circulatory system so that it is sensitive to the environmental stimuli.

1.4 Improved Respiratory Frequency Expression

Exercise presents the organism with the task of rapidly and optimally adapting to the requirements imposed upon it. One of these tasks is to increase ventilation in order to meet the accelerated metabolic demand for O_2 by the exercising muscle systems and the corresponding need to vent the CO_2 byproduct.

A ventilatory stimulus could be considered a physiological variation which acts upon the respiratory centers and supplies information about the respiratory requirements of the body. There are two classifications of ventilatory stimuli: humoral and neural. Humoral stimuli involve modifications in the physical or chemical properties of the circulating blood that stimulate the respiratory centers either directly through the blood or via afferent nerve endings located in receptors in contact with the vessels. These are termed chemoreceptors and baroreceptors. The other stimuli are classified as neural stimuli. They originate in the brain or in cutaneous, mucosal, or deep peripheral receptors. Generally, these respond to localized conditions. Humoral and neural factors are postulated as controlling respiratory frequency.

The complexities of the interactions between neural and humoral control are manifested during exercise. The individual must increase ventilation to a level sufficient to provide the additional O_2 intake and CO_2 venting demanded by the body's high level of exercise metabolism. However, exercising subjects ventilate at a rate that exceeds the increases that would be dictated solely by arterial P_{CO_2}, pH, and P_{O_2} alone. (7) The difference between the humoral requirements and the actual ventilatory rate must then be a function of neural stimuli. This could be the result of neural pathways between the motor cortex and the respiratory centers and feedback from the forementioned proprioceptors. The neural factors assume even greater significance when ventilation is plotted as a function of exercise level and duration; however, there seems to be an upper limit of neural stimulation. It is noted that there is a rapid increase in perspiration immediately after the onset of exercise; this component has been postulated to be strictly neurological in nature.

An important question about ventilation, both for resting states and during exercise, concerns the actual frequency of respiration. It is obvious that identical ventilation requirements can be fulfilled either with a series of rapid, shallow inspirations or with long, deep ventilations.

The ventilation formulation in the respiratory system model is a satisfactory representation. The respiratory frequency expression is the one for which modifications are proposed. It is desirable to have a physiologically based expression for respiratory frequency since this could become an important interfacing component for the respiratory-pulsatile cardiovascular system model.

1.5 Acknowledgements

The author wishes to acknowledge the NASA-ASEE Summer Faculty Research Program for its support during particular phases of the study. Continuation of the research was supported in part by the General Electric Company (Purchase Order No. 036-E31001-T1494) and the Kansas State University Engineering Experiment Station. Special gratitude is extended to the personnel of the General Electric Company for their system programming and evaluation support in addition to Mr. John Schmalzel of Kansas State University.

2. EVALUATION OF EXERCISE SUBROUTINE MODIFICATIONS IN THE RESPIRATORY SYSTEM MODEL

2.1 Statement of Objectives

With the respiratory control system model functioning as an independent system certain modifications of the exercise subroutine allow for a more realistic response to exercise stimulation. These modifications apply to both on- and off-transient responses. Evaluation of these modifications which preserve the neural and humoral control of ventilation is desired.

2.2 System Response Before Implementation of Modifications

The discussion in this section refers to the respiratory system functioning independently with all modifications relating to the computer program as listed in the Appendix of Gallagher's report. (7) Some of the modifications are included in the integrated circulatory-respiratory system model in addition to the modifications required for the interfacing of the two systems.

For implementation and evaluation of exercise subroutine modifications for the respiratory control system simulations a spectrum of exercise levels were simulated. Appropriate magnitudes and lengths of exercise levels were implemented. These ranged in magnitude from the resting state to a submaximal exercise level of 250 watts and in durations of 2.5 to 12.0 minutes depending upon the exercise increment.

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, 1/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)

Figures 2 and 3 illustrate the type of responses generated by the system before the modifications were introduced. In general, the greater the exercise level the more pronounced are the variables' transient responses. If one would superimpose a variable's response for a wide range of exercise levels a family of curves illustrating trends in the variable's response to exercise stimulation would be evident. After careful examination of the system's responses to each exercise level the 200 watt level was chosen as the base run from which exercise subroutine modifications were evaluated.

For the following discussion of the simulation deficiencies refer to Figure 3. Inspired ventilation, V_I, contains a reasonable neurological component as illustrated by the immediate on-set of ventilation when exercise is initiated.

This is followed by a slowly rising V_I response, the humoral component. Sufficient ventilation is not available in order to properly regulate the arterial O_2 and CO_2 tensions as demonstrated by these 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

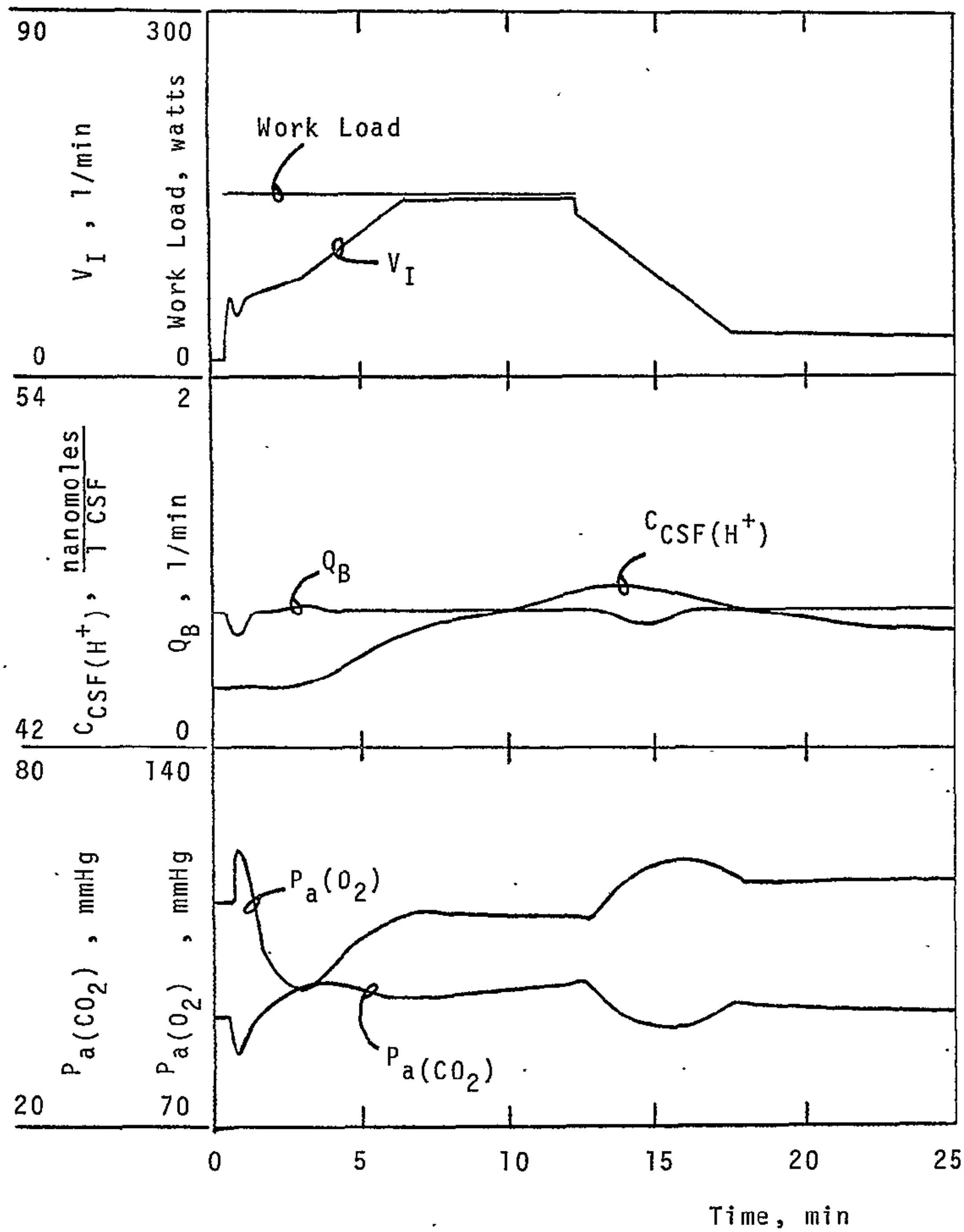

Figure 2. Selected variables from the respiratory system simulation of an exercise (work load) excitation of 150 watts prior to exercise subroutine modifications.

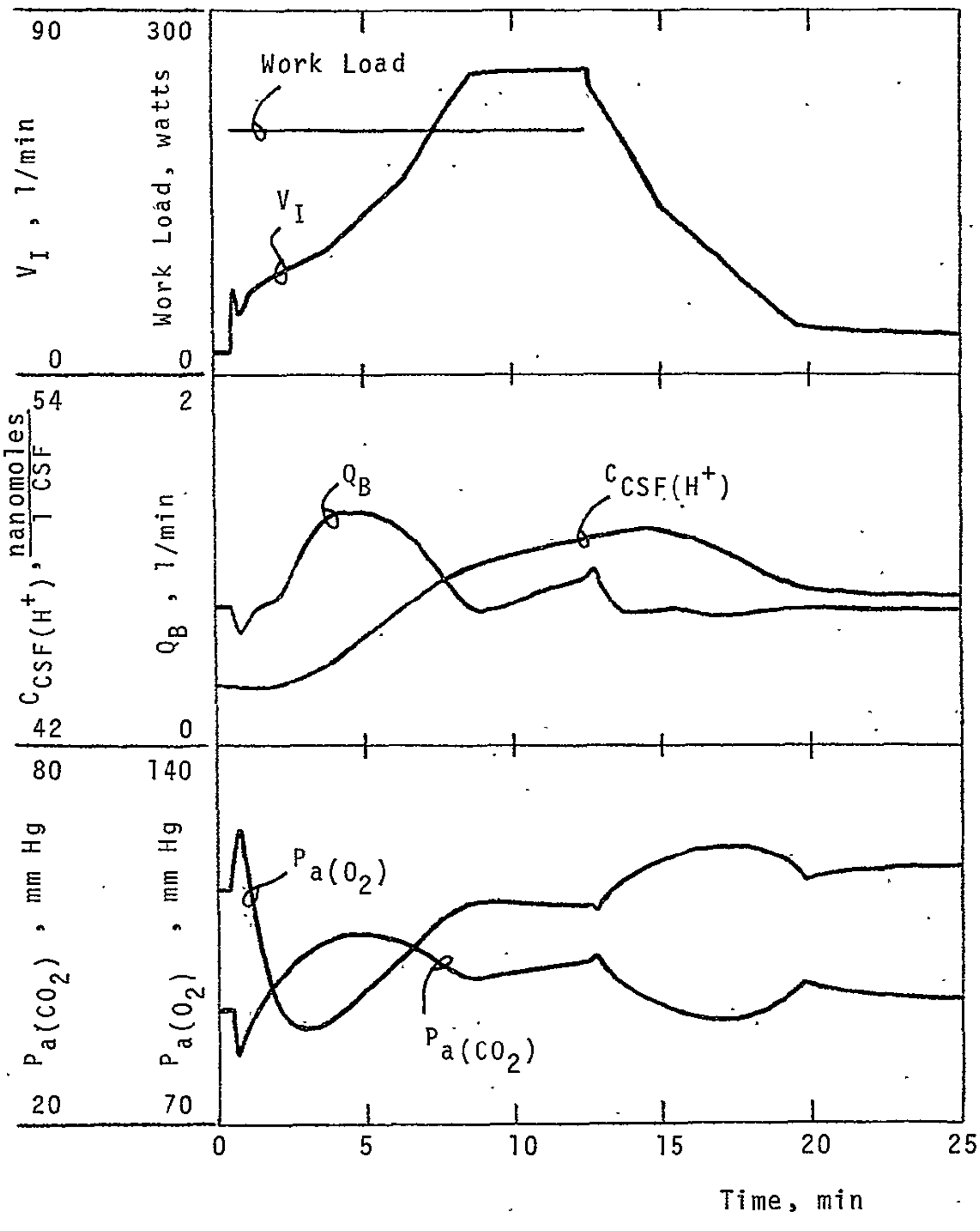

Figure 3. Selected variables from the respiratory system simulation of an exercise (work load) excitation of 200 watts prior to exercise subroutine modifications.

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 3 is the simulation's inadequate regulation of cerebral blood flow. This response correlates with an insufficient ventilation rate.

The off-transient exercise response provides a ventilation rate that exceeds the necessary rate. In other words, the ventilation rate causes an increase in arterial O_2 tension and a decrease in arterial CO_2 tension which could be smoothed with proper modification of the exercise subroutine. In addition, the piece-wise linear off-transient V_I response is not physiologically justifiable.

2.3 System Response After Implementation of Modifications

Three basic modifications were implemented in the respiratory system program yielding improved simulations. These changes are reflected in the system responses for the respiratory control system independent of the circulatory system simulation. Consequently, these program changes are not contained in the program listing in the Appendix. Variations of some of these expressions with the integrated system are discussed in Section 3.

In compliance with Åstrand and Rodahl (9) a change in the functional relationship between steady-state O_2 requirement and exercise level (SSO2W(WORK)) was made. The functional discontinuities listed in the statements of subroutine SSO2W(X) were removed yielding the relationship

$$\begin{aligned} SSO2W(X) &= (X/75.) + .215*(75.-X)/75., \quad 0 \leq X < 75 \\ &= -.072 + X/70., \quad 75 \leq X \leq 250 \\ &= 3.5, \; X > 250 \quad \text{for } X = WORK \end{aligned} \tag{2-1}$$

For a 200-watt exercise level this change increased the steady-state O_2 requirement by 4.5% to 2.785 l/min and correspondingly increased steady-state ventilation approximately 6.4%. (10) Thus, this subroutine dictates the steady-state level of required O_2 for an exercise stimulus and can be easily altered to meet individual demands.

Another 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. The VTIME expression which was applicable for both the on-transient and off-transient responses to exercise stimulation was originally programmed as

VTIME = TCT*(CXT-TIMEON)/9.2 . (2-2)

Modification of this expression yielded for the on-transient case the expression

VTIME = 1.1-1.1*EXP(-TCT*(CXT-TIMEON)/1.92) (2-3)

and for the off-transient case

VTIME = 1.1-1.1*EXP(-TCT*(CXT-TIMEON)/3.84). (2-4)

Here,

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 4 illustrates the responses utilizing the forementioned modifications. The modifications retain the neurological component of inspired ventilation, V_I, and allows steady-state ventilation to be approached much more swiftly with a slight positive derivative in the ventilation rate prevailing until exercise is terminated. The faster response in ventilation rate, which is more acceptable physiologically speaking, provides good regulation of the arterial O_2 and CO_2 tensions during the initial portion of the exercise stimulus in addition to good regulation of cerebral blood flow.

Although not a critical problem, the off-transient response needs some refinement. The build-up of H^+ concentration in the CSF compartment suggests further modifications in the metabolism formulations. Cerebral blood flow, although not unstable, possesses a response which should be smoother.

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 5. Justifiable regulation of $P_{a(CO_2)}$ and $P_{a(O_2)}$ is achieved. Q_B

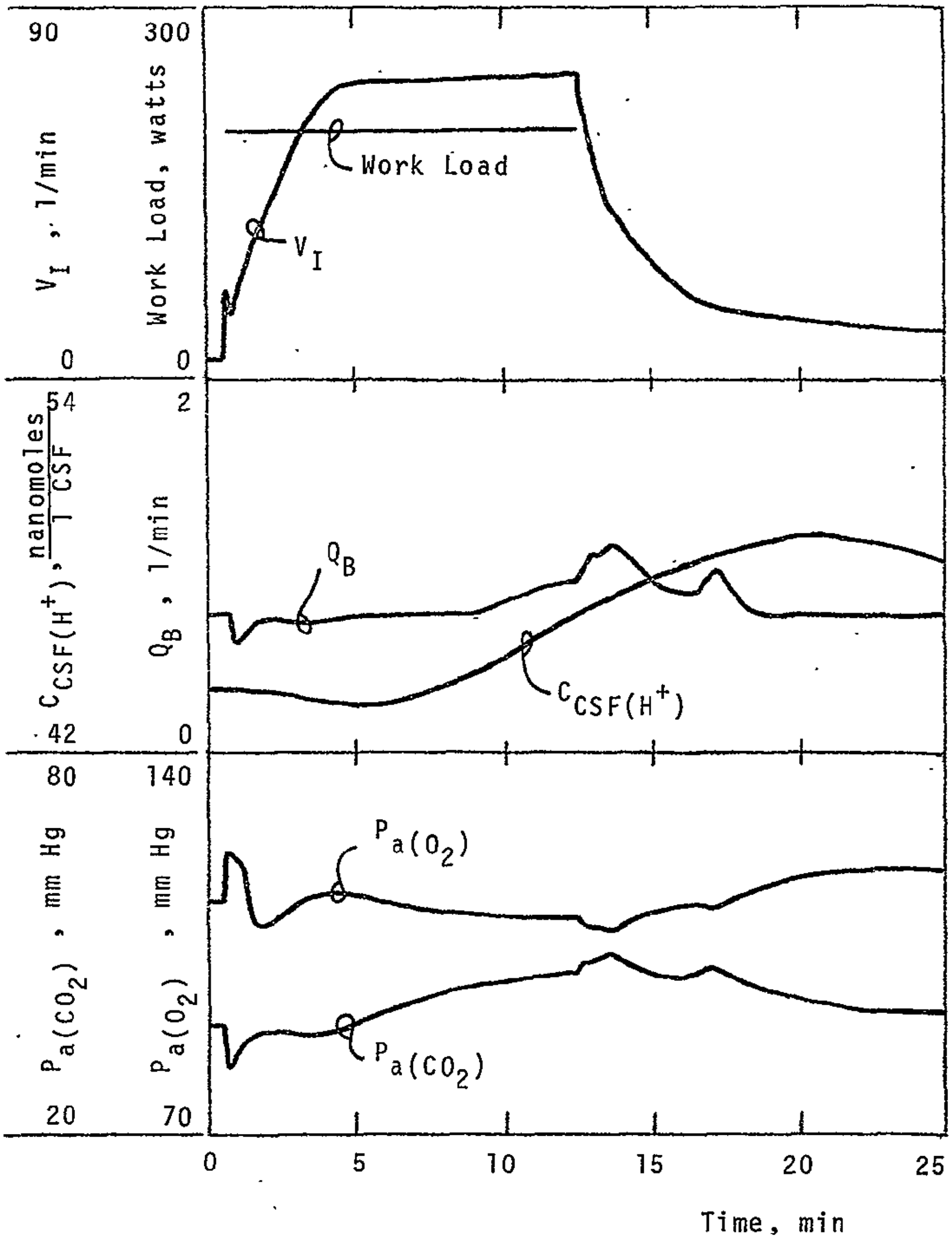

Figure 4. Selected variables from the respiratory system simulation of an exercise (work load) excitation utilizing exercise subroutine modifications.

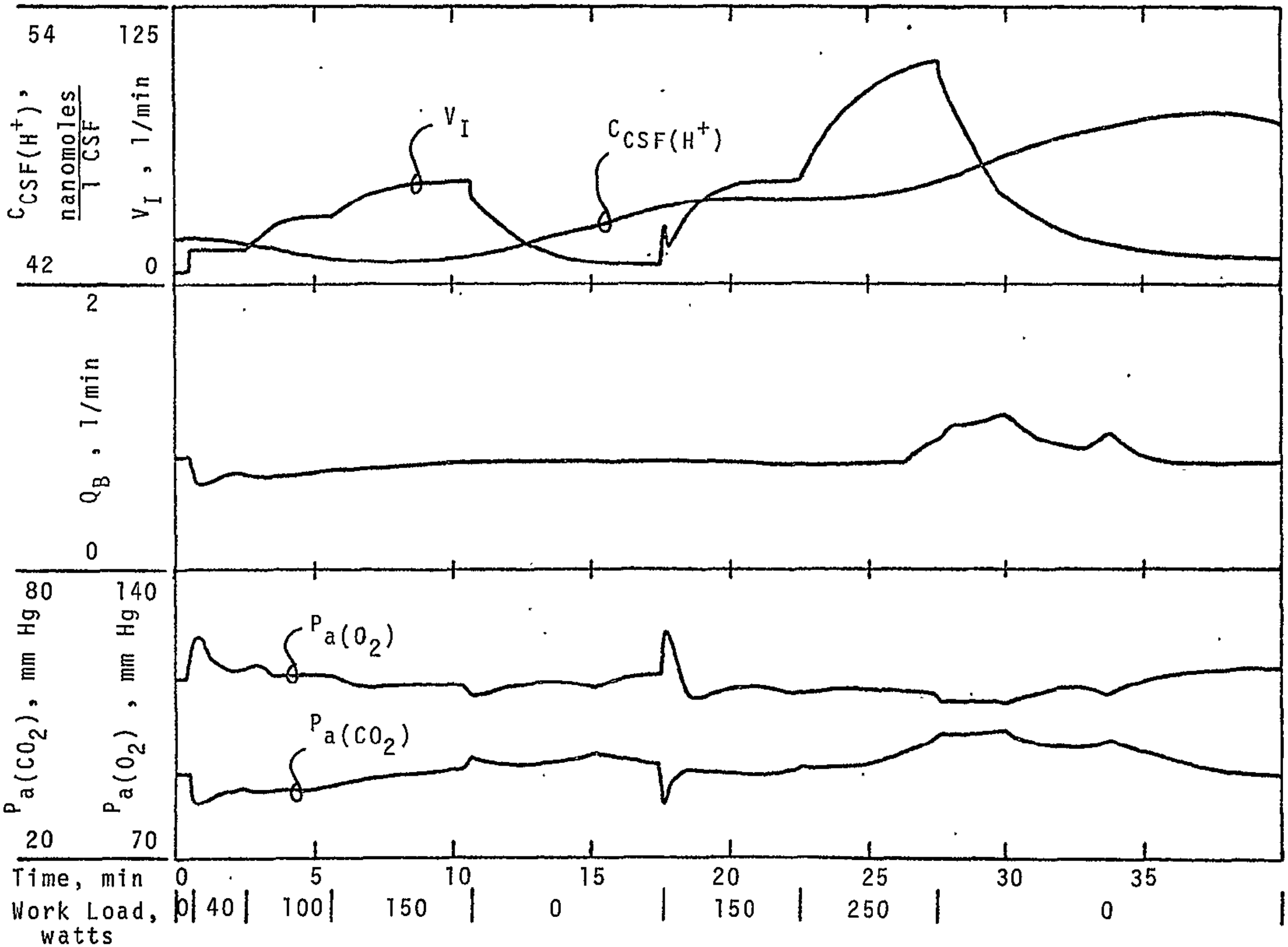

Figure 5. Selected variables from the respiratory system simulation of several exercise (work load) excitations utilizing exercise subroutine modifications.

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.

The third modification which could be implemented without appreciable sacrifice in the simulation's fidelity 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 justifiable requirement for a differential 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. Note that the program listing in the Appendix does not contain this substitution.

```
      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.

With preliminary evaluations of this modification there was demonstrated a small variation in the responses of the simulations using the two differential equation routines in the initial transient responses. Since the variables are changing most rapidly during this time interval this phenomenon should be expected. With due consideration given to the variety of simulations that have been performed with the respiratory model it appears that this modification would present the most difficulties when simulating extreme variations in environmental gaseous concentrations. Simple exercise stimulus variations should be handled without difficulty.

3. INTEGRATION OF PHYSIOLOGICAL SYSTEMS

3.1 Statement of Objectives

One of the major objectives of the overall research effort is to identify appropriate variables and subsystem components that can be utilized in an integration scheme for the physiological system models. Specific concentration within the present research effort is with the circulatory and respiratory systems. Supporting the objective is the establishment of an evaluation procedure. With exercise being the primary stimulus the proposed integration scheme for the circulatory-respiratory system is evaluated for both normal and stressed physiological system states providing partial fulfillment of the objectives. Section 3.5 presents descriptive material aligned with the objectives of the integration plans involving other physiological systems.

3.2 Circulatory-Respiratory System Integration Scheme

In Section 1.3 a description, including a block diagram (Figure 1), of the integrated circulatory-respiratory system model was presented. The three stimuli - exercise, parameter, and environmental variations - were discussed with reference to their important forcing capabilities. This section contains a discussion of the interfacing component of the overall system. Refer to Figure 1 for the pictorial representation.

With regard to the exercise phenomenon it is important to consider both aerobic and anerobic oxygen deficits and debts. As an improvement upon the formulation of the O_2 metabolic rate for the tissue compartment (humoral forcing component of inspired ventilation) in the respiratory system simulation the following interface was established. The total O_2 metabolic rate for the body is given as

$$\frac{(RMO + DOB)}{1000} = RMT(2) + C(26)$$

$$= MR_{T(O_2)} + MR_{B(O_2)} \qquad (3\text{-}1)$$

where

RMO = rate of O_2 deli blood to the muscle tissue, ml/min.,

DOB = rate of O_2 delivery by the blood to the non-muscle tissue, ml/min.,

RMT(2) = $MR_{T(O_2)}$ = metabolic rate of O_2 in the tissue compartment, l/min., and

C(26) = $MR_{B(O_2)}$ = metabolic rate of O_2 in the brain compartment, l/min.

RMO and DOB taken from the circulatory system are functions of several physiological variables; thus yielding a more reasonable description of O_2 requirements during exercise. 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. Here

$$QLO = (QLN)(LVM)(HSL)(AUH)(HMD)(HPL) \qquad (3\text{-}2)$$

where

QLO = left ventricle output, l/min

QLN = output of left ventricle under normal conditions, l/min.,

LVM = effect of arterial pressure loading factor on left ventricle,

HSL = basic strength of left ventricle,

AUH = degree of autonomic stimulation of left ventricle,

HMD = degree of deterioration of left ventricle caused by low coronary blood flow, and

HPL = degree of hypertrophy of left ventricle.

Refer to Guyton (3) and White (6) for a detailed description of the terms in Eq. (3-2).

In the respiratory system model cardiac output, Q = C(10), is described by a first-order differential equation and depends only on specific levels of arterial O_2 and CO_2 tensions. (2) Based upon the comparison of these two formulations and the complexity of altering each, the decision was made to allow the respiratory system component to receive cardiac output from the circulatory system component. 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 component is a constant (Hb = C(17)) alterable by an input data card. In the circulatory system this term is continuously calculated, thus it is provided to the respiratory system as

$$\frac{HM \cdot OSA}{200} = Hb = C(17) \qquad (3\text{-}3)$$

where

HM = hematocrit

OSA = arterial oxygen saturation, and

Hb = arterial blood oxygen capacity, l O_2/l blood.

In turn, the oxygen volume attached to hemoglobin in the aortic blood is developed in the respiratory system. The circulatory system utilizes this term in the expression

$$OVA = 1000 \cdot CHBA$$

where

$CHBA = C_{a(HbO_2)}$ = arterial hemoglobin concentration, $l\ O_2/l$ blood,

OVA = oxygen volume attached to hemoglobin in aortic blood.

This latter interface relationship is important in providing a possible pathway to the circulatory system for an environmental stimulus (alterations in gaseous composition). 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. The forementioned features of the interface system contribute to a more physiologically reliable representation of the variables than formerly existed in the individual systems.

The complete computer program for the integrated system is listed in the Appendix. However, there are some modifications which should be mentioned in comparing the individual respiratory system program with the respiratory system component of the integrated program. The original format and namelist statements are changed to comment statements.

The following comment statements are listed at the beginning of the respiratory system program, SUBROUTINE GRODIN. These identify the flow of variables between the two systems.

FOLLOWING FROM GUYTON TO GRODIN.

GUYTON	GRODIN		
QLO	C(10)	(URZ1)	CARDIAC OUTPUT.
(RMO+DOB)/1000.	RMT(2)+C(26)	(URZ2)	TOTAL METABOLIC RATE OF BODY.
(HM*OSA)/200.	C(17)	(URZ3)	BLOOD OXYGEN CAPACITY.
URZ4	URZ4	(URZ4)	FLG. 1 = 1ST. TIME GRODIN CALLED. 2 = GUYTON JUST OUTPUT. 3 = GUYTON JUST OUTPUT AND DETECTED END RUN. 0 = NOT ABOVE.
URZ5	URZ5	(URZ5)	WORK LEVEL (WATTS)

FOLLOWING FROM GRODIN TO GUYTON

GUYTON	GRODIN		
OVA/1000.	CHBA	(RUZ1)	OXYGEN VOLUME IN AORTIC BLOOD.

In Subroutine RC12 the Guyton segment of the program is sent the work load change.

In order for the circulatory and respiratory systems' programs to be compatible with their formulation of oxygen requirements for various exercise levels, modifications were made in Subroutines FUNCTION SSO2W(X) and FUNCTION SSVENT(X). The original Subroutine FUNCTION SSO2W(X) is presented below.

```
      FUNCTION SSO2W(X)
C CALCULATION OF STEADY-STATE OXYGEN REQUIREMENTS FOR VARIOUS LEVELS
C OF WORK LOAD (X = WATTS).
      IF(X.GT.250.) GO TO 1
      IF(X.LT.75.) GO TO 2
      SSO2W = -.072 + X/70.
      RETURN
1     SSO2W = 3.5
      RETURN
2     SSO2W = (X/75.) + .215*(75.-X)/75.
      RETURN
      END
```

The modification of the above subroutine yields

```
      FUNCTION SSO2W(X)
C CALCUALTION OF STEADY-STATE OXYGEN REQUIREMENTS FOR VARIOUS LEVELS
C OF WORK LOAD (X = WATTS).
      SSO2W = .195 + (X/84.15)
      IF (X.GT.210.) SSO2W = 2.7
      RETURN
      END
```

This modification produces a reduced level of steady-state oxygen requirement compared to the original respiratory program. The original Subroutine FUNCTION SSVENT(X) is presented below.

```
      FUNCTION SSVENT(X)
C  CALCULATION OF STEADY-STATE VENTILATION RATE AS A FUNCTION
C  OF TISSUE OXYGEN METABOLIC RATE
   IF (X.LE..215) SSVENT = 5.398
```

```
      IF((X.GT..215). AND.(X.LT.2.))SSVENT = 25.*X
      IF(X.GE.2.)SSVENT = 50.+50.*(X-2.)
      RETURN
      END
```

The modification of the above subroutine yields

```
      FUNCTION SSVENT(X)
C  CALCULATION OF STEADY-STATE VENTILATION RATE AS A FUNCTION
C  OF TISSUE OXYGEN METABOLIC RATE
      IF(X.LE..195)SSVENT = 5.398
      IF(X.GE.2.)SSVENT = 55.36 + 50.*(X-2.)
      IF((X.GT..195).AND.(X.LT.2.))SSVENT = 27.68*X
      RETURN
      END
```

A necessary condition that must be fulfilled for the integrated system to function properly is that both subsystems must be operating with the same steady-state values prior to application of an exercise stimulus. After steady-state conditions are established for any particular type of normal or abnormal environmental or physiological condition, the integrated system components will function in concert for all parameter or stimuli disturbances. One key used in determining when steady-state conditions are reached is the observance of a minimal change in variable values C(1) - C(14) of the respiratory system model. These variables are related to the compartmental gaseous concentrations, cardiac output, and cerebral blood flow.

Documentation of initial physiological variable values are necessary so that both of the systems are functioning under compatible initial conditions for all levels of exercise. As an example of the type of documentation required, steady-state resting cardiac output is adjusted to 5.12 l/min in both models. All other variables which are dependent upon this variable are adjusted accordingly. Model modifications such as these are deemed necessary if both models are going to function in concert.

The printed output data combines the forms of both individual systems. (6,7) In addition to the tabular form of the respiratory system model's output, the following circulatory system variables are printed.

SECS = seconds

PA = arterial pressure, mm Hg,

QLO = left ventricular output, l/min.,

PLA = left atrial pressure, mm Hg,

PRA = right atrial pressure, mm Hg,

VP = plasma volume, l,

VPF = free fluid in interstitial spaces of lungs, l,

VTS = total interstitial fluid volume, l,

VUD = urinary output, l/min.,

RMO = rate of oxygen delivery to muscle tissue, ml/min., and

DOB = rate of oxygen delivery to non-muscle tissue, ml/min.

Also, special plotting routines are available and provide for excellent qualitative analysis and indicate variable trend setting phenomena. This feature of the simulation set-up is very useful when one is observing trends in a variable's response to a family of excitations, i.e. exercise levels.

3.3 Exercise Response for Nonstressed Physiological System States

As described in the previous section, in order to establish a base run, appropriate initial conditions have to be obtained for the respiratory system component. Basically, cardiac output and metabolic rates must be compatible between the two systems.

The input data as shown in Appendix 6.1, Table 2 of the reference by Gallagher (7) 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 listed in Table 2.

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

Table 2 Continued

Input Data Card No.	Variable	Value
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.

Included here is a brief description of a simulation run for the nonstressed physiological system which correlated very well with a simulation performed with the individual respiratory system. Refer to Figure 5. The stimuli were a series of exercise levels with specific durations as shown here.

Circulatory System	Respiratory System	
Exercise Level		Duration
(EXC)	(Work load, watts)	(min)
1.000	0	0.5
12.900	40	3.0
38.500	100	3.0
65.880	150	5.0
1.000	0	9.0

For each of the exercise levels and their corresponding transient and steady-state responses the integrated system provided a slightly 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 cerebral blood flow. All other physiological variables were altered accordingly. Although no definite trend was established, the VI-VE difference was altered when compared to the independently functioning respiratory system.

Similar types of unstressed physiological system simulations were performed under altered environmental conditions. To evaluate the initial conditions for the respiratory system model the input data as shown in Appendix 6.1, Table 2 of the reference by Gallagher (7) 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.

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 provided a physiological condition similar to that experienced at sea level. An interesting experiment involved 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 were similar to those obtained for the normal environmental conditions using the integrated system or for the respiratory system functioning independently.

3.4 Exercise Response for Stressed Physiological System States

A significant benefit is achieved in using the integrated system as a means of determining respiratory system response to exercise when the circulatory system is not optimally functioning. In this way one can demonstrate the dependency of the respiratory system, in particular the ventilation rates, upon abnormal (stressed) functioning of the circulatory system. Thus, by observing easily monitored physiological variables noninvasive evaluation of circulatory system malfunctioning is achieved.

The simulations involving exercise stimulation and the stressed circulatory system are implemented in the following manner. Under the influence of normal or physiologically compatible environmental conditions the circulatory system is stressed (parameter variation). Examples of stressful situations include malfunctioning of the renal system, excessive fluid intake, unilateral or bilateral heart failure, regional volume loading, anemia, or hematocrit level variations. All of these are situations that could have been encountered in recent spaceflights or while performing normal routine earth-bound tasks; consequently, interest is keen on such simulations. Steady-state conditions are then established for the stressed condition with the appropriate variable changes realized for the respiratory system. The exercise stimulus is then applied to the integrated system.

Justification for the above sequence of steps is stated in the following manner. Two types of systems are involved - a long-term model (circulatory) and a short-term model (respiratory). For a given stressed circulatory system state several hours or days of simulated time might be required for the system to approach steady-state conditions. Simulation with the integrated system is not necessary for this period of time. Only after stressed steady-state conditions are reached is it necessary for the integrated system to become operative. Exercise stimulation is associated with rapid transient responses. It is applied for short periods of time; therefore, the short-term model is compatible for this time segment.

Examples of variable responses for a stressed circulatory system under the influence of an exercise stimulus are shown in Figures 6-8. The stressed circulatory state was a bilateral heart failure. The pumping capabilities of both the left and right ventricles were reduced, simulating a mild heart attack. A simulated recovery period of approximately 2 weeks established the stressed steady-state conditions. Responses to various levels of exercise were observed with a comparison of 100 and 150 watt exercise stimuli illustrated in Figures 6-8. The exercise stimulus was applied for 5 minutes followed by a 5 minute period of no exercise. Included in these illustrations are only a few of the more significant variable responses. Direct comparison of the responses for the two exercise levels illustrates the dependency of each variable upon exercise stimulation for the particular stressed state. A more detailed comparison may be observed from the tabular output data. Many details need to be refined before this particular system can be faithfully used in a quantitative predictive and/or diagnostic role. However, preliminary studies have been encouraging.

3.5 Interfacing Possibilities for Physiological Systems' Models

This section contains a brief summary of some possible integration schemes for the respiratory, cardiovascular, thermoregulatory, and the circulatory (long-term) system models. Even

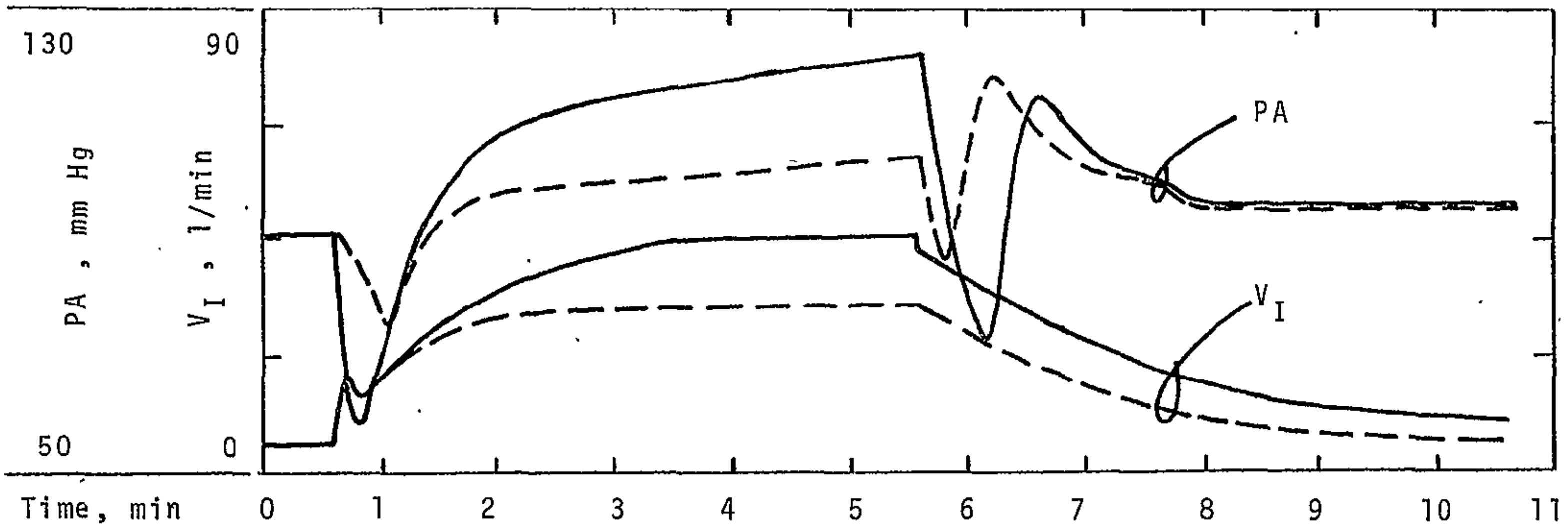

Figure 6. Arterial pressure and inspired ventilation rate for 100 watt (— — —) and 150 watt (———) exercise levels.

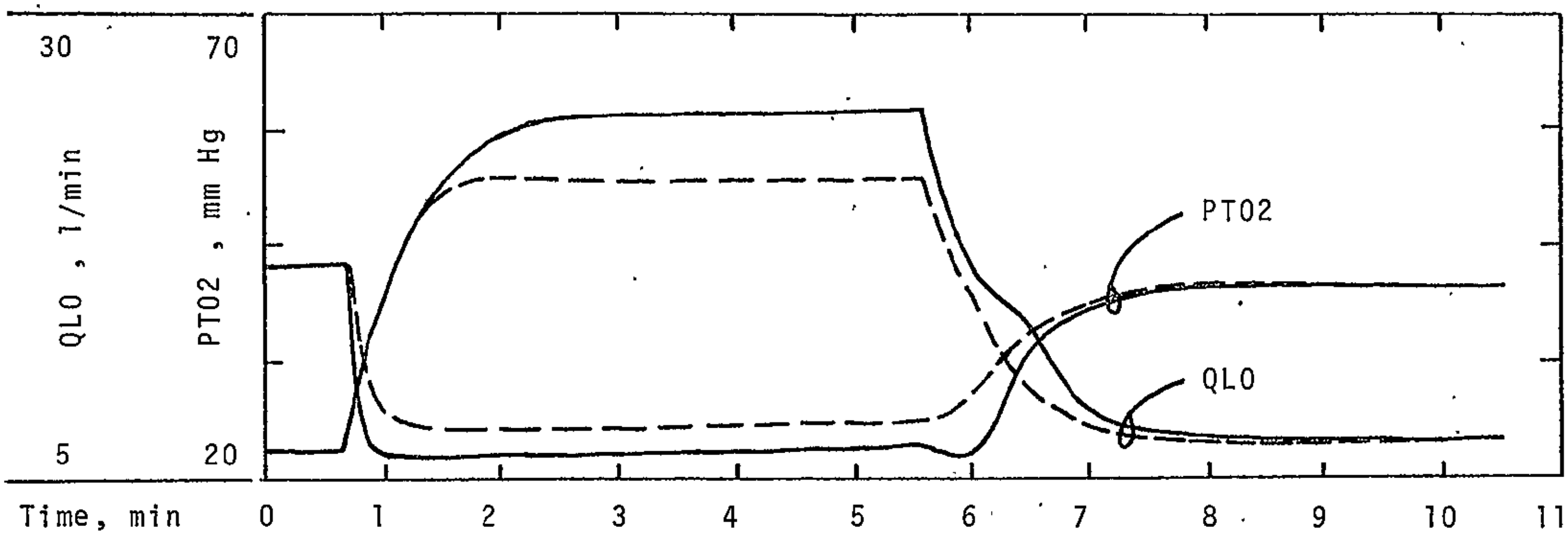

Figure 7. Cardiac output and tissue oxygen pressure for 100 watt (— — —) and 150 watt (———) exercise levels.

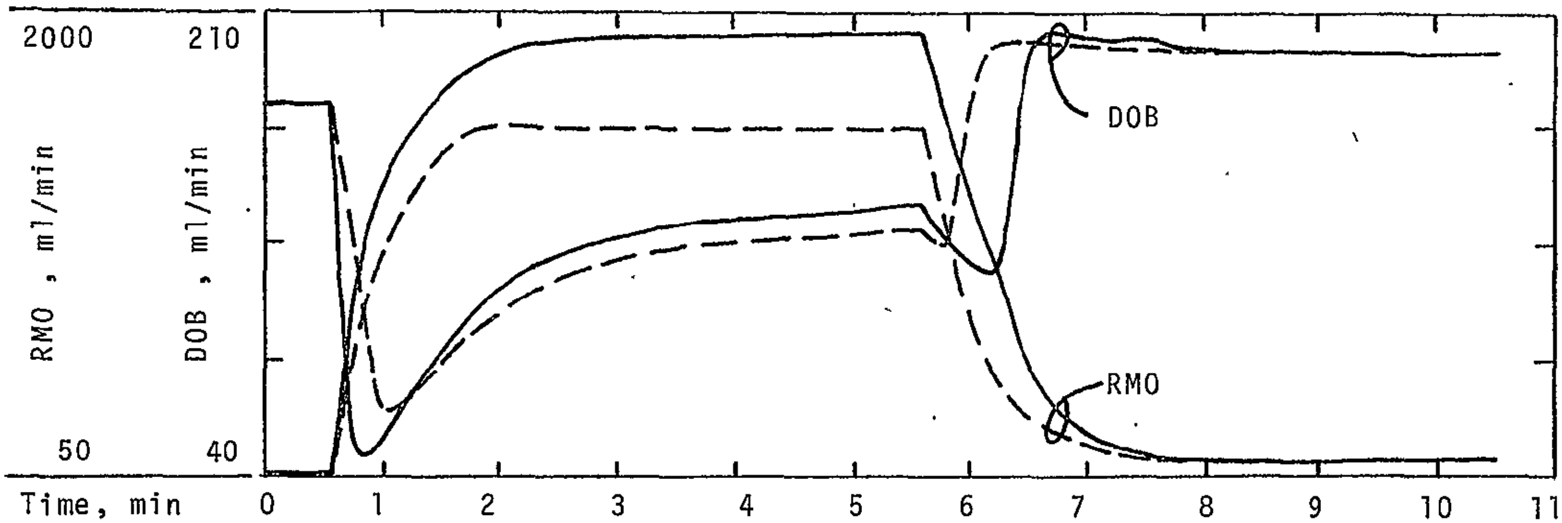

Figure 8. Rate of oxygen delivery by the blood to muscle (RMO) and non-muscle (DOB) tissues for 100 watt (— — —) and 150 watt (———) exercise levels.

though there remains considerable uncertainty involving the details of the interfacing plans the overall goal has some definitive aspects. The objective is a whole-body algorithm which simulates physiological system responses to specific conditions and excitations directly related to those encountered in recent manned spaceflights (Skylab).

Since there is a logical separation in the classification of models, long-term and short-term, it seems advisable to mold a total system which minimizes the interfacing structure and uses the aspect of simulated time to its best advantage. Thus, a plan which seems most encouraging at this time utilizes a separation between short-term and long-term models. Each of the short-term models will interact with the other short-term models yielding appropriate transient responses for the stimuli.

The respiratory and pulsatile cardiovascular system models' interface relies heavily upon compartmental blood flows and blood gas (O_2 and CO_2) concentrations. The respiratory model would receive the following variables: cardiac output, cerebral blood flow, pulmonary vascular volume, and metabolic rate. The role of metabolic rate as a function of exercise would be handled in the respiratory system in a similar manner as described in the interface of the circulatory-respiratory system (Section 3.2).

The respiratory model would be responsive to environmental conditions. It would supply the cardiovascular system with a physiologically justified description of respiratory frequency, arterial CO_2 and O_2 concentrations, and an intrathoracic pressure variable. Some of the weaker features of the respiratory system model will be enhanced by inputs from the cardiovascular system. A similar statement applies for transferal of information in the opposite direction. 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 individual respiratory program.

A minimal degree of compartment redefining seems necessary with the above approach. If additional compartmentalization is deemed necessary the tissue compartment of the respiratory system could be subdivided to correspond to the legs, abdominal cavity, thoracic cavity, and upper extremities as described in the cardiovascular system model. A restructuring of all blood flows and metabolic formulations would be necessary. With minor modifications the other two compartments, brain and lungs, and their associated variables could be related to the head and pulmonary segments in the cardiovascular system.

The void of a compatible definition for compartmental blood flow and the dependency of compartments on the exercise phenomenon are two major obstacles in the integration of the respiratory and thermoregulatory systems. A more refined definition of blood flow may be achieved in the thermal model if a transition is made from lumped core regions to distributed core regions. However, this change would not yield itself to an easily implemented interface since all of the core, muscle, fat, and skin are lumped into a tissue compartment in the respiratory system.

Under the influence of exercise it is reasonable to assume that the muscle compartment plays the dominating role as far as O_2 and CO_2 functions are concerned. Thus, the interrelationships among blood level parameters could be defined as follows. Arterial O_2 and CO_2 tensions could be supplied to the muscle model along with a fractional supply of total cardiac output. In return the muscle compartment would supply a description of O_2 and CO_2 metabolic rates, and O_2 and CO_2 gas tensions which would be interpreted as tissue compartment variables in the respiratory system.

The importance of the effects of the environmental temperature should be included in the respiratory component of the respiratory-thermoregulatory system. Temperature effects on total cardiac output (related to skin blood flow), ventilation rates, and metabolic rates are important. Additional terms or functions which are proportional to selected temperature deviations might be added to the calculation of cardiac output and the ventilatory controller equation to compensate for environmental temperature variations.

Sections 3.2 - 3.4 presented an integration of the respiratory and circulatory systems. It allowed for a minimal reorganization of the existing systems and yet simulated with reasonable accuracy the influence of the exercise stimulus. Further compartmentalization of the respiratory system would no doubt be a part of the next level of complexity if the integration effort between these two systems were extended. With emphasis on the exercise stimulus the tissue compartment in the respiratory system would be subdivided into (1) muscle, (2) renal, and (3) non-muscle, non-renal, and fat compartments. This partitioning would be in agreement with the major compartments of the circulatory system model. Blood flow and metabolism for each of the compartments would be developed as functions of O_2 requirements and CO_2 production in addition to normal basal levels and neural control. The combined blood flow of these compartments plus the cerebral blood flow would total the cardiac output. In comparison to the interface system described in Section 3, total cardiac output might be handled in the same manner.

4. RESPIRATORY FREQUENCY FORMULATION

4.1 Statement of Objectives

Respiratory frequency is a term which can be related to the establishment of a sufficient O_2 supply and the proper venting of CO_2. It is also an important driving force in the pulsatile cardiovascular system thus possessing the potential use as an interfacing component for the respiratory and pulsatile cardiovascular system model. Consequently, a physiologically compatible expression for respiratory frequency is desired.

4.2 Proposed Respiratory Frequency Expression

Separation of the factors causing ventilation rate, respiratory frequency, and the different pulmonary lung volumes is practically impossible. Some humoral and neural control mechanisms have been experimentally justified while many others remain undefined.

Carbon dioxide can stimulate the respiratory centers directly and indirectly through the carotid and aortic chemoreceptors. For example, hyperventilation which decreases $P_{A_{CO_2}}$ by several millimeters of Hg results in a decrease in ventilation. Variations in CO_2 concentration necessarily involve changes in blood pH due to the combination of CO_2 with H_2O to form carbonic acid, and the subsequent dissociation to form H^+ ions. This confounds efforts to distinguish CO_2 from the H^+ ion effects. There are small chemosensitive respiratory areas on the surface of each side of the medulla oblongata near the entry point of the 8th, 9th and 10th cranial nerves. This region is very sensitive to changes in H^+ ion concentration in the cerebrospinal fluid (CSF). Because CO_2 diffuses from the bloodstream into the CSF compartment much more rapidly than do free H^+ ions, the stimulus to the medullary centers is primarily due to CO_2. The impact of the CSF compartment's H^+ ion concentration is discussed in detail by Gallagher (7) including changes in its weighting in the ventilation controller equation.

Changes in arterial O_2 concentration to levels below normal also have a strong stimulating effect on the chemoreceptors located bilaterally in the bifurcations of the common carotid arteries (carotid bodies) and along the arch of the aorta (aortic bodies). Their afferent neurons pass to the medulla through Hering's nerves to the glossopharyngeal nerves and through the vagi respectively.

Understanding neural control of respiration is more elusive. In addition to neural pathways in the medulla that seem to have inherent inspiratory and expiratory patterns of rhythmicity, there are also other neural factors that influence respiration. Stretch receptors located in the visceral pleura and throughout the lungs give rise to the "Hering-Breuer" stretch reflexes which act through the vagus nerve to inhibit continued inspiration (or expiration) to certain limits of expansion or contraction. The Hering-Breuer reflex also contributes to cyclic respiratory rhythmicity.

There are also other stretch receptors located throughout the body in joints and muscle tissues that give proprioceptive feedback. The immediate emotional state of the organism also acts to modify respiratory patterns. Speech, fear, rage and other stresses serve to alter respiration.

One approach to the establishment of a respiratory frequency expression involves a work formulation. In this context work is associated with respiration itself. Otis, et al. (11) found that for low levels of ventilation the frequency of breathing could be fairly accurately predicted by utilizing a minimum rate of work criterion. The problem definition assumed a sinusoidal airflow pattern, passive expiration, a linear elastic element and nonlinear resistance. Differential work was defined as

$$dW = A(t) + B(t) + C(t)$$

$$dW = KVdV + K^{1}a^{2} \sin^{2}bt\ dt + K^{11}a^{3} \sin^{3}bt\ dt \qquad (4\text{-}1)$$

where

$A(t)$ = elastic work

$B(t)$ = viscous work

$C(t)$ = work done in overcoming turbulent resistance.

By graphing elastic, viscous, turbulent, and total work as functions of respiration frequency there emerged a frequency that minimized work for a constant alveolar ventilation. Also, it was determined that for too low a frequency a greater amount of elastic work was required to produce the large tidal volumes. In addition, for high frequencies, work was wasted in ventilating the dead space with each breath.

Yamashiro and Grodins (12), assuming negligible turbulent resistance ($C(t) \rightarrow 0$) and noting that the terms in the series expansion of $B(t)$ were orthogonal with respect to the period T, minimized the rate of work done in breathing by using the equation

$$\frac{dW}{dt} = \dot{W}f = KfV_T^{2}/2 + K^{1} \sum_{i=1}^{\infty} a_i^{2}/4 \qquad (4\text{-}2)$$

and the constant alveolar ventilation and dead space constraint,

$$V_T = V_D + \mathring{V}_A/f. \qquad (4\text{-}3)$$

Terminology used in Equations 4-2 and 4-3 follows:

f = respiratory frequency, bpm

V_T = tidal volume, l

K^1 = total respiratory resistance

a_i = i^{th} Fourier coefficient of airflow infinite series

V_D = dead space volume, l

$\dot{V}_A$ = minute alveolar ventilation, l/min

Utilizing an optimization procedure with Equations 4-2 and 4-3 an optimal frequency was obtained as

$$f_{opt} = ((1 + 32RC\dot{V}_A/V_D)^{1/2}-1)/16RC \qquad (4\text{-}4)$$

with the same terminology as before in addition to

RC = time constant associated with resistance and elastance of the tissues. (Experimentally determined to be .015 min)

Yamashiro and Grodins (12) stated that since the airflow pattern was assumed periodic with no specific describing function the optimal work was achieved with a constant flow rate during inspiration and a decreasing exponential flow rate during expiration. This was associated with passive breathing.

Examination of predicted optimal respiratory frequencies for optimal and sinusoidal airflow patterns indicate that sinusoidal airflow can require up to a 11.7% increase in work cost when compared to the optimal airflows. The situation is altered if active expiration is considered. For active expiration the optimal airflow pattern assumes the shape of a square wave with maximum and minimum values of $\pm 2(V_D f + \dot{V}_A)$. Comparison with sinusoidal airflow indicates a 23.4% work cost increase if the pattern is sinusoidal.

Research involving active expiration seems to provide the transition to the study of airflow patterns during exercise. Yamashiro and Grodins (13) examined the minimization of work during exercise when functional residual capacity (FRC), the airflow pattern, and respiratory frequency were included as controlled variables. The result of their derivation yielded the optimal frequency expression

$$f_{opt} = ((1+32((1+a)/a)RC\mathring{V}_A/V_D)^{1/2}-1)/16((1+a)/a)RC. \qquad (4\text{-}5)$$

The only term which has not been previously defined is "a". Here "a" is a ratio of inspiratory elastance (K_I) to expiratory elastance (K_E).

When correlated with experimentally determined curves, a time constant (RC) of 0.015 min. was obtained. This compared with a similar value of 0.011 min. in research reported by Mead. (14) The value of "a" was assumed to be 1.95 based on data taken by Rahn, et al. (15)

At levels of ventilation near rest, the experimental data appears consistent with the expression for respiratory frequency associated with a sinusoidal airflow pattern and constant expiratory reserve volume (ERV). This is Equation 4-4. However, at greater respiratory rates, the expression which accounts for FRC (Equation 4-5) provides the best fit with experimental data.

Based upon the previous discussion and the importance of exercise in the simulations associated with the project's goals a recommendation to implement Equation 4-5 in the respiratory program appears reasonable. This formulation would be substituted in Subroutine RC12 for the expression

```
FREQ = 8.1 + 7.815*(RMT(2) + C(26))
```
(4-6)

which gives an empirical representation of respiratory frequency as a function of O_2 utilization. This change would require a modification in the calculation of dead space ventilation. Using the discussions of the cited references an empirical formulation for dead space ventilation as a function of exercise level could be established. Upon implementation of the appropriate variable designations an improvement in the calculation of respiratory frequency is proposed.

5. CONCLUSIONS AND RECOMMENDATIONS

Modifications of the individual respiratory system model have produced a system which simulates the effects of exercise in a manner which is acceptable with regard to regulation of O_2 and CO_2. The neural and humoral control of ventilation during on- and off-transient exercise stimulation is justified. Likewise, other variables are altered according to the regulation of gas tensions and ventilation rates.

Improvement of physiological system models is always possible. Such is the case with the respiratory frequency expression. With projected plans for using the respiratory frequency as an interfacing variable between the cardiovascular and respiratory systems it is desirable that the expression be valid for the types of simulations performed. The proposed expression has met with success with various levels of exercise as discussed in the references of Section 4. However, there is no sound documentation as to the percentage contribution of humoral and neural control as given by this frequency expression. This constitutes another level of complexity in both experimental and theoretical respiratory research.

To fulfill the goals of the research effort, future work should emphasize the integration of the short-term and long-term models so that an adequate whole-body algorithm is realized. There are many problems that will arise as the integrations of the interacting physiological systems are achieved.

Results of this study are encouraging since a minimal amount of individual system modification was necessary for the integration of the circulatory and respiratory systems. Perhaps features of this approach can be applied to other integration endeavors.

Continued improvement of the integrated systems will help establish a better understanding of the interrelated physiological processes, especially those which are influenced by altered environments or stressed physiological states. Obviously, the continued development of appropriate data integration and display routines should parallel the modeling phases.

The next phase of the project will undoubtedly be an enlightening experience with significant gains made in the establishment of techniques and useful procedures for integrating complex physiological systems. As an additional benefit of the modeling effort it is hoped that correlation of simulated and experimental data will provide potential noninvasive diagnostic and therapeutic capabilities for both stressed and nonstressed physiological states.

6. APPENDIX

6.1 Integrated Circulatory-Respiratory System

```
C     PROGRAM GUYTON
C     CIRCULATORY DYNAMICS - CIRCLE
C             CIRCE1
      INTEGER URZ4
      REAL LVM,I,IFP,LPD,KF,KE1,KOD,KIR,KIL KI,KCD,KED,KN1,KN3
      REAL NAE,NED,NID,NOD,I1,LPK,KID,MC2,MCZ,KCZ,HPL,HPR,I2,I3,MMD
      DIMENSION FUN1(14),FUN2(14),FUN3(14),FUN4(14),FUN6(14),FUN7(14)
      COMMON/ARRAY/T,I,VBD,VVS,VPA,VAS,VLA,VRA,VAE,PA,PAM,LVM,
     *            VRE,PRA,QPN,VPE,PPA,PP1,LPA,RPA,RVM,VLE,PLA,QLN,PL1,
     *            V1B,RPV,RPT,PGL,QPO,Q5 ,VVE,VV8,PVS,PGV,RVG,QVC,AVE
      COMMON/ARRAY/CN2,CN3,RVS,PGS,RTP,CAC,QRO,QLO,CVS,DPA,DAS,DLA,DRA,
     *            PA1,AUC,AUB,AUN,AU6,AU2,AU8,DAU,AUJ,AU ,AUD,AUH,VV4,
     *            AU9,AUM,AU4,VIF,PO1,PTT,PTS,PIF,CPI,PTC,CPP,PPC,PVG
      COMMON/ARRAY/PC ,PCD,VTC,PLD,VTL,VTD,VPD,DPL,CP1,DPC,DPI,LPD,DLP,
     *            DPP,CHY,PPM,PGR,CPG,PGP,CF1,PGX,PGC,PGH,PGZ,VGD,VG ,
     *            FPF,GP1,GP2,GPD,AAR,RR ,GFN,APD,GLP,PFL,GFR,TPR,VUD
      COMMON/ARRAY/RFK,NOD,NED,NAE,VEC,CKE,KOD,KE1,KIR,KIE,KCD,KED,CKI,
     *            CNA,CCD,VID,KE ,KI ,VIC, 1 ,VTY,Z  ,VTZ,VUZ,TVZ,PPZ,
     *            DFZ,X  ,I2 ,PRL,VTS,VP ,PRP,IFP,GPR,KN3,KN1,AMR,AMP
      COMMON/ARRAY/AM1,AMC,AM2,AM3,AM5,AM ,ANE,AGK,ANP,AN1,ANC,AN2,AN3,
     *            AN5,ANM,VB ,HM1,HM ,R1 ,VIE,VIB,VIM,RC2,PO2,RKC,RC1,
     *            RCD,VPC,RSN,OVA,BFN,DOB,QOM,P1O,OSV,POT,PDO,POR,AR1
      COMMON/ARRAY/AR2,PCC,AR3,ARM,CNB,GFN,AH7,AHR,AH ,AHC,AH1,AH2,AH4,
     *            AHM,CNY,CNX,VV1,VV2,VV5,VV6,VV7,TVD,VTW,HSR,HSL,NID,
     *            SR ,VVR,RAR,CV ,CN7,AUX,AUK,AUZ,Y  ,CFC,CPK,PCE,CPR
      COMMON/ARRAY/LPK,DPO,HYL,KID,AMT,ANT,POK,PON,A1K,A2K,A3K,CNR,CNZ,
     *            AHK,SRK,V9 ,V2D,Z1 ,Z2 ,Z3 ,Z4 ,Z5 ,Z6 ,Z7 ,Z8 ,HMK,
     *            HKM,POV,POZ,RDO,OO2,RBF,MO2,POA,POY,ANU,POR,GF2,HMD
      COMMON/ARRAY/DHM,POQ,I3 ,U  ,VP1,T1 ,GF3,GF4,AUP,AUV,RV1,AUY,OUT,
     *            DSP,AHZ,AHY,OSA,PPI,CPN,POS,PLF,PPD,PPN,PPO,PFI,DFP,
     *            VPF,PPR,PPC,PMS,PMP,HR ,CPF,PCP,DA1,DLZ,OPY,OPZ,GPZ
      COMMON/ARRAY/NOZ,KCZ,VIZ,HPR,HPL,STH ALO,EXC,O2M,PA2,PP2,SVO,AUL,
     *            VV9,O2A,Q1 ,EXE,ARF,QRF,RSM,BFM,RAM,OVS,PVC,PMO,QOM,
     *            PMC,P2O,MMO,PDO,POE,AMM A4K,POM,OMM,PM1,PM3,PM4,EX1
      COMMON/ARRAY/Q2 ,Q3 ,PM5,PK1,Z9 ,Z10,Z11,Z12,Z13,Z14,Z15,Z16,PK2,
     *            PK3,FIS,STA,PAR,GBL,ANY,ANZ,ANX,ANV,ANW,ANR,AUO,AUR,
     *            AUS,A37B,H1 ,A2 ,A3 ,DUMMY(19),TITLE(400),DUMNY(40)
      COMMON/NUMERO/K,NO(20),NTIMEC,UNITS,NZ,NTIMEP,NN,MAXNC,NTIME
     1 ,IPNEXT
      COMMON/STORE/NG1,NG2,NG3,NG4,NG5,NG6,NG7,NG8,NG9,DT,TLP,TNP,ND,
     *            TM,TMM,NFIRST,ZZ(15),OLY(9),OBY(9),YMIN(10),YMAX(10),
     *            N,PT(18),BETA(10),NGRAPH(10),GRAPH(10),HEAD(19),NOEXP
     *            ,DTMAX
      COMMON/TAPE/TOTAL
      DATA FUN1(1),FUN1(2),FUN1(3),FUN1(4),FUN1(5),FUN1(6),FUN1(7),
     *FUN1(8),FUN1(9),FUN1(10),FUN1(11),FUN1(12),FUN1(13),FUN1(14)/
     *0.,1.04,60.,1.025,125.,.97,160.,.88,200.,.59,240.,0.,240.,0./
      DATA FUN2(1),FUN2(2),FUN2(3),FUN2(4),FUN2(5),FUN2(6),FUN2(7),
     *FUN2(8),FUN2(9),FUN2(10),FUN2(11),FUN2(12),FUN2(13),FUN2(14)/
     *-100.,0.0,-6.,0.0,-3.,.75,-1.,2.6,2.,9.8,8.,13.5,1000.,13.5/
      DATA FUN3(1),FUN3(2),FUN3(3),FUN3(4),FUN3(5),FUN3(6),FUN3(7),
     *FUN3(8),FUN3(9),FUN3(10),FUN3(11),FUN3(12),FUN3(13),FUN3(14)/
     *0.0,1.06,20.,.97,24.,.93,30.,.8,38.,.46,45.,0.,45.,0./
      DATA FUN4(1),FUN4(2),FUN4(3),FUN4(4),FUN4(5),FUN4(6),FUN4(7),
     *FUN4(8),FUN4(9),FUN4(10),FUN4(11),FUN4(12),FUN4(13),FUN4(14)/
     *-100.,0.,-4.,0.,-1.,3.6,3.,9.4,6.,11.5,10.,13.5,1000.,13.5/
      DATA FUN6(1),FUN6(2),FUN6(3),FUN6(4),FUN6(5),FUN6(6),FUN6(7),
     $FUN6(8),FUN6(9),FUN6(10),FUN6(11),FUN6(12),FUN6(13),FUN6(14)/
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      *-100.,10000.,0.,70.,.4,9.3,.8,3.3,1.2,1.3,1.6,.43,100.,0./
       DATA FUN7(1),FUN7(2),FUN7(3),FUN7(4),FUN7(5),FUN7(6),FUN7(7),
      *FUN7(8),FUN7(9),FUN7(10),FUN7(11),FUN7(12),FUN7(13),FUN7(14)/
      *0.,7.,30.,6.25,60.,3.,100.,1.,160.,.15,400.,.05,400.,.05/
C
   90 CALL PUTIN
      URZ4 = 1
C
      IF(I .GT. 0.5) I=0.5
C
 100  CALL PUTOUT(URZ4,URZ5)
C
C
C
C
C  FOLLOWING FROM GUYTON TO GRODIN...
C       GUYTON             GRODIN
C        QLO                C(10)      (URZ1)CARDIAC OUTPUT.
C  (RMO+DOB)/1000.        RMT(2)+C(26)(URZ2)TOTAL METABOLIC RATE OF BODY.
C   (HM*OSA)/200.           C(17)      (URZ3)BLOOD OXYGEN CAPACITY.
C       URZ4                URZ4       (URZ4)FLG  1=1ST.TIME GRODIN CALLED
C                                                 2=GUYTON JUST OUTPUT.
C                                                 3=GUYTON JUST OUTPUT
C                                                   AND DETECTED END RUN.
C                                                 0=NOT ABOVE.
C       URZ5                URZ5       (URZ5)WORK LEVEL(WATTS)
C
C  FOLLOWING FROM GRODIN TO GUYTON.....
C       GUYTON             GRODIN
C        OVA              CHBA*1000.  (RUZ1)OXYGEN VOLUME IN AORTIC BLOOD
C
C
  102 URZ1 = QLO
      URZ2 = (RMO + DOB)/1000.
      URZ3 = (HM * OSA)/200.
C
      CALL GRODIN(URZ1,URZ2,URZ3,URZ4,URZ5,RUZ1)
      URZ4 = 0
C
      T = T + I2
C
      CALL HEMO (FUN1,FUN2,FUN3,FUN4)
C     CALL HEMO        (AM1,ANM,ANU,ANY,ANZ,ARM,AUH,AUM,AUY,AVE,BFM,BFN,
C    *                  CN2,CN3,CN7,CV ,DAS,DLA,DPA,DRA,DVS,FIS,HMD,HPL,
C    *                  HPR,HSL,HSR,I2 ,LVM,PA ,PAM,PA2,PC ,PGL,PGS,PLA,
C    *                  PPA,PP1,PP2,PRA,PP1,PVS,QAO,QLN,QLO,QPC,QRF,QRN,
C    *                  QRO,QVO,RAM,RAR,RBF,RPA,RPT,RPV,RSM,RSN,RVG,RVM,
C    *                  RVS,U  ,VAE,VAS,VBD,VIM,VLA,VLE,VP ,VPA,VPE,VRA,
C    *                  VRC,VRE,VVE,VVR,VVS,VV7,VV8,X  ,FUN1,FUN2,FUN3,
C    *                  FUN4)
C
      CALL AUTO        (AU ,AUB,AUC,AUH,AUJ,AUK,AUL,AUM,AUN,AUO,AUP,AUQ,
     *                  AUR,AUS,AUV,AUX,AUZ,AU4,AU6,AU8,A1B,DAU,EXC,EXE,
     *                  EX1,I2 ,PA ,PA1,POQ,POT,P2O,STA,VVR,VV9,Y  ,Z,
     *                  Z8 ,Z12)
C
      IF(I3.LE.I2)GO TO 168
      IF(ABS(DAU-AUJ).GT.CA1)GO TO 100
  110 IF (ABS(QAO-QLO).GT..2)GO TO 100
      IF (ABS(QAO-QPO).GT..2)GO TO 100
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```
      IF (ABS(QAO-QRO).GT..4)GO TO 100
C
  169 CALL HORMON    (AM ,AMC,AMP,AMR,AMT,AM1,ANM,CKE,PA,Z,FUN7,
     *                AGK,ANC,ANP,ANR,ANT ANV,ANW,AN1,CNA,CNE,GFN,
     *                I  ,REK,A2 ,A3)
C
      CALL BLOOD     (HKM,HM ,HMK,I  ,POT POY,PO1,PO2,RC1,RC2,RCD,RKC,
     *                VB ,VIB,VIE,VIM,VP ,VRC)
C
      CALL MUSCLE    (ALO,AMM,AOM,AUP,A4K BFM,EXC,HM ,I  ,MMO,OMM,OSA,
     *                OVA,OVS,O2A,POD,PK1,PK2,PK3,PMO,PM1,PM3,PM4,PM5,
     *                POE,POM,PVO,P2O,QOM RMO,VPF,Z5 ,Z6,RUZ1)
C
      CALL AUTORG    (AOM,ARM,AR1,AR2,AR3,A1K,A2K,A3K,BFN,DOB,HM ,I,
     *                MO2,OSV,OVA,O2M,POA POB,POC,POD,POK,PON,POR,POT,
     *                POV,POZ,P10,QO2,RDO,Z  ,Z4 ,Z7)
C
      CALL ADH       (AH ,AHC,AHK,AHM,AHY AHZ,AH7,AH8,AUP,CNA,CN8,CNR,
     *                CNZ,I  ,PPA,Z)
C
      CALL MISC1     (AHM,AU4,AU8,I  ,SR  SRK,STH,TVD,TVZ,VEC,VIC,VTW,
     *                VV5,VV6,VV7,Z  ,V9)
C
      CALL HEART     (AUR,DHM,HMD,HR ,I   PA ,PMC,PMP,PMS,POT,PRA,QAO,
     *                QLO,RTP,SVO,VAE,VLE,VPE,VRE,VVE,H1)
C
      CALL CAPMBD    (BFN,CFC,CPI,CPP,DFP,I  ,IFP,PC ,PCD,PIF,PLD,PPC,
     *                PRP,PTC,PTS,PTT,PVG,PVS,RVS,TVD,VG ,VID,VIF,VP,
     *                VPD,VTC,VTD,VTL,VTS,VUD,Z  ,Z1 ,FUN6)
C
      I=I*1.2+T-T1
      I1=ABS(VP1/VPD/I)
      IF(I1.LT.I) I=I1
      IF(I3+T-T1.LT.I) I=I3+T-T1
      T=I+T1
      T1=T
C
      CALL PULMON    (CPF,CPP,CPN,DFP,I  ,PCP,PFI,PLA,PLF,POS,PPA,PPC,
     *                PPD,PP1,PPN,PPO,PPR,VP ,VPD,VPF,Z  ,Z3)
C
      CALL MISC2     (HPL,HPR,HSL,HSR,I,PA,PPA,POT,STH,Z10,Z11,Z13)
C
      CALL PROTEN    (CHY,CPG,CPI,CPK,CPP,CPR,CP1,DLP,DLZ,DPC,DPI,DPL,
     *                DPO,DPY,GPD,GPR,I  ,IFP,LPK,PC ,PCE,PGX,PRP,VG ,
     *                VTL,Z  ,PPD)
C
      CALL KIDNEY    (AAR,AHM,AM ,APD,ART,AUM,CNE,CNX,CNY,GBL,GFN,GFR,
     *                GF2,GF3,GF4,GLP,I  ,NAE,NED,NID,NOD,NOZ,PA ,PAR,
     *                PFL,PPC,RBF,REK,RFN,RR ,STH,TRR,VIM,VUD,Z)
C
      CALL IONS      (AM ,CCD,CKE,CKI,CNA,I  ,KCD,KE ,KED,KI ,KID,KIE,
     *                KIR,KOD,NAE,REK,VEC,VIC,VID,VP ,VPF,VTS,Z)
C
      CALL GELFLO    (CHY,CPG,CPI,GPR,HYL,IFP,PGC,PGH,PGP,PGR,PGX,PIF,
     *                PRM,PTC,PTS,PTT,VG ,VGD,VIF,VRS,VTS,V2D,FUN6)
C
      GO TO 100
      END

      SUBROUTINE PUTIN
```

```
C
      COMMON/ARRAY/A(400),TITLE(400),COL(70),ALPHA(20)
      COMMON/NUMERO/K,NO(20),NTIMEC,UNITS,NZ,NTIMEP,NN,MAXNO,NTIME
     1 ,IPNEXT
      COMMON/STORE/NG1,NG2,NG3,NG4,NG5,NG6 NG7,NG8,NG9,DT,TLP,TNP,ND,
     *             TM,TMM,NFIRST,ZZ(15),OLY(9),OBY(9),YMIN(10),YMAX(10),
     *             N,PT(18),BETA(10),NGRAPH(10),GRAPH(10),HEAD(19),NOEXP
     *             ,DTMAX
      DATA ALL/'ALL '/,BLANK/'    '/,SAME/'SAME'/
      DO 1 J=1,400
      A(J)=0.
    1 TITLE(J)=BLANK
      NZ=0
      NTIMEP=1
      NN=1
      MAXNO=1
    2 READ(5,100) VALUE,NUMBRO,SYMBOL
  100 FORMAT       (F13.6,2X,I5,2X,A4)
      IF(MAXNO.LT.NUMBRO) MAXNO=NUMBRO
      IF(NUMBRO.EQ.0) GO TO 3
      A(NUMBRO)=VALUE
      TITLE(NUMBRO)=SYMBOL
      GO TO 2
    3 DSP=A(286)
      READ(5,101) NOEXP,(HEAD(J),J=1,19)
  101 FORMAT(I4,19A4)
   31 READ(5,200) (ALPHA(J),J=1,20)
  200 FORMAT       (20A4)
  201 IF(ALPHA(1).EQ.SAME) GO TO 32
      IF(ALPHA(1).NE.ALL) GO TO 4
      READ(5,300) NTIMEC,UNITS
      WRITE(6,102) NOEXP,(HEAD(J),J=1,19)
      WRITE(6,71) UNITS,(TITLE(J),A(J),J=1,MAXNO)
      GO TO 31
    4 DO 5 K=1,20
      IF(ALPHA(K).EQ.BLANK) GO TO 6
    5 CONTINUE
      K=21
    6 K=K-1
      DO 10 J=1,K
      L=1
    7 IF(ALPHA(J).EQ.TITLE(L)) GO TO 9
      L=L+1
      IF(L.LT.MAXNO+1) GO TO 7
    9 COL(J)=A(L)
      NO(J)=L
   10 CONTINUE
      GO TO 34
   32 DO 33 J=1,K
      ALPHA(J)=BETA(J)
      NO(J)=NGRAPH(J)
   33 COL(J)=GRAPH(J)
   34 READ(5,300) NTIMEC,UNITS,IPNEXT
  300 FORMAT(I6,A4,I2)
      WRITE(6,102) NOEXP,(HEAD(J),J=1,19)
  102 FORMAT(1H1///20X,'EXP ',I4,19A4///)
      IF(K.GT.10) GO TO 70
      WRITE(6,21) UNITS, (ALPHA(J),J=1,K)
   21 FORMAT('0 ',A4,10(6X,A4,1X))
      WRITE(6,22) (COL(J),J=1,K)
```

```
   22 FORMAT(' ',5X,'0',2X,F10.4,9(1X,F10.4))
      GO TO 31
   70 WRITE(6,71) UNITS,(ALPHA(J),COL(J),J=1,K)
   71 FORMAT(60X,2HO ,A4//5(4X,A4,' = ',F10.4,4X))
   31 RETURN
      END

      SUBROUTINE PUTPUT(URZ4,URZ5)
      INTEGER URZ4
C
      COMMON/ARRAY/A(400),TITLE(400),COL(20),ALPHA(20)
      COMMON/NUMERO/K,NO(20),
     *              NTIMEC,UNITS,NZ,NTIMEP,NN,MAXNO,NTIME
     1 ,IPNEXT
      COMMON/STORE/NG1,NG2,NG3,NG4,NG5,NG6,NG7,NG8,NG9,DT,TLP,TNP,ND,
     *             TP,TMM,NFIRST,ZZ(15),OLY(9),OBY(9),YMIN(10),YMAX(10),
     *             N,PT(18),BETA(10),NGRAPH(10),GRAPH(10),HEAD(19),NOEXP
     *             ,DTMAX
      COMMON/TAPE/TOTAL
      DATA SECS/'SECS'/,TMIN/'MINS'/,HOUR/'HOUR'/,DAYS/'DAYS'/
      DATA ALL/'ALL '/,BLANK/'    '/
C
C     WATEXC(13,2) IS RELATION BETWEEN WATTS AND PARAMETER EXC (FROM
C     DR.WHITE) TO ALLOW THE COMBINING OF GRODIN WITH GUYTON.
C
      DIMENSION WATEXC(13,2)
      DATA WATEXC/1.,5.,10.,20.,30.,40.,50.,60.,70.,80.,90.,100.,120.,
     1 0.,16.6,32.2,59.1,93.,103.,123.,140.,157.,170.,182.,193.,212./
C
      T=A(1)
C
C      ICONVT IS FLG     1=CONVERT EXC (A(3 9)) TO WATTS FOR GRODIN.
C                        0=DO NOT CONVERT EXC TO WATTS.
      ICONVT = 0
      IF(URZ4 .EQ. 1 ) ICONVT = 1
C
      NTIME  = T/1440.
      IF(UNITS .EQ. SECS) NTIME = T * 60.
      IF(UNITS .EQ. TMIN) NTIME  = T
      IF(UNITS .EQ. HOUR) NTIME  = T/60.
      IF(NTIME .LT. NTIMEP) GO TO 65
C
C     HERE IF TO PRINT.
    6 IF(URZ4 .NE. 1) URZ4 = 2
      IF(ALPHA(1) .NE. ALL) GO TO 7
      WRITE(6,71) NTIME,UNITS,(TITLE(J),A(J),J=1,MAXNO)
      GO TO 51
    7 DO 20 I = 1,K
      I1 = NO(I)
      COL(I) = A(I1)
   20 CONTINUE
      IF(K .GT. 10) GO TO 70
      WRITE(6,21) UNITS, (ALPHA(J),J=1,K)
   21 FORMAT('0 ',A4,10(6X,A4,1X))
      WRITE(6,31) NTIME,(COL(J),J=1,K)
   31 FORMAT(' ',I6,2X,F10.4,9(1X,F10.4))
      GO TO 51
   70 WRITE(6,71) NTIME,UNITS,(ALPHA(J),COL(J),J=1,K)
   71 FORMAT(///56X,I5,1X,A4//5(4X,A4,' = ',F10.4,4X))
   51 NTIMEP = NTIME + IPNEXT
```

```
C
C   SEE IF TIME TO STOP PRESENT TIME STEP.
   53 IF(NTIMC.LT.NTIMEC) GO TO 65
   54 READ(5,400) NTIMEC,CUNITS,IPNEXT,SYMBOL,CVALUE
  400 FORMAT(I6,A4,I2,A4,E13.6)
C
C     BLANK TIME STEP CARD ENDS RUN.
      IF(SYMBOL.EQ.CUNITS) GO TO 66
      IF(CUNITS.NE.BLANK) GO TO 59
      IF(A(2).GT..5) A(2)=.5
  450 DO 55 MN=1,MAXNO
      IF(SYMBOL.EQ.TITLE(MN)) GO TO 57
   55 CONTINUE
   57 WRITE(6,58) NTIME,UNITS,SYMBOL,A(MN),CVALUE
   58 FORMAT(/15X,'AT',I5,1X,A4,' INTO THE SIMULATION, THE VALUE OF ',
     *                 A4,'WAS CHANGED FROM ',F10.3,'  TO ',F10.3/)
      A(MN)=CVALUE
C    SET FLG.INDICATION CHGED.WORK LOAD IF EXC INPUT.
      IF(MN .EQ. 319) ICONVT = 1
      GO TO 54
   59 UNITS  = CUNITS
      NTIMEP = T / 1440. + IPNEXT
      IF(UNITS .EQ. SECS) NTIMEP = T * 60. + IPNEXT
      IF(UNITS .EQ. TMIN) NTIMEP = T + IPNEXT
      IF(UNITS .EQ. HOUR) NTIMEP  = T / 60  + IPNEXT
C
      NTIMEC= NTIMEP+ NTIMEC - IPNEXT
C
C     CONVERT EXC TO WATTS FOR GRODIN IF HAVENT ALREADY.
   65 IF(ICONVT .EQ. 0) GO TO 650
C
      URZ5 = 0.
      IF(A(319) .LE. 1.) GO TO 650
      DO 805 JJ = 2,13
      JJ2 = JJ
      IF(A(319) .LE. WATEXC(JJ,1)) GO TO 806
  805 CONTINUE
      URZ5 = 212.
      GO TO 650
  806 URZ5 =  WATEXC(JJ2-1,2) +(((A(319)-WATEXC(JJ2-1,1))/
     1  (WATEXC(JJ2,1) - WATEXC(JJ2-1,1)))  *  (WATEXC(JJ2,2) -
     2  WATEXC(JJ2-1,2)))
C
  650 RETURN
C
C  HERE IF DETECTED END OF RUN(BLANK TIME STEP CARD).
   66 URZ4 = 3
      RETURN
      END

      SUBROUTINE FUNCTN(TH,POL,TAB)
      DIMENSION TAB(14)
      N=14
      DO 110 I=1,N,2
      IF(TAB(I)-TH) 110,120,110
  110 CONTINUE
      GO TO 140
  120 POL=TAB(I+1)
  130 RETURN
  140 NN=N-2
```

```
      DO 150 I=1,NN,2
      IF(TAB(I) .LT. TH .AND. TAB(I+2) .GT. TH) GO TO 160
  150 CONTINUE
      WRITE(6,100) TH
  100 FORMAT(5X,' ***** CURVE LIMITS EXCEEDED ***** ',G12.6//)
      IF(TH .LT. TAB(1)) PCL=TAB(2)
      IF(TH .GT. TAB(N-1)) PCL=TAB(N)
      GO TO 130
  160 POL=TAB(I+1)+(TAB(I+3)-TAB(I+1))*((TH-TAB(I))/(TAB(I+2)-TAB(I)))
      GO TO 130
      END

      SUBROUTINE HEMO (FUN1,FUN2,FUN3,FUN4)
      DIMENSION FUN1(14),FUN2(14),FUN3(14),FUN4(14)
C     SUBROUTINE HEMO (AMM,ANM,ANU,ANY,ANZ,ARM,AUH,AUM,AUY,AVE,BFM,BFN,
C    *                 CN2,CN3,CN7,CV ,DAS,DLA,DPA,DRA,DVS,FIS,HMD,HPL,
C    *                 HPR,HSL,HSR,I2 ,LVM PA ,PAM,PA2,PC ,PGL,PGS,PLA,
C    *                 PPA,PP1,PP2,PRA,PR1,PVS,QAO,QLN,QLO,QPO,QRF,QRN,
C    *                 QRO,QVO,RAM,RAR,RBF RPA,RPT,RPV,RSM,RSN,RVG,RVM,
C    *                 RVS,U  ,VAE,VAS,VBD VIM,VLA,VLE,VP ,VPA,VPC,VRA,
C    *                 VRC,VRF,VVE,VVR,VVS VV7,VV8,X  ,FUN1,FUN2,FUN3,
C    *                 FUN4)
C     REAL I2,LVM
C     DIMENSION FUN1(14),FUN2(14),FUN3(14).FUN4(14)
      REAL LVM,I,IFP,LPD,KE,KE1,KOD,KIR,KI. ,KI,KCD,KED,KN1,KN3
      REAL NAE,NED,NID,NOD,I1,LPK,KID,MO2,HOZ,KCZ,HPL,HPR,I2,I3,MMO
      COMMON/ARRAY/T,I,VBD,VVS,VPA,VAS,VLA.VRA,VAE,PA,PAM,LVM,
     *              VRE,PRA,QRN,VPE,PPA,PP1.CPA,RPA,RVM,VLE,PLA,QLN,PL1,
     *              A1B,RPV,RPT,PGL,GPP,QS ,VVE,VVB,PVS,PGV,RVG,QVO,AVE
      COMMON/ARRAY/CN2,CN3,RVS,PGS,RTP,QAO,QRO,QLO,DVS,CPA,DAS,DLA,DRA,
     *              PA1,AUC,AUB,AUN,AU6,AU2,AU8,DAU,AUJ,AU ,AUQ,AUH,VV4,
     *              AU9,AUM,AU4,VIF,PC1,PTT,PTS,PIF,CPI,PTC,CPP,PPC,PVG
      COMMON/ARRAY/PC ,PCD,VTC,PLO,VTL,VTC,VPD,DPL,CPI,DPC,DP1,LPD,DLP,
     *              DPP,CHY,PPM,PGP,CPG,PCP,GF1,PGC,PGX,PGH,PG2,VGD,VG ,
     *              EPH,GP1,GP2,GPD,AAR,PR ,RFN,APD,GLP,PFL,GFR,TRR,VUD
      COMMON/ARRAY/REK,NOD,NED,NAE,VFC,CK3,KOD,KE1,KIP,KIE,KCD,KED,CKI,
     *              CNA,CCD,VID,KE ,KI ,VIC,I1 ,VTY,Z  ,VTZ,VUZ,TVZ,PPZ,
     *              DFZ,X  ,I2 ,PR1,VTS,VP ,PRP,IFP,GPR,KN3,KN1,AMR,AMP
      COMMON/ARRAY/AM1,AMC,AM2,AM3,AM5,AM ,CNE,AGK,ANP,AN1,ANC,AN2,AN3,
     *              AN5,AN4,VB ,HM1,HM ,H1 ,VIE,VIB,VIM,RC2,PO2,RKC,RC1,
     *              PCD,VPC,RSN,OVA,BFN,DO3,AOM,P10,OSV,POT,PCD,POB,AR1
      COMMON/ARRAY/AR2,PCC,AP3,ARM,CNB,GFN,AH7,AH8,AH ,AHC,AH1,AH2,AH4,
     *              AH4,CNY,CNX,VV1,VV2,VV5,VV6,VV7,TVD,VTW,HSR,HSL,NIC,
     *              SP ,VVR,RAR,CV ,CN7,AUX,AUK,AUZ,Y  ,CFC,CPK,PCF,CPR
      COMMON/ARRAY/LPK,DPO,HYL,KID,AMT,ANT,POK,PUN,A1K,A2K,A3K,CNP,CNZ,
     *              AHK,SRK,V9 ,V2D,Z1 ,Z2 ,Z3 ,Z4 ,Z5 ,Z6 ,Z7 ,Z8 ,HMK,
     *              HKM,PCV,PCZ,RDU,GF2,RBF,MC2,POA,POY,ANU,POP,GF2,HMD
      COMMON/ARRAY/DHM,POQ,I3 ,U  ,VP1,T1 ,GF3,GF4,AUP,AUV,RV1,AUY,OUT,
     *              DSP,AHZ,AHY,USA,PP1,CPM,POS,PLF,PPO,PPN,PPO,PF1,DFP,
     *              VPF,PPR,PKC,PMS,PMP,HR ,CPF,PCP,PA1,DLZ,DPY,DPZ,GPZ
      COMMON/ARRAY/MOZ,KCZ,VIZ,HPP,HPL,STF,ALC,EXC,C2M,PA2,PP2,SVO,AUL,
     *              VV9,O2A,O1 ,EXE,APF,QRF,PSM,BFM,RAM,DVS,PVO,RMD,QOM,
     *              PMD,P2O,MMO,PDO,PGE,AMI,A4K,PCM,CMM,PV1,PM3,PM4,CX1
      COMMON/ARRAY/Q2 ,O3 ,PM5,PK1,Z9 ,Z10,Z11,Z12,Z13,Z14,Z15,Z16,PK2,
     *              PK3,FIS,STA,PAR,GBL,ANY,ANZ,ANX,ANV,ANW,ANR,AUO,AUR,
     *              AUS,A378,H1 ,A2 ,A3 ,DUMMY(19),TITLE(400),DUMMY(40)
      COMMON/NUMERO/K,NO(20),NTIMEC,UNITS.NZ,NTIMEP,NN,MAXNC,NTIME
      COMMON/STORE/NG1,NG2,NG3,NG4,NG5,NG6,NG7,NG8,NG9,DT,TLP,TNP,ND,
     *              TM,TMM.NFIRST,ZZ(15),GLY(9),GBY(9),YMIN(10),YMAX(10),
     *              N,PT(18),BETA(10),NGRAPH(10),GRAPH(10),HEAD(19),NOEXP
```

```
                    ,DTMAX
C
C     CIRCULATORY DYNAMICS BLOCK
C    HEMODYNAMICS
C
      VBD=VP+VPC-VVS-VAS-VLA-VPA-VRA
      VVS=VVS+DVS*I2+VBD*.3986
      VPA=VPA+DPA*I2+VBD*.155
      VAS=VAS+DAS*I2+VBD*.261
      VLA=VLA+DLA*I2+VBD*.128
      VRA=VRA+DRA*I2+VBD*.0574
      VAE=VAS-.495
      PA=VAE/.00355
      IF(PA.LT.0.) PA=.0001
      PAM=100./PA
      PA2=PA/AUH
      CALL FUNCTN(PA2,LVM,FUN1)
      VRE=VRA-.1
      PRA=VRE/.005
      CALL FUNCTN(PRA,QRN,FUN2)
      VPE=VPA-.30625
      PPA=VPE/.0048
      PP1=.026*PPA
      IF(PP1.LT.0.) PP1=10.**(-12)
      RPA=PP1**(-.5)
      PP2=PPA/AUH
      IF(PP2.LE.0.) PP2=.0001
      CALL FUNCTN(PP2,RVM,FUN3)
      VLE=VLA-.4
      PLA=VLE/.01
      CALL FUNCTN(PLA,QLN,FUN4)
      RPV=1./(PLA+20.)/.0357
      RPT=RPV+RPA
      PGL=PPA-PLA
      QPO=PGL/RPT
      ANU=ANM
      IF (ANU.LT..8)ANU=.8
      VVE=VVS-VVR-(ANU-1.)*ANY
      VV8=VVE-VV7
      IF(VV8.LT..0001)VV8=.0001
      PVS=VV8/CV
      PR1=PRA
      IF (PRA.LT.0.)PR1=0.
      RVG=2.738/PVS
      QVO=(PVS-PR1)/RVG
      CN3=CN3+(((PC-17.)*CN7+17.)*CN2-CN3)*.1
      AVE=(AUM-1.)*AUY+1.
      RVS=AVE*(1./CN3)*VIM*((ANU-1.)*ANZ+1.)
      PGS=PA-PVS
      RSN=RAR*ARM*ANU*AUM*PAM*VIM+RVS*1.79
      BFN=PGS/RSN
      RSM=ANU*VIM*PAM*AUM*AMM*RAM
      BFM=PGS/RSM
      QAO=BFN+BFM+RBF+(PA-PRA)*FIS
      QLN=LVM*QLN*AUH*HSL*HMD*HPL
      QRO=QRN*((1.-QRF)*AUH*RVM*HSR*HMD*HPR+QRF*QLO/QLN)
      QPO=QLO+(QPO-QLO)/U
      QVO=QRO+(QVO-QRO)/X
      DVS=QAO-QVO
      DPA=QRO-QPO
```

```
      DAS=QLC-QAC
      DLA=QPC-QLC
      DRA=QVO-QRO
      RETURN
      END

      SUBROUTINE AUTO (AU ,AUB,AUC,AUH,AUJ,AUK,AUL,AUM,AUN,AUO,AUP,AUQ,
     *                 AUP,AUS,AUV,AUX,AUZ,AU4,AU6,AU8,A1B,DAU,EXC,EXE,
     *                 EX1,I2 ,PA ,PA1,POQ,POT,P2O,STA,VVR,VV9,Y  ,Z,
     *                 Z8 ,Z12)
      REAL I2
C
C     AUTONOMIC CONTROL BLOCK
C
 120  EXE=(8.-P2O)*EX1+(EXC-1.)*Z12
      POQ=POT
      IF (POQ.GT.8.)POQ=8.
      IF (POQ.LT.4.)POQ=4.
      PA1=PA*POQ/8.-EXE
      AUC=0.
      IF(PA1.LT.80.)AUC=.03*(80.-PA1)
      IF(PA1.LT.40.)AUC=1.2
      AUB=0.
      IF(PA1.LT.170.)AUB=.014286*(170.-PA1)
      IF(PA1.LT.40.)AUB=1.83
 123  A1B=(AUB-1.)*AUX+1.
 124  AUN=0
      IF(PA1.LT.50.)AUN=.2*(50.-PA1)
      IF(PA1.LT.20.)AUN=6.0
      AU6=A1B-AU4
      AU8=AUK*(AU6-1.)
      DAU=DAU+(AUC+AU6+AUN-DAU)/Z/Y
      AUJ=AUJ+(DAU-AUJ)*I2*6./Z8
      IF(AUJ.LT.0.)AUJ=0.
      IF(AUJ-1.)126,127,127
 126  AU=AUJ**AUZ
      GO TO 128
 127  AU=(AUJ-1.)*AUZ+1.
 128  IF(STA.GT..00001)AU=STA
      AUO=AU-1.
      AUP=AUO*AUQ+1.
      AUH=AUO*AUV+1.
      AUR=AUO*AUS+1.
      VVR=VV9-AUL*AUP
      AUM=.15+.85*AUP
      RETURN
      END

      SUBROUTINE HORMON(AM ,AMC,AMP,AMR,AMT,AM1,ANM,CKE,PA,Z,FUN7,
     *                  AGK,ANC,ANP,ANR,ANT,ANV,ANW,AN1,CNA,CNE,GFN,
     *                  I  ,REK,A2 ,A3)
      DIMENSION FUN7(14)
      REAL I
C
C*******************************************************************************
C
C     ALDOSTERONE CONTROL BLOCK
C
C*******************************************************************************
  168 AMR=CKE/CNA/A3-A2
```

```
      IF(AMR.LT.0.)AMR=0.
      CALL FUNCTN (PA,AMP,FUN7)
      AM1=AM1+(ANM*AMP*AMR-AM1)/Z
      AMC=AMC+(AM1-AMC)*(1.-EXP(-I/AMT))
      AM=20.039-19.8*EXP(-.0391*AMC)
C*****************************************************************************
C
C     ANGIOTENSIN CONTROL BLOCK
C
C*****************************************************************************
      CNE=152.-CNA
      IF(CNE.LT.1.)CNE=1.
      ANR=((17.75-GFN*CNA)*AGK+1.)*REK
      ANW=ANW+((ANR-1.)*10.-ANW)*ANV*I
      IF(ANW.LT..0)ANW=0.
      ANP=ANR+ANW
      IF(ANP.GT.100.)ANP=100.
      IF(ANP.LT..01) ANP=.01
      AN1=AN1+(ANP-AN1)/Z
      ANC=ANC+(AN1-ANC)*(1.-EXP(-I/ANT))
      ANM=4.0-3.3*EXP(-.0967*ANC)
      IF(ANM.LT..7)ANM=.7
      RETURN
      END

      SUBROUTINE BLOOD (HKM,HM ,HMK,I  ,POT,POY,PO1,PO2,RC1,RC2,RCD,RKC,
     *                  VB ,VIB,VIE,VIM,VP ,VRC)
      REAL I
C
C     RED CELLS AND VISCOSITY BLOCK
C-----------------------------------------------------------------------------
C     BLOOD VISCOSITY
C-----------------------------------------------------------------------------
 170  VB=VP+VRC
      HM=100.*VRC/VB
      VIE=HM/(HMK-HM)/HKM
      VIB=VIE+1.5
      VIM=.3333*VIB
C-----------------------------------------------------------------------------
C     RED BLOOD CELLS
C-----------------------------------------------------------------------------
      RC2=RKC*VRC
      PO2=PO1-POT
      IF(PO2.LT..2375)PO2=.2375
      RC1=POY*PO2
      RCD=RC1-RC2
      VRC=VRC+RCD*I
      RETURN
      END

      SUBROUTINE MUSCLE(ALO,AMM,ACM,AUP,A4K,BFM,EXC,HM ,I  ,MMO,OMM,OSA,
     *                  OVA,CVS,O2A,POD,PK1,PK2,PK3,PMO,PM1,PM3,PM4,PM5,
     *                  POE,POM,PVO,P2O,QOM,RMO,VPF,Z5 Z6,RUZ1)
      REAL I,MMO
C
C     MUSCLE BLOOD FLOW CONTROL AND PO2 BLOCK
C
 180  OSA=ALO-VPF*.5
C      RUZ1 IS OXYGEN VOL.IN AORTIC BLOOD(CHBA) FROM GRODIN.
      OVA = RUZ1 * 1000.
```

```
      OVS=OVS+((BFM*OVA-RMO)/HM/5./BFM-OVS)/Z6
      PVO=57.14*OVS
      RMO=(PVO-PMO)*PMS/(PM1**PK3-PM4)
      QOM=QOM+(RMO-MMO)*(1.-EXP(-I/Z5))
      PMO=PK2/(PK1-QOM)
      PM1=PMO
      IF(PM1.LT.PM3)PM1=PM3
      P2O=PMO
      IF(P2O.GT.8.)P2O=8.
      AOM=(AUP-1.)*O2A+1.
      MMO=AOM*OMM*EXC*(1.-(8.0001-P2O)**3./512.)
      PDO=PVO-40.
      POE=POM*PDO+1.
      IF(POE.LT..005)POE=.005
      AMM=AMM+(POE-AMM)*(1.-EXP(-I/A4K))
      RETURN
      END

      SUBROUTINE AUTORG(AOM,ARM,AR1,AR2,AR3,A1K,A2K,A3K,BFN,DOB,HM ,I,
     *                  MO2,OSV,OVA,O2M,POA,POB,POC,POD,POK,PON,POR,POT,
     *                  POV,POZ,P1O,QO2,PDO,Z  ,Z4 ,Z7)
      REAL I,MO2
C
C     NON-MUSCLE OXYGEN DELIVERY BLOCK
C     AND NON-MUSCLE LOCAL BLOOD FLOW CONTROL BLOCK
C-----------------------------------------------------------------------
C     AUTOREGULATION,RAPID
C-----------------------------------------------------------------------
      OSV=OSV+((BFN*OVA-DOB)/HM/5./BFN-OSV)/Z7
      POV=OSV*57.14
      RDO=POT**3.
      IF(RDO.LT.50.)RDO=50.
      DOB=(POV-POT)*2896.5/RDO
      MO2=AOM*O2M*(1.-(8.0001-P1O)**3./512.)
      QO2=QO2+(DOB-MO2)*(1.-EXP(-I/Z4))
      POT=QO2*.00333
      P1O=POT
      IF(POT.GT.8.)P1O=8.
      POD=POV-POR
      POB=POB+(POK*POD+1.-POB)/Z
      IF(POB.LT..2)POB=.2
      AR1=AR1+(POB-AR1)*(1.-EXP(-I/A1K))
      ARM=AR1*AR2*AR3
C-----------------------------------------------------------------------
C     AUTOREGULATION,INTERMEDIATE
C-----------------------------------------------------------------------
      POA=POA+(PON*PDO+1.-POA)/Z
      IF (POA.LT..5)POA=.5
      AR2=AR2+(POA-AR2)*(1.-EXP(-I/A2K))
C-----------------------------------------------------------------------
C     AUTOREGULATION,LONG-TERM
C-----------------------------------------------------------------------
      IF(POD)194,192,192
  192 POC=POZ*POD+1.
      GO TO 196
  194 POC=POZ*POD*.33+1.
  196 IF (POC.LT..3)POC=.3
      AR3=AR3+(POC-AR3)*I/A3K
      RETURN
      END
```

```
      SUBROUTINE ADH   (AH  ,AHC,AHK,AHM,AHY,AHZ,AH7,AH8,AUP,CNA,CNB,CNR,
     *                  CNZ,I   ,PRA,Z)
      REAL I
C
C     ANTIDIURETIC HORMONE
C
      CNB=CNA-CNR
      AHZ=.2*PRA
      AHY=AHY+(AHZ-AHY)*.0007*I
      AH8=AUP-1.
      IF(AH8.LT.0.)AH8=0.
      IF(CNB.LT.0.)CNB=0.
      AH=AH+(CNZ*CNB+AH8-AHZ+AHY-AH)/Z
      IF(AH.LT.0.)AH=0.
      AHC=AHC+(.3333*AH-AHC)*(1.-EXP(-I/AHK))
      AHM=6.*(1.-EXP(-0.1808*AHC))
      IF(AHM.LT..3)AHM=.3
      RETURN
      END

      SUBROUTINE MISC1 (AHM,AU4,AU,I   ,SR  ,SRK,STH,TVD,TVZ,VEC,VIC,VTW,
     *                  VVE,VV6,VV7,Z   ,V9)
      REAL I
C
C*****************************************************************************
C
C     VASCULAR STRESS RELAXATION BLOCK
C
C*****************************************************************************
      VV6=VV6+(SR*(VVE-V9  )-VV7-VV6)/Z
      VV7=VV7+VV6*(1.-EXP(-I/SRK))
C*****************************************************************************
C
C     THIRST AND DRINKING BLOCK
C*****************************************************************************
C
      TVZ=(.01*AHM-.009)*STH
      TVD=TVD+(TVZ-TVD)/Z
      IF(TVD.LT.0.)TVD=0.
      VTW=VIC+VEC
C*****************************************************************************
C
C     AUTONOMIC CONTROL BLOCK
C     ADAPTATION OF BARORECEPTORS
C
C*****************************************************************************
      AU4=AU4+AU8*I
      RETURN
      END

      SUBROUTINE HEART (AUR,CHM,HMD,HR  ,I   ,PA  ,PMC,PMP,PMS,PPT,PRA,QAO,
     *                  QLE,RTP,SVO,VAE,VLE,VPE,VRE,VVE,HM)
      REAL I
C
C     HEART HYPERTROPHY OR DETERIORATION BLOCK
C
C-----------------------------------------------------------------------------
C     HEART VICIOUS CYCLE
C-----------------------------------------------------------------------------
```

```
      DHM=(PCT-6.)*.0025
      HMD=HMD+DHM*I
      IF (HMD.GT.1.)HMD=1.
C-----------------------------------------------------------------------
C    MEAN CIRCULATORY PRESSURES
C-----------------------------------------------------------------------
      PMC=(VAE+VVE+VRE+VPE+VLE)/.11
      PMS=(VAE+VVE+VRE)/.09375
      PMP=(VPE+VLE)/.01625
C***********************************************************************
C
C    HEART RATE AND STROKE VOLUME BLOCK AND TOTAL PERIPHERAL RESISTANCE
C
C***********************************************************************
      HR=(32.+HI *AUR+PRA*2.)*((HMD-1.)*.5+1.)
      PTP=(PA-PRA)/QAO
      SVC=QLO/HR
      RETURN
      END

      SUBROUTINE CAPMBD(BFN,CFC,CPI,CPP,DFP,I  ,IFP,PC ,PCD,PIF,PLD,PPC,
     *                  PRP,PTC,PTS,PTT,PVG,PVS,RVS,TVD,VG ,VID,VIF,VP,
     *                  VPD,VTC,VTD,VTL,VTS,VUD,Z  ,Z1,FUN6)
      DIMENSION FUN6(14)
      REAL I,IFP
C
C    CAPILLARY MEMBRANE DYNAMICS BLOCK
C
 130  PTT=(VTS/12.)**2.
      VIF=VTS-VG
      CALL FUNCTN (VIF,PTS,FUN6)
      PIF=PTT-PTS
      CPI=IFP/VIF
      PTC=.25*CPI
      CPP=PRP/VP
      PPC=.4*CPP
      PVG=PVS*1.79*BFN
      PC=PVG+PVS
      PCD=PC+PTC-PPC-PIF
      VTC=VTC+(CFC*PCD-VTC)/Z
      PLD=7.8+PIF-PTT
      VTL=VTL+(.004*PLD-VTL)/Z
      IF(VTL.LT.0.)VTL=0.
      VTD=VTC-VTL-VID
      VTS=VTS+VTD*I
      VPD=VPD+(TVD-VTC+VTL-VUD-DFP-VPD)/Z1
      RETURN
      END

      SUBROUTINE PULMON(CPF,CPP,CPN,DFP,I  ,PCP,PFI,PLA,PLF,POS,PPA,PPC,
     *                  PPD,PPI,PPN,PPC,PPP,VP ,VPD,VPF,Z  ,Z3)
      REAL I
C
C    PULMONARY DYNAMICS AND FLUIDS BLOCK
C
      VP=VP+(VPD*I)/Z3
C
 200  PCP=.45*PPA+.55*PLA
      PPI=2.-.150/VPF
      CPN=PPR/VPF
```

```
      POS=CPN*.4
      PLF=(PPI+11.)*.0003
      PPO=PLF*CPN
      PPN=(CPP-CPN)*.000225
      PPD=PPD+(PPN-PPO-PPD)/Z
      IF(PPR+PPD*I-.025.LT.0.)PPD=(.025-PPR)/I
      PFI=(PCP-PPI+POS-PPC)*CPF
      DFP=DFP+(PFI-PLF-DFP)/Z
      IF(VPF+DFP*I-.001.LT.0.)DFP=(.001-VPF)/I
      VPF=VPF+DFP*I
      PPR=PPR+PPD*I
      RETURN
      END

      SUBROUTINE MISC2 (HPL,HPR,HSL,HSR,I,PA,PPA,POT,STH,Z10,Z11,Z13)
      REAL I
C
C*******************************************************************************
C
C     HEART HYPERTROPHY OR DETERIORATION BLOCK
C
C*******************************************************************************
      HPL=HPL+(((PA/100./HSL)**Z13)-HPL)*I/57600.
      HPR=HPR+(((PPA/15./HSR)**Z13)-HPR)*I/57600.
C*******************************************************************************
C
C     TISSUE EFFECT ON THIRST AND SALT INTAKE
C
C*******************************************************************************
      STH=(Z10-POT)*Z11
      IF(STH.LT.1.)STH=1.
      IF(STH.GT.8.)STH=8.
      RETURN
      END

      SUBROUTINE PROTEN(CHY,CPG,CPI,CPK,CPP,CPR,CP1,DLP,DLZ,DPC,DPI,DPL,
     *                  DPO,CPY,GPD,GPR,I   ,IFP,LPK,PC  ,PCE,PGX,PRP,VG  ,
     *                  VTL,Z   ,PPD)
      REAL I,IFP,LPK
C
C     TISSUE FLUIDS,PRESSURES AND GEL BLOCK
C
C-------------------------------------------------------------------------------
C     PLASMA AND TISSUE FLUID PROTEIN
C-------------------------------------------------------------------------------
  135 DPL=DPL+(VTL*CPI-DPL)/Z
      IF (PC.LT.0.)PC=0.
      DPC=DPC+(CPK*(CPP-CPI)*PC**PCE-DPC)/Z
      DPI=DPC-DPL
      DLZ=LPK*(CPR-CPP)
      IF(CPP.GT.CPR)DLZ=4.*DLZ
      DLP=DLP+(DLZ-DLP)/Z
      PRP=PRP+(DLP-DPO+DPL-DPC-PPD)*I
C-------------------------------------------------------------------------------
C     GEL PROTEIN DYNAMICS
C-------------------------------------------------------------------------------
  141 PGX=CHY**2*.01332*CPG+CPG
      GPD=GPD+(.0005*(CPI-PGX)*VG-GPD)/Z
      GPR=GPR+GPD*I
      IFP=IFP+(DPI-GPD)*I
```

```
      RETURN
      END

      SUBROUTINE KIDNEY(AAR,AHM,AM ,APD,ARF,AUM,CNE,CNX,CNY,GBL,GFN,GFR,
     *                  GF2,GF3,GF4,GLP,I   ,NAE,NED,NID,NOD,NOZ,PA ,PAR,
     *                  PFL,PPC,RBF,REK,RFN,RR ,STH,TRR,VIM,VUD,Z)
      REAL I,NAE,NED,NID,NOD,NOZ
C
C     KIDNEY DYNAMICS AND EXCRETION BLOCK
C
 142  GF3=((GFN/.125-1.)*GF4)+1.
      IF(GF3.GT.15.)GF3=15.
      IF(GF3.LT..4)GF3=.4
      AAR=31.67*VIM*(AUM*ARF+1.-ARF)*GF3
      RR=AAR+51.66*VIM
      PAR=PA-GBL
      RFN=PAR/RR
      RBF=REK*RFN
 150  APD=AAR*RFN
      GLP=PAR-APD
      PFL=GLP-PPC-18.
      GF1=GFN
      GFN=GFN+(PFL*.00781-GFN)*GF2/Z
      IF (ABS(GFN-GF1).GT..002)GO TO 142
      GFR=GFN*REK
      TRR=.8*GFR+.025*REK-.001*REK/AM/AHM
      VUD=VUD+(GFR-TRR-VUD)/Z
      IF(VUD.LT..0002)VUD=.0002
C-----------------------------------------------------------------------
C     KIDNEY SALT OUTPUT AND SALT INTAKE
C     (SEE ALSO ELECTROLYTES AND CELL WATER BLOCK)
C-----------------------------------------------------------------------
      NOZ=1000.*VUD/AM/(CNE/CNX+CNY)
      NOD=NOD+(NOZ-NOD)/Z
      NED=NID*STH-NOD
      NAE=NAE+NED*I
      RETURN
      END

      SUBROUTINE IONS  (AM ,CCD,CKE,CKI,CNA,I   ,KCD,KE ,KED,KI ,KID,KIE,
     *                  KIR,KOD,NAE,REK,VEC,VIC,VID,VP ,VPF,VTS,Z)
      REAL I,KCD,KE,KED,KI,KID,KIE,KIR,KOD,NAE
C
C     ELECTROLYTES AND CELL WATER BLOCK
C
 160  VEC=VTS+VP+VPF
      CKE=KE/VEC
      KOD=(.00042*CKE+.00014*AM*CKE)*REK
      KIR=2850.+140.*CKE
      KIE=KIR-KI
      KCD=KCD+(KIE*.013-KCD)/Z
      KI=KI+KCD*I
      KED=KID-KCD-KOD
      KE=KE+KED*I
      CKI=KI/VIC
      CNA=NAE/VEC
      CCD=CKI-CNA
      VID=VID+(.01*CCD-VID)/Z
      VIC=VIC+VID*I
      RETURN
```

```
      END

      SUBROUTINE GELFLD(CHY,CPG,CPI,GPR,HYL,IFP,PGC,PGH,PGP,PGR,PGX,PIF,
     *                  PRM,PTC,PTS,PTT,VG ,VGD,VIF,VRS,VTS,V2D,FUN6)
      DIMENSION FUN6(14)
      REAL IFP
C
C    GEL FLUID DYNAMICS
  140 CHY=HYL/VG
      PRM=-5.9*CHY+24.2
      PGR=.4*CHY
      CPG=GPR/VG
      PGP=.25*PGX
      PGC=PGP+PGR
      VIF=TS-VG
      CALL FUNCTN (VIF,PTS,FUN6)
      PIF=PTT-PTS
      CPI=IFP/VIF
      PTC=.25*CPI
      PGH=PIF+PTS+PRM
      VGD=V2D*(PIF+PGC-PTC-PGH)
      VG=VG+VGD
      IF(VG.LT.0.)VG=0.
      IF(.012.LT.ABS(VGD)) GO TO 140
      RETURN
      END

      SUBROUTINE GRODIN(URZ1,URZ2,URZ3,URZ4,URZ5,RUZ1)
C
C
C  FOLLOWING FROM GUYTON TO GRODIN.....
C       GUYTON             GRODIN
C        QLC                C(10)     (URZ1) CARDIAC OUTPUT.
C  (RMO+DUB)/1000.      RMT(2)+C(26)  (URZ2) TOTAL METABOLIC RATE OF BODY
C   (HM*OSA)/200.           C(17)     (URZ3) BLOOD OXYGEN CAPACITY.
C       URZ4                URZ4      (URZ4) FLG  1=1ST.TIME GRODIN CALLED.
C                                                 2=GUYTON JUST OUTPUT
C                                                 3=GUYTON JUST OUTPUT
C                                                   AND DETECTED END RUN.
C                                                 0=NOT ABOVE.
C       URZ5                URZ5      (URZ5) WORK LEVEL(WATTS).
C
C  FOLLOWING FROM GRODIN TO GUYTON.....
C       GUYTON             GRODIN
C       OVA/1000.           CHBA      (RUZ1) OXYGEN VOL.IN AORTIC BLOOD.
C
C     C(40)
C  ALVEOLAR VOL GAS FUNCTIONS
C       1    FA(CO2)
C       2    FA( O2)
C       3    FA(N2)
C
C  GAS CONCENTRATIONS IN BRAIN.
C       4    CB(CO2)
C       5    CB(O2)
C       6    CB(N2)
C
C  GAS CONCENTRATIONS IN TISSUE.
C       7    CT(CO2)
C       8    CT(O2)
```

```
C       9   CT(N2)
C  CARDIAC OUTPUT.
C      10   Q
C  CEREBRAL BLOOD FLOW.
C      11   QB
C  GAS TENSION IN CSF.
C      12   PCSF(CO2)
C      13   PCSF(O2)
C      14   PCSF(N2)
C
C  LENGTH OF SIMULATION RUN.
C      15   TMAX
C  WEIGHTING OF H+CONC IN CSF VERSUS VENOUS BLOOD OF BRAIN.
C      16   CENTRAL SENSITIVITY PARTITION
C  BLOOD OXYGEN CAPACITY
C      17   (HB)
C  TIME CONSTANTS IN CARDIAC OUTPUT AND CEREBRAL BLOOD FLOW RESPONSES.
C      18   R1
C      19   R2
C
C  CONTROLLER EQUATION SENSITIVITY WEIGHTINGS.
C      20   CENTRAL SENSITIVITY COEFFICIENT
C      21   CAROTID BODY SENSITIVITY COEFFICIENT
C
C  VOLUMES OF LUNG,BRAIN,AND TISSUE
C      22   KL
C      23   KB
C      24   KT
C
C  BRAIN METABOLIC RATE OF CO2 PRODUCTION.
C      25   MRB(CO2)
C  BRAIN METABOLIC RATE OF O2 CONSUMPTION.
C      26   MRB(O2)
C  GAS DIFFUSION COEFF.FOR BLOOD-BRAIN BARRIER.
C      27   DCO2
C      28   DO2
C      29   DN2
C
C  BAROMETRIC PRESSURE.
C      30   B
C  VOL.FRACTION OF INSPIRED GAS.
C      31   FI(CO2)
C      32   FI(O2)
C      33   FI(N2)
C
C  VOL.OF CSF.
C      34   KCSF
C  INITIAL TIME
C      35   T
C  COMPUTER TIME STEP.
C      36   H
C  CONTROLLER EQUATION CONSTANT(MAINTAINS RESTING PA(CO2) APPROX.40).
C      37   VI(N)
C  VALUE FOR RESTING ALVEOLAR VENTILATION.
C      38   VI(55)
C  OUTPUT PRINT INCREMENTS (ALSO PRINTS AT .5MIN.INCRIMENTS).
C      39   PRINT-ALL TIME
C
C      SV(18,50)
C  ARTERIAL GAS CONCENTRATIONS AT LUNG EXIT.
```

```
C       1   CA(CO2)
C       2   CA(O2)
C       3   CA(N2)
C
C   VENOUS GAS CCNCENTRATIONS AT BRAIN EXIT.
C       4   CVB(CO2)
C       5   CVB(O2)
C       6   CVB(N2)
C
C   VENOUS GAS CONCENTRATIONS AT TISSUE EXIT.
C       7   CVT(CO2)
C       8   CVT(O2)
C       9   CVT(N2)
C
C   CARDIAC OUTPUT.
C      10   C
C   CEREBRAL BLCCD FLCW.
C      11   QB
C   TISSUE BLCCD FLOW.
C      12   QT
C   ARTERIAL H+ CONCENTRATION.
C      13   CA(H+)
C   ARTERIAL O2 TENSION.
C      14   PA(O2)
C
C      15   --
C   TOTAL GAS CONCENTRATIONS AT BRAIN EXIT.
C      16   CVB(CO2) + CVB(O2) + CVB(N2)
C   TOTAL GAS CONCENTRATIONS AT TISSUE EXIT.
C      17   CVT(CO2) + CVT(O2) + CVT(N2)
C   TIME.
C      18   T
C      VTRAN(18)
C   ARTERIAL GAS CONCENTRATIONS AT BRAIN ENTRANCE.
C       1   CAB(CO2) = CA(CO2)(T - TAB)
C       2   CAB(O2) = CA(O2)(T - TAB)
C       3   CAB(N2) = CA(N2)(T - TAB)
C
C   VENCUS BRAIN GAS CONCENTRATION AT LUNG ENTRANCE.
C       4   CVB(CO2)(T- TVB)
C       5   CVB(O2)(T - TVB)
C       6   CVB(N2)(T - TVB)
C
C   VENOUS TISSUE GAS CONCENTRATION AT LUNG ENTRANCE.
C       7   CVT(CO2)(T- TVT)
C       8   CVT(O2)(T - TVT)
C       9   CVT(N2)(T - TVT)
C
C   ARTERIAL GAS CONCENTRATIONS AT TISSUE ENTRANCE.
C      10   CAT(CO2) = CA(CO2)(T - TAT)
C      11   CAT(O2) = CA(O2)(T - TAT)
C      12   CAT(N2) = CA(N2)(T - TAT)
C
C   ARTERIAL H+ CONCENTRATION AT CAROTID BODIES'SITE.
C      13   CAO(H+) = CA(H+)(T - TAO)
C   ARTERIAL O2 TENSION AT CAROTID BODIES'SITE.
C      14   PAO(O2) = PA(O2)(T - TAO)
C   ARTERIAL H+ CCNCENTRATICN AT BRAIN ENTRANCE.
C      15   CAB(H+) = CA(H+)(T - TAB)
C   TOTAL GAS CONCENTRATION FROM BRAIN AT LUNG ENTRANCE.
```

```
C      16   (CVB(CO2) + CVB(O2) + CVB(N2))(T-TVB)
C  TOTAL GAS CONCENTRATION FROM TISSUE AT LUNG ENTRANCE.
C      17   (CVT(CO2) + CVT(O2) + CVT(N2))(T - TVT)
C
C     D(15)
C   FOR D(15) THE SYMBOLS B=BAROMETRIC PRESSURE, 47=WATER VAPOR PRESS.,
C  K=CONVERSION FACTOR FOR ATM TO MMHG, A=SOLUBILITY COEFF.OF GASES,
C  H=COMPUTER TIME STEP, HB=BLOOD OXYGEN CAPACITY
C       1   B - 47
C       2   K ACO2
C       3   K AO2
C       4   K AN2
C       5   K AN2 (B - 47)
C       6   K AO2 (B - 47)
C       7   K AN2 (B - 47)
C       8   0.16 + 2.3(HB)
C       9   863/(B - 47)
C      10   0.62
C      11   K ACSF(CO2)
C      12   K ACSF(O2)
C      13   K ACSF(N2)
C      14   2*H
C      15   1.99*H
C     F(20)
C  COMPARTMENTAL GAS TENSIONS AND CONCENTRATIONS.
C       1   PA(O2)
C       2   K ACO2 PA(CO2)
C       3   PB(O2)
C       4   K ACO2 PB(CO2)
C       5   PT(O2)
C       6   K ACO2 PT(CO2)
C       7   PA(CO2)
C       8   PA(O2)
C       9   CA(O2)
C      10   CA(N2)
C      11   CA(CO2) + CA(O2) + CA(N2)
C      12   CVB(O2)
C      13   CVT(O2)
C
C  PRODUCT OF DIFFUSION COEFFS.AND GAS DIFFERENTIALS ACROSS BLOOD-BRAIN
C  BARRIER.
C      14   DCO2 (PB(CO2) - PCSF(CO2))
C      15   DO2 (PB(O2) - PCSF(O2))
C      16   DN2 (PB(N2) - PCSF(N2))
C
C      17   PB(O2)
C      18   PB(N2)
      INTEGER UR24
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), CC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), OF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      DIMENSION XNB(4,2), DJ(4), CDJ(6), IDJ(2)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, CC, A, D, F, VOL, RMT, BC, OF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, K, N
      COMMON/R/ XDS,XHH,CXT,WORK,DUM1,DUM2,DUM3,WORK2,RMTB,RMTB2,TIMEOF
     1  ,RMLIN
C
C
```

```
C
C     SEE IF THIS 1ST TIME GRODIN CALLED.
       IF(URZ4 .NE. 1 ) GC TO 370
C
C
C     HERE IF THIS 1ST TIME GRODIN CALLED.
C
C       DATA FOR INITIAL CONDITIONS
       WRITE (6,5)
     5 FORMAT (/'  , GRCDINS: RESPIRATORY CONTRCL MODEL')
300    CONTINUE
       WRITE(6,90)
    90 FORMAT('0  RESPIRATORY CHEMOSTAT -- INPUT DATA'/)
C      DATA FOR INITIAL CONDITIONS
       DO 10 I = 1,40
       READ(5,19C,END=301) C(I),(XN(I,J),J=1,2)
    10 CONTINUE
C    ESTABLISH CCMPUTER STEP INCEPENDENT OF INPUT DATA.
C         FOLLOWING  TIME STEP TO MAKE GRODIN COMPATABLE TO GUYTON.
       C(36) = .003
   190 FORMAT (5X,F15.0,5X,2A4)
       DO 20 I = 1,4
       IP40 = I + 40
       READ   (5,190) BC(I), (XNB(I,J), J = 1,2)
    20 CONTINUE
       DO 30 I = 1,2
       READ  (5,190) RMT(I), (XNB(I,J), J = 1,2)
       IP40 = I + 44
    30 CONTINUE
       DO 40 I = 1,2
       READ   (5,190) DJ(I), (XNB(I,J), J = 1,2)
       IP40 = I + 46
    40 CONTINUE
C
C
       C(10) = URZ1
       C(17) = UPZ3
       RMT(2) =  UPZ2 - C(26)
C    OUTPUT INPUT + ABOVE 3 VARIABLES FROM GUYTON.
       J = 1
       DO 75 I = 1,8
       JJ = J+4
       WRITE(6,92) J, (C(I1),I1=J,JJ)
    92 FORMAT(' ',I2,2X,5(F9.4))
       J = J + 5
    75 CONTINUE
       WRITE(6,92) J, (BC(I),I=1,4)
       J = 45
       WRITE(6,92) J, RMT(1), RMT(2), DJ(1), DJ(2)
C
C   FI(CO2)
       DUM1=C(31)
C   FI(O2)
       DUM2=C(32)
C   FI(N2)
       DUM3=C(33)
       WORK=0.
       WORK2=0.
C   METABOLIC RATE OF C2 CONSUMPTION IN TISSUE.
       RMTB=RMT(2)
```

```
      RMTB2=RMT(2)
C
      TIMEOF=0.
      XDS=0.
      XMH = 10. * C(36)/.003
      MMM=0
201   CONTINUE
      XDS=XDS+XMH
      IF(MMM.EQ.1)XDS=XDS+C(36)
      MMM=1
      C(35)=C.
      C(40)=0.
C
C     INITIAL GUESSES FOR ITERATIVE LOOPS
C   ARTERIAL CONCENTRATION OF CO2.
      CC(1) = 0.6
C   BRAIN CONCENTRATION OF CO2.
      CC(2) = C(4)

C   BRAIN CO2 TENSION.
      CPB = 50.0
C   TISSUE CO2 TENSION.
      CPT = 50.C
      IF(XDS.GT.XMH) GOTO202
C     SETS VARIOUS CONSTANTS AND AGGREGATES OF CONSTANTS.
C   TMAX.
      C(15) = C(15) + .0001
C   PRINT ALL TIME.
      C(39) = C(39) + .0001
      DO 200 I = 27,29
C   FACTOR OF 1-E-7 MULTIPLYING DIFFUSION COEFFICIENTS.
      C(I) = C(I) * 1.E-7
  200 CONTINUE
 202  CONTINUE
      IPK = 1
      M = 14
      N = 5
      IOJ(1) = C
C      SOLUBILITY COEFFICIENTS.
C   A(1)= (ALPHA)CO2, A(2)= (ALPHA)O2, A(3)= (ALPHA)N2,
C   A(4)= (ALPHA)CO2, A(5)= (ALPHA)O2, A(6) = (ALPHA)N2
      A(1) = 0.51
      A(2) = 0.024
      A(3) = 0.013
      A(4) = C.51
      A(5) = 0.024
      A(6) = 0.C13
C   ATM/MMHG CONVERSION FACTOR.
      SK = 0.00132
C   CARBONIC ACID DISSOCIATION CONSTANT.
      CADK = 795.0
C   VOL(1)-VOL(10)= VOLUMES USED IN CALCULATION OF VARIABLE TIME DELAYS.
      VOL(1) = 0.015
      VOL(2) = 1.062
      VOL(3) = 0.188
      VOL(4) = 0.06
      VOL(5) = 0.188
      VOL(6) = 2.94
      VOL(7) = 0.735
      VOL(8) = 1.062
```

```
      VOL(9) = 0.009
      VOL(10)= 1.062
C
C  (METABOLIC RATE OF CO2 IN BRAIN + TISSUE.) / SAME FOR O2
      QF(6) = (C(25) + RMT(1))/(C(26) + RMT(2))
C   B-47
      D(1)=C(30)-47.
      DO 210 I = 2,4
C  PRODUCTS OF CONVERSION FACTORS AND SOLUBILITY COEFFICIENTS.
      D(I) = SK*A(I-1)
      D(I+9) = SK*A(I+2)
C
      D(I+3) = D(1)*D(I)
  210 CONTINUE
C  FACTOR USED IN ESTABLISHING CA(CO2)
      D(8) = 0.16 + 2.3*C(17)
C
      D(9) = 863.0/D(1)
C  FACTOR USED IN ESTABLISHING CB(CO2).
      D(10) = 0.62
C  MANIPULATION OF COMPUTER TIME STEP.
      D(14) = C(36)*2.0
      D(15) = D(14) - .01*C(36)
C
      CALL RC3
      CALL RC4
      CALL RC5 (CPB, F(4), C(4), BC(2))
      CALL RC21 (CHB(2), F(3), F(4), C(4), CH(2), CPH(2))
      CALL RC19 (CPB, CHB(2), CC(2), BC(1), F(4))
      CALL RC5 (CPT, F(6), C(7), BC(3))
      CALL RC21 (CHB(3), F(5), F(6), C(7), CH(3), CPH(3))
      CALL RC19 (CPT, CHB(3), CC(3), BC(1), F(6))
      CALL RC20
      CALL RC7
      CALL RC8
      CALL RC9
      CALL RC10
      CALL RC11
C   FORCE PRINTOUT
      URZ4 = 2.
      CALL RC12(URZ4,URZ5)
      GO TO 60
   50 CALL RC15
      CALL RC16
C
C
   60 RUZ1 = CHB(1)
      RETURN
C
C
C     NORMAL ENTRY FROM GUYTON.
  370 C(10) = URZ1
      C(17) = URZ3
      RMT(2) = URZ2 - C(26)
      CALL RC13
      CALL RC12(URZ4,URZ5)
C
C
C      SEE IF GUYTON SAYS END OF RUN.
      IF(URZ4 .EQ. 3 ) GO TO 80
```

```
      IF(C(35).GE.XMH) GO TO 201
C
   70 CALL RC14
      UU = AMOD(C(35), D(14))
      IF (UU .LT. .0001 .OR. UU .GT. D(15))     GOTO50
      GOTO 60
C
C  HERE WHEN GUYTON SAID END OF RUN.
   80 IF (C(37) .GT. 1.0E-5)       GO TO 250
  220 CTERM = 0.0
      IF (VTRAN(14) - 104.0)       230, 240, 240
  230 CTERM = (23.6E-9)*((104.0 - VTRAN(14))**4.9)
  240 C(37) = C(20)*(C(16)*VTRAN(15) + (1.0 - C(16))*CH(4))
     1        + C(21)*VTRAN(13) + CTERM - VI
      I = 37
      WRITE(6,192)I,C(I), (XN(I,J), J = 1,2)
  250 DO 260 I = 1,14
      WRITE(6,192)I,C(I), (XN(I,J), J = 1,2)
  260 CONTINUE
301   CONTINUE
      STOP
  192 FORMAT (I3,2XF15.5,5X2A8)
  194 FORMAT (1H1)
      END

      SUBROUTINE RC8
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), OF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       TPK, LOC, ITERX, INDEX, I, J, K, N
C     CALCULATES TRANSPORT TIMES
C      EQUATIONS 8.10 THRU 8.14  .
C6969           FORMAT(1H 7HSUB RC8)
      DO 870 I = 1,5
      DT = C(35) - SV(18,1)
      ND = 1
      GO TO (810,812,814,816,810), I
  810 NC = 11
      NB = 10
      GO TO 820
  812 NC = 10
      NB = 11
      GO TO 820
  814 NC = 10
      NB = 12
      GO TO 820
  816 NC = 12
      NB = 10
      QA = QF(1)
      GO TO 822
  820 QA = C(NC)
  822 DO 860 J = 1,2
      GO TO (834,824), J
  824 NC = NB
      ND = K + 1
      IF (K)             826, 826, 832
  826 IF (NC - 12)       830, 828, 830
```

```
828 QA = SV(NC,1) - (SV(NC,1) - QF(1))*DT/(C(35) - SV(18,1))
    GO TO 834
830 QA = SV(NC,1) - (SV(NC,1) - C(NC))*DT/(C(35) - SV(18,1))
    GO TO 834
832 QA = SV(NC,ND) - (SV(NC,K) - SV(NC,ND))*DT/D(14)
834 IJ = 2*I + J - 2
    AB = VOL(IJ) * (C(36)/.0078125)
    AA = DT*(QA + SV(NC,ND))/2.0
    DO 838 K = ND,49
    IF (AA - AB)          836, 836, 840
836 AA = AA + C(36)*(SV(NC,K) + SV(NC,K+1))
838 CONTINUE
    K = 49
    WRITE (6,890) I
840 DA = AA- AB
    K = K -1
    IF (K)                842, 842, 846
842 DV = SV(NC,1) - QA
    IF (DV)                850, 844, 850
844 DT = DA/QA
    GO TO 860
846 DV = SV(NC,K+1) - SV(NC,K)
    IF (DV)                850, 848, 850
848 DT = DA/SV(NC,K)
    GO TO 860
850 DT = (SV(NC,K+1) - SQRT (SV(NC,K+1)**2 - DV*DA/C(36)))/(DV/D(14))
860 CONTINUE
    TAU(I) = C(35) - SV(18,K + 1) - DT
870 CONTINUE
    RETURN
890 FORMAT (5X27HSV ARRAY EXCEEDED ON CYCLE I2)
    END

    SUBROUTINE RC12(URZ4,URZ5)
    INTEGER URZ4
    DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
   1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
   2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
   3          DQ(4)
    COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
   1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
   2       IRK, LOC, ITERX, INDEX, I, J, M, N
    COMMON/R/ XDS,XMH,CXT,WORK,DUM1,DUM2,DUM3,WORK2,RMTB,RMTB2,TIMEOF
   1  ,RMLIN
    CXT=C(35)+XDS-10.
    IF(CXT.LE.0.)CXT=+0.
C   RESPIRATORY FREQUENCY.
    FREQ=8.1+7.815*(RMT(2)+C(26))
C   DEAD SPACE VENTILATION
    DEADVT=.1107*FREQ+.0785*VE
C   C(31)=(DEADVT*C(1)+VE*DUM1)/(DEADVT+VE)
C   C(32)=(DEADVT*C(2)+VE*DUM2)/(DEADVT+VE)
C   C(33)=(DEADVT*C(3)+VE*DUM3)/(DEADVT+VE)
C   MINUTE VOLUME.
    TVNT=DEADVT+(VE+VI)/2.
C   HEART RATE.
    HRATE=43.8*(RMT(2)+C(26))+54.5
C
C
C   SEE IF WORKLOAD HAS CHANGED.
```

```
      IF(URZ5 .NE. WORK) GO TO 500
C
C
      IF(MARKER.EQ.0) GOTO101
 1    WORK=WORK2
      MARKER=1
C
C  SYSTEM RESPONSES: TIME CONSTANTS FOR WORK LOAD LEVELS(INCREASING).
      IF(WORK.LE.0.)GOTO2
      IF(WORK.GE.50.) TCT=2.3/(2.*WORK/200.)
      IF(WORK.LT.50)TCT=4.6
C  TISSUE O2 METABOLIC RATE.
C       RMT(2) COMES FROM GUYTON.
      VTIME=1.1-1.1*EXP(-TCT*(CXT-TIMEON)/1.92)
C  TERM USED IN VI THAT IS A COMPONENT OF TRANSIENT RESPONSE RELATED
C  TO WORK LOAD.
      RMLIN =SSO2W(WORK)-(SSO2W(WORK)-RMTB2 *(1.-VTIME)
      IF(VTIME.GE.1.) RMLIN=SSO2W(WORK)
C  TISSUE CO2 METABOLIC RATE.
      RMT(1)=.88*RMT(2)
      IF(TVNT.GT.37.) RMT(1)=(TVNT+40.77)*RMT(2)/88.5
      IF(URZ4 .EQ. 0) GO TO 1230
      WRITE (6,333) RMT(1),RMT(2)
 333  FORMAT(  '0',1X,25HCHANGE IN METABOLIC RATES,5X,7HMRCO2= ,F10.4,
     1  5X,6HMRO2= ,F10.4,/)
2     CONTINUE
C
      IF(URZ4 .EQ. 0) GO TO 1230
C
C  HERE IF GOING TO PRINTOUT.
C  ARTERIAL N2 TENSION.
 1210 PAN2 = D(1)*C(3)
C  TISSUE O2 TENSION.
      PTO2 = C(8)/D(3)
C  TISSUE N2 TENSION.
      PTN2 = C(9)/D(4)
C  CEREBROSPINAL FLUID PH , EQUATION 6.2 .
      PHSCF = 9. - PCF1(CH(4))
C  VENOUS BRAIN H+ CONCENTRATION , EQUATION 4.7 .
      HVB   = CANK*F(4)/(CC(2) - F(4))
C  VENOUS BRAIN PH , EQUATION 4.6 .
      PHVB  = 9. - PCF1(HVB)
C  VENOUS TISSUE H+ CONCENTRATION , EQUATION 5.7 .
      HVT   = CANK*F(6)/(CC(3) - F(6))
C  VENOUS TISSUE PH , EQUATION 5.6 .
      PHVT  = 9. - PCF1(HVT)
C  RESPIRATORY QUOTIENT (ALVEOLAR).
      RQ = ((C(11)*VTRAN(4) + QF(1)*VTRAN(7))/C(10) - CC(1))/
     1       (F(9) - (C(11)*VTRAN(5) + QF(1)*VTRAN(8))/C(10))
      QF(5) = QF(6) - RQ
C
      WRITE (6,1810) CXT, RQ, QF(5)
C
      WRITE (6,1815)    (C(I), I = 1,3), (DC(I), I = 1,3), F(7), F(1),
     1       PAN2
      WRITE (6,1820)   CC(1), F(9), F(10), F(7), F(1), PAN2, CH(1),
     1       CPH(1), CHB(1)
      WRITE (6,1825)    (C(I), I = 4,6), (DC(I), I = 4,6), CPB, F(17),
     1       F(18), CH(2), CPH(2)
      WRITE (6,1830)    (C(I), I = 7,9), (DC(I), I = 7,9), CPT, PTO2,
```

```
     1       PTN2, CH(3), CPH(3)
      WRITE (6,1835)   (DC(I), I = 12,14), (C(I), I = 12,14), CH(4),
     1       PHCSF
      WRITE (6,1840)   CC(2), F(12), C(6), CPB, F(17), F(18), HVB,
     1       PHVB, CHB(2)
      WRITE (6,1845)   CC(3), F(13), C(9), CPT, PTO2, PTN2, HVT,
     1       PHVT, CHB(3)
      WRITE (6,1850)   (TAU(I), I = 1,5), VI, VE, C(10), C(11), DC(10),
     1       DC(11)
      WRITE (6,1855) FREC,TVNT,DEADVT,HRATE
 1230 RETURN
 1290 FORMAT (5H XXXX5X7F10.4)
 1292 FORMAT (9F10.4)
 1805 FORMAT (1H1)
 1810 FORMAT (1H06X4HTIMEF10.4,74X6HALV RQF10.4,3X7HRQ DIFF,F8.4/
     1        16X3HCO28X2HO28X2HN27X21HD E R I V A T I V E S9X4HPCO26X
     2        3HPO27X3HPN27X4H(H+)7X2HPH5X4HHCO2)
 1815 FORMAT (3X8HALVEOLAR9F10.4)
 1820 FORMAT (3X8HARTERIAL3F10.4,30X,5F10.4,F8.4)
 1825 FORMAT (6X5HBRAIN11F10.4)
 1830 FORMAT (5X6HTISSUE11F10.4)
 1835 FORMAT (8X3HCSF30X9F10.4)
 1840 FORMAT (4X7HV BRAIN3F10.4,30X,5F10.4,F8.4)
 1845 FORMAT (3X8HV TISSUE3F10.4,30X,5F10.4,F8.4)
 1850 FORMAT (5X18HTRANSPORT TIMES --4X2HAB8X2HVB8X2HVT8X2HAT8X2HAC2X
     1  2H**4X2HVI8X2HVE8X1HO9X2HFB7X11HDERIVATIVES/21X,10F10.4,F8.4)
 1855 FORMAT(3X,9HRESP FREQ,F10.4,5X,13HMINUTE VOLUME,F10.4,5X,
     1  15HDEAD SPACE VENT,F10.4,10X,10HHEART RATE,F10.4)
C
C
C   HERE GUYTON SENT WORK LOAD CHANGE.
  500 WORK2 = URZ5
      WRITE(6,305) WORK2,CXT
  305 FORMAT('0',20('*')/' CHG.IN WORK LOAD, WORK=',F7.2,'WATTS ',
     1 '(AT ',F10.4,'MINS)')
      TIMEON=CXT
C  SYSTEM RESPONSES: TIME CONSTANTS FOR WORK LOADS AND TISSUE O2
C  METABOLIC RATE.
      IF(WORK2.GE.WORK)RMTB2=RMT(2)
C  DECREASING WORK LOADS
      IF(WORK2.LT.WORK) RMT4=RMT(2)
      IF(WORK2.LT.WORK)RMTB=SSO2W(WORK2)
      IF((WORK2.LT.WORK).AND.(WORK.GE.50.))   TCT=2.3/(2.*WORK/200.)
      IF((WORK2.LT.WORK).AND.(WORK.LT.50.))TCT=4.6
      IF(WORK2.GE.WORK) GOTO1
  101 WORK=WORK2
      MARKER=0
C  TISSUE O2 METABOLIC RATE.
C        RMT(2) COMES FROM GUYTON.
      VTIME=1.1-1.1*EXP(-TCT*(CXT-TIMEON)/3.84)
C  TERM USED IN VI THAT IS A COMPONENT OF TRANSIENT RESPONSE RELATED
C  TO WORK.LOAD.
      RMLIN =RMTB-(RMTB-RMT4)*(1.-VTIME)
      IF(VTIME.GE.1.) RMLIN=RMTB
C  TISSUE CO2 METABOLIC RATE.
      RMT(1)=.88*RMT(2)
      IF(TVNT.GT.37.) RMT(1)=(TVNT+40.77)*RMT(2)/88.5
      IF(URZ4 .EQ. 0) GO TO 1230
      WRITE (6,333) RMT(1),RMT(2)
      GOTO2
```

```
      END

      SUBROUTINE RC3
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LCC, ITERX, INDEX, I, J, K, N
C6969             FORMAT(1H 7HSUB RC3)
C     SETS TIME-DEPENDENT EXPRESSIONS
C  TISSUE BLOOD FLOW.
      QF(1) = C(10) - C(11)
C  ARTERIAL O2 TENSION.
      F(1) = D(1)*C(2)
C  ARTERIAL CO2 CONCENTRATION.
      F(2) = D(5)*C(1)
C  BRAIN O2 CONCENTRAION / (CONV.FACTOR*SOLUBILITY COEFF.FOR O2)
      F(3) = C(5)/D(3)
C  (CONV.FACTOR*SOLUBILITY COEFF.FOR CO2) * BRAIN CO2 TENSION.
      F(4) = D(2)*CPB
C  TISSUE O2 CONCENTRATION / (CONV.FACTOR*SOLUBILITY COEFF.FOR O2)
      F(5) = C(8)/D(3)
C  (CONV.FACTOR*SOLUBILITY COEFF.FOR CO2) * TISSUE CO2 TENSION.
      F(6) = D(2)*CPT
C  ARTERIAL CO2 TENSION.
      F(7) = D(1)*C(1)
C  ARTERIAL O2 TENSION.
      F(8) = D(1)*C(2)
      RETURN
      END

      SUBROUTINE RC4
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LCC, ITERX, INDEX, I, J, K, N
C     ITERATES FOR CC(1), ARTERIAL CO2 CONCENTRATION
C6969             FORMAT(1H 7HSUB RC4)
  410 CALL RC21 (CHB(1), F(1), F(2), CC(1), CH(1), CPH(1))
      X = (CC(1) - F(2))/(0.01*F(7))
      X = RCF1(X)
C  SEE EQUATION 3.1,  X= CA(CO2) .
      X = BC(1) + 0.375*(C(17) - CHB(1)) + F(2) - D(8)*(X - 0.14)
C  CC(1) = CA(CO2) .
      CALL RC6 (CC(1))
      CC(1) = CC(1) + 2.0*(X - CC(1))/3.0
C3000 FORMAT(1H ,5HCC(1),5X,E16.6)
      IF (ITERX)   420, 410, 420
  420 RETURN
      END

      SUBROUTINE RC5 (CP, FB, CCB, BHC)
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
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```
     3            DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1          TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2          IRK, LOC, ITERX, INDEX, I, J, H, N
C     ITERATES FOR BRAIN AND TISSUE PCO2
C6969             FORMAT(1H 7HSUB RC5)
  510 X = (CCB - FB)/(0.01*CP)
      X = RCF1(X)
C  SEE EQUATION 4.1,  X = PB(CO2) .
      X = (-BHC + CCB + D(10)*(X - 0.14))/0 2)
C  CP = PB(CC2) .
      CALL RC6 (CP)
      CP = CP + (X - CP)/10.0
C  CEREBRAL BLOOD FLOW.
      FB = D(2)*CP
C3000 FORMAT(1H ,4HCP= ,E16.6,4HFB= E16.6,5HCCB= E16.6,5HBHC= E16.6)
      IF (ITERX)    520, 510, 520
  520 RETURN
      END

      SUBROUTINE RC6 (Y)
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15 , F(20), VOL(10), RMT(2),
     2           BC(4), QF(6), TAU(5), CC(3)  CHB(3), CH(4), CPH(3),
     3           DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1          TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2          IRK, LOC, ITERX, INDEX, I, J, H, N
C     CHECKS CONVERGENCE OF ITERATIVE PROCEDURES
C      RC4 : X=CA(CO2), Y=CC(1)  .
C      RC5 : X=PB(CO2), Y=CP  .
C      RC19 : X=CVB(CO2), Y=CVC .
C6969             FORMAT(1H 7HSUB RC6)
      ITERX = 0
      DIFF = ABS ((X - Y)/Y)
      IF (DIFF - 1.0E-5)    620, 620, 630
  620 ITERX = 1
  630 RETURN
      END

      SUBROUTINE RC7
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1          TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2          IRK, LOC, ITERX, INDEX, I, J, H, N
      COMMON/P/ XDS,XMH,CXT,WORK,DUM1,DUM2,DUM3,WORK2,RMTB,RMTB2,TIMEOF
     1  ,RMLIN
C6969             FORMAT(1H 7HSUB RC7)
C     FILLS SV ARRAY WITH INITIAL CONDITION
      CALL RC16
      IF(XDS.GT.XMH) GOTO2
      DO 725 I = 1,17
      DO 720 J = 2,50
      SV(I,J) = SV(I,1)
  720 CONTINUE
  725 CONTINUE
 2    CONTINUE
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      DO 730 J = 2,50
      SV(18,J) = SV(18,J - 1) - D(14)
  730 CONTINUE
C3000 FORMAT(1H ,12H18SV S D(14),6(3X,E16.5)/1H ,6(3X,E16.6)/1H ,7(3X,E1
C    C6.6))
      RETURN
      END

      SUBROUTINE RC9
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C     SETS VALUES IN VTRAN ARRAY
C6969               FORMAT(1H 7HSUB RC9)
      DO 960 I = 1,5
      TA = TAU(I) - (C(35) - SV(18,1))
      LOC = TA/D(14)
      IF (LOC - 49)    904, 904, 902
  902 WRITE (6,990) I,LOC
      LOC = 49
  904 XLOC = LOC
      TB = XLOC*D(14)
      DT = TA - TB
      GO TO (910,920,930,940,950), I
  910 DO 914 J = 1,3
C  LUNG TO BRAIN CO2,O2,N2 TIME DELAYED ARTERIAL CONCENTRATIONS.
      VTRAN(J) = RCF3(J)
  914 CONTINUE
C  LUNG TO BRAIN H+ TIME DELAYED ARTERIAL CONCENTRATION.
      VTRAN(15) = RCF3(13)
      GO TO 960
  920 DO 924 J = 4,6
C  BRAIN TO LUNG CO2,O2,N2 TIME DELAYED VENOUS CONCENTRATIONS.
      VTRAN(J) = RCF3(J)
  924 CONTINUE
C  BRAIN TO LUNG COMBINED CO2,O2,N2 TIME DELAYED VENOUS CONCENTRATIONS.
      VTRAN(16) = RCF3(16)
      GO TO 960
  930 DO 934 J = 7,9
C  TISSUE TO LUNG CO2,O2,N2 TIME DELAYED VENOUS CONCENTRATIONS.
      VTRAN(J) = RCF3(J)
  934 CONTINUE
C  TISSUE TO LUNG COMBINED CO2,O2,N2 TIME DELAYED VENOUS CONCENTRATIONS.
      VTRAN(17) = RCF3(17)
      GO TO 960
  940 DO 944 J = 1,3
C  LUNG TO TISSUE CO2,O2,N2 TIME DELAYED ARTERIAL CONCENTRATIONS.
      VTRAN(J+9) = RCF3(J)
  944 CONTINUE
      GO TO 960
C  LUNG TO CAROTID SITE H+ TIME DELAYED ARTERIAL CONCENTRATION.
  950 VTRAN(13) = RCF3(13)
C  LUNG TO CAROTID SITE O2 TIME DELAYED ARTERIAL TENSION.
      VTRAN(14) = RCF3(14)
  960 CONTINUE
C     NAMELIST/DDNM/VTRAN
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      RETURN
  990 FORMAT (5X27HSV ARRAY EXCEEDED ON CYCLE I2,12H WITH LOC = ,I4)
      END

      SUBROUTINE RC10
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C6969               FORMAT(1H 8HSUB RC10)
C     COMPUTES EMPIRICAL FUNCTIONS FOR ACRDIAC OUTPUT AND BRAIN BLOOD
C     FLOW DIFFERENTIAL EQUATIONS
      DQ(1) = 0.
      DQ(2) = 0.
C   F(8) = PA(O2) .
      IF (F(8) - 104.0)              1008, 1024, 1024
C   (DELTA)QB(O2) , EQUATION 7.9 .
 1008 DQ(2) = (((7.6559E-8*F(8) - 2.324E-5)*F(8) + 2.6032E-3)*F(8)
     1       - 0.1323)*F(8) + 2.785
 1016 IF (DQ(2))                     1024, 1044, 1044
 1024 DQ(2) = 0.0
C
C     IF PCO2 GT 60 DQ(3) STAYS AT ITS VALUE AT 60 - - OLD ROUTINE SETS
C     THE VALUE OF DQ(3) EQUAL TO 0
C
 1044 IF (F(7) - 38.0)               1048, 1052, 1052
C   (DELTA)QB(CO2) , EQUATION 7.11 .
 1048 DQ(4) = (8.0163E-4*F(7) - 3.1073E-2)*F(7) + 2.3232E-2
      RETURN
 1052 IF (F(7) - 44.0)               1056, 1056, 1060
 1056 DQ(4) = 0.0
      RETURN
C   (DELTA)QB(CO2) , EQUATION 7.13 .
 1060 DQ(4) = (((-2.1748E-7*F(7) + 9.3918E-5)*F(7) - 1.2947E-2)*F(7)
     1       + 0.7607)*F(7) - 15.58
C     NAMELIST/D6/DQ.F
      RETURN
      END

      SUBROUTINE RC11
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1        SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C     CALCULATES DIFFERENTIAL EQUATIONS
C6969               FORMAT(1H 8HSUB RC11)
      CALL RC17
C  EQUATION 10.1 .
      DC(1) = (VI*C(31) - VE*C(1) + D(9)*(F(11)*VTRAN(4) + QF(1)
     1        *VTRAN(7) - C(10)*CC(1)))/C(22)
C  EQUATION 10.2 .
      DC(2) = (VI*C(32) - VE*C(2) + D(9)*(F(11)*VTRAN(5) + QF(1)
     1        *VTRAN(8) - C(10)*F(9)))/C(22)
C  EQUATION 10.3 .
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      DC(3) = (VI*C(33) - VE*C(3) + D(9)*(C(11)*VTRAN(6) + QF(1)
     1        *VTRAN(9) - C(10)*F(10)))/C(22)
C  EQUATION 10.4 .
      DC(4) = (C(25) + C(11)*(VTRAN(1) - CC(2)) - F(14))/C(23)
C  EQUATION 10.5 .
      DC(5) = (-C(26) + C(11)*(VTRAN(2) - F(12)) - F(15))/C(23)
C  EQUATION 10.6 .
      DC(6) = (C(11)*(VTRAN(3) - C(6)) - F(16))/C(23)
C  EQUATION 10.7 .
      DC(7) = (RMT(1) + QF(1)*(VTRAN(10) - CC(3)))/C(24)
C  EQUATION 10.8 .
      DC(8) = (-RMT(2) + QF(1)*(VTRAN(11) - F(13)))/C(24)
C  EQUATION 10.9 .
      DC(9) = QF(1)*(VTRAN(12) - C(9))/C(24)
      DC(10) = 0.
C
C
C  DEPENDANCE OF CARDIAC OUTPUT ON TISSUE
C  UTILIZATION OF OXYGEN.
      XAB=5.5 *(RMT(2)-.215)+6.-C(10)
      IF((RMT(2).GT..215).AND.(XAB.GT.0.))DC(10)=DC(10)+XAB/.010
C
C
C  EQUATION 7.7 .
      DC(11) = (-C(11) + 0.75 + DQ(2) + DQ(4))/C(19)
C  EQUATION 1.10 .
      DC(12) = F(14)/(C(34)*D(11))
C  EQUATION 1.11 .
      DC(13) = F(15)/(C(34)*D(12))
C  EQUATION 1.12 .
      DC(14) = F(16)/(C(34)*D(13))
C     NAMELIST/AB/DC
      RETURN
      END

      SUBROUTINE RC13
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2         BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, II, N
C6969              FORMAT(1H 8HSUB RC13)
C     SOLVES M DIFFERENTIAL EQUATIONS BY FOURTH-ORDER RUNGE-KUTTA AND
C     ADAMS-MOULTON PREDICTOR-CORRECTOR METHODS
C     NAMELIST/DBG/C,DC,SC
      IF (IRK - 4)        1304, 1356, 1356
 1304 DO 1352 INDEX = 1,4
      DO 1308 I = 1,M
      RK(I,INDEX) = DC(I)
 1308 CONTINUE
      GO TO (1312, 1320, 1328, 1340), INDEX
 1312 DO 1316 I = 1,M
      SC(I,IRK+1) = C(I)
      SC(I,IRK) = DC(I)
 1316 CONTINUE
      TI = C(35)
 1320 C(35) = TI + C(36)/2.0
      DO 1324 I = 1,M
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      C(I) = SC(I,IRK+1) + C(36)*RK(I,INDEX /2.0
 1324 CONTINUE
      GO TO 1336
 1328 C(35) = TI + C(36)
      DO 1332 I = 1,M
      C(I) = SC(I,IRK+1) + C(36)*RK(I,INDEX)
 1332 CONTINUE
 1336 CALL RC14
      GO TO 1352
 1340 DO 1344 I = 1,M
      C(I) = SC(I,IRK+1) + C(36)*(RK(I,1) + 2.0*RK(I,2) + 2.0*RK(I,3)
     1        + RK(I,4))/6.0
 1344 CONTINUE
      IRK = IRK + 1
 1352 CONTINUE
      RETURN
 1356 DO 1360 I = 1,M
      SC(I,5) = C(I)
      SC(I,4) = DC(I)
      C(I) = SC(I,5) + C(36)*(55.0*SC(I,4) - 59.0*SC(I,3) + 37.0*SC(I,2)
     1        - 9.0*SC(I,1))/24.0
 1360 CONTINUE
      C(35) = C(35) + C(36)
      NC35=C(35)/C(36) + .1
      C(35)=C(36)*NC35
 1364 CALL RC14
      DO 1368 I = 1,M
      SC(I,1) = C(I)
      C(I) = SC(I,5) + C(36)*(9.0*DC(I) + 19.0*SC(I,4) - 5.0*SC(I,3)
     1        + SC(I,2))/24.0
 1368 CONTINUE
      DO 1372 I = 1,M
      IF (ABS  (C(I) - SC(I,1)) - 1.0E-3)  1372, 1372, 1364
 1372 CONTINUE
      DO 1376 I = 1,M
      DO 1376 J = 1,3
      SC(I,J) = SC(I,J+1)
 1376 CONTINUE
      RETURN
      END

      SUBROUTINE RC14
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C     CALLS OTHER SUBROUTINES IN C BLOCK
C6969              FORMAT(1H 8HSUB RC14)
      CALL RC3
      CALL RC8
      CALL RC9
      CALL RC4
      CALL RC5 (CPB, F(4), C(4), BC(2))
      CALL RC21 (CHB(2), F(3), F(4), C(4), CH(2), CPH(2))
      CALL RC19 (CPB, CHB(2), CC(2), BC(1), F(4))
      CALL RC5 (CPT, F(6), C(7), BC(3))
      CALL RC21 (CHB(3), F(5), F(6), C(7), CH(3), CPH(3))
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      CALL RC19 (CPT, CHB(3), CC(3), BC(1), F(6))
      CALL RC10
      CALL RC20
      CALL RC11
      RETURN
      END

      SUBROUTINE RC15
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1       SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2         BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3         DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1     TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2      IRK, LOC, ITERX, INDEX, I, J, K, N
C6969           FORMAT(1H 8HSUB RC15)
C     NAMELIST/SCH/SV
C     SHIFTS VALUES IN SV ARRAY
      DO 1530 I = 1,18
      DO 1520 J = 1,49
      JM = 51 - J
      JMM = JM - 1
      SV(I,JM) = SV(I,JMM)
 1520 CONTINUE
 1530 CONTINUE
      RETURN
      END

      SUBROUTINE RC16
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1         SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2         BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3         DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1      TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2      IRK, LOC, ITERX, INDEX, I, J, K, N
      COMMON/P/ XDS,XMH,CXT,WORK,DUM1,DUM2,DUM3,WORK2,RMT8,RMT82,TIMEOF
     1  ,RMLIN
C6969           FORMAT(1H 8HSUB RC16)
C     SETS VALUES FOR SV ARRAY
C  ARTERIAL CO2 CONCENTRATION.
      SV(1,1) = CC(1)
C  ARTERIAL O2 CONCENTRATION.
      SV(2,1) = F(9)
C  BRAIN VENOUS CO2 CONCENTRATION.
      SV(4,1) = CC(2)
C  ARTERIAL N2 CONCENTRATION.
      SV(3,1) = F(10)
C  BRAIN VENOUS O2 CONCENTRATION
      SV(5,1) = F(12)
C  BRAIN VENOUS N2 CONCENTRATION.
      SV(6,1) = C(6)
C  TISSUE VENOUS CO2 CONCENTRATION.
      SV(7,1) = CC(3)
C  TISSUE VENOUS O2 CONCENTRATION.
      SV(8,1) = F(13)
C  TISSUE VENOUS N2 CONCENTRATION.
      SV(9,1) = C(9)
C  CARDIAC OUTPUT.
      SV(10,1) = C(10)
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C  CEREBRAL BLOOD FLOW.
      SV(11,1) = C(11)
C  TISSUE BLOOD FLOW.
      SV(12,1) = QF(1)
C  ARTERIAL H+ CONCENTRATION.
      SV(13,1) = CH(1)
C  ARTERIAL O2 TENSION.
      SV(14,1) = F(1)
C  INITIAL TIME.
      SV(15,1) = 0.0
C  TOTAL GAS CONCENTRATIONS AT BRAIN EXIT.
      SV(16,1) = SV(4,1) + SV(5,1) + SV(6,1)
C  TOTAL GAS CONCENTRATIONS AT TISSUE EXIT.
      SV(17,1) = SV(7,1) + SV(8,1) + SV(9,1)
C  SIMULATED TIME.
      SV(18,1) = C(35)
      RETURN
      END

      SUBROUTINE RC17
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, CC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
      COMMON/R/ XDS,XMH,CXT,WORK,DUM1,DUM2,DUM3,WORK2,RMTB,RMTB2,TIMEDF
     1  ,RMLIN
C     NAMELIST/BAC/CH(4),CADK,C(11),C(12),BC(4),C(37),C(38),VTRAN(14),
C    1TERM,VI,C(20),C(16),VTRAN(15),C(21),VTRAN(13),C(37),D(9),C(11),
C    2VTRAN(16),QF(1),VTRAN(17),C(10),F(11),
C6969             FORMAT(1H 8HSUB RC17)
C     CALCULATES VENTILATION
C  CFS H+ CONCENTRATION , EQUATION 6.1 .
      CH(4)   = CADK*C(11)*C(12)/BC(4)
      IF (C(37) .GT. 1.0E-5)       GO TO 1708
 1704 VI = C(38)
      GO TO 1730
 1708 TERM = 0.0
C  DECISION ON ARTERIAL O2 TENSION AT CAROTID BODIES'SITE.
      IF (VTRAN(14) - 104.0)       1710, 1720, 1720
 1710 TERM = (23.6E-9)*((104.0 - VTRAN(14) **4.9)
C  CONTROLLER EQUATION AS A FUNCTION OF HUMORAL TERMS.
 1720 VI = C(20)*(C(16)*VTRAN(15) + (1.0 - C(16))*CH(4))
     1       + C(21)*VTRAN(13) + TERM - C(37)
C  INCLUSION OF NEURAL COMPONENT AS A FUNCTION OF WORK LOAD.
      SVNT2=SSVENT(SSO2W(WORK))  -VI
      IF((SVNT2.GT.0.).AND.(SVNT2.LE.15.))   VI=VI+SVNT2
      IF(SVNT2.GT.15.)  VI=VI+15.
C
C  DESCRIPTION OF TRANSIENT VENTILATION RESPONSE.
      SVNT =SSVENT(RMLIN ) -VI
      IF(SVNT.GT.0.5)   VI=VI+0.75*SVNT
C
C  EXPIRED VENTILATION RATE, EQUATION 11.1 .
 1730 VE = VI + D(9)*(C(11)*VTRAN(16) + QF(1)*VTRAN(17) - C(10)*F(11))
      IF (VI .LT. 0.0 .OR. VE .LT. 0.0)     GO TO 1740
      RETURN
 1740 VI = 0.0
```

```
      VE = 0.0
      RETURN
      END

      SUBROUTINE RC19 (CPA, CVHBA, CVC, BHCA, FC)
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C     NAMELIST/DM2/CPA,CVHBA,CVC,BHCA,FC
C6969            FORMAT(1H 8HSUB RC19)
C     ITERATES FOR VENOUS BRAIN AND VENOUS TISSUE CO2 CONCENTRATION
C  TERM USED IN EQUATION 4.2 .
 1910 X = (CVC - FC)/(0.01*CPA)
C  LOGARITHM SUBROUTINE.
      X = RCF1(X)
C  EQUATION 4.2 .
      X = BHCA + 0.375*(C(17) - CVHBA) - D(8)*(X - 0.14) + FC
      CALL RC6 (CVC)
      CVC = CVC + 2.0*(X - CVC)/3.0
      IF (ITERX)        1920, 1910, 1920
 1920 CONTINUE
      RETURN
      END

      SUBROUTINE RC20
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C     NAMELIST/NMF/F
C6969            FORMAT(1H 8HSUB RC20)
C     SETS TIME DEPENDENT EXPRESSIONS
C  ARTERIAL OXYGEN CONCENTRATION INCLUDING EFFECTS OF HEMOGLOBIN.
      F(9) = D(6)*C(2) + CHB(1)
C  ARTERIAL NITROGEN CONCENTRATION.
      F(10) = D(7)*C(3)
C  TOTAL ARTERIAL GAS CONCENTRATION AT LUNG EXIT.
      F(11) = CC(1) + F(9) + F(10)
C  VENOUS BRAIN OXYGEN CONCENTRATION INCLUDING EFFECTS OF HEMOGLOBIN.
      F(12) = C(5) + CHB(2)
C  VENOUS TISSUE OXYGEN CONCENTRATION INCLUDING EFFECTS OF HEMOGLOBIN
      F(13) = C(8) + CHB(3)
C  OXYGEN TENSION IN BRAIN.
      F(17) = C(5)/D(3)
C  NITROGEN TENSION IN BRAIN.
      F(18) = C(6)/D(4)
C  PRODUCT OF DIFFUSION COEFFS.AND DIFFERENTIAL BRAIN - CSF GAS TENSIONS
      F(14) = C(27)*(CPB - C(12))
      F(15) = C(28)*(F(17) - C(13))
      F(16) = C(29)*(F(18) - C(14))
C
      RETURN
      END
```

```
      SUBROUTINE RC21 (CHBA, FA, FD, CCA, CHA, CPHA)
      DIMENSION C(40), XN(40,2), SV(18,50)  VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3 , CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE  VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C6969             FORMAT(1H BHSUB RC21)
C     NAMELIST/PB/CHBA,FA,FD,CCA,CHA,CPHA
C     COMPUTES H+ ION, PH, AND OXYHEMOGLOBIN
C  ARTERIAL H+ CONCENTRATION.
      CHA = CADK*FD/(CCA - FD)
C  ARTERIAL PH.
      CPHA = 9.0 - RCF1(CHA)
C  DEVELOPMENT OF EXPRESSION USED IN CALCULATION OF ARTERIAL
C  OXYHEMOGLOBIN SATURATION.
      X = RCF2(CPHA)
      X = -X * FA
      X = (1.0 - EXP (X))**2
      X=ABS(X)
C
C  ARTERIAL OXYHEMOGLOBIN CONCENTRATION.
      CHBA = X*C(17)
      RETURN
      END

      FUNCTION RCF1(W)
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C     LOGARITHM TO BASE 10
      RCF1    = 0.43429448 * ALOG(W)
      RETURN
      END

      FUNCTION RCF2(ZZ)
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1       TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2       IRK, LOC, ITERX, INDEX, I, J, M, N
C     OXYHEMOGLOBIN - PH EMPIRICAL FUNCTION
C       EQUATION 3.4 ,
      RCF2  =(((0.0066815*ZZ)-0.10098)*ZZ + 0.44921)*ZZ-0.454
      RETURN
      END

      FUNCTION RCF3(KK)
      DIMENSION C(40), XN(40,2), SV(18,50), VTRAN(18), RK(14,4),
     1          SC(14,5), DC(14), A(6), D(15), F(20), VOL(10), RMT(2),
     2          BC(4), QF(6), TAU(5), CC(3), CHB(3), CH(4), CPH(3),
     3          DQ(4)
```

```
      COMMON/Z/ C, XN, SV, VTRAN, RK, SC, DC, A, D, F, VOL, RMT, BC, QF,
     1        TAU, CC, CHB, CH, CPH, DQ, VE, VI, CPB, CPT, CADK, X, DT,
     2        IRK, LOC, ITERX, INDEX, I, J, M, N
C      VTRAN FUNCTION
C   VARIABLES WITH TIME DELAYS USED IN EQUATIONS 8.1-8.1 .
      RCF3 = SV(KK,LOC) + (SV(KK,LOC + 1) - SV(KK,LOC))*DT/D(14)
      RETURN
      END

      FUNCTION SSO2W(X)
C   CALCULATION OF STEADY-STATE OXYGEN REQUIREMENTS FOR VARIOUS LEVELS
C   OF WORK LOAD (X=WATTS).
      SSO2W = .195 + (X/84.15)
      IF(X .GT. 210.) SSO2W = 2.7
      RETURN
      END

      FUNCTION SSVENT(X)
C   CALCULATION OF STEADY-STATE VENTILATION RATE AS A FUNCTION OF TISSUE
C   OXYGEN METABOLIC RATE.
      IF(X.LE..195) SSVENT=5.398
      IF(X.GE.2.)SSVENT=55.36+50.*(X-2.)
      IF((X.GT..195).AND.(X.LT.2.))SSVENT=27.68*X
      RETURN
      END
```

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