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SUBJECT: Study Report, The Development of a Whole-Body Algorithm, by Franklin J. Kay, Ph.D.

The attached study report was submitted to G. E. by Dr. Franklin J. Kay in partial fulfillment of his subcontract. The report details a plan for the development of a whole-body algorithm.

R. C. Croston, Ph.D.

Attachment
/db

CONCURRENCES

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ASD 4028

STUDY REPORT

ON

THE DEVELOPMENT OF A WHOLE-BODY ALGORITHM

by

Franklin J. Kay, Ph. D.

November 12, 1973

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I. Introduction

The whole-body algorithm is envisioned as a mathematical model that utilizes human physiology to simulate the behavior of vital body systems. The objective of this model is to determine the response of selected body parameters within these systems to various input perturbations, or stresses. Perturbations of interest are exercise, chemical unbalances, gravitational changes, and other abnormal environmental conditions. This model will then provide for a study of man's physiological response in various space applications, underwater applications, normal and abnormal workloads and environments, and the functioning of the system with physical impairments or decay of functioning components.

Many methods or approaches to the development of a whole-body algorithm have been considered. Of foremost concern is the determination of the subsystems to be included, the detail of the subsystems and the interaction between the subsystems. The approach selected is to use the subsystems that are currently in existence, specifically:

1. Guyton's model for Circulatory, Fluid and Electrolyte Regulation,
2. Grodins' Respiratory model
3. Stolwijk's model for Thermoregulation
4. Croston's Cardiovascular Exercise model

These models were selected after careful study and with cognizance of the differences in parameters, control systems, and various approximations used as constant parameters or set points.

A whole-body algorithm must be versatile so modifications can be performed without total disruption of the system. The model needs to change as data are added from experiments being conducted, new information is gained from the literature, or results from the model indicate an inappropriate approximation has been made.

This report will describe the subsystems, delineate interfaces between the subsystems, and indicate an approach for the development of the whole-body algorithm.

II. Background

Previous work has been done to couple subsystems and determine response, but with the exception of Guyton, the models were not integrated or really interacting. Walters (17) defined a model for combined steady-state and thermal. Weissman (14) developed a model for combined respiratory-thermoregulation based on the models of Stolwijk and Grodins and made suggestions for the improvement of this model. These models lack the refinement and detail required in the planned whole-body algorithm.

Guyton (4) has integrated the circulatory, fluids, and electrolytes subsystems with sufficient detail to be considered a tremendous step in the right direction. This model includes circulatory dynamics, pulmonary dynamics, regional blood flow control, and its relationship to P_{O_2}, tissue fluids and pressures, heart rate, and stroke volume.

The previous listing is a very brief coverage of work that may be listed as some background information relevant to this work. The following pages describe the subsystems that have been selected for use in the development of this whole-body algorithm.

For the whole-body algorithm the cardiovascular model should be able to yield fairly accurate values of mean, systolic, and diastolic pressures and mean flow rates in major vascular beds, but the high frequency, low amplitude harmonics contained in the pressure and flow pulses are not needed.

With these considerations, two models appear to be necessary for the cardiovascular subsystem. Croston's model is a short and intermediate term model that responds to transient inputs such as exercise. For the long term model, Guyton, Coleman, and Granger (4) have developed a circulatory model that is very complex and quite broad in its coverage. This model is being used and studied by White (5), (6). A discussion of these models follow.

Croston's Cardiovascular Model

A mathematical model and digital computer simulation of the human cardiovascular system and its controls have been developed to simulate transient

responses to bicycle ergometer exercise. The Croston model (1) includes gravity effects, muscle pumping, venous tone, venous valves, respiratory frequency, and intrathoracic pressure effects.

Complex cardiovascular control hypotheses are modeled for the control of the heart period, peripheral flow resistances, venous tone, and other controlled variables. Metabolic control models utilize simple mathematical models of oxygen uptake, oxygen deficit, and accumulating metabolites to simulate a transient metabolic state.

The uncontrolled cardiovascular circulatory system is broken into 28 model sections, as shown in Figure 1, to describe pulsatile blood flows, pressures and volumes. This circulatory system model is combined with the models of the controlling systems shown in Figure 2 to simulate transient responses to exercise.

Command inputs to the model are assumed to be from the chemoreceptors, proprioceptive inputs from muscular activity, and somatic anticipation inputs. Other inputs needed are the exercise workload, work rate, gravity, oxygen requirement for rest and cardiac output.

Outputs can be tabulated as oxygen uptake, oxygen deficit, total metabolites, heart rate, various blood flows, systolic pressure, mean pressure, diastolic pressure, stroke volume, venous pressures, and arterial pressures. A complete description of the model is available in the work by Croston (2) and a user's manual for the simulation (3).

Guyton's Circulatory Model

The systems analysis of overall circulatory regulation developed by Guyton, Coleman, and Granger (4) considers a large number of the physiological subsystems that affect blood flow. This analysis consists of 354 blocks. Each block represents one or more mathematical functions that describe some physiological facet of circulatory regulation. The analysis presented is based on cumulative knowledge of the circulation and on experimental data.

The analysis is based on 18 different major systems that enter into circulatory control. In Appendix 1 is a listing of these systems and a chart listing

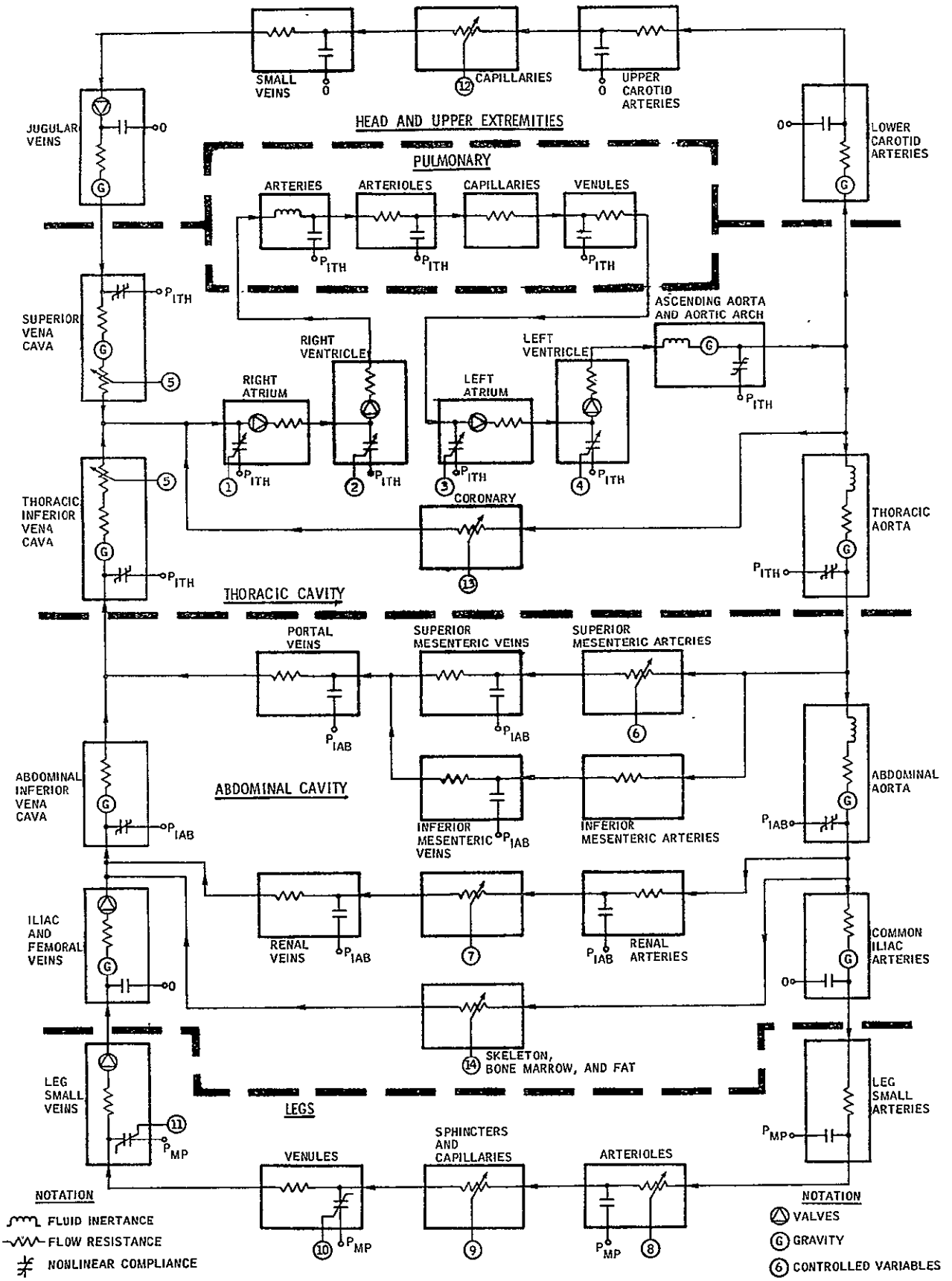


FIGURE 1

CIRCULATORY MODEL BLOCK DIAGRAM

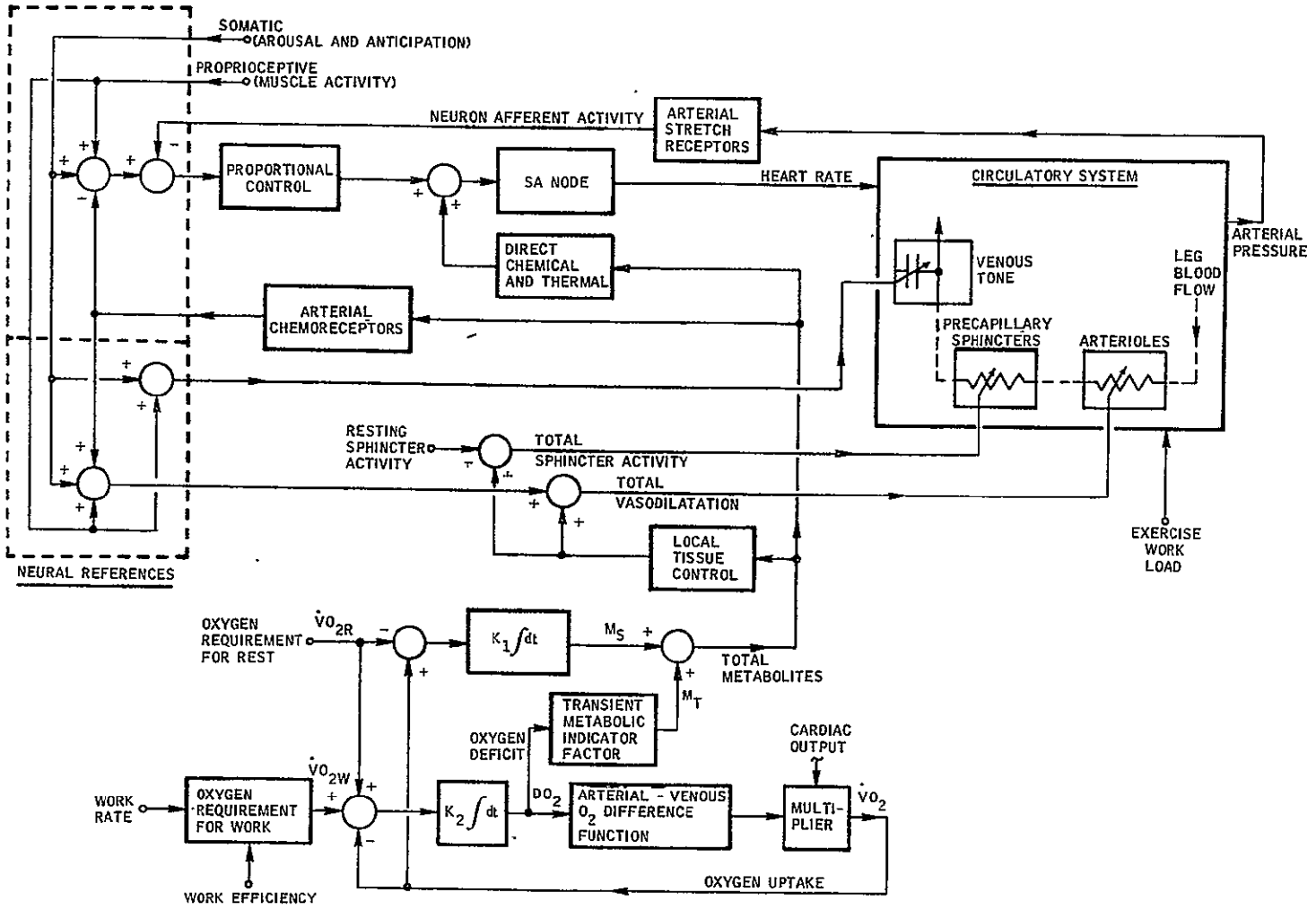


FIGURE 2

BLOCK DIAGRAM OF THE CONTROLLING SYSTEM

the inputs and outputs for each of these systems. White (6) has broken this overall block diagram into a series of color coded block diagrams that illustrate inputs, outputs, variables, and constants for this system. Reference to the document by White and the appendix of this document when studying Guyton's model will greatly aid in its understanding.

The circuit of the blood flow in the Guyton model is divided into five volume segments: the aorta, the veins, the right atrium, the pulmonary arteries, and the combination of pulmonary veins and left atrium. This division of the blood flow is illustrated in Figure 3. Comparison of this blood flow circuitry and that of the Croston model illustrated in Figure 1 points out the difference in the number of volume segments. This division is indicative of the difficulites to be encountered in the development of the whole-body algorithm, because each of the models were developed independently with no thought of combining with other models.

The Guyton model includes fluid and electrolyte balance as part of the system. Also included in this model are ventricular muscle strength, hypertrophy of the heart, deterioration of the heart, autonomic and sympathetic stimulation. These factors enable the simulation user to calculate the effect of changes in these parameters on circulation. The inclusion of such parameters as cardiac hypertrophy, cardiac deterioration, etc., clearly indicate that the Guyton model was developed to be a long term model. This feature makes it very attractive as a companion to the Croston model to be used in the whole-body algorithm.

Respiratory System

The respiratory system model of Grodins (8) has been selected for use in the development of the whole-body algorithm. Grodins' model is a closed-loop control system as illustrated in Figure 4 taken from reference 10. Typical of a closed loop control system is a controlled system and a controlling system. Grodins has divided the controlled system into three compartments (lung, brain, tissue) as shown in Figure 5. The lungs are treated as a box of constant volume, uniform content, and zero dead space ventilated by a continuous emidirectional stream of gas. If the alveolar RQ differs from unity, the rates of inspired and expired gas will differ.

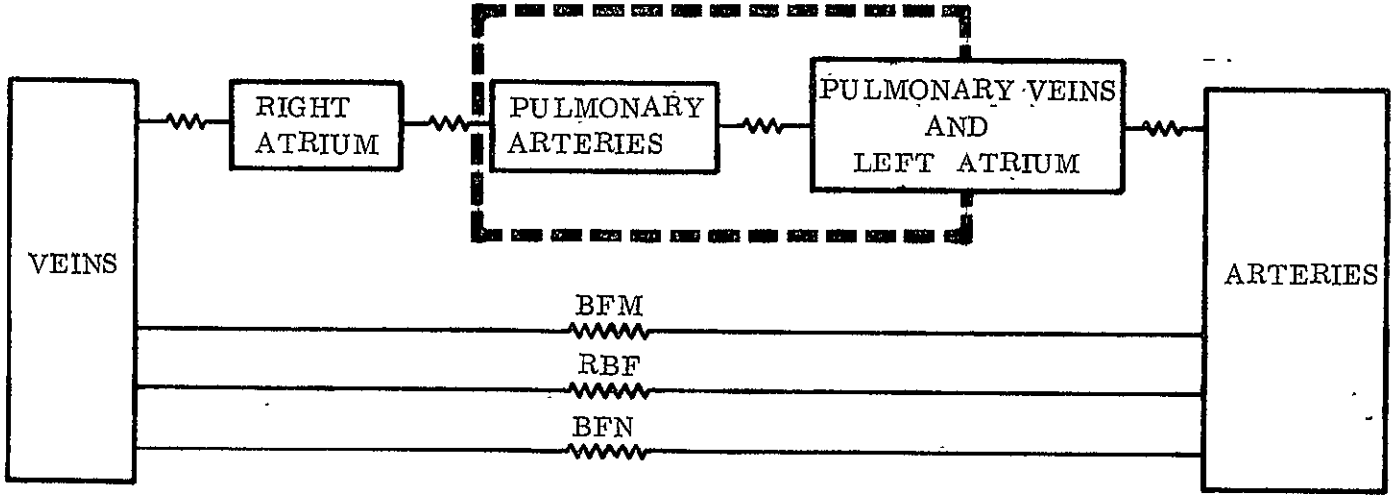


FIGURE 3. BLOOD VOLUMES IN THE GUYTON MODEL

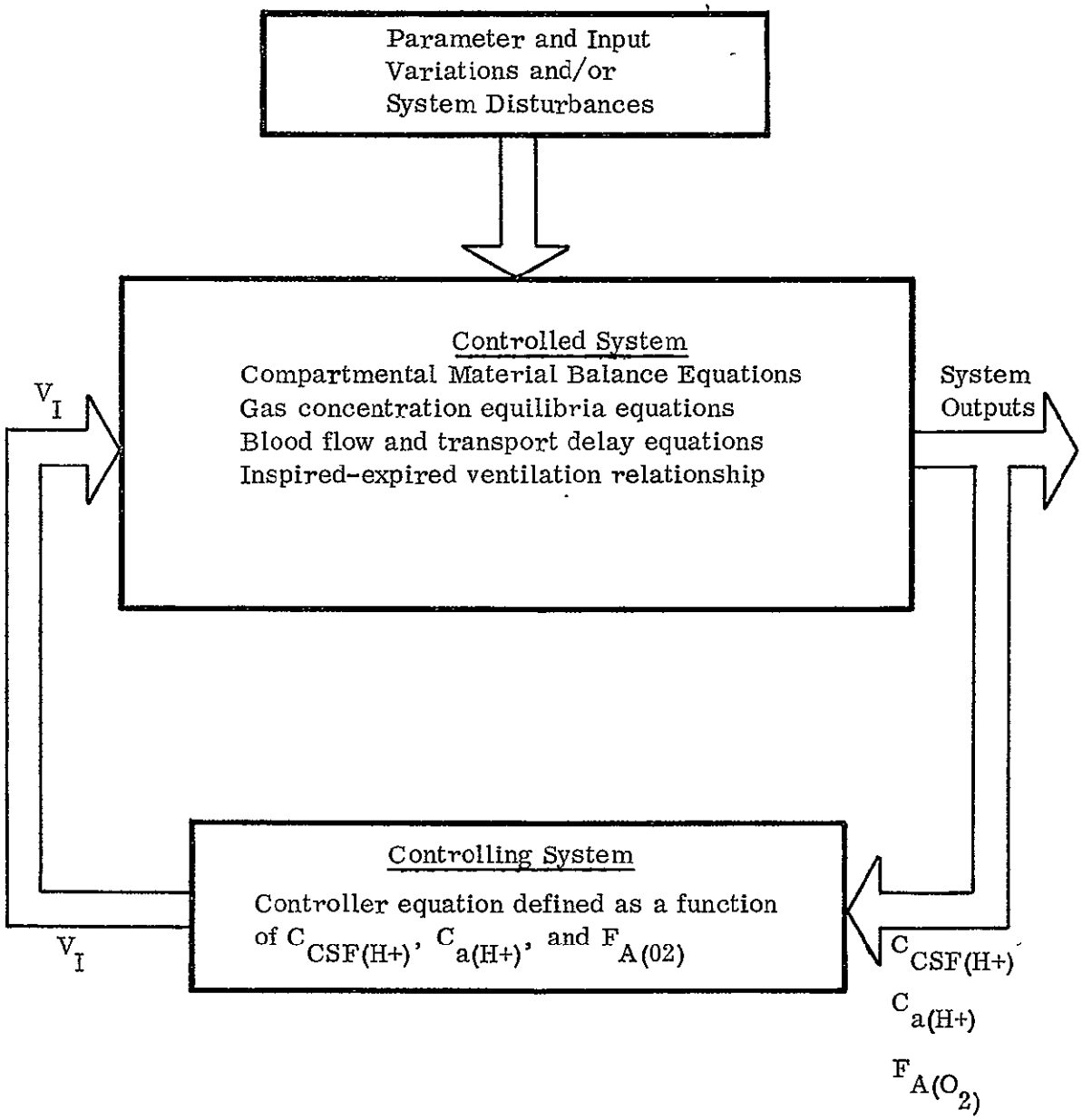


FIGURE 4. RESPIRATORY FEEDBACK CONTROL SYSTEM

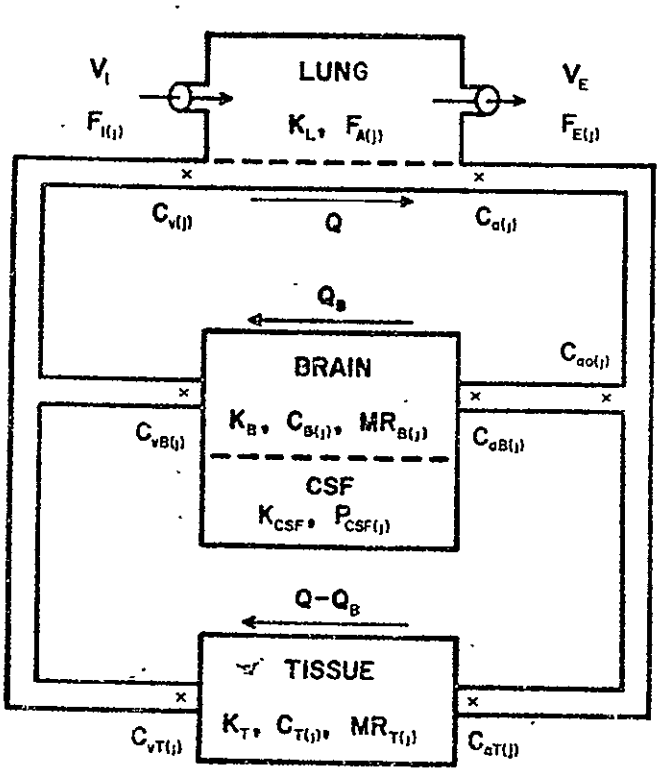


FIGURE 5. CONTROLLED SYSTEM. SYMBOLS DEFINED IN REFERENCE 8.

The blood passes through the lungs and after a transport delay that is dependent on vascular volume and blood flow rate, the arterial blood arrives at the brain or tissue compartment. In this model CO_2 and O_2 exchange rates are governed by metabolism.

The brain compartment communicates with the cerebrospinal fluid reservoir via a membrane permeable to respiratory gases only. The diffusion rates across the membrane are proportional to their tension gradients.

Venous blood exiting the brain combines with venous blood from the tissue after a time delay forming mixed venous blood. After another delay this mixed venous blood enters the lungs to complete the cycle of gas transport and exchange. Total cardiac output and local blood flow have been found to vary as functions of arterial CO_2 and O_2 tensions (8), in Guyton's (4) circulatory model the control utilizes only O_2 tensions.

The actual physiological control system is composed of receptor elements which monitor chemical concentrations, afferent nerves which transmit this information to the central nervous system, the neural centers, motor nerves to the respiratory muscles, the muscles, and finally the thorax-lung pump which they drive. In the model of this system, the procedure is to go directly from chemical concentrations at receptor sites as the inputs to ventilation as the output.

The equations governing this system are readily available in the previously referenced material. The controller equation uses only three of the many outputs of the controlled system ($C_{CSF(H^+)}$, $C_{a(H^+)}$, $F_{A(O_2)}$) as shown in Figure 4.

Thermoregulatory System

A dynamic mathematical model of physiological regulation of body temperature in man has been developed by Stolwijk (11) and modified by General Electric and others (15). The thermoregulatory system is modeled as a control system and a controlled system. The controlled system is the mathematical representation of the thermal characteristics of the different parts of the body. Thermal loads act on the controlled system and cause a response that may be considered

as a stress or a strain. Sensor mechanisms as part of the control system feel these changes and induce corrective action to reduce or control the effect of the loading within acceptable limits.

A total of 41 nodes is used to represent the thermal characteristics of the body with four nodes each representing the head, trunk, arms, hands, legs, and feet. The forty-first node represents the central blood compartment. The four nodes representing each of the segments are composed of concentric layers treated as core, muscle, fat, and skin. Each node has the appropriate metabolic heat preduction, convective heat exchange with the central blood compartments, and conductive heat exchange with adjacent compartments. The nodes representing the skin exchange heat with the environment via radiation, convection, and evaporation.

The thermoregulatory model receives temperature signals from all compartments and after integration and processing the control system causes appropriate commands to be sent to all appropriate compartments changing metabolic heat production, blood flow or the rate of sweat secretion.

A schematic of the system is shown in Figure 6 and a flow diagram taken from Reference 1 is shown as Figure 7.

The thermoregulatory system presented is basically concerned with the effects of external temperature (environment) and the effects of exercise. The controlling system is developed to maintain a heat balance utilizing all facets of heat transfer. Control equations consist of the product of a control coefficient and a central temperature signal, the product of a control coefficient and an integrated skin temperature signal, and a third term consisting of a control coefficient, a central temperature signal, and skin temperature signal. These control equations affect the temperature change by controlling blood flow, causing a sweating response, or instigating the muscular activity of shivering.

This system is based on a man with a body weight of 74.1 Kg and a surface area of 1.89 m^2. Inputs to the system are thermal properties, geometric or volume parameters, work rate, basal conditions, environmental conditions, and time or duration of the exposure.

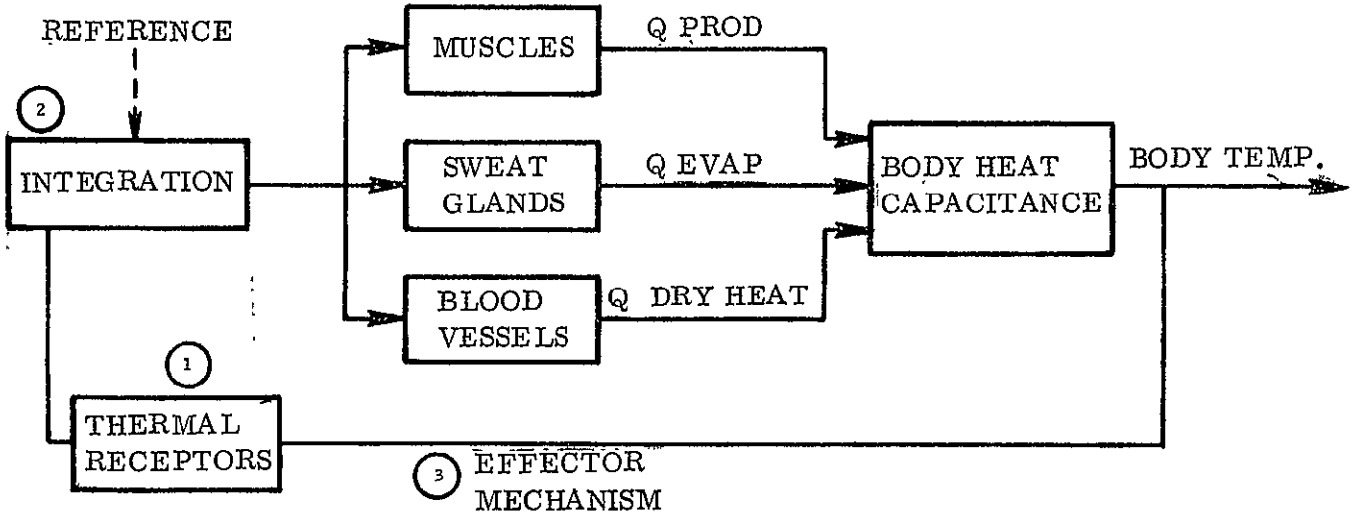


FIG. 6 BLOCK DIAGRAM OF THE THERMOREGULATION SYSTEM

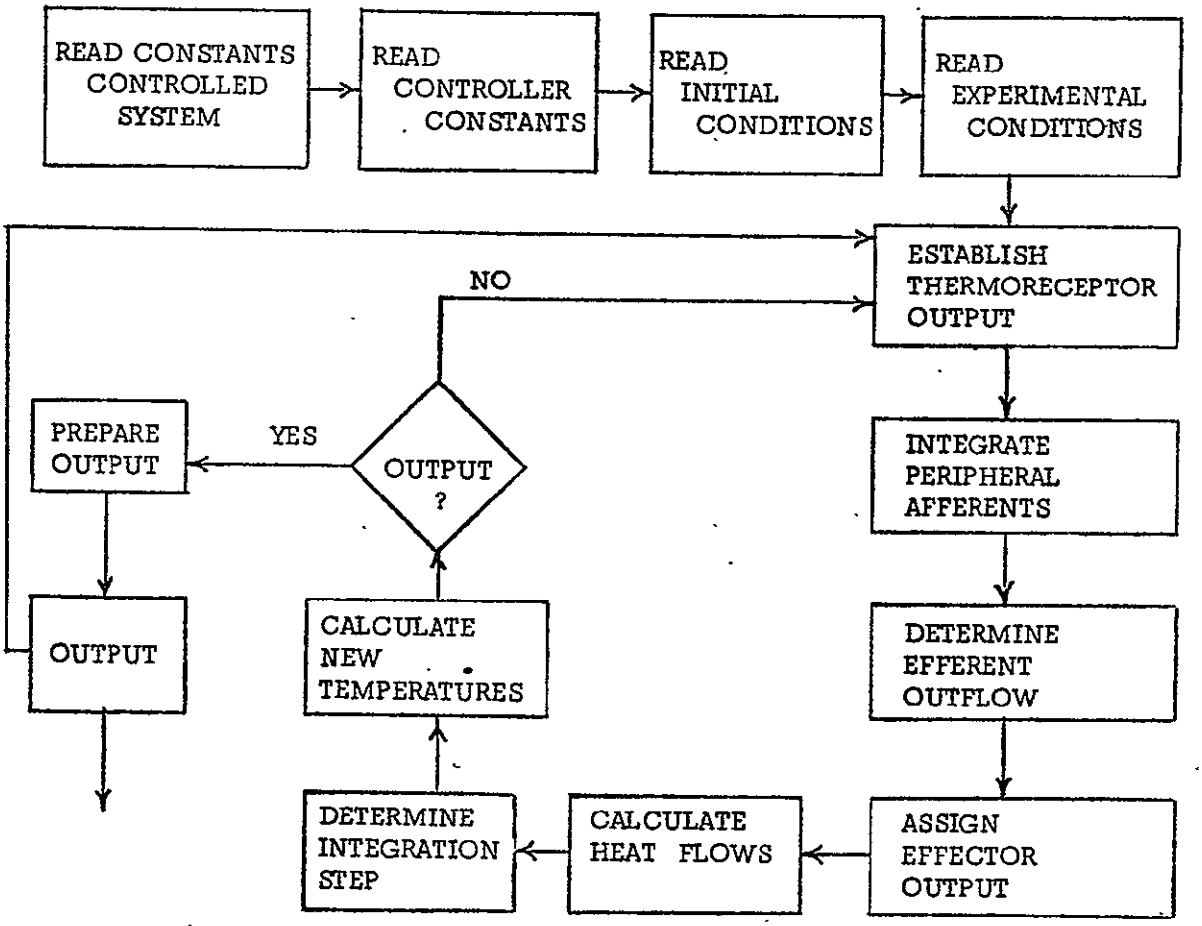


FIGURE 7. COMPUTATIONAL BLOCK DIAGRAM FOR THE THERMOREGULATORY MODEL

The Whole-Body Algorithm

The design of the whole-body algorithm is governed by many factors. Most important of these factors is the accuracy of the model in simulating the true physiological responses, and the ability of the model to produce the information required to compare with experiments being conducted in the space program. The significance of these statements is that each of the subsystem models must provide outputs concerning vital parameters, as well as providing certain information necessary for the interfacing of the subsystems.

A whole-body algorithm implies the existence of a mathematical simulation of all the important physiological functions. These functions now exist to a finite degree of detail in models developed by Grodins (8), Guyton (4), Stolwijk (11), and Croston (2). To incorporate these models into a total system, the cardiovascular subsystem is chosen as the central model.

Using the cardiovascular subsystem as the central model and the research done by Kuchar and Sittel (12) the following considerations can be listed as necessary basic cardiovascular parameters.

Required Vital Parameters

To assess the body's state of health and its response to stresses induced into the system as disturbances, the following cardiovascular parameters are required as stated in Reference (12).

1. Total Cardiac Output
2. Mean, systolic, and diastolic central arterial pressures.
3. Total peripheral resistance
4. Heart rate
5. Stroke volume
6. Blood flow rates through the following vital organs:

   Heart
   Lungs
   Kidneys
   Liver

7. Blood Volumes stored in the above organs.

Outputs Required by the Thermoregulatory Model

This listing consists of important regional blood flow rates and blood volumes to be used in the thermoregulatory subsystem model (11).

8. Blood flow rates through the skin, fat, muscle and core of each of the following regions:

    Head
    Arms
    Hands
    Legs
    Feet
    Trunk

9. Blood volumes stored in each of these regions.

Outputs Required by Respiratory Model

This listing consists of blood flow rates and blood transport delay times associated with the transport of blood gases between the lungs, brain-CSF receptors, and tissues (8).

10. Blood flow rates through the following organs:

    Lungs
    Brain

11. Transport delay times for:

    Lung to Brain
    Lung to Tissue
    Brain to Lung
    Tissue to Lung
    Lung to Carotid Body

Outputs Required by the Fluid Balance Model

This listing consists of circulatory parameters involved in renal function.

12. Renal arterial blood pressure
13. Glomerular blood pressure
14. Total blood volume.

These considerations can be met with these and additional parameters available for output from a whole-body algorithm based on:

1. Croston's Cardiovascular Exercise Model
2. Guyton's Model of Circulatory, Fluid and Electrolyte Regulation in the Human System
3. Grodins' Respiratory Control System
4. Stolwijk's Temperature Regulation in Man

This model is illustrated in Figure 8 with Guyton's model as the central element in the whole-body system. Since Guyton's model contains fluid and electrolyte regulation as well as circulatory requirements it controls more parameters than any of the other subsystems and increases its importance.

Since the whole-body algorithm is to be used to simulate stress states as well as the normal physiology, the system must have the capability to modify parameters within the subsystems so they each respond properly to thermal stresses, gravitational fields, exercise, and other stress states. These subsystems must interface in such a manner that an input to one of the subsystems will modify the appropriate parameters in all affected subsystems.

Special cases exist where the whole-body system may be too slow or all the information isn't desired. Such a case may be the effect of lower body negative pressure, gravity-directional change, etc. In this case, the capability to utilize only a subsystem model or two subsystem models must exist. If the tilt example is used and the effect on mean arterial pressure, systolic, etc., is desired as a transient function, it should not be necessary to consider thermal control or perhaps even respiration. This illustrates need for a long term model and a short term model. Croston's model provides the capability of determining the details of pulsatile blood flow for examples such as this and for exercise. Guyton's model provides the capability of intermediate and long term observation and experimentation and can be coupled to the Croston model and used to provide initial value input at any time for short term information.

The approach discussed to this point has listed the parameters required of the cardiovascular subsystem, but has not listed the parameters from the other subsystems that can affect the cardiovascular subsystem. These problems have

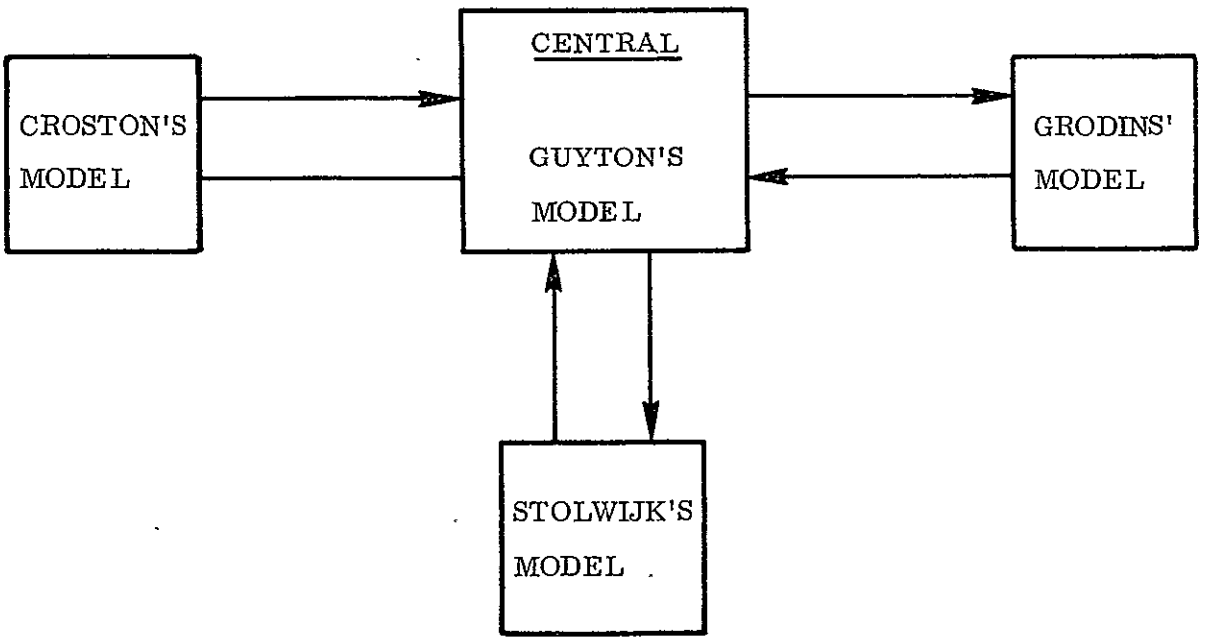


FIGURE 8. SCHEMATIC OF THE WHOLE BODY ALGORITHM

been discussed in working groups throughout this summer and many possibilities were found to exist. In any case, the effects of exercise and other stresses must be input to the system so they will be properly distributed and not be redundant.

Inputs to the cardiovascular subsystem (12) from outside the subsystem model are:

1. Strength and orientation of the gravitational field.
2. Total work rate and work rates of legs, feet, arms, hands, trunk, and head.
3. Thermal loads on legs, feet, arms, hands, trunk, and head.
4. Partial pressure of CO_2 in the arterial flow to the head, also in muscles and tissue.
5. Partial pressure of O_2 in the arterial flow muscle, tissue, etc.

The interfacing of the subsystems has been considered from the viewpoint of the effects obtained by interfacing two systems at a time rather than all at once - then these can be interfaced.

Thermoregulatory - Respiratory System (14)

These two systems were coupled in a study performed by Weissman (14) using the common parameters:

1. Cardiac Output, Q,
2. Blood flow to the brain, Q_B,
3. Work rates.

Since these parameters are common to the two subsystems they can be interactive in this manner. However, each subsystem retained its individuality and was coupled through a transfer program that converted the units of one system into the units of the other system. The thermal model is based on a blood flow of 4.8966 l./min. while the respiratory is based on a blood flow of 6.0 l/min. The output of this system was based on the larger of the two sets of values predicted by the system. Each subsystem determines its own blood flow by completely different equations controlling the Q and Q_B. The integration was performed on the basis

of one step in the thermal program, then one step in the respiratory program, with the larger value being accepted.

In the whole-body system both these models will receive their cardiac output from the cardiovascular subsystem and alleviate the problems illustrated in the Weissman report. These two subsystems also have different divisions of the body that was neglected by the simple comparison of common parameters in the work of Weissman.

Thermoregulatory - Cardiovascular (Guyton)

Blood flow in the Guyton model is divided into three paths:

1. Muscle blood flow,
2. Renal blood flow,
3. Non-muscle, non-renal blood flow,

and in the Stolwijk model there are multiple blood flow segments (a comparison of blood flow is included as Appendix 2). The interfacing of these systems is through the blood flow, resistance to blood flow, and exercise. For the whole-body system with the Guyton model as the central system the appropriate blood flows can be picked off as outputs from the three divisions listed above.

A combination of these two models was suggested by Fulcher (17) as shown in Figure 9 and in the included example:

Integration of Stolwijk Skin Blood Flow and Guyton Skin Blood Flow/Compartment

$$BF = \frac{BFB + SKIN\ V(I) * DILAT}{1 + SKINC(I) * STRICT}$$, where,

BF = Skin blood flow in a body segment, e.g., leg

BFB = Basal blood flow to skin in a body segment, e.g., leg

SKINV = Fraction of vasodilatation command to body segment, e.g,, leg

SKINC = " " vasoconstriction command to body segment, e.g., leg

DILAT = Total efferent vasodilation command

= CDIL*WARM(1) + SDIL*WARMS + PDIL*WARM(1)*WARMS

where,

CDIL = Coeff. for vasodilatation and from head core

SDIL = " " " " " skin

WARM(1) = Output of warm receptors in head core

WARMS = Total integrated output from skin warm receptors

PDIL = Coeff. for vasodilatation and from product of head core and skin.

STRICT = CCON*COLD(1) + SCON*COLDS + PCON*COLD(1)*COLDS

= Total efferent vasoconstriction command

where,

CCON = Coeff. for vasoconstriction and from head core

COLD(1) = Output of cold receptors in head core

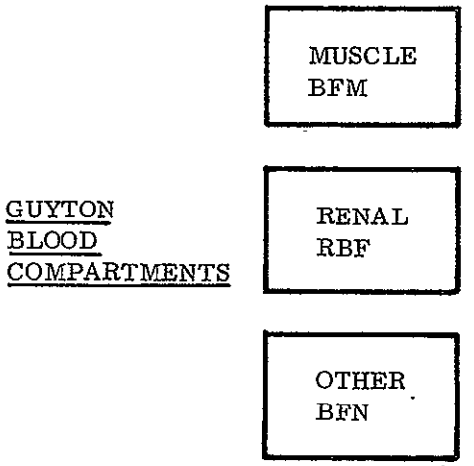
SCON = Coeff. for vasoconstriction and from skin

COLDS = Total integrated output from skin cold receptors

PCON = Coeff. for vasoconstriction and from product of head core and skin.

An interaction of the two subsystems as shown in Figure 9 provides the total system with an environmental response and exercise response. New variables are brought into the thermal through the resistance of muscle circulation (RAM) term in the Guyton model that enables the thermal model to be sensitive to other effects. The other significant point is that with the suggested change the skin blood flow will be controlled by the thermal model.

The Guyton model will receive skin blood flow requirements, sweat rate, shiver rate, and respiratory H_2O loss from the thermal model. The thermal model will in turn receive blood flows for the muscle, core, and fat from Guyton. Both systems will have added controlled variables from this interaction.



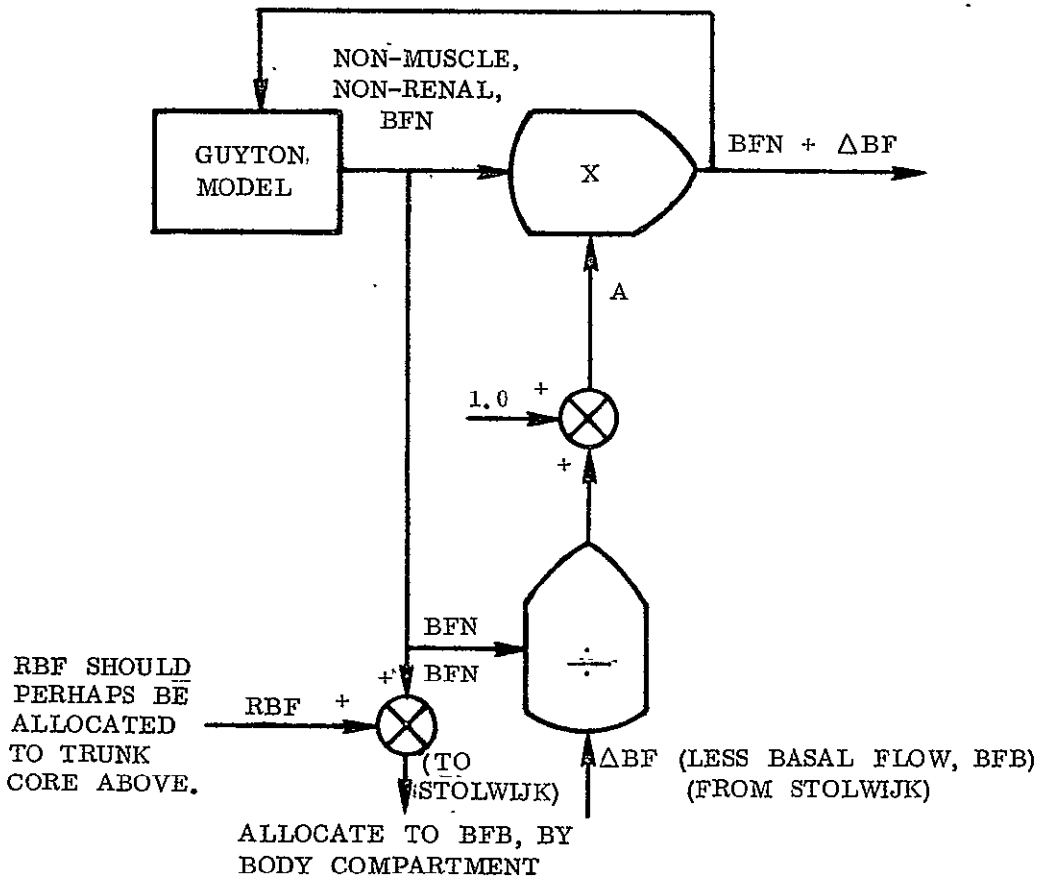
WE WANT TO MODIFY BFN TO REFLECT CHANGES IN SKIN BLOOD FLOW DUE TO TEMPERATURE CHANGES

PROBLEM: (1) FIND A

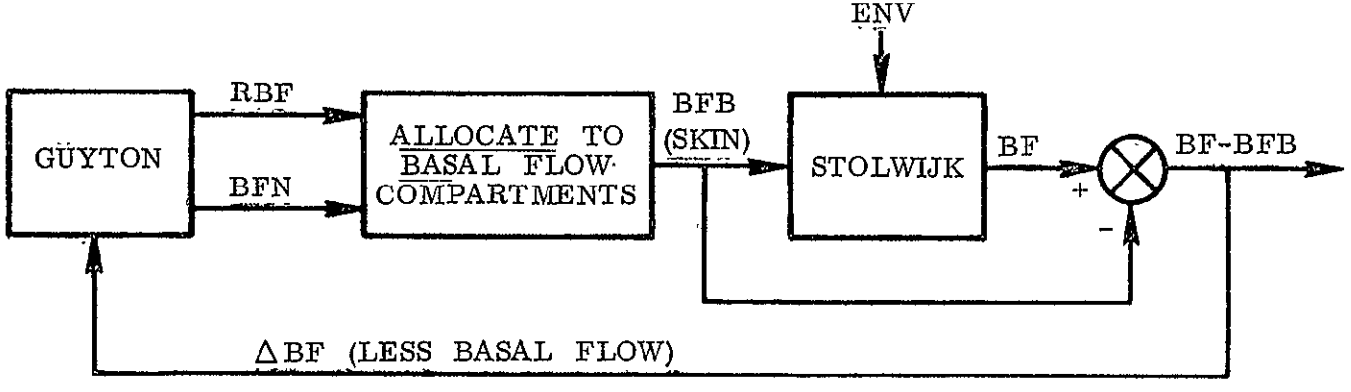
$$BFN^{*}A = BFN + \Delta BF.$$

SOLU: $A = \frac{BFN + \Delta BF}{BFN} = 1 + \frac{\Delta BF}{BFN}$

GRAPHICALLY, IN SIGNAL FLOW FORMAT,



EXAMPLE NO. 1



EXAMPLE NO. 2 FIND BF, LESS BASAL FLOW, BFB.

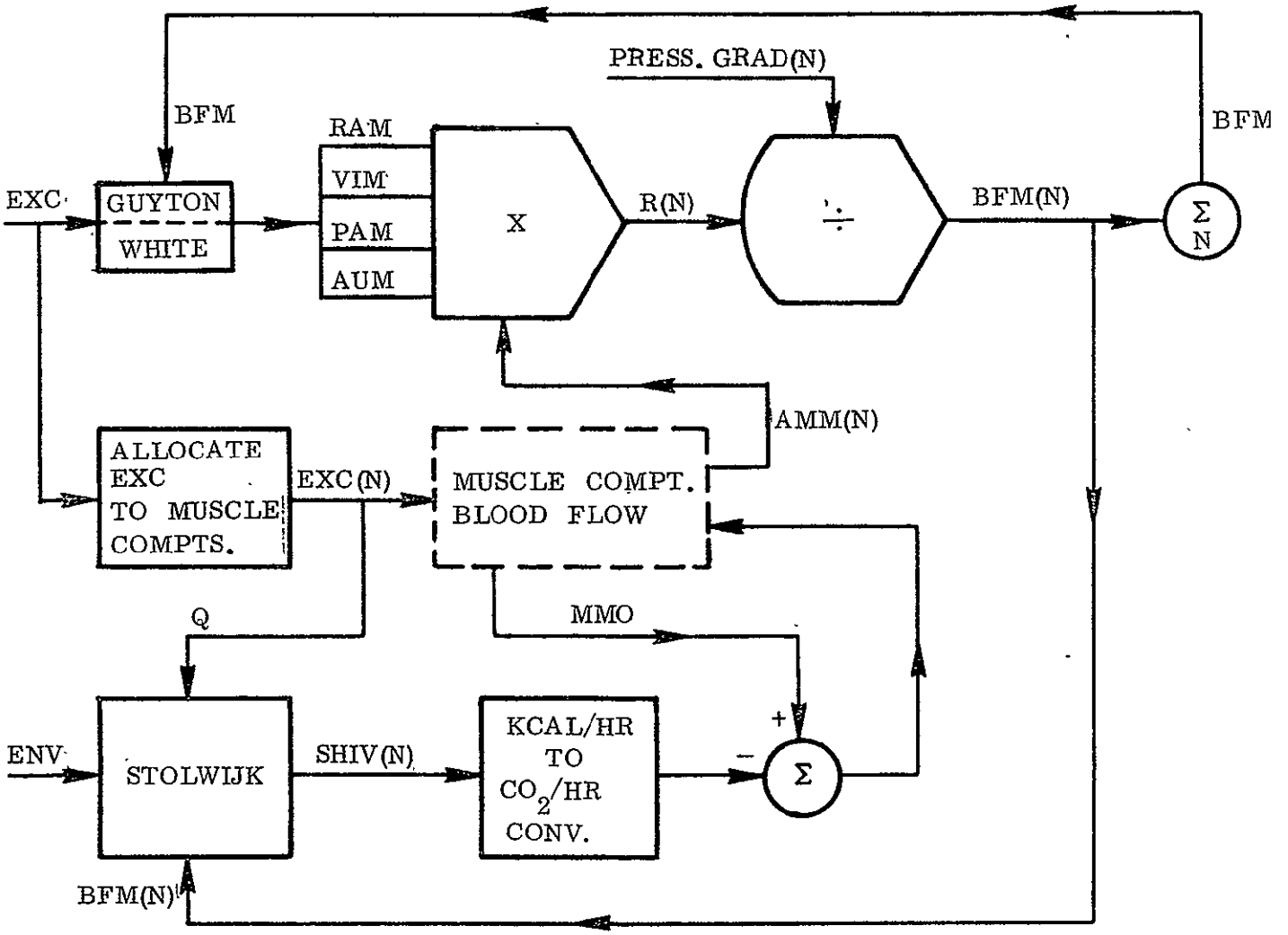


FIGURE 9. COMBINATION OF THERMOREGULATORY-CARDIOVASCULAR

Respiratory (Grodins) - Cardiovascular (Guyton)

The basic commonalities between these two subsystems are the blood flow and the metabolic rates. Since the cardiac output, brain blood flow, and tissue blood flow in the Grodins' model are empirically determined, these values can be obtained directly from the Guyton model. The Guyton model can in turn receive gas concentrations to be used in the control functions from the respiratory model. An interfacing of these two subsystems as considered by Gallagher (16) is shown as Figure 10. The basal conditions in these two models differ requiring changes to be made. Guyton has based his model on a 45 year old man that allows a maximum of 2.5 $^{L.}O_2$ uptake under exercise while Grodins' allows a maximum of 3.5 $^{l.}O_2$ uptake based on a 25 year old man.

The compatibility of these models can be worked out, but baseline experimental data must be provided to determine the maximum values of oxygen uptake versus work load in watts. Also, the basal conditions between the two models must be compatible.

Croston - Guyton Combination

The combination of these two models provides a broad experimental base for the whole-body algorithm. Short term transient experiments can be performed on the Croston model to obtain specific results for special case studies. Uncoupling the Croston model to run particular experiments may be desirable, but the fluids and electrolyte subsystem is contained in the Guyton model. Consideration of this fact may require running a few time steps on the Croston model, feeding this output into the Guyton model for one integration, and continuing this process until all the desired information has been obtained.

One possibility for interfacing the Guyton-Croston models is illustrated in Figure 11 as suggested by Croston (16). This connection would provide the effect of strength factors, hypertrophy, viscous changes in the blood, and other factors inherent in the Guyton model to be incorporated in the Croston model, while providing the capability of monitoring pulsatile flows and pressures that aren't available in the Guyton model.

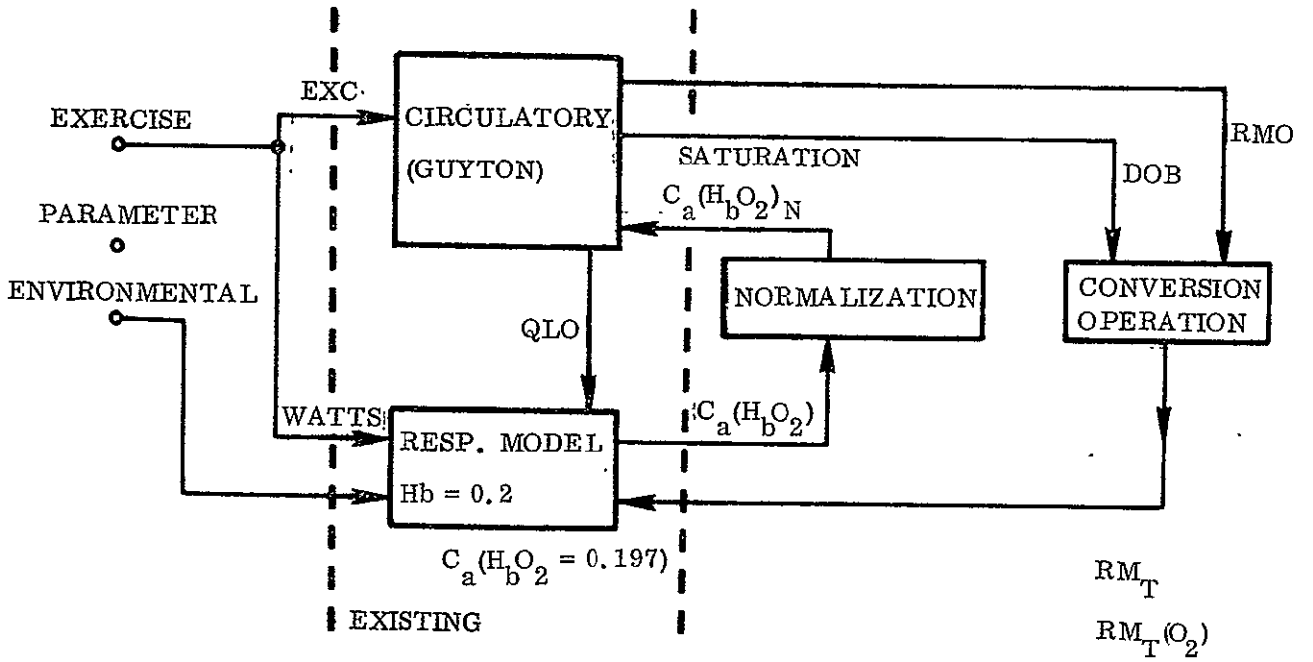


FIGURE 10. COMBINATION OF THE CIRCULATORY AND RESPIRATORY MODELS

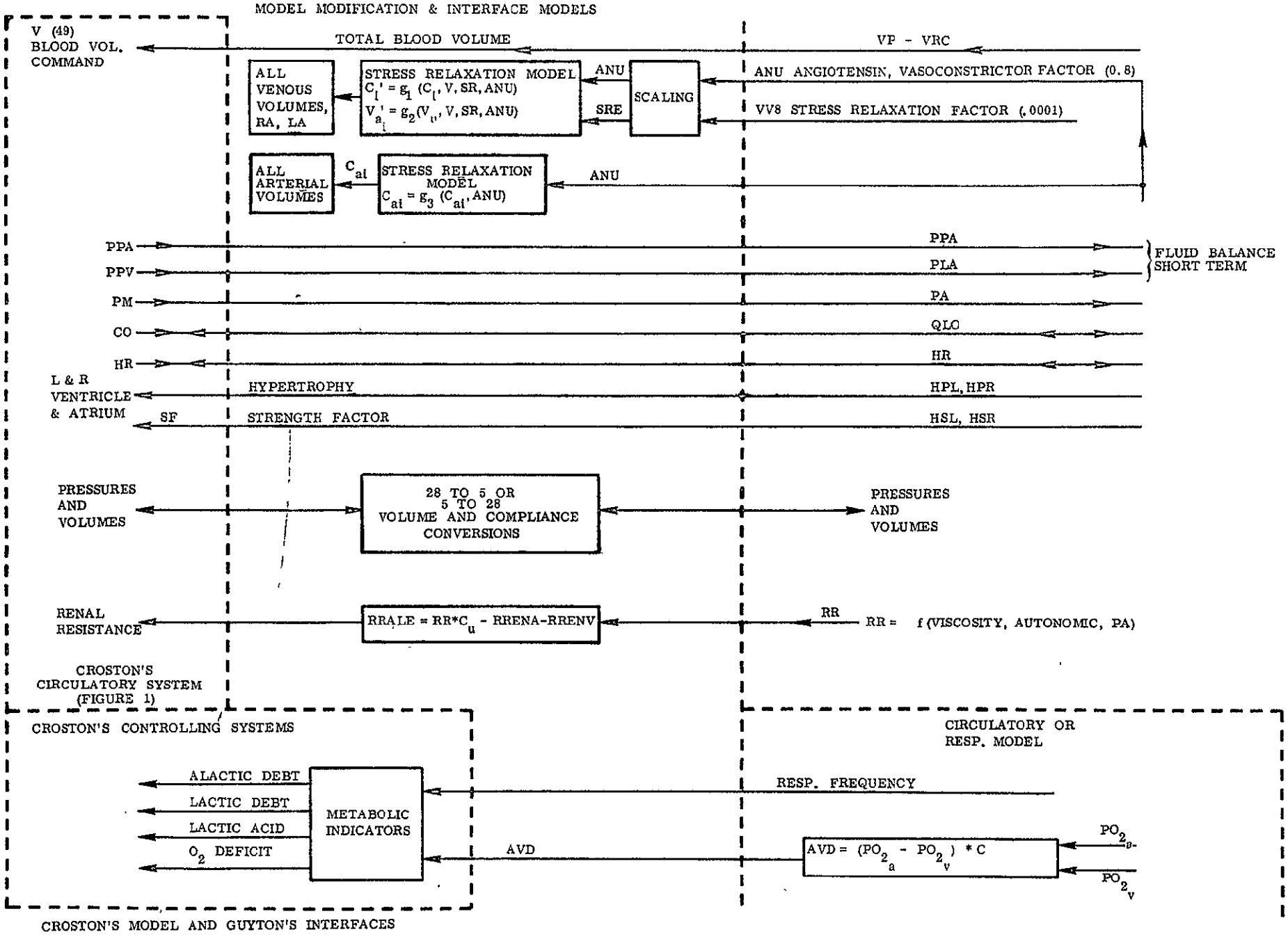


FIGURE 11. CROSTON'S MODEL AND GUYTON'S INTERFACES

Conclusions

The whole-body algorithm can be developed using the suggestions contained in this report. It would be wise to implement the models in a step-by-step fashion rather than putting them all together as a whole-body algorithm. First, the Guyton model and the Respiratory model could be coupled and verified versus an experimental base. Secondly, the thermal model could be incorporated with these models and validated to give a limited whole-body algorithm. Then the Croston model could be incorporated as it is the most detailed and will have more interfacing points than the other models. This addition will provide a whole-body algorithm that is limited only by the detail of the model, the lack of physiological experimental data to further refine the model, and the lack of knowledge of certain physiological phenomena. Such a model provides a basis for studying physiological phenomena and a basic model which can be refined as new parameters are recognized or needed.

Although this discussion may indicate that the task is easy, any such idea will quickly be dispelled from simply considering any two of the subsystems. All these subsystems were developed with different goals in mind; each model assumes or calculates common parameters using different approaches; each model was developed to obtain certain outputs and developed to these outputs satisfy experimental results. To further complicate the interfacing baseline data such as:

1. Blood volumes
2. Basal metabolism
3. Maximum exercise levels
4. Control systems
5. Units
6. Variable names
7. Volume divisions

all differ in the various subsystems. Integration time constants and integration schemes within each subsystem differ and will create much consternation with the systems integration. These details can only be worked out directly at the program level, so the final solution is reached by total commitment to the task and many man-hours of work.

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APPENDIX 1

Circulation: Overall Regulation

Guyton, Coleman, & Granger

Systems:

1. Non-Muscle Oxygen Delivery
2. Non-Muscle Local Blood Flow Control
3. Autonomic Control
4. Heart Rate and Stroke Volume
5. Muscle Blood Flow Control and $P0_2$
6. Vascular Stress Relaxation
7. Circulatory Dynamics
8. Pulmonary Dynamics and Fluids
9. Red Cells and Viscosity
10. Heart Hypertrophy or Deterioration
11. Kidney Dynamics and Excretion
12. Capillary Membrane Dynamics
13. Tissues, Fluids, Pressures, and Gel
14. Thirst and Drinking
15. Antidiuretic Hormone Control
16. Angiotensin Control
17. Aldosterone Control
18. Electrolytes and Cell Water

Following this listing of systems is a breakdown that indicates the outputs and inputs for each of the systems.

Input to Circulatory Dynamics			Output from (Subsystem)
Variable	Defined	Units	
HMD	Cardia Depressant effect of Hypoxia		Heart Hypertrophy or Deterioration
HPR	Hypertrophy effect on heart, ratio to normal		" " "
VB	Blood Volume		Capillary Membrane Dynamics
PC	Capillary Pressure		" "
RBF	Renal Blood Flow		Kidney Dynamics and Excretion
VV7			Vascular Stress Relaxation
VVR	Diminished Vascular Volume Caused by Sympathetic Stimulation		Autonomic Control
ANU 35 x 36 x	Nonrenal effect of angiotensin		Angiotensin Control
AMM	Muscular vascular constriction caused by local tissue control, ratio to resting state		Muscle Blood Flow Control and $P0_2$
AVE	Sympathetic Vasoconstrictor Effect on Veins		Autonomic Control
ARM	Vasoconstrictor effect of all types of Autoregulation		Non-Muscle Local Blood Flow Control
VIM	Blood Viscosity (Ratio)		Red Cells & Viscosity
AUM 35 x 36 x	Sympathetic Vasoconstrictor Effect on Arteries		Autonomic Control
AUH 29, 49, x 58, 51, x	Autonomic Stimulation of Heart (Ratio to normal)		" "

Output from Circulatory Dynamics			Input to (Subsystem)
Variable	Defined	Units	
QLO	Left Ventricle Output		Pulmonary Dynamics and Fluids
PPA	Pulmonary Arterial Pressure		" " " "
PPA	" " "		Heart Hypertrophy or Deterioration
PRA	Right Atrial Pressure		Heart Rate and Stroke Volume
HSR	Basic Strength of Right Ventricle		Heart Hypertrophy or Deterioration
HSL	Basic Left Ventricular Strength		" " "
PRA	Right Atrial Pressure		Antidiuretic Hormone Control
PA	Aortic Pressure		Kidney Dynamics and Excretion
PA	" "		Aldosterone Control
PA	" "		Angiotensin "
PA	" "		Heart Hypertrophy or Deterioration
PA	" "		Autonomic Control
BFN	Blood Flow in Non-Muscle Non-Renal Tissues		Capillary Membrane Dynamics
RVS	Venous Resistance		" "
BFM	Muscle Blood Flow		Muscle Blood Flow Control and $P0_2$
BFN	Blood Flow in Non-Muscle, Non-Renal Tissues		Non-Muscle Oxygen Delivery
QLO	Output of Left Ventricle		Heart Rate & Stroke Volume
PVS	Average Venous Pressure		Capillary Membrane Dynamics
VVE	Excess Venous Volume Before Stress Relaxation		Vascular Stress Relaxation

(SUBSYSTEM)

HEART RATE AND STROKE VOLUME

INPUT

VARIABLE	DEFINED	UNITS	FROM
PRA	Right Atrial Pressure		Circulatory Dynamics
HMD	Cardia Depressant Effect of Hypoxia		Heart Hypertrophy or Deterioration
AU	Overall Activity of Autonomic System, Ratio to Normal		Autonomic Control
QLO	Output of Left Ventricle		Circulatory Dynamics

OUTPUT

(NONE SHOWN)

SUBSYSTEM

NON-MUSCLE OXYGEN DELIVERY

VARIABLE	DEFINED	UNITS	FROM
	INPUT		
OVA	Oxygen Volume in Aortic Blood		Muscle Blood Flow Control and $P0_2$
BFN	Blood Flow in Non-Muscle Non-Renal Tissues		Circulatory Dynamics
AOM	Autonomic Effect on Tissue Oxygen Utilization		Muscle Blood Flow Control and $P0_2$
HM	Hematocrit		Red Cells and Viscosity
	OUTPUT		TO
POV	Non-Muscle Venous $P0_2$		Non-Muscle Local Blood Flow Control
POT	Non-Muscle Cell $P0_2$		Autonomic Control

NON-MUSCLE LOCAL BLOOD FLOW CONTROL

	INPUT	FROM
POV	Non-Muscle Venous $P0_2$	Non-Muscle Oxygen Delivery
	OUTPUT	**TO**
ARM	Vasoconstrictor Effect of all types of Autoregulation	Circulatory Dynamics

VASCULAR STRESS RELAXATION

Input	VVE	Excess Venous Volume Before Stress Relaxation	Circulatory Dynamics
Output	VV7	Increased Vascular Volume Caused by Stress Relaxation	" "

AUTONOMIC CONTROL

	INPUT	FROM
POT	Non-Muscle Cell PO_2	Non-Muscle Oxygen Delivery
PA	Aortic Pressure	Circulatory Dynamics
P2O	Muscle Cell PO_2	Muscle Blood Flow Control and PO_2
	OUTPUT	**TO**
EXC	Exercise Activity, Ratio Norm	Muscle Blood Flow Control and PO_2
AU	Overall Activity of Autonomic System, Ratio to Normal	Heart Rate & Stroke Volume
AU	" " "	Muscle Blood Flow Control and PO_2
AU	" " "	Antidiuretic Hormone Control
VVR	Diminished Vascular Vol. caused by Sympathetic Stimulation	Circulatory Dynamics
AUH	Autonomic Stimulation of Heart, Ratio to normal	" "
AUM	Sympathetic Vasoconstrictor effect on arteries	" "
AUM	" "	Kidney Dynamics and Excretion
AVE	Sympathetic Vasoconstrictor on veins	Circulatory Dynamics

MUSCLE BLOOD FLOW CONTROL & PO_2

	INPUT	FROM
VPF	Pulmonary Free Fluid Volume	Pulmonary Dynamics & Fluids
HM	Hematocrit	Red Cells & Viscosity
BFM	Muscle Blood Flow	Circulatory Dynamics
EXC	Exercise Activity, Ratio to activity at rest	Autonomic Control
AU	Overall activity of autonomic system, ratio to normal	

	OUTPUT	TO
P20	Muscle Cell PO_2	Autonomic Control
AMM	Muscle Vascular Constriction caused by local tissue control, ratio to resting state.	Circulatory Dynamics

PULMONARY DYNAMICS AND FLUIDS

	INPUT	FROM
PPA	Pulmonary Arterial Pressure	Circulatory Dynamics
PLA	Left Atrial Pressure	" "
PPC	Plasma Colloid Osmotic Pressure	Capillary Membrane Dynamics
CPP	Plasma Protein Concentration	" "

	OUTPUT	TO
VPF	Pulmonary Free Fluid Volume	Muscle Blood Flow Control and PO_2
PPD	Rate of Change of Protein in Pulmonary Fluids	Capillary Membrane Dynamics
DFP	Rate of Increase in Pulmonary Free Fluid	" "
VPF	Pulmonary Free Fluid Volume	Electrolytes and Cell Water

RED CELLS AND VISCOSITY

	INPUT	FROM
POT	Non-Muscle Cell PO_2	Non-Muscle Oxygen Delivery
VB	Blood Volume	Capillary Membrane Dynamics

	OUTPUT	TO
VIM	Blood Viscosity (Ratio to Normal Blood)	Circulatory Dynamics
VIM	" " " "	Kidney Dynamics and Excretion
VRC	Volume of Red Blood Cells	Capillary Membrane Dynamics
HM	Hematocrit	Muscle Blood Flow Control and PO_2
HM		Non-Muscle Oxygen Delivery

HEART HYPERTROPHY OR DETERIORATION

	INPUT		FROM
PA	Aortic Pressure	mm(hg)	Circulatory Dynamics
HSL	Basic Left Ventricular Strength		" "
PPA	Pulmonary Arterial Pressure	mm(hg)	" "
HSR	Basic Strength of Right Ventricle		" "
POT	Non-Muscle Cell PO_2		Non-Muscle Oxygen Delivery

	OUTPUT	TO
HPL	Hypertrophy Effect on Left Ventricle	Circulatory Dynamics
HPR	Hypertrophy Effect on heart, ratio to	" "
HMD	Cardia Depressant Effect of Hypoxia	" "
HMD	" " " "	Heart Rate & Stroke Volume

KIDNEY DYNAMICS AND EXCRETION

	INPUT	FROM
AUM	Sympathetic Vasoconstrictor effect on arteries	Autonomic Control
VIM	Blood Viscosity (Ratio to Normal Blood)	Red Cells & Viscosity
PA	Aortic Pressure	Circulatory Dynamics
PPC	Plasma Coloid Osmotic Pressure	Capillary Membrane Dynamics
AM	Aldosterone Multiplier, /normal effect	Aldosterone Control
AHM	Antidiuretic Multiplier, /normal effect	Antidiuretic Hormone Control
CNE	Sodium Concentration Abnormality causing 3rd factor effect	Angiotensin Control

	OUTPUT	TO
RFN	Renal Blood Flow if Kidney is not damaged.	Angiotensin Control
RBF	Renal Blood Flow	Circulatory Dynamics
REK	Percent of Normal Renal Function	Angiotensin Control
REK	" " " " "	Electrolytes & Cell Water
NOD	Rate of Renal Excretion of Sodium	" " "

CAPILLARY MMEBRANE DYNAMICS

	INPUT	FROM
VUD	Rate of Urinary Output	Kidney Dynamics and Excretion
RVS	Venous Resistance	Circulatory Dynamics
BFN	Blood Flow in Non-Muscle Non-Renal Tissues	" "
PPD	Rate of change of Protein in Pulmonary Fluids	Pulmonary Dynamics & Fluids
VRC	Volume of Red Blood Cells	Red Cells & Viscosity
DFP	Rate of Increase in Pulmonary Free Fluid	Pulmonary Dynamics & Fluids
PIF	Interstitial Fluid Pressure	Tissue Fluids, Pressures, and Gel
PTC	Interstitial Fluid Colloid Osmotic Pressure	" " "
VTL	Rate of Systemic Lymph Flow	" " "
DPL	Rate of Systemic Lymphatic return of protein	" " "
CPI	Concentration of Protein in free Interstitial Fluid	" " "
TVD	Rate of Drinking	Thirst & Drinking
PVS	Average Venous Pressure	Circulatory Dynamics

CAPILLARY MEMBRANE DYNAMICS (Continued)

	OUTPUT	TO
PPC	Plasma Colloid Osmotic Pressure	Kidney Dynamics & Excretion
PPC	" " " "	Pulmonary Dynamics & Fluids
PC	Capillary Pressure	Circulatory Dynamics
VB	Blood Volume	" "
VB	" "	Red Cells & Viscosity
CPP	Plasma Protein Concentration	Pulmonary Dynamics & Fluids
VTC	Rate of Fluid Transfer Across Systemic Capillary membranes	Tissue Fluids, Pressures and Gel
DPC	Rate of loss of Plasma Proteins Through Systemic Capillaries	" " "
VP	Plasma Volume	Electrolytes & Cell Water

TISSUE FLUIDS, PRESSURES, AND GEL

	INPUTS	FROM
VID	Rate of Fluid Transfer between interstitial fluid & cells.	Electrolytes & Cell Water
DPC	Rate of loss of Plasma Proteins through Systemic Capillaries	Capillary Membrane Dynamics
VTC	Rate of Fluid Transfer across systemic capillary membranes	" " "

	OUTPUTS	TO
VTS	Total Interstitial Fluid of Volume	Electrolytes & Cell Water
CPI	Concentration of Protein in Free Interstitial Fluid	Capillary Membrane Dynamics
DPL	Rate of Systemic Lymphatic return of Protein	" " "
VTL	Rate of Systemic Lymph Flow	" " "
PTC	Interstitial Fluid Colloid Osmotic Pressure	" " "
PIF	Interstitial Fluid Pressure	" " "

THIRST AND DRINKING

	INPUT	FROM
AHM	Antidiuretic Hormone Multiplier, / of normal effect	Antidiuretic Hormone Control
POT	Non-Muscle Cell PO_2	Non-Muscle Oxygen Delivery

	OUTPUT	TO
TVD	Rate of Drinking	Capillary Membrane Dynamics
STH	Effect of Tissue Hypoxia on Salt and Water Intake	Electrolytes and Cell Water

ANTIDIURETIC HORMONE CONTROL

	INPUT	FROM
CNA	Extracellular Sodium Concentration	Electrolytes & Cell Water
AU	Overall activity of Autonomic system, /to normal	Autonomic Control
PRA	Right Atrial Pressure	Circulatory Dynamics

	OUTPUT	TO
AHM	Antidiuretic Hormone Multiplier, / of normal effect	Thirst & Drinking
AHM	" " "	Kidney Dynamics and Excretion

ANGIOTENSIN CONTROL

	INPUT	FROM
REK	Percent of normal Renal Function	Kidney Dynamics & Excretion
RFN	Renal Blood Flow if Kidney is not damaged	" " "
PA	Aortic Pressure	Circulatory Dynamics
CNA	Extracellular Sodium Concentration	Electrolytes & Cell Water

	OUTPUT	TO
ANM	Angiotensin multiplier effect on vascular resistance, ratio to	Circulatory Dynamics
ANM	normal	Aldosterone Control
CNE	Sodium Concentration Abnormality causing third factor effect	Kidney Dynamics and Excretion

ALDOSTERONE CONTROL

	INPUT	FROM
ANM	Angiotensin multiplier effect on vascular resistance, ratio to normal.	Angiotensin Control
PA	Aortic Pressure	Circulatory Dynamics
CKE	Extracellular Potassium Concentration	Electrolytes & Cell Water
CNA	Extracellular Sodium Concentration	" " " "

	OUTPUT	TO
AM	Aldosterone Multiplier, ratio of normal effect	Kidney Dynamics & Excretion
AM	" " " "	Electrolytes & Cell Water

ELECTROLYTES & CELL WATER

	INPUT	FROM
AM	Aldosterone Multiplier	Aldosterone Control
REK	Percent of Normal Kidney Function	Kidney Dynamics & Excretion
NOD	Rate of Renal Excretion of Sodium	" " " "
STH	Effect of Tissue Hypoxia on Salt and Water Intake	Thirst and Drinking
VPF	Pulmonary Free Fluid Volume	Pulmonary Dynamics and Fluids
VD	Plasma Volume	Capillary Membrane Dynamics
VTS	Total Interstitial Fluid Volume	Tissue Fluids, Pressures and Gel

	OUTPUT	TO
VID	Rate of Fluid Transfer between interstitial fluid and cells	Tissue Fluids, Pressures, and Gel

APPENDIX 2

BLOOD FLOW COMPARISON FOR THE THERMAL & CARDIOVASCULAR MODELS

	Guyton		Stolwijk
	Calculated	Tabulated	
Skin	24	18 l./hr.	11.89 l./hr.
(Skeletal) Muscle	60-108	45	11.69
Fat	Other (10.5)	-	3.67
Non-Muscle Non-Renal	(Breakdown (Includes Skin)		Core ----------
Cerebral		45	Head 48
Heart		9	
Bronchial		9	
Liver		81	Trunk 232.0
Bone		15	
Thyroid		3.0	
Adrenal		1.5	
Other	(10.5-Fat)	10.5	Arms Hands 3.14 Legs Feet ----------
			283.14
Renal	72	66	Let Renal = 66
		292.5	
TOTAL		303.0 l./hr	310.39 l./hr.

APPENDIX 2 (Cont'd)

BLOOD FLOW COMPARISONS

In Core

Stolwijk (S)		Guyton (G)
(Includes RBF)	= 283.14 l./hr.	174.0 l./hr.
minus 66 (RBF)	= 217.14	

217.14
174.00
43.14 l./hr. Difference S G

Muscle

11.69 45.0

45.0
11.7
33.3 l./hr. Difference G S

Skin

11.89 18.0 to 24.0

18.00
11.9
6.1 l./hr. G S

43.14 Core S ~ G 39.4 Muscle & Skin G ~ S