A coupled model of the cardiorespiratory and thermoregulatory systems

by

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NOMENCLATURE

Symbol	Description
A	Body surface area (m^2)
C_P	Heat capacity of the body (kcal/kg*°C)
C_P^B	Heat capacity of the blood (kcal/kg*°C)
h	Overall convective heat transfer coefficient (kcal/m^2*min*°C)
$\Delta H_V^{H2O}(T_C)$	Heat of vaporization of water at T_C (kcal/kg)
K_{CM}	Conductivity between core and muscle layers (kcal/min*°C)
K_{MS}	Conductivity between muscle and skin layers (kcal/min*°C)
m	Body mass (kg)
m_J	Mass of compartment J [J = (C)ore, (M)uscles, or (S)kin] (kg)
M_{air}	Molecular weight of air
M_{water}	Molecular weight of water
M_{OJ}	Metabolic oxygen generation rate or carbon dioxide consumption rate in the Jth compartment [J = (C)ore, (M)uscles, or (S)kin] at rest (L/min) M_{OJ} is converted to kcal/min for the energy balances
ΔM	Additional metabolic conversion rate (in the muscles compartment) due to exercise (L/min). $\Delta M = 0$ at rest. Also converted to kcal/min for the energy balances.

ΔM_{sh}	Metabolic conversion rate (in the muscles compartment) due to shivering (L/min)
p	Partial pressure of the component (mmHg)
p^*	Vapor pressure (mmHg)
P_{total}	Total pressure of the system [as defined] (mmHg)
Q_A	Ventilation rate (L/min)
Q_B	Total blood flow rate [Cardiac Output] (L/min)
Q_J	Blood flow to compartment J [J = (C)ore, (M)uscles, or (S)kin] (L/min)
Q_V	Sweat rate [evaporative heat loss] (kcal/min)
RQ	Respiratory Quotient
S_{O2}	Percent saturation of hemoglobin with oxygen
t	Time (min)
T_C	Core temperature (^oC)
T_A	Ambient temperature (^oC)
T_M	Muscle temperature (^oC)
T_S	Skin temperature (^oC)
V_A	Volume of air in the lungs (L)
V_J	Volume of blood and equivalent dissolved gas in compartment J [J = (C)ore, (M)uscles, or (S)kin] (L)
x_A	Concentration fraction of oxygen or carbon dioxide in the arterial blood (exiting the lungs)

x_J	Concentration fraction of oxygen or carbon dioxide leaving the Jth compartment [J = (C)ore, (M)uscles, or (S)kin]
x_V	Concentration fraction of oxygen or carbon dioxide in the venous blood (returning to the lungs)
y_A	Volume fraction of oxygen or carbon dioxide in the gas exiting the lungs
y_I	Volume fraction of oxygen or carbon dioxide in the gas entering the lungs
α_J	The gain in a control equation
γ	Absolute humidity of the air (kg H_2O/kg air)
λ	Partition coefficient ([dissolved gas volume/tissue volume]/[dissolved gas volume/blood volume])
ρ	Density of the blood (kg/L)

INTRODUCTION

Numerous mathematical models have been developed to describe thermoregulation in the human body. Many of them are based on the "three cylinder" approach which divides the body into three distinct layers consisting of core, muscle, and skin which are "wrapped around" each other as shown in Figure 1. While this simple approach is fairly useful for modeling conductive transport, that is, temperature changes produced by heat conducted between adjacent materials of different temperatures, it often ignores or over-simplifies the heat being exchanged through convective means, without regard to metabolic demands. Since blood is flowing between and among the different layers, heat exchange and oxygen transport are both being performed by the vascular system.

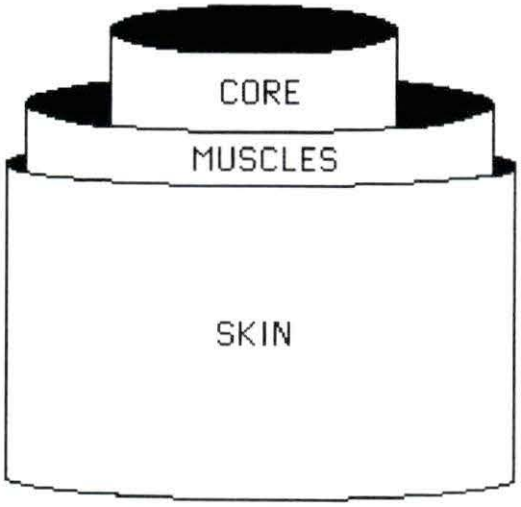


Figure 1: Typical three-cylinder thermoregulation model.

In the early 1960s, Wissler developed a model which included all of the basic exchange elements, such as conduction, convection, and sweating, plus a division of the body into multiple cylindrical sections. It also included radial temperature variations (Wissler, 1964). More recently, the 41-Node METMAN Program was developed by NASA researchers to expand this approach further. They included overall oxygen consumption and carbon dioxide production calculations based on the metabolic rate, but did not compartmentalize their analysis to differentiate between the changing concentrations in the various body elements. In 1979, Kuznetz, using the 41-Node Man as a basis, introduced temperature variations in angular as well as radial directions to study non-uniformity of ambient conditions and internal heat generation.

In this work, we believe that the next important step in the development of this type of model should be to combine it with a metabolic circulatory modeling approach. Mitchell (1977) performed whole body mass and energy balances, primarily to describe the dynamics of working muscle, but did not attempt to develop a compartmentalized model using those balances. Leigh (1984) described some early attempts to do this in which the body was divided into tissue and lung compartments, with metabolism being added to the tissues and heat being exchanged with the environment. Temperature was considered to be uniform throughout the body, however, and only one energy balance was included. This is clearly an incomplete description of human thermoregulation. Since flowing blood carries energy, oxygen, and carbon dioxide, a combined approach is necessary to

understand the changes and limitations that take place when an external effect, such as exercise level, ambient temperature, or gravity is altered.

Quite separately, models of the circulatory system have been developed to describe blood flows that carry oxygen, carbon dioxide, and water, but most of them have not included the changes in temperature which are also occurring. The coupled model in this work combines these approaches in order to better describe the thermoregulatory and circulatory effects resulting from dynamic changes from steady-state behavior (see Figure 2). For example, when a person exercises, increased muscle blood flow is required to deliver additional oxygen to muscles. Blood flow to the skin usually also needs to be increased to meet the growing demand for heat transfer resulting from more heat being produced by the muscles. At least 80 percent of the energy released by oxygen consumption must go to thermal forms and ultimately, be dissipated as heat from the skin and respiratory tract (Mitchell, 1977). It is this contest between oxygen needs and temperature regulation that this work addresses.

Figure 2a

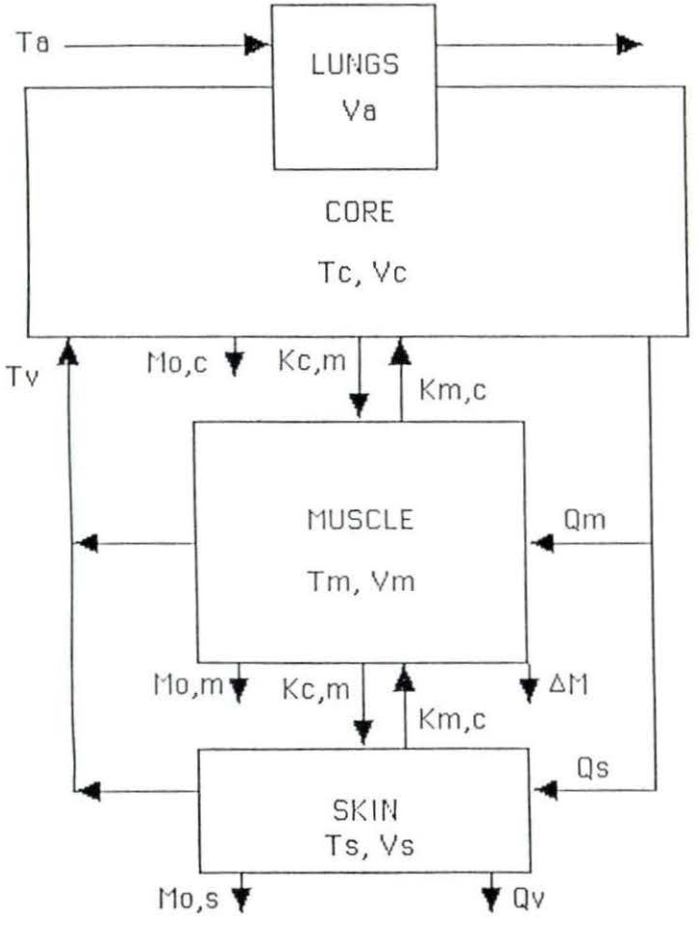


Figure 2b

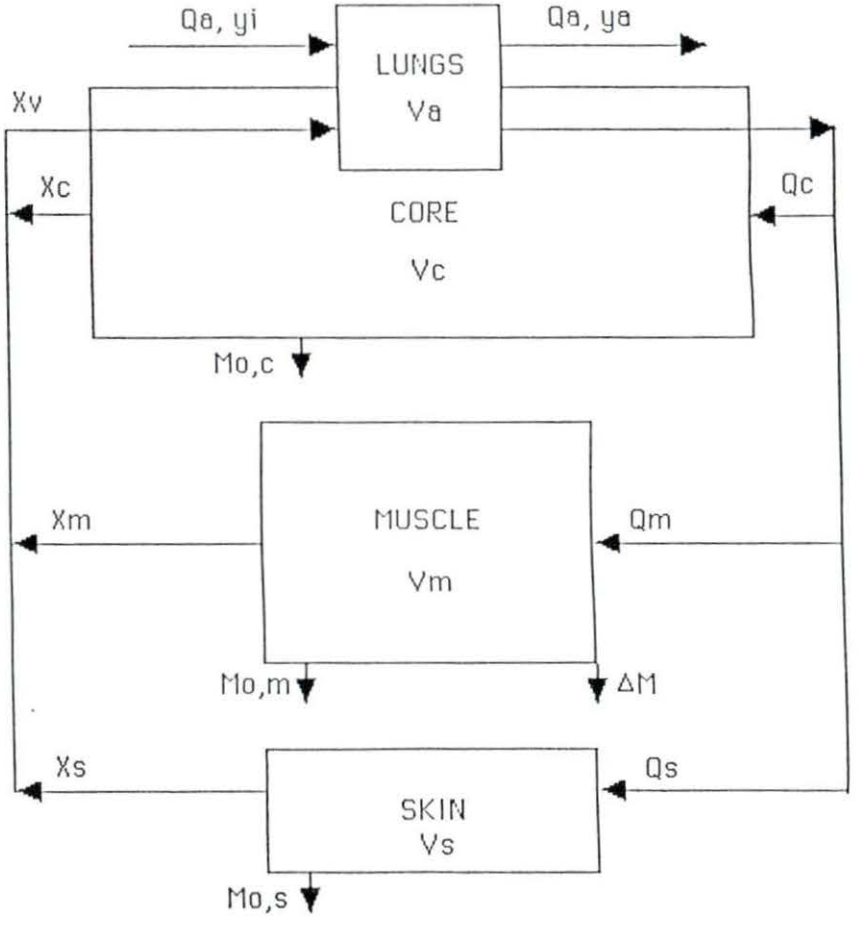


Figure 2: Temperature regulation model (a) and oxygen transport model (b).

INCREASING BLOOD FLOWS DURING EXERCISE

Increasing Blood Flow to Muscles and Skin -- The Partitioning Effect

How are increases in blood flow to muscles and skin accomplished? Some possible mechanisms include; a re-direction of the blood flow from certain internal organs to the periphery of the body (muscles and skin), an increased cardiac output (the volumetric flow rate of blood ejected from the heart) due to an increased heart rate or an increase in intravascular fluid volume, or a combination of these mechanisms.

Partitioning of increased blood flow to skin from working muscles during exercise will limit the delivery of oxygen to muscles, and thus reduce the ability to maintain a high rate of ATP resynthesis, which represents the energy production required in exercising. Partitioning more blood flow to muscles from skin, however, will limit the rate of heat transfer from the core to the skin, causing a rapid rise in the body core temperature. Theories of Rowell, Blackmon, Martin, Mazzarella, and Bruce (1965) suggest that instead of either of these mechanisms, blood flow through specialized tissue beds is reduced during exercise. For example, splanchnic and renal blood flow have been shown to decrease during increased levels of exercise (from Nadel, 1980). These theories suggest that this effect might compensate for the increased need of the skin, which requires extra blood flow to transfer some of the additional heat produced during mild or moderate exercise to the surroundings. In fact, Rowell (1974) determined that vasoconstriction (a decrease in the diameter of blood vessels, especially arteries,

brought about by contraction of their muscular walls) of these two regions during moderate exercise under heat stress could account for the redistribution of 600 to 800 ml/min of blood flow to the skin. At maximum vasoconstriction of splanchnic and renal blood vessels, about 2.2 L/min of blood flow can be redistributed to working muscles and/or skin.

This partitioning effect could also occur between working and resting muscles. If the blood flow is confined to a specific muscular region, blood flow to other muscles could be decreased. Johnson and Rowell (1975) showed that, while skin blood flow to the arms increased during leg exercise, muscle blood flow decreased in that region. Both the metabolic and temperature regulation requirements are probably not capable of being met at higher levels of exercise or exercise performed under heat stress through this means, however.

The means by which these partitioning effects occur involves reflexes that dilate or constrict certain blood vessels. During mild exercise, skeletal muscle vasodilation occurs to increase blood flow through the working muscles. A fall in the partial pressure of oxygen, a rise in the partial pressure of carbon dioxide, a rise in muscle temperature, and accumulation of metabolites (especially potassium) are the local mechanisms responsible for this response (Ganong, 1993). In this case, the amount of oxygen being supplied to the muscles over time is increased, but the total muscle blood volume increases very little because muscles continue to contract and then relax during exercise.

For the skin, however, the blood volume increases along with a rise in skin blood flow when cutaneous blood vessels dilate (Rowell, 1977). If taken to extremes, this central volume change can become compromising to stroke volume and central blood pressures. When these core volumes and pressures decrease while heart rate rises during prolonged exercise, it is referred to as "cardiovascular drift." When skin temperatures are maintained at a constant low value during exercise, this cardiovascular drift can be eliminated (Rowell, 1974).

Increasing Cardiac Output -- Problems Maintaining Blood Volume

Increased blood flow to the periphery will reduce central (core) blood volume, reducing cardiac filling pressure and compromising stroke volume (the amount of blood ejected in one contraction of the left heart). When stroke volume is reduced with the heart rate being held constant, cardiac output is also reduced because a smaller volume of blood is expelled from the heart in the same amount of time. If the heart rate is correspondingly increased, cardiac output can be maintained and will even increase in proportion to oxygen uptake, but this compensatory response has limits. During mild exercise in cool conditions, cardiac output typically does not change significantly, but the A-V oxygen difference (the difference between the oxygen concentration in the arteries and the veins) increases (with increasing oxygen uptake) and heart rate increases to compensate for the decreased stroke volume (Ekelund, 1967). A maximum cardiac output of around 22 L/min (approximately a four-fold increase from rest) can be

reached in a typical person with a maximum oxygen uptake of 3.7 L/min in a relatively cool environment (Rowell, 1977). Both of these values are highly prone to individual variations and are given with wide ranges in most references. For the purposes of our model, we set maximum oxygen uptake at 2.66 L/min which is calculated for a standard 70 kg. man using Ganong's (1993) formula:

Maximum Oxygen Uptake = (38 ml/kg/min)X(Body Mass)

Since this calculation for maximum oxygen uptake results in a much lower value than is often observed, the sensitivity of the model to changes in maximum oxygen uptake was tested in a later part of this work (see p. 63). Maximum cardiac output was allowed to vary according to the increase in muscle blood flow which will be discussed in detail later.

Besides the reduced blood flow circulating in the core due to increased peripheral requirements, blood volume is reduced due to loss of intravascular water to the tissues, especially active muscle tissues, during exercise. The results of Harrison, Edwards, and Leitch (1975) indicate that more protein may go into the vascular compartment during exercise to increase oncotic pressure, and favor water retention by the blood. They were able to show this for the recovery or post-exercise period, but failed to obtain supporting evidence that it was a factor during the time of exercise. Of course, fluid is also lost from the body through sweat from the skin; one important thermoregulatory response to the increased heat generated in the muscles which is discussed in detail in a later part of this work. During low intensity exercise, this effect may be negligible, but if the skin temperature is

high or the exercise is more intense, it could become significant (Nadel, Cafarelli, Roberts, and Wenger, 1979). In fact, Rowell (1974) found that maximum cardiac output, which was hypothesized to increase in the heat to account for the increase in skin blood flow, actually was lower when exercising heavily in the heat than in cooler conditions, presumably because so much water was lost through sweat that heart rate could not increase enough to compensate for the reduced stroke volume.

Under these conditions, the amount of water being diverted from the vascular system to the internal tissues (including muscles) may be negligible because of the extreme high rates of sweating that will result. According to Nadel (1980), "above a critical water deficit, all body fluid compartments, including blood, are reduced in volume." Senay and Christensen (1965) showed that osmotic pressure could act as an indicator of body volume changes (from Harrison, Edwards, and Fennessy, 1978). Generally, when the volume is reduced, core temperatures are higher, cardiac output decreases, and lactic acid (lactate) concentration increases, but usually not enough to indicate that oxygen is not being sufficiently supplied to the muscles (Nadel, Fortney, and Wenger, 1980).

Dehydration is an important factor, especially during exercise in the heat, and can become a limitation to the physical work capacity. When cardiac filling pressure is reduced during dehydration when the blood volume is decreased, it has been theorized that antidiuretic hormone (ADH) release is controlled from the hypothalamus, and that this has a direct effect on the hypothalamic neurons that mediate

thermoregulation (Nadel, Fortney, and Wenger, 1980). Hortsman and Horvath (1972) showed that forearm blood flows, which supply both skin and muscle, could not be maintained during dehydration, so the storage of thermal energy in the body increased dramatically, causing body temperatures to increase. Sodium, Na^+, loading is another factor which may affect blood volume. It has been shown to increase the core temperature during exercise. During sodium loading, the concentration of intravascular Na^+ increases so that the peripheral circulation is reduced. Both dehydration and Na^+ loading are presumed to decrease the effectiveness of the sweating mechanism (Nadel and Horvath, 1977).

The Competition -- When Muscle Blood Flow is Favored

If the exercise is continued to very high levels, vasoconstriction occurs (blood vessels become smaller to keep blood in the core and maintain stroke volume). When this happens, the rate of heat transfer from the core to the skin becomes insufficient and core temperature continues to rise. It has been shown in numerous experiments (Nadel, 1980) that metabolic circulatory regulation will be given precedence over temperature regulation in this case.

Cutaneous vasoconstriction is just one reflex which will favor oxygen delivery at the expense of thermoregulation. Increases in cutaneous venomotor tone (the basal amount of muscle contraction controlled through reflex activity) and an increasing degree of tone during exercise will occur (Nadel, 1980). An upward shift in the core

temperature threshold for cutaneous vasodilation will also cause blood to shift toward the core by making the blood vessels of the skin stay constricted, even at higher temperatures (Nadel, Fortney, and Wenger, 1980). All of these reflexes will help to maintain the core blood volume (stroke volume), but will also reduce the heat transfer rate from the core to the skin (Nadel, 1983).

Early theories often supported the idea that, during maximal exercise, only the metabolic demands of the exercising muscles are important. As a result of the measures which serve to protect the metabolic circulatory demands, many cardiovascular researchers tended to ignore thermoregulatory effects. However, more recent evidence shows that heat dissipation is also an important consideration. The central circulation can often meet increased demands for heat dissipation so "...thermoregulatory factors can influence the central circulation during exercise" (Saltin, 1970).

In addition to increased redistribution of blood flow from splanchnic and renal areas and non-exercising muscles, Rowell (1983) suggests that vasoconstriction may also occur to some extent in exercising muscles to redirect blood flow to the skin. He states that at exercise levels up to about sixty percent of the maximum oxygen uptake, "muscle blood flow could decrease enough to provide skin with an additional liter or so of blood flow each minute ..." without decreasing oxygen uptake. Conflicting experimental results have not provided any direct evidence to support this theory, but increases in lactate concentrations and decreases in oxygen uptake have been shown.

If cardiac output decreases too much during maximal exercise levels, cardiac filling and arterial blood pressures can become compromised. To prevent this from happening, compensatory responses must occur within the cardiovascular system (Nadel, 1985). Nadel (1984) states that it is probably blood pressure receptors that insure adequate muscle blood flow. Experiments of Rowell, Murray, Brengelmann, and Kraning (1969) showed that at a skin temperature of about 38°C cardiac output started to level off after 10 to 15 minutes of exercise. Brengelmann, Johnson, Hermansen, and Rowell (1977) associate this break in conditions with the point where blood pressure regulation starts to dominate the vasodilation response which was serving to increase skin blood flow. Sheriff, Wyss, Rowell, and Scher (1987) hypothesized that a nerve-acting "pressor substance" accumulates in the muscle, causing the systemic arterial pressure to be increased. They concluded that "pressor responses are apparently generated when O_2 delivery falls below some critical level, causing accumulation of a pressor substance, the release of which is linked to a metabolic event that precipitates lactate accumulation." This is also commonly called the muscle chemoreflex.

Mechanoreflexes in the muscles, or arterial mechanoreflexes (also called baroreflexes), also serve to maintain blood pressure during exercise. When exercise begins, vagal withdrawal serves to increase heart rate to maintain cardiac output, and the baroreflex is set to a higher blood pressure. Vagal activity normally limits the maximum heart rate. During mild exercise, vagal withdrawal can raise heart rate and cardiac output enough to raise the blood pressure to this higher

level. When the level of exercise is more extreme, a point is reached where vagal withdrawal can no longer serve to increase the heart rate. When heart rate exceeds this range of vagal withdrawal, sympathetic nervous activity is increased (mostly by the muscle chemoreflex described above). This sympathetic nervous activity can serve to cause further increases in heart rate. There is usually a "blood pressure error", a mismatch between cardiac output and vascular conductance, because this response is slower. Sympathetic vasoconstriction must then occur to increase blood pressure (Rowell and O'Leary, 1990).

Limitations of Muscle Blood Flow

Circulatory requirements of the muscles may be favored over those of the skin when a competition exists, but they must also be limited. Exercise cannot be increased indefinitely, and oxygen uptake reaches a maximum at some point beyond which the subject cannot continue to use a higher rate of oxygen by the muscles. It has been shown to occur, typically, when about 80 to 85 percent of the cardiac output perfuses active muscles while inactive tissues are maximally vasoconstricted (Rowell, 1974). The maximum oxygen uptake of any particular individual is set by many factors, such as the degree of training. Many have hypothesized that circulatory delivery of oxygen is the single limiting step in the maximum oxygen uptake that is attainable. It has been shown that the rate of increase in cardiac output declines as the oxygen uptake approaches its maximum (Saltin, 1964).

The Fick Principle relates maximum oxygen uptake to the functional capacity of the cardiovascular system as a product of the maximum cardiac output and the maximum A-V oxygen difference (Rowell, 1974). Rowell (1974) also suggests that a better definition might be to redefine cardiac output as a ratio of maximal arterial mean pressure divided by minimum total peripheral resistance (if cardiac output is controlled by pressure regulation). According to Jones and Lindstedt (1993), this maximum rate of oxygen consumption is not mechanically limiting to muscle because anaerobic metabolic pathways can be utilized to generate more power, but aerobic capacity is limited and this limits maximal sustained performance. Core temperature is often measured as a function of oxygen uptake (muscle metabolism) and numerous sources (including Davies, Brotherhood, and Zeidifard (1976); Nielsen (1971); and Saltin and Hermansen (1966)) have determined that it is more closely related to the individual's percentage of maximum oxygen uptake than to the absolute amount of oxygen they use (from Rowell, 1983).

AMBIENT TEMPERATURE CHANGES

Ambient temperature is another important factor in determining the behavior of the body's circulation. Brouha was one of the first to propose (in 1960) that cardiac output should increase during exercise in the heat to meet increased circulatory requirements and prolong the duration of work possible (from Nadel, Cafarelli, Roberts, and Wenger, 1979). At rest, total cardiac output remains relatively unchanged up to an ambient temperature of 115°F (46.1°C). However, at such extremely high temperatures, skin blood flow can comprise over fifty percent of the cardiac output (Roddie, 1983).

At higher temperatures, resting cardiac output was shown to increase, which was associated with decreased A-V oxygen differences. Damato, Lau, Stein, Haft, Kosowsky, and Cohen (1968) concluded from their studies of this phenomenon that up to 115°F (46.1°C) ambient temperature, the skin blood flow could be increased enough to maintain the thermal balance by diverting blood flow from resting internal organs to the skin without increasing cardiac output. Arterial pressure decreases were also observed throughout the temperature range they studied, 78-125°F (25.6°C-51.7°C) in a hot, dry environment. Decreases in stroke volume by water lost through sweat appear to be compensated for by increased heart rates.

When exercise is performed in hot environments, even at moderate levels, however, problems with maintaining adequate blood flows to both muscles and skin occur. Compensations for these problems are similar to the compensatory actions that take place during more severe

exercise under cool conditions, but they are usually encountered more quickly since skin blood flow is already increased dramatically by the heat stress.

When exercising in a cool environment, skin blood flow remains low initially and cutaneous veins refill very slowly after muscles compress them during the action of exercise. This moves the majority of the skin blood volume to the central (core) regions and helps to maintain stroke volume and pressures. This is not the case when exercising in the heat. Muscles still compress cutaneous veins, but they refill so rapidly that the result is not as effective in displacing blood centrally (Rowell, 1983).

Mild exercise, if prolonged under heat stress, can produce increases in the cardiac output by two to three L/min to help meet the increased demands for skin blood flow. Arterial pressures can still be maintained in this case, but stroke volume has been shown to decrease continuously. If the level of exercise is more intense, cardiac output cannot continue to increase over time. Numerous conflicting sources have shown that oxygen uptake may increase, decrease, or remain constant during this period (Rowell, 1974). Since we know that the blood flow decreases, this effect must be a result of the dynamic changes in the A-V oxygen difference, which we can calculate by the mass balances.

Stroke volume still decreases, even though heart rate increases considerably. When the heart rate reaches a maximum at around 200 beats/min, a fall in cardiac output should result (Rowell, 1983). Maximal muscle blood flow cannot be reached because maximal cardiac

output is never reached. Also, as a result of the reduced stroke volume, maximal heart rate and A-V oxygen difference are reached at a lower oxygen uptake. This means that the peak oxygen uptake is reduced under these conditions. Rowell (1974) defines the peak oxygen uptake as the highest oxygen uptake observed under specific circumstances. This is not always the same as the maximum oxygen uptake, which determines the cardiovascular system functional capacity and does not change. Other possible reasons for peak oxygen uptake being reduced in the heat include increased sympathetic activity vasoconstricting muscle blood vessels and allowing more cardiac output to go to the skin (as was previously discussed) and/or a reduction in the subject's tolerance to work in the heat, which is not very likely to be the cause in every case.

TEMPERATURE CHANGES: WHERE HEAT TRANSFER BECOMES IMPORTANT

Heat Influences on Muscle Metabolism -- The Value of Negative Work Experiments

Many researchers have postulated that high muscle temperatures may be optimal to ATP reaction. The rate of glycolysis and ATP utilization are both higher in heated muscle, but endurance times are shorter. Edwards, Harris, Hultman, Kaijser, Koh, and Nordesjo (1972) suggested that this early fatigue may be due to a reduction in the rate of regeneration of ATP from anaerobic glycolysis, so the muscle contraction cannot be sustained. Results of Jessen and Kuhnen (1990) show that low ambient temperatures could exert a direct effect on muscle metabolism and they also suggest that "the relationship between low skin temperature and metabolic rate (which they found experimentally) essentially reflects the influence of low muscle temperature on metabolic processes at a cellular level, i.e., the dependence of peak metabolic rate on muscle temperature."

Others have addressed the issue as to whether or not muscle temperature is limiting to exercise. There is no direct evidence that muscle temperature contributes to fatigue but, since muscle temperature rarely rises above 40°C, it has been suggested that this temperature may be a limiting factor. Nadel (1983) found that subjects obtained muscle temperatures near 41°C during eccentric exercise (negative work), but failed to prove that this higher temperature is not limiting. Still, most of the evidence indicates that it is not. Muscle

biopsy samples have shown that, even at high intensities, there is little indication of anaerobiosis. Also, Knuttgen, Nadel, Pandolf, and Patton (1982) found that training did not affect muscle temperatures and, thus, was not a factor that contributes to trained athletes being more resistant to fatigue. Guyton (1976) does state that body temperatures above 41.1°C can cause cellular damage.

Many of the experiments performed to study metabolism and heat effects involve the comparison of positive and negative work. Positive work exercise is the typical type of exercise used to study thermoregulation. The muscles contract concentrically, producing metabolic heat and causing body temperatures to rise. During negative work exercise, muscles resist elongation due to an external force so excess heat, in addition to metabolic heat, is added to the muscles (Nadel, Bergh, and Saltin, 1972). These "negative work" experiments are especially helpful in studying thermal load, when muscles do not require as much blood to transport excess oxygen. Since extra heat is produced, temperature effects can be observed at lower muscle blood flow rates and lower metabolic rates. Core temperatures remain lower during negative work exercise while muscle and skin temperatures are higher.

Temperature Measurements and Local Effects

One problem that has been generally encountered in the area of temperature regulation is the physical measurement of temperatures. How do we measure a core, muscle, or skin temperature when the

actual temperature may vary greatly between different areas of the body? Core temperature, in our model, for example, includes everything in the body that is not muscle or skin. Most models include this concept of core temperature, but it surely cannot be measured experimentally in humans. In fact, most of the individual components of the core are not accessible to temperature measurements. So what information do we use to test our models? Typically, tympanic, rectal, or esophageal temperature measurements are used to estimate the core. Nadel (1977) believes that esophageal temperature is the best indicator because tympanic temperature can be influenced by ambient temperature and rectal temperature has a very slow response time. Several others agree with this, but, unfortunately, much of the earlier experimental data only include rectal or tympanic temperature measurements.

Skin temperature is usually taken to be a weighted average of the various areas of the skin, taking into account both area and sensitivity. Local effects of skin temperatures can be considerable. Most experiments performed to study blood flow effects hold the local temperature of the skin surrounding the muscle constant in order to reduce these local effects. Brengelmann (1977), for example, held local forearm temperatures at 36°C or less when studying forearm blood flow measurements.

Core Temperature Elevation During Exercise -- A Change in Set Point?

In 1938, M. Nielsen became the first researcher to experimentally show that "internal body temperature increases during muscular exercise and eventually arrives at a new steady state that is roughly proportional to the absolute exercise intensity and independent of ambient temperature (between 5 and 30°C)." (Nadel, 1983). Many other studies have agreed with this and have shown conversely that skin temperature is a linear function of ambient temperature and independent of metabolic rate (Stolwijk, Saltin, and Gagge, 1968). More recently, Wyndham, Strydom, Morrison, duToit, and Kraan (1954) were one of the first to determine that core temperature does vary with environmental temperature. In fact, it also varied in Nielsen's graphs, but he plotted his data on a coarser scale (Brengelmann, 1977). Davies (1979) presented results which were directly contrary to those of Nielsen and several others. He found that the rise in core temperature (rectal temperature) was <u>not</u> independent of ambient temperature from 5 to 30°C, using experiments with higher relative work loads and more convective cooling. Also, skin temperature will rise with metabolic rate if the skin blood flow is high and evaporative heat loss (convective cooling) cannot be maintained at a high enough level to satisfy the energy balances.

A highly debated question has been whether temperature or heat content is the regulated variable in thermoregulation. It is now generally agreed that temperature must be the regulated variable and the body has no known sensors for heat flow or heat content. The

temperature difference will provide heat flow, but evidence shows that it is not what is regulated; the body probably does not have thermal sensors at every depth of the epidermal layer (Nadel, 1977).

Many subsequent arguments have arisen from this concerning whether or not core temperature is adjusted to a higher "set point" in exercise, as it appears to be in fever. As the energy balances which follow show, when a subject exercises, muscle metabolism (ΔM) increases and the temperatures increase. They will eventually reach a new steady-state where heat production is balanced by heat dissipation, but this does not mean that there is a new, regulated core temperature.

THE MODEL EQUATIONS

The "Standard Man" Concept

Much of the research that has been done in the area of exercise physiology has concentrated on individual differences that affect performance. Many of the factors described here can be affected by external factors such as the degree to which an individual is acclimated to his or her surroundings or each individual's own relative level of fitness. Stroke volume, for example, is related to heart size, but can be affected by other factors. Both cardiac output and stroke volume can be increased through aerobic training. (Jones and Lindstedt, 1993) For the purposes of our model, we have used the concept of a "standard man" developed by Seagrave (1971) to obtain typical values for the physiological parameters that were used here.

Energy Balances

Energy balances on each of three compartments (core, muscles, and skin) include terms for energy consumption in that compartment, thermal energy flowing into or out of that compartment with blood flows (which are the same flows that carry oxygen throughout the circulatory system), and the energy conducted between adjacent compartments.

The blood entering the core compartment is assumed to be a mixture of blood leaving the muscles and skin. Its temperature, T_V is calculated as an average so that:

$$T_V = \frac{Q_M T_M + Q_S T_S}{Q_M + Q_S}$$

and the energy balance for the core is:

$$m_C C_P \frac{dT_C}{dt} = M_{0,C} - K_{CM}(T_C - T_M) - (Q_M + Q_S)\rho C_P^B(T_C - T_V) + Q_A \rho C_P^B(T_A - T_C) + Q_A \rho_{air}(\gamma^{amb} - \gamma^{exp})\Delta H_V^{H2O}(T_C)$$

where the last two terms account for energy loss through the respiratory system. The difference between the absolute humidities of the inspired and expired air ($\gamma^{amb} - \gamma^{exp}$) can be simplified in terms of pressures and molecular weights so:

$$(\gamma^{amb} - \gamma^{exp}) = \frac{M_{H2O}}{M_{air}}\left(\frac{p^*_{in}}{760 - p^*_{in}} - \frac{p^*_{out}}{760 - p^*_{out}}\right)$$

These vapor pressures can be calculated using the Antoine equation with coefficients for water (Felder and Rousseau, 1986).

The muscle equation includes both a resting energy consumption term (M_{OM}) and a term for added metabolism (ΔM) resulting from exercise:

$$m_M C_P \frac{dT_M}{dt} = M_{0,M} + K_{CM}(T_C - T_M) + \Delta M - K_{MS}(T_M - T_S) + Q_M \rho C_P^B (T_C - T_M)$$

The skin equation contains two additional terms to account for the release of heat from the skin to the environment. Q_V represents the evaporative loss (the amount of water that is vaporized) and $hA\Delta T$ is the overall heat convected from the skin to the surrounding air:

$$m_S C_P \frac{dT_S}{dt} = M_{0,S} + K_{MS}(T_M - T_S) - Q_V - hA(T_S - T_A) + Q_S \rho C_P^B (T_C - T_S)$$

Figure 2a showed the basic model used to derive these equations.

Mass Balances (Oxygen)

Next, a simple mass balance is performed around each of the four compartments of the model with respect to the oxygen volume (see Figure 2b). Oxygen is brought into each compartment through the blood stream and also the air entering the lungs, in the first balance given below. A portion is metabolized (consumed) by the cells in the three compartments to which it is carried and the rest leaves the compartments, again through the blood stream. In the lung compartment, it is considered that only gas exchange between the air and the blood takes place. Oxygen uptake by the lung tissues may be included as a part of the core/tissues compartment.

$$V_A \frac{dy_A^{O_2}}{dt} = Q_A\left(y_I^{O2} - y_A^{O2}\right) + Q_B\left(x_V^{O2} - x_A^{O2}\right)$$

$$V_C^{O2} \frac{dx_C^{O2}}{dt} = Q_C\left(x_A^{O2} - x_C^{O2}\right) - M_{0,C}^{O2}$$

$$V_M^{O2} \frac{dx_M^{O2}}{dt} = Q_M\left(x_A^{O2} - x_M^{O2}\right) - M_{0,M}^{O2} - \Delta M^{O2}$$

$$V_S^{O2} \frac{dx_S^{O2}}{dt} = Q_S\left(x_A^{O2} - x_S^{O2}\right) - M_{0,S}^{O2}$$

The metabolism of oxygen in these equations is related to the metabolism of energy in the energy balances by the calorific oxygen equivalent statement given with a dependence on the respiratory quotient (which will be discussed in the next section):

$$\frac{\text{kcal energy}}{\text{L oxygen}} = 1.23 \times RQ + 3.816$$

This equation was obtained from the data given by Brobeck (1974).

The volume terms that multiply the derivative terms in all of these equations are actually combined volumes of the gas being considered (oxygen in this case) in a given compartment and in the blood in that compartment. For example,

$$V_C^{O2} = V_{BC} + \lambda^{O2} V_{CC}$$

where V_{BC} is the volume of blood in the core and V_{CC} is the total core volume.

In this case, the partition coefficient, λ^{O2}, is close to zero since oxygen is almost immediately used by the cells and does not remain in the tissue space in a significant amount. This partition coefficient for oxygen is assigned a value of 0.024, so $V_C{}^{O2}$ is just slightly larger than the volume of blood in the tissues. In the following case, the partition coefficient for carbon dioxide is closer to one, $\lambda^{CO2} \sim 0.57$, so $V_C{}^{CO2}$ is much larger than the volume of blood in the tissue compartment.

Mass Balances (Carbon Dioxide)

The carbon dioxide mass balances are analogous to the oxygen mass balances except the metabolism terms are added to the right-hand side of the equations; carbon dioxide is generated instead of being consumed by the cells of each compartment. This metabolism can be related to the metabolism of oxygen by:

$$RQ = \frac{M^{CO2}}{M^{O2}} = 0.8 + 0.083 \times \Delta M \ (L\ O_2 / min)$$

This relationship is an approximation which is derived from the ratio of carbon dioxide production (200 ml/min) to oxygen consumption (250 ml/min) at rest and STP conditions for a standard man (Seagrave, 1971) and the assumption that the respiratory quotient increases linearly to reach a value of 1.0 at the maximum oxygen uptake.

This "respiratory quotient" is strongly dependent on the diet of the subject. It is always equal to 1.00 for carbohydrates, which have

exactly enough oxygen to oxidize all the hydrogen in the molecule. Just enough respiratory oxygen must be added to combine with the carbon in the carbohydrate molecule to produce the same amount of carbon dioxide. Fats typically produce a much lower respiratory quotient, around 0.707. The average respiratory quotient for proteins is 0.801. So the approximation we are using would vary between 0.71 and 1.0 depending on the type and amount of food the subject consumes and the level of exercise. Generally, shortly after a meal, most of the food is metabolized to carbohydrates, raising the respiratory quotient. When the subject has not eaten for a longer period of time, such as at night, little carbohydrate is present, and the value of the respiratory quotient is lowered, approaching that which would occur for fat metabolism (Guyton, 1976).

The respiratory quotient also depends on the level of exercise being performed because, as exercise becomes more strenuous, more carbohydrates are used, so it increases toward unity. It may even appear to exceed one during anaerobic work because lactic acid accumulates and combines with bicarbonate base and the respiratory compensation that takes place leads to decreased alveolar and arterial P_{CO_2}. The carbon dioxide which is released through the lungs can therefore exceed the amount of metabolically produced carbon dioxide (Mountcastle, 1974).

$$V_A \frac{dy_A^{CO2}}{dt} = Q_A\left(y_I^{CO2} - y_A^{CO2}\right) + Q_B\left(x_V^{CO2} - x_A^{CO2}\right)$$

$$V_C^{CO2} \frac{dx_C^{CO2}}{dt} = Q_C\left(x_A^{CO2} - x_C^{CO2}\right) + M_{0,C}^{CO2}$$

$$V_M^{CO2} \frac{dx_M^{CO2}}{dt} = Q_M\left(x_A^{CO2} - x_M^{CO2}\right) + M_{0,M}^{CO2} + \Delta M^{CO2}$$

$$V_S^{CO2} \frac{dx_S^{CO2}}{dt} = Q_S\left(x_A^{CO2} - x_S^{CO2}\right) + M_{0,S}^{CO2}$$

The Oxygen/Hemoglobin Dissociation Curve

$y_A{}^{O2}$ (the volume fraction of oxygen in the alveolar gas of the lungs) can be related to $x_A{}^{O2}$ (the volume fraction of oxygen in the pulmonary capillary blood) through the oxygen/hemoglobin dissociation curve. When oxygen is dissolved in the blood, approximately 99% of it combines with the protein hemoglobin to be transported through the circulatory system. Since this is true, we can say that the relationship between the percentage saturation of hemoglobin with oxygen in the blood and the partial pressure of oxygen in the lungs will specify an equilibrium relation between $x_A{}^{O2}$ and $y_A{}^{O2}$.

In 1925, Adair developed the following equation which relates percent saturation (S_{O2}) to oxygen tension (or partial pressure, P^{O2}):

$$S_{O_2} = \frac{100p^{O_2}\left(c_1 + p^{O_2}\left(c_2 + p^{O_2}\left(c_3 + p^{O_2}\right)\right)\right)}{\left(c_4 + p^{O_2}\left(c_5 + p^{O_2}\left(c_6 + p^{O_2}\left(c_7 + p^{O_2}\right)\right)\right)\right)}$$

(from Willis, Clapham, and Mapleson, 1987).

The c_i's in this equation are empirically determined coefficients. In 1972, Thomas found improved values for these constants to be:

$c_1 = -2000$ $c_2 = 2045$

$c_3 = 15$ $c_4 = 2400000$

$c_5 = 31100$ $c_6 = 2400$

$c_7 = 15$

These values also fit well with the standard curve developed by Severinghaus in 1966.

The value for partial pressure used in this equation can be obtained from the mass balance as:

$$(P^{O2})_{standard} = (y_A{}^{O2})(P_{total})$$

where P_{total} is taken to be 713 mmHg on a dry basis at STP.
It must be corrected for the influences of core temperature and carbon dioxide partial pressure:

$$\left(p^{O2}\right)_{virtual} = \left(p^{O2}\right)_{standard} \times 10^{\left(0.024\left[37 - T_C\right] + 0.06\left[\log 40 - \log P^{CO2}\right]\right)}$$

where 37°C is the temperature where the standard curve has been calculated and 40 mmHg is the carbon dioxide partial pressure of the standard curve (Kelman, 1966).

Percent saturation can be converted to $x_A{}^{O2}$ by:

$$x_A^{O_2} = \frac{S_{O_2}}{100} \times \left(0.201 \text{ ml } O_2 / \text{ ml blood}\right)$$

Since at complete saturation there is 1.34 ml oxygen at STP per gram of hemoglobin, and about 15 grams of hemoglobin per deciliter of blood (Ganong, 1993), 0.201 ml O2/ ml blood was chosen as the saturated value for our standard man model.

The Carbon Dioxide Dissociation Curve

A similar equilibrium relationship can be used to relate y_A^{CO2} to x_A^{CO2}. The so-called "carbon dioxide dissociation curve" used here relates x_A^{CO2} (in ml of carbon dioxide per liter of blood) to the partial pressure of carbon dioxide in the lungs:

$$CO_2 \text{ content (ml/ L)} = 462e^{0.00415p^{CO2}} - 340e^{-0.0445p^{CO2}} + 0.62(97.5 - S_{O_2})$$

This formula was developed by Meade in 1972 and is based on the empirical data of Comroe (1963). The standard curve is given at an oxyhemoglobin saturation level of 97.5% and a correction factor is added to account for changes in S_{O2}.

A further correction for core temperature changes proposed by Nunn in 1965 and utilized by Thomas in 1972 is given by:

$$p_T^{CO2} = \left(p_{37^\circ C}^{CO2}\right) \times 10^{0.019(T_C - 37)}$$

P^{CO2} at 37°C can be calculated from the mass balance on carbon dioxide, as was done in the case of oxygen:

$$(P_{37^{\circ}C}^{CO2}) = (y_A^{CO2})(P_{total})$$

The Model

These equations and the control relations in the following chapter have been used to create a model which was developed on Matlab using the Simulink modeling package on a DEC Station (Model 2100) workstation. The equations were solved using a fifth order Runge-Kutta method available in Simulink.

THE CONTROLLERS

Skin Blood Flow

The literature concerning the subject of thermoregulation is often contradictory. Contrary to the results of Wenger, Roberts, Stolwijk, and Nadel (1975), Benzinger (1959) claimed that skin temperature does not contribute to the control of skin blood flow. He also observed that thermoregulatory sweating is independent of skin temperature. Wenger et al. (1975) relate these findings to the possibility of a significant contribution of skin temperature to tympanic temperature, which Benzinger measured.

Brengelmann, Wyss, and Rowell (1973) found that increases in forearm blood flow were due almost entirely to increases in core temperature and were unaffected by skin temperature. Most later studies disagree with this and Wenger et al. (1975) attribute Brengelmann et al.'s conclusion to the fact that it depends entirely on the assumption that core temperature has a relationship with heart rate independent of its relationship with forearm blood flow. Wenger et al. assert that Brengelmann et al.'s results really only support that control of forearm blood flow is similar to control of skin blood flow. Rowell (1983) states that skin temperature appears to be a more important factor in determining skin blood flow during exercise than during rest. He also asserts that changes in skin temperature may modulate vasoconstrictor outflow to skin which is increased during heavy exercise. Still, he maintains that core temperature activates

vasodilation and has about a twenty-fold greater influence on skin blood flow than skin temperature (Rowell, 1977).

In our model, we have used a proportional controller for skin blood flow based on core temperature, so:

$$Q_S = Q_{S,0} + \alpha_1 (T_C - T_{C,0})$$

The maximum Q_S in our model is set at 3.0 L/min. If the calculated value of Q_S by this equation becomes greater than 3.0, the model switches to use this constant value for Q_S. According to Ganong (1993), skin blood flow typically ranges between 0.02 and 3.0 L/min. Rowell (1974), however, has reported that skin blood flows between 7 and 8 L/min can be attained at high levels of exercise and/or high ambient temperatures.

The gain, α_1, was set at 0.9 to yield skin temperatures similar to those found in literature, especially in comparison with the data of Saltin, Gagge, and Stolwijk (1968). At the same time, Q_C is allowed to decrease by 0.7 L/min from the resting state to simulate the effects of repartitioning of blood flow. This change occurs before cardiac output begins to increase.

Muscle Blood Flow

To model the increase in muscle blood flow during exercise, we have used a proportional controller based on oxygen concentration in the blood leaving the muscles.

$$Q_M = Q_{M,0} + \alpha_2 \left(x_M^{O2} - x_{M,0}^{O2} \right)^2$$

The concentration term was squared in order to reduce errors. The gain, α_2, was set at 5500. This value was chosen so that $x_M{}^{O2}$ reaches 0.044 at the maximum oxygen uptake, as is discussed on page 41.

Sweating Rate

In 1949, Robinson described the sweating rate during exercise as a linear function of internal body temperatures. He said that skin temperature also influences sweating, but to a lesser degree than core temperature (Nadel, 1983). According to Benzinger (1961), skin temperature suppresses sweating below 33°C while skin temperatures above 33°C do not affect sweating rate (from Brengelmann, 1977). Saltin and Hermansen (1966) state that "sweat rate during work in a constant environmental temperature is linearly related to metabolic rate." They propose that an increasing temperature in the hypothalamus elicits a sweating rate related to the individual aerobic work capacity. Stolwijk, Saltin, and Gagge (1968) confirmed this finding and also showed that sweat rate can be described as a linear function of core and skin temperature.

More recent studies have shown that muscle temperatures may also play a role. It is often difficult to determine if certain factors cause something to happen or are a result of something else causing changes to a system. This is certainly the case in the initiation of sweating

during exercise. A rapid rise in muscle temperature parallels a rise in sweating (Saltin, Gagge, and Stolwijk, 1968), but they probably do not directly affect each other. Work in the muscles generates heat, causing the muscle temperature to increase. When muscle temperatures increase, core temperatures increase, skin temperatures increase, and sweating is initiated. Although the muscle temperature rise was indirectly the cause for sweating to occur, it is probably not involved in the control mechanisms used to signal the sweating response. Most researchers conclude that it is impossible using the data they are able to collect to differentiate between core and muscle temperatures to find their individual effects on sweating, so it has not been demonstrated whether or not signals are sent from the muscles to the thermoregulatory center. B. Nielsen (1966) showed, in fact, that muscle temperature could not be the stimulus for correlating sweat rate with total heat production, because muscle temperature differs for the same rate of total heat production for positive and negative work.

Control of sweat rate does pose an especially difficult problem, in that Stolwijk, Saltin, and Gagge's (1968) linear model may not always be adequate. Wyndham and Atkins (1968) found that sweat rate control is too complex to model with a simple function of core and skin temperature. They suggest using non-linear control. Finally, Davies (1979) concluded that sweat rate can be expressed as a linear function of core and skin temperature during sub maximal work, but not during more severe work. His results showed that thermoregulation is only passive during extreme hard work where it becomes physical instead of

physiological, that is, the evaporative process becomes controlling and the circulatory transport of heat is insignificant compared to sweat rate control.

When exposure to heat or exercise is prolonged, sweat rate is decreased. The question is often asked concerning why this occurs. Some postulate that there is a change in the "set point" for the central nervous system control of the threshold temperature at which sweating begins. Many others support the idea that there is a decrease in sweat gland responsiveness to neuroglandular signals (Nadel, 1977).

We have not yet included this effect in our model and have based the heat loss through sweat (water evaporation) on Stolwijk, Saltin, and Gagge's (1968) linear model discussed above. The general form of this equation is:

$$Q_V = 3.42(T_C - 36.6°C) + 0.51(T_S - 33.3°C)$$

where Q_V is in kcal/min. It is assumed that all water lost through sweating is replaced so that the total body water content does not decrease.

Ventilation Responses

When oxygen uptake is increased, another compensatory response to bring more oxygen into the blood stream and remove the excess carbon dioxide that is produced is an increase in ventilation. It has been postulated that this results from either baroreceptor reflexes or the

increased catecholamine level of the blood. (Ekelund, 1967). Also, it is possible that the increased concentration of potassium in the plasma which occurs during exercise stimulates peripheral chemoreceptors. Ganong (1993) states that body temperature increases may also play a role or the respiratory center may become more sensitive to carbon dioxide to provide the stimulus for ventilation changes. Oxygen may also play some part, since as the amount of oxygen in the inspired air is increased, breathing rate decreases. Robinson (1974) observed that small reductions in P^{O2} which do not affect the ventilation in resting subjects, cause substantial ventilation changes in subjects who are performing severe work. It is, most likely, some combination of these stimuli that regulates ventilation.

The majority of the carbon dioxide found in the blood is in the form of bicarbonate (HCO_3^-). The rest is either dissolved, or in carbamino compounds. This is why the acid/base balance in the blood is especially important during exercise. When exercising muscles produce carbon dioxide, a large amount of it is converted to bicarbonate, increasing the pH in the blood. The opposite effect occurs in the lungs, where the increased ventilation rate removes excess carbon dioxide, lowering the pH. The balance between these two events must be carefully maintained to preserve a near neutral pH in the body and avoid the problems associated with alkalosis or acidosis.

There is usually a brief, abrupt ventilation increase at the onset of exercise, thought to be due mostly to psychic stimuli, but ventilation soon levels off and continues to increase more slowly as exercise is prolonged. First there is an increase in the depth of respiration, then

an increase in respiratory rate as the exercise becomes more strenuous. During mild to moderate exercise, arterial pH, carbon dioxide partial pressure, and oxygen partial pressure all remain relatively constant (Ganong, 1993).

When the level of exercise becomes more severe, greater amounts of lactic acid may be produced by the muscles, and the bicarbonate must be utilized as a buffer. More carbon dioxide is liberated and ventilation increases further. The partial pressure of carbon dioxide then decreases as the partial pressure of oxygen increases due to this respiratory compensation for the resulting metabolic acidosis. Some of the lactic acid (about 20 percent) is metabolized to produce more carbon dioxide, so the respiratory quotient can increase considerably (Ganong, 1993).

Ventilation control in our model is based on the chemoreflex control model of Duffin (1972):

$$Q_A = 0.83\left[60 - \frac{60\left(p_a^{O2} - 25\right)}{\left(p_a^{O2} - 25\right) + 2.5}\right] + \frac{115\left(p_a^{CO2} - 37\right)}{\left(p_a^{CO2} - 37\right) + 70} +$$

$$\left[\frac{\left(p_a^{CO2} - 40\right)}{\left(p_a^{CO2} - 40\right) + 70}\right] \times \left[2220 - \frac{2220\left(p_a^{O2} - 25\right)}{\left(p_a^{O2} - 25\right) + 2.5}\right]$$

Shivering

When the ambient temperature is significantly cool and the subject is at rest, core temperature starts to fall and triggers a shivering

response. The muscle metabolism automatically increases to produce heat. This shivering response is triggered by hypothalamic stimulation, as will be discussed in the next chapter. The primary motor center for shivering, which is normally inhibited, becomes activated and transmits impulses that increase the skeletal muscle tone. This causes an initial increase in metabolism and, when the muscle tone rises above a threshold level, initiates the muscle contractions of shivering. At maximum shivering, body heat production can increase by a factor of five (Guyton, 1976).

Since the typical thermal comfort zone for core temperature ranges between 36.6 and 37.1°C (Astrand and Rodahl, 1977), we have set a controller in our model to automatically increase muscle metabolism when core temperature falls below 36.6°C so that:

$$\Delta M_{sh} = \alpha_{sh}(36.6 - T_C)$$

The value chosen for $\alpha_{sh} = 0.3$ is based on the steady state values for core and skin temperatures given by Coffey and Seagrave (1972) at ambient temperatures as low as 18°C.

OTHER REGULATORY FACTORS AND THEIR LIMITATIONS

Minimum Oxygen Concentrations and Effects on the Dissociation Curves

The changes in ventilation that occur during exercise are closely related to the changes that are occurring at the cellular level. When muscles are exercising, more oxygen diffuses out of the blood stream (more oxygen is removed from hemoglobin) and the resulting venous P^{O2} drops severely. The P^{O2} in venous blood leaving the cells can only decrease to the value in equilibrium with the oxygen present in the cells and fluid layer between the blood and cells (interstitial fluid). Guyton (1976) states that, in heavy exercise, muscle cells can utilize oxygen at such a rapid rate that interstitial fluid P^{O2} can fall as low as 15 mmHg. At this pressure, about 4.4 ml of oxygen remains bound with hemoglobin in each 100 ml of blood. In our model, we have, therefore, set $X_M{}^{O2}$ at 0.044 ml O2/ml blood when oxygen uptake reaches its maximum. Also, we prevent $X_C{}^{O2}$ from decreasing below 0.044 ml O2/ml blood when Q_C decreases in diverting blood flow from internal organs to the muscles during exercise.

The fraction of blood that gives up its oxygen to the tissues is known as the utilization coefficient. Normally it is about 0.25. The highest value that can be obtained for the overall body is 0.75 to 0.85 during strenuous exercise. In local areas, if the blood flow is very slow and/or the metabolic rate is very high, the utilization coefficient can approach 1.0 (where all of the oxygen is removed) (Guyton, 1976).

Another change that takes place during exercise is that the small arteries in the muscles are dilated to increase blood flow, so the distance that the oxygen molecule must travel from the blood to the muscle tissue cells is greatly decreased. Also, the rise in temperature and accumulation of carbon dioxide (the Bohr effect) serve to shift the curve to the right, this too facilitating oxygen extraction from the blood (Ganong, 1993).

The carbon dioxide dissociation curve is also affected by these changes. The Haldane effect (the tendency of oxygen binding with hemoglobin to displace carbon dioxide from the blood) is even more significant for promoting carbon dioxide transport than the Bohr effect is for promoting oxygen transport (Guyton, 1976). When oxygen and hemoglobin combine, the acidity of the hemoglobin is increased, so carbon dioxide is less likely to combine with hemoglobin and the hydrogen ions in the acidified blood combine with bicarbonate ions forming carbonic acid and then releasing carbon dioxide from the blood. Therefore, both release of carbon dioxide in the lungs and pickup of carbon dioxide from the cells are enhanced by the Haldane effect.

The Role of the Nervous System

Thermoregulatory adjustments that take place involve local responses as well as more general reflex responses. When exercise is begun, a rise in core temperature is sensed by central thermodetectors, primarily in the anterior hypothalamus and spinal cord, to provide the signal for increased skin blood flow and the initiation of sweating.

Cutaneous temperature receptors (especially cold receptors) located in the subcutaneous tissues signal the hypothalamic temperature centers about changes in skin temperature; such as those brought about by a change in ambient temperature. Cutaneous veins will not react to exercise or local cooling when body skin temperature is elevated. Reflex responses activated by cold are controlled from the posterior hypothalamus and their stimulation causes a shivering response. Reflex responses activated by heat are controlled from the anterior hypothalamus and their stimulation causes cutaneous vasodilation and sweating (Ganong, 1993).

The sympathetic nervous system is especially important in regulating circulatory control. Increased sympathetic nervous outflow in proportion to the severity of exercise causes increased heart rates. This is believed to be accompanied by increased sympathetic vasomotor outflow to visceral organs, such as renal and splanchnic beds, which causes their constriction. In heat stress without exercise, sympathetic nervous outflow increases in proportion to the rise in arterial blood temperature.

When cutaneous vasodilation is opposed by vasoconstriction during exercise in the heat, it is sympathetic nervous activity that causes the vasoconstriction. This is also this stimulus that is thought to vasoconstrict exercising muscles to help meet thermoregulatory demands. Vagal activity is also important in man, but evidence shows that man relies more on sympathetic activity, in contrast to some other species, such as the dog, which rely more on vagal activity. Some

other animals, most notably primates, rely on sympathetic activity to an even greater extent than humans (Rowell, 1974).

Chemical Factors and Hormonal Regulation

Chemical factors are also important in the control of constriction or dilation of blood vessels. An increase in calcium ion concentration will stimulate smooth muscle contraction, leading to vasoconstriction. Increasing potassium ion concentration will have the opposite effect, inhibiting smooth muscle contraction and causing vasodilation. If the concentration of magnesium ions is increased, an even more powerful vasodilation effect results from smooth muscle inhibition (Guyton, 1976).

If the osmolality of the blood is increased, arteriolar dilation results. This can occur due to increases in sodium ions, glucose, or other nonvasoactive substances. Acetate and citrate are the only anions that have shown significant effects on blood vessels. Their presence can cause mild vasodilation (Guyton, 1976).

pH can also have an effect on arteriolar dilation. A slight decrease in hydrogen ion concentration causes arteriolar constriction, but a severe decrease can cause dilation. Any level of increase in hydrogen ion concentration appears to cause dilation of arterioles (Guyton, 1976).

Carbon dioxide has a varied effect on vasodilation/constriction. In most parts of the body, an increase in the carbon dioxide concentration will cause moderate vasodilation. In the brain, it will cause even more

severe vasodilation, but if it acts on the vasomotor center, it can become a powerful vasoconstrictor (Guyton, 1976). It is possible that this is an important factor during exercise, and that carbon dioxide only begins acting on the vasomotor center when the maximal oxygen uptake is approached and central blood volume is being compromised.

Several hormones have also been shown to have significant dilation and constriction effects on the blood stream. Angiotensin is the most powerful vasoconstrictor. Vasopressin has a similar vasoconstricting effect, but acts only on the arterioles (angiotensin acts on the veins, as well). Vasopressin's main effect is the control of reabsorption of water from the renal tubules, but it can also act to substantially increase arterial pressure (Guyton, 1976).

Histamine is a powerful dilator for arterioles. Bradykinin also causes vasodilation and it has been claimed that it plays a role in regulating skin blood flow. In fact, many of the small polypeptides that are known as kinins are believed to be involved in blood flow regulation (Guyton, 1976).

Norepinephrine and epinephrine are secreted from the adrenal medulla when the sympathetic nervous system is stimulated. Norepinephrine is universally a vasoconstrictor. Epinephrine is often a constrictor, but in some vascular beds (including most types of muscle) it acts as a vasodilator. Serotonin can also act as a vasoconstrictor or a vasodilator, depending on the area of circulation or condition. Some prostaglandins cause vasoconstriction while others cause vasodilation (Guyton, 1976).

The Importance of Vasoconstriction and Related Effects

Vasoconstriction is discussed throughout this work as a primary means for preserving central blood volume and central pressures. Other factors may also contribute to this effect, but usually they are not as significant. The force of ventricular contraction could increase (increased inotropic influence), for example, to help increase the ejection fraction. This cannot occur, however, when the heart rate is high and cardiac filling time is short (Nadel, Fortney, and Wenger, 1980). Venomotor adjustments can also be an important factor. When peripheral veins are constricted, blood is still shifted centrally to serve in maintaining central blood volume, cardiac filling pressure, cardiac output, etc. Still, vasoconstriction, not venoconstriction, of the skin is most important in maintaining central pressures because it aids in reducing the rate at which cutaneous veins fill (Rowell, 1977).

MODEL VALIDATION

The Basic Model with Exercise

The basic model was developed for a 30°C ambient temperature and steady-state resting conditions ($\Delta M = 0$). This ambient temperature was chosen because it is very close to the minimum for humans to maintain a resting thermal balance. Astrand and Rodahl (1977) state that nude humans require an ambient temperature of 28°C to have a resting metabolic rate within the thermal comfort zone. This means that, at this temperature, no shivering should be present, but skin blood flow should be very low. The 30°C ambient temperature was chosen as the setpoint level for our controllers because more data could be found to test the model at this temperature than at 28°C.

We can see that changes in exercise at this ambient temperature produce the expected increases in temperatures. At rest, muscle temperature is lower than core temperature, and skin temperature is much lower than muscle temperature. When exercise is begun, muscle temperature quickly increases to a value greater than core temperature. Core temperature also increases after a short, initial dip. This dip has been observed by Saltin and Hermansen (1966) as a common trend during the first 3 minutes of exercise. Skin temperature also increases, quickly at first, with a slight, subsequent dip, then a rise again to a new steady state. The initially fast rise presumably occurs because the evaporative heat loss, Qv, which is mainly a

function of core temperature, also falls initially then begins to increase.

Figure 3 shows comparisons of our model predictions with the results of Saltin, Gagge, and Stolwijk (1968) for subjects exercising at three different work loads in a 30°C environment. The predictions for sweat rate match well with the empirical equation used in its prediction. The gain on the equation for skin blood flow is set so that core temperature matches the measured value for rectal temperature at the lowest level of exercise. Results then show that at the lower exercise levels, skin temperature is underpredicted while it is slightly overpredicted at the highest exercise level. Muscle temperature is universally underpredicted in this case. The most likely reasons for this will be discussed in the next chapter.

Changing Ambient Temperatures and Exercising

When ambient temperatures are increased or decreased, the model is allowed to approach a new steady-state in the changed environment to simulate a subject being introduced into a new environment and achieving a thermal balance. If the environment is cold enough to cause the subject's core temperature to fall below 36.6°C, he will shiver, bringing his temperature back up. If he then starts to exercise, shivering will stop as soon as his core temperature warms up above 36.6°C.

Figure 4 shows a comparison between Saltin and Hermansen's (1966) values for esophageal, rectal, and muscle temperatures measured after

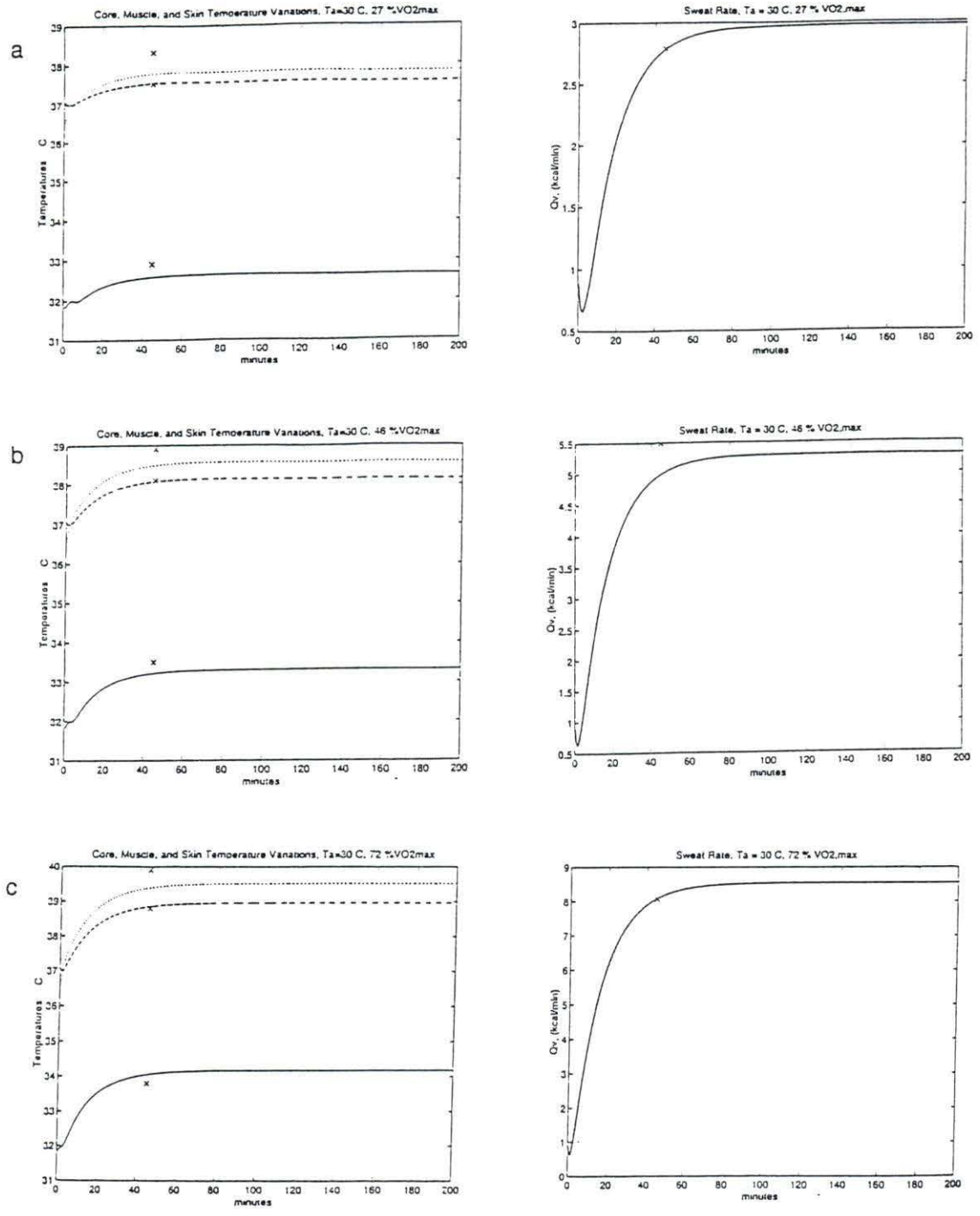
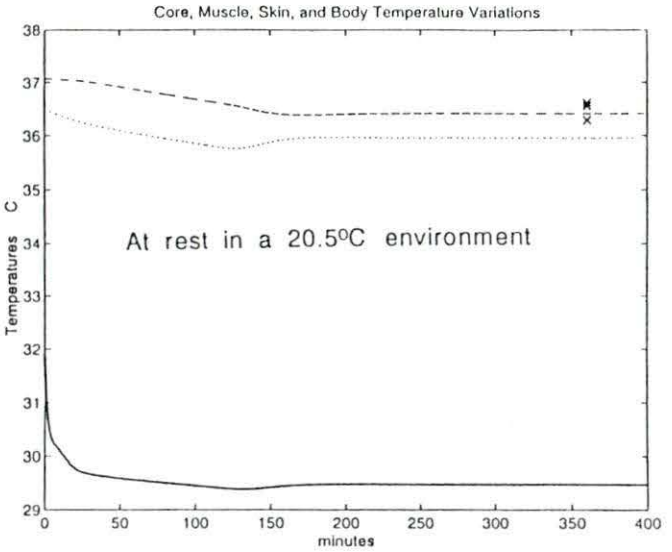
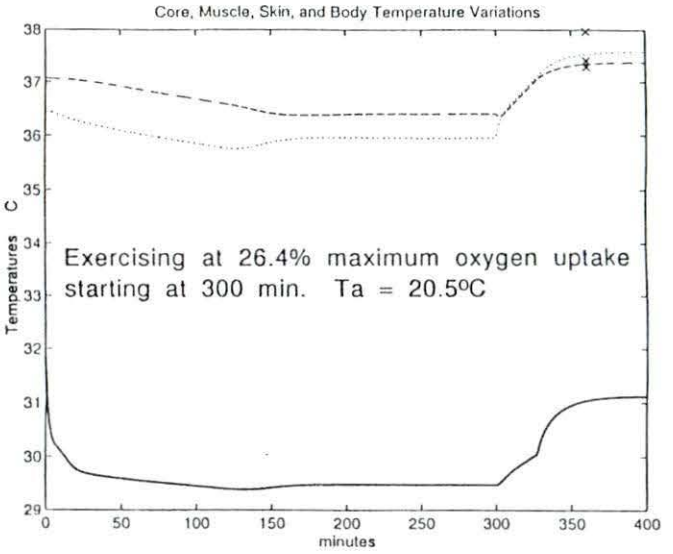
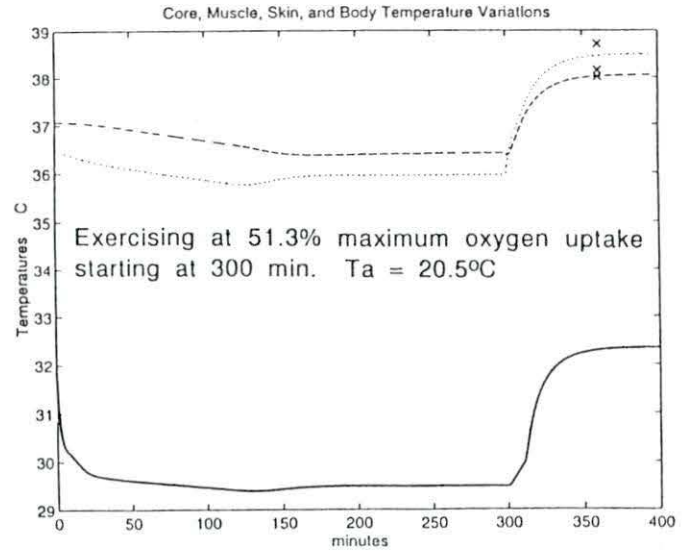


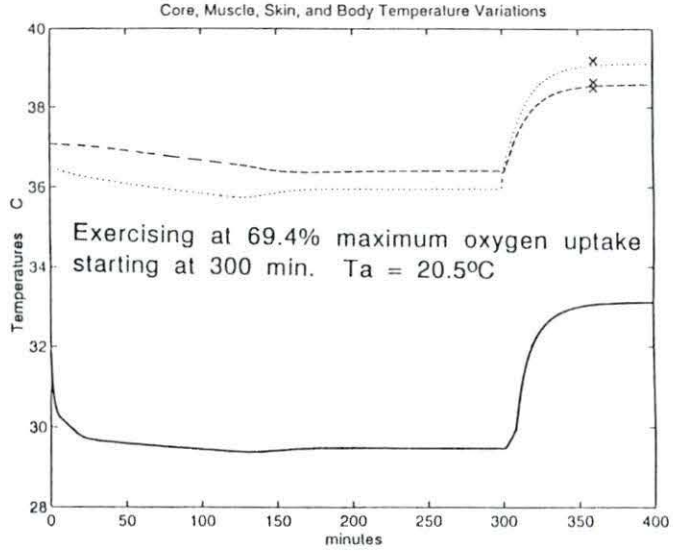
Figure 3: Measured values (X) for rectal, muscle, and skin temperatures and heat lost through sweat (data taken from Saltin, Gagge, and Stolwijk (1968)) compared with model predictions for core (---), muscle (.....), and skin(___) temperatures and Q_V.

Figure 4: Predicted values for core (---), muscle (.....), and skin (____) temperature compared with the data (X) of Saltin and Hermansen (1966).


Core, Muscle, Skin, and Body Temperature Variations
At rest in a 20.5°C environment
Temperatures C
minutes


Core, Muscle, Skin, and Body Temperature Variations
Exercising at 26.4% maximum oxygen uptake
starting at 300 min. Ta = 20.5°C
Temperatures C
minutes


Core, Muscle, Skin, and Body Temperature Variations
Exercising at 51.3% maximum oxygen uptake
starting at 300 min. Ta = 20.5°C
Temperatures C
minutes


Core, Muscle, Skin, and Body Temperature Variations
Exercising at 69.4% maximum oxygen uptake
starting at 300 min. Ta = 20.5°C
Temperatures C
minutes

60 min of exercise in a 20.5°C environment. The resting values are slightly underpredicted by our model; shivering is apparently greater in the resting subjects or they are wearing more clothes. The core temperature prediction usually falls between the measured values for rectal and esophageal temperatures during exercise. Muscle temperature is underpredicted by the model. At higher exercise levels, the predicted value is closer to the measured.

Steady-State Comparisons

As shown in previous examples, temperatures throughout the body typically increase to a new steady state when exercise is performed. Skin temperature, however, has been shown to increase, decrease, or stay the same, depending primarily on the environment in which the exercise is taking place and on the rate of skin blood flow and evaporative heat loss. Other variables predicted by the model also change as expected when exercise is simulated. Steady-state values for oxygen concentration throughout the blood stream decrease while carbon dioxide concentrations increase. Sweat rate, ventilation rate, muscle and skin blood flow rates, and cardiac output all increase while blood flow to the tissues decreases.

Rowell (1974) compared cardiac output distributions in cool (25.6°C) and hot (43.3°C) environments at various exercise levels. The predictions of this model are compared to his results in Figure 5. The total cardiac output is larger in our model. This appears to be due to the muscle blood flow rate controller being set to maintain a higher

flow rate in all conditions. The major trends are similar except for skin blood flow, which is overestimated during exercise in cool conditions and underestimated during exercise in hot conditions. Rowell (1986) gives evidence that this may occur because exercise increases the threshold core temperature at which skin blood flow begins to increase. If this is true, skin blood flow is increased more by a change in resting ambient temperature than by exercising in a cool environment.

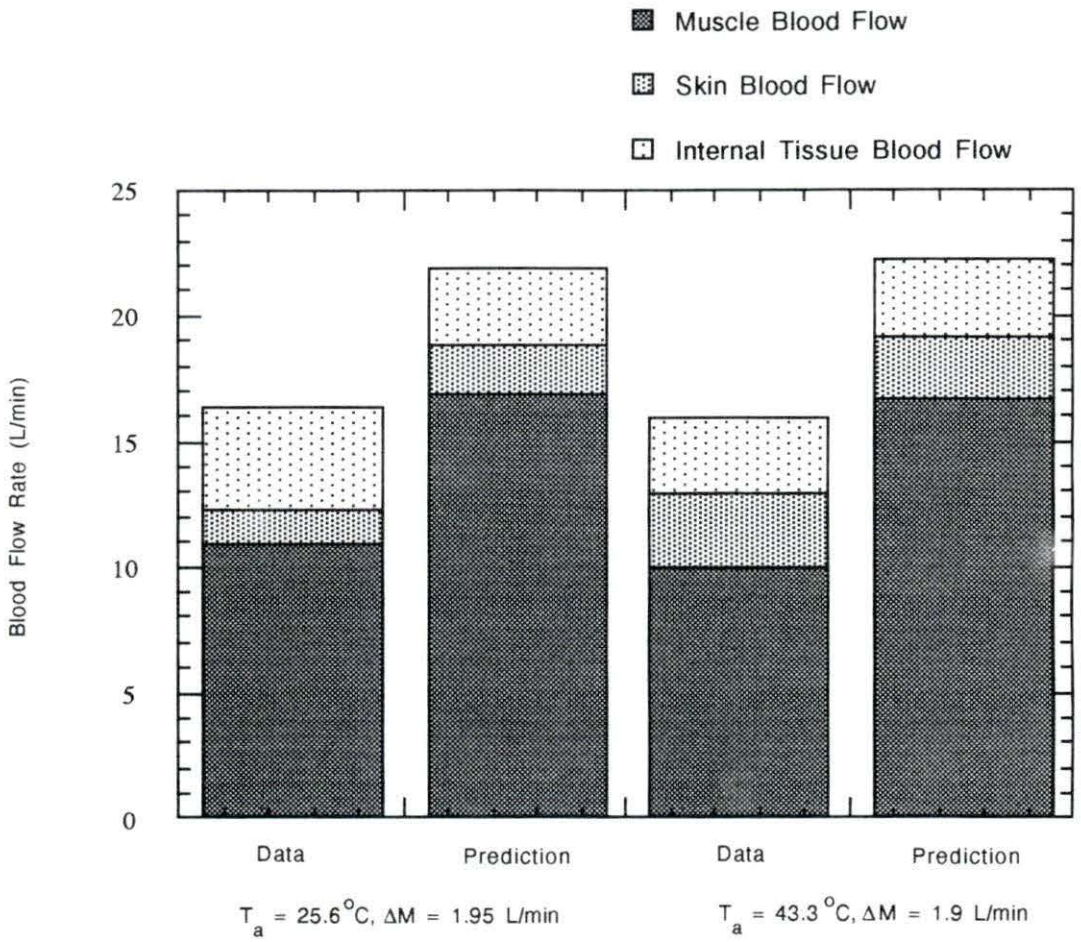


Figure 5: Comparisons between data from Rowell (1974) and the model predictions during exercise at the given temperature.

The measured value for blood flow to internal tissues is decreased more during exercise in heat. Our model predicts that it is already at its minimum value during exercise in the cooler conditions. This could also be explained by the fact that we are assuming Q_C decreases to a minimum before cardiac output begins to increase. Evidence shows that this assumption is fairly reasonable for heat stress conditions, but, as has been found for skin blood flow, the same might not be true for exercise with no heat stress.

Another variable which is often studied in experiments involving the cardiovascular system is the A-V oxygen difference. It is easy to measure through blood sampling and, as shown in Figure 6, comparable to our model results. Two major differences between these two plots need to be pointed out. First, our model predicts that oxygen concentration in the muscles is higher at rest than in the mixed venous blood. This is most likely due to an overestimated resting muscle blood flow rate in our model. In fact, when $Q_{M,0}$ was reset at 0.55 L/min our results showed that $X_M{}^{O2}$ was lower than $X_V{}^{O2}$ at rest. It could also be explained by the assigned distribution of resting metabolic rate if our model underpredicts oxygen consumption by the muscles at rest.

The second distinguishable difference between these plots is that the difference between muscle venous and mixed venous oxygen content of the measured values continuously decreases until there is little difference between them. In the predicted results, muscle oxygen content quickly decreases, but then the difference between muscle and mixed oxygen content becomes nearly constant and much larger than is measured. This could be the result of several factors. It has been

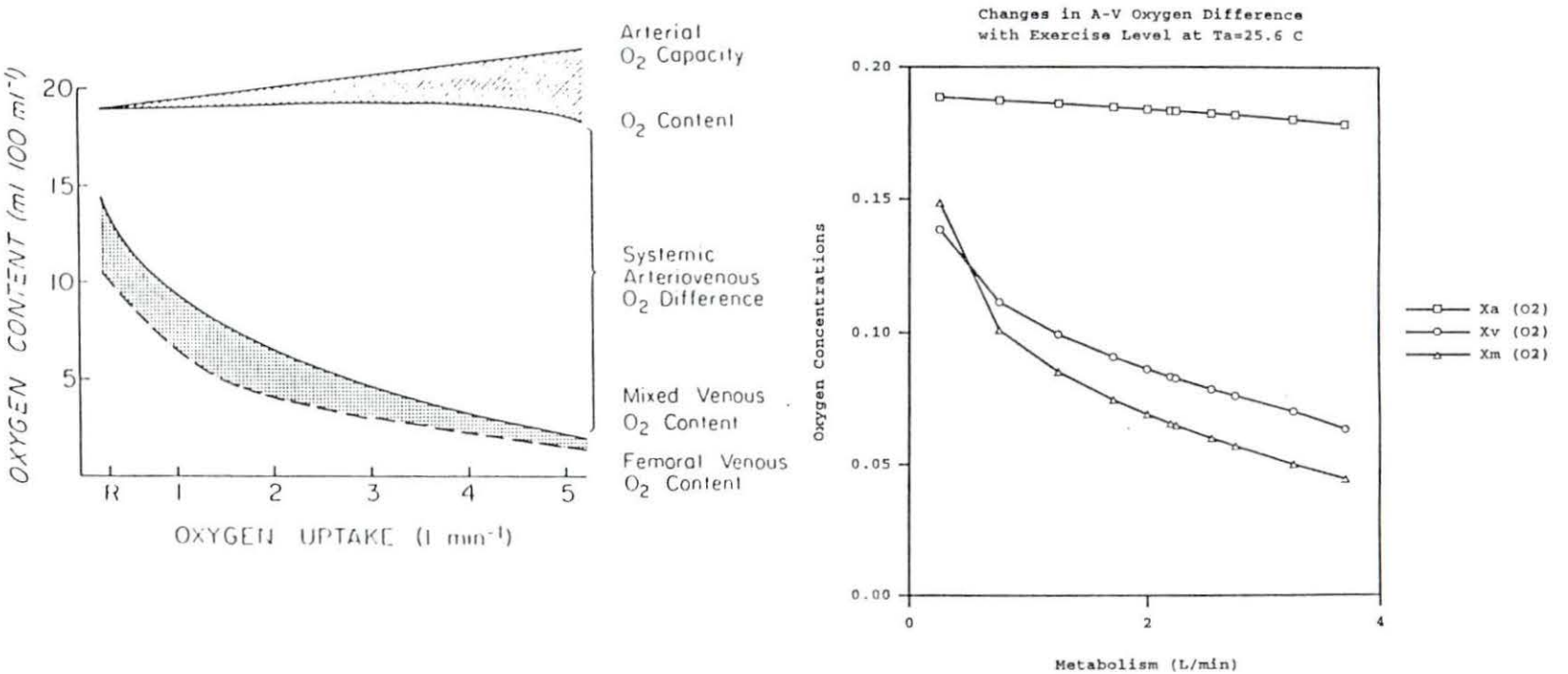


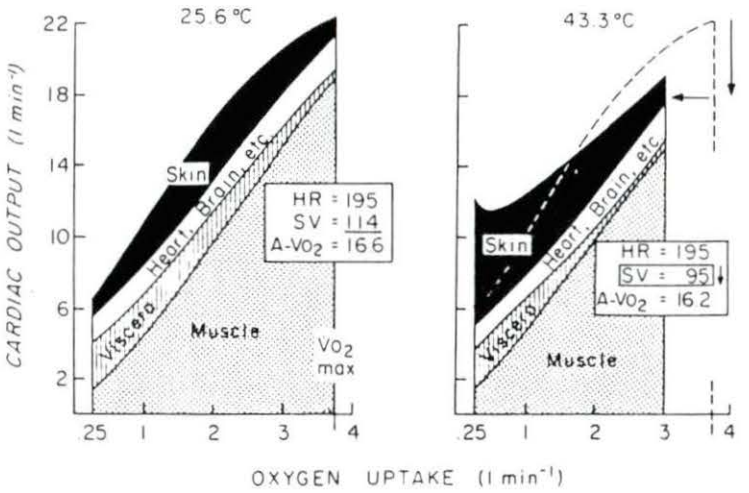
Figure 6: Oxygen content data (taken from Rowell, 1986) compared to model predictions.

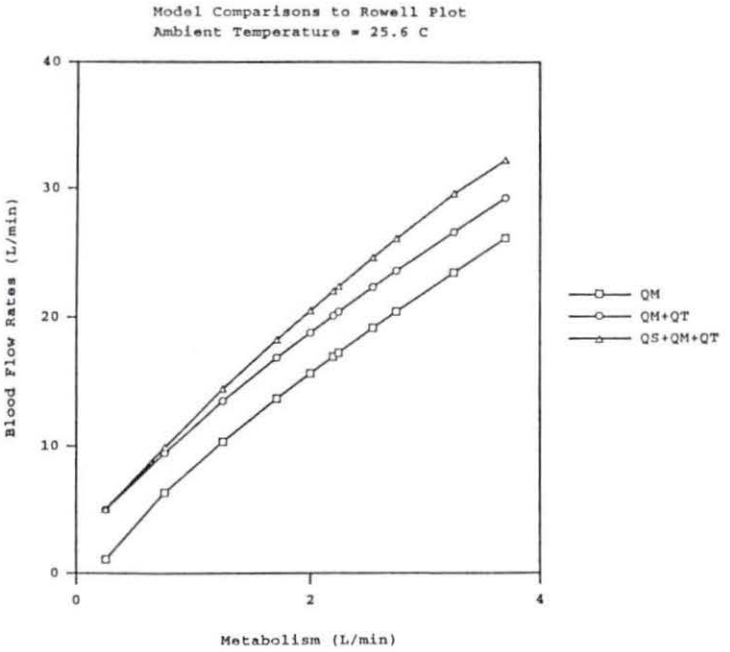
shown that skin blood flow in our model is overpredicted in this case, so the calculation of mixed venous oxygen content would be high. Rowell does not give a temperature at which his data were obtained, but states that data from various studies were used. Even if skin blood flow was high, much of the blood would remain pooled in the cutaneous veins and the oxygen content of the mixed venous sample would not be as affected by it as much as our calculations would indicate.

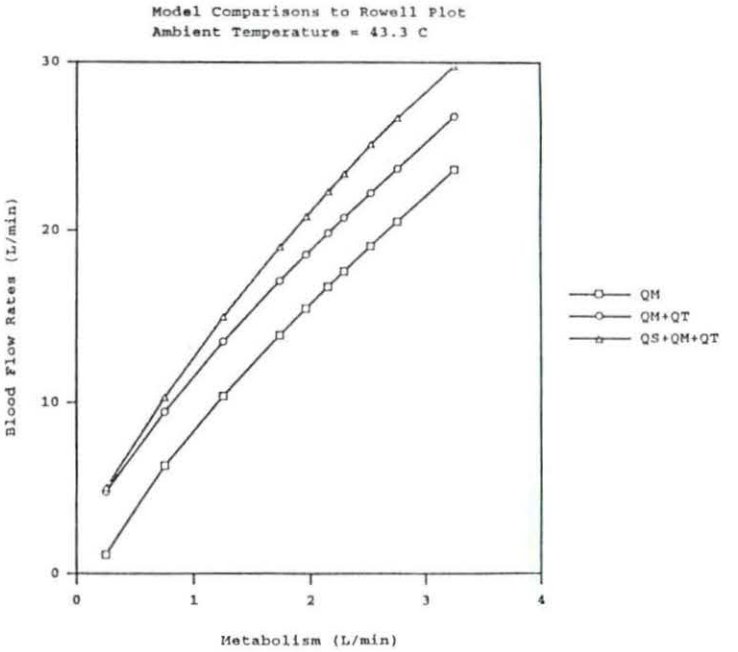
Other apparent differences between model predictions and measured values can be explained by where the parameters of the model were set. Maximum oxygen uptake in our model is not as high and muscle venous oxygen content is not allowed to decrease as much as in these results. These parameters were set according to average values given in literature. The observed trends, mainly that the A-V oxygen difference increases during exercise up to the maximum oxygen uptake, are the same.

Figure 7 shows steady-state results for the blood flow model predictions at various oxygen uptakes up to the maximum oxygen uptake, and a comparison with the theoretical blood flow distribution of Rowell (1986). At 25.6°C, both predictions are comparable. A few differences do exist. In the model, skin blood flow continuously increases during exercise and does not begin to level out as it does in Rowell's diagram. Our maximum cardiac output is higher, as set by the gain on the skin blood flow controller. This is in agreement with data from other sources. Lastly, blood flow to internal tissues decreases to a minimum initially in our model, but the theory of Rowell shows that during exercise at this temperature, cardiac output rises significantly

Figure 7: The theory of Rowell (1986) compared to model predictions for blood flow distributions in 25.6°C and 43.3°C ambient temperatures.


25.6 °C
43.3 °C
CARDIAC OUTPUT (l min⁻¹)
OXYGEN UPTAKE (l min⁻¹)
Skin
Heart, Brain, etc.
Viscera
Muscle
HR = 195
SV = 114
A-Vo2 = 16.6
HR = 195
SV = 95
A-Vo2 = 16.2
Vo2 max


Model Comparisons to Rowell Plot
Ambient Temperature = 25.6 C
Blood Flow Rates (L/min)
Metabolism (L/min)
QM
QM+QT
QS+QM+QT


Model Comparisons to Rowell Plot
Ambient Temperature = 43.3 C
Blood Flow Rates (L/min)
Metabolism (L/min)
QM
QM+QT
QS+QM+QT

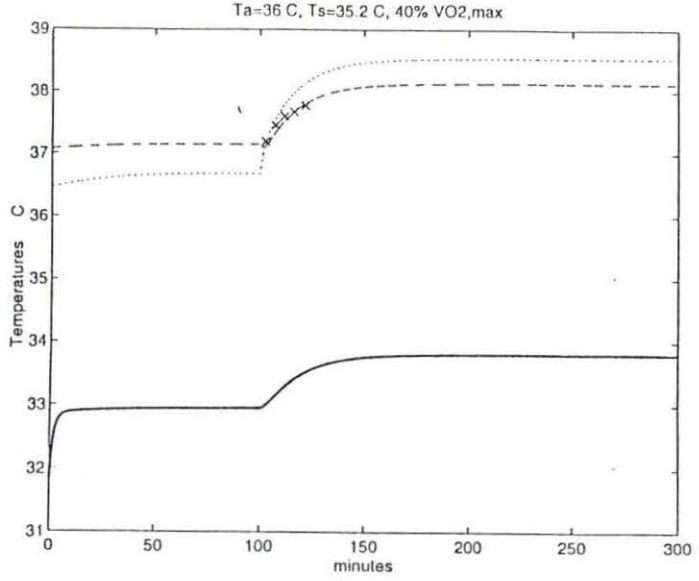
before it starts to decrease.

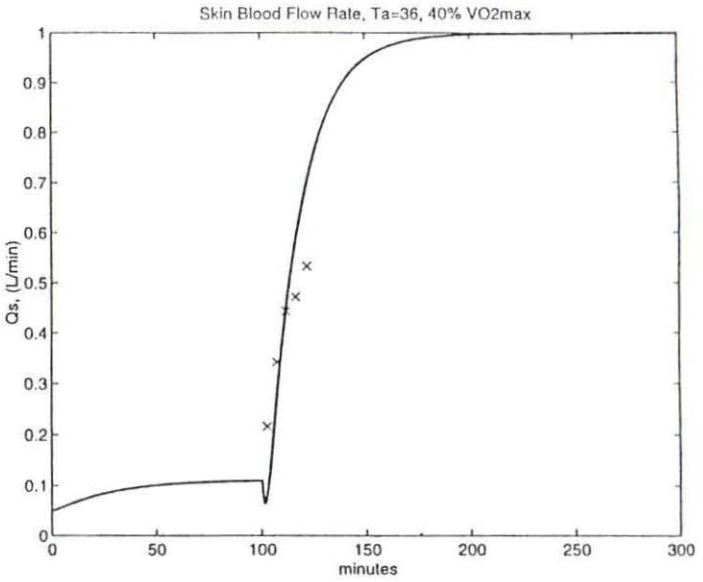
At 43.3°C, more significant differences in the predictions occur. Most obviously, Rowell's skin blood flow is initially higher (by several L/min) than our model prediction shows. It then decreases sharply at low levels of exercise and continues to decrease more slowly as exercise becomes more strenuous. In our model, skin blood flow increases up to a maximum then stays constant. The same comparisons can be made about internal tissue blood flow as were made in the 25.6°C case. In Rowell's prediction here, visceral blood flow decreases to a smaller minimum while blood flow to the heart, brain, etc. increases slightly. Rowell states that the maximum oxygen uptake attainable in this case will be lower than at the cooler temperature. He attributes this to a reduction in stroke volume and states that the maximum cardiac output attainable will also be lowered. We assume complete water replacement in our model, but the maximum oxygen uptake appears to be reached at a similar metabolism level, limited in our case by the extremely high temperatures observed (T_c > 41.1°C) at oxygen uptakes near 3 L/min.

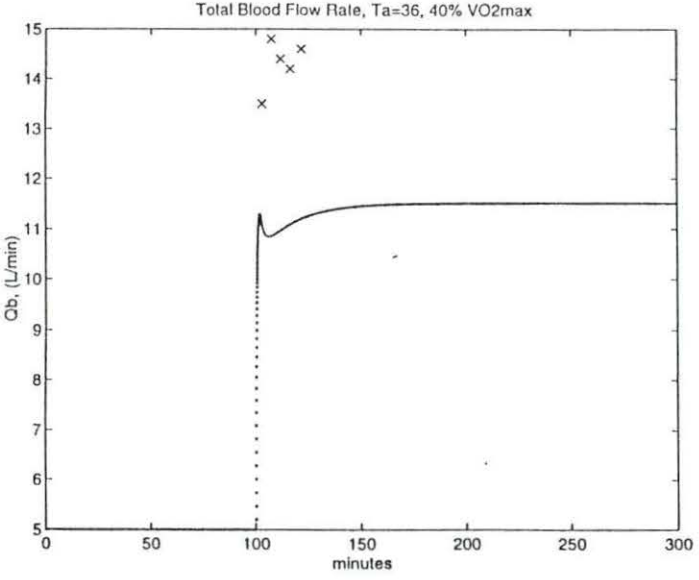
Dynamic Validations

Dynamic changes in esophageal temperature, skin blood flow, and cardiac output during the first few minutes of exercise were recorded by Nadel, Cafarelli, Roberts, and Wenger (1979). Sample comparisons with the model predictions are given in Figure 8. Temperature and skin blood flow predictions appear to be good in most cases. The predicted

Figure 8: Model predictions for core (---), muscle (.....), and skin (___) temperatures, cardiac output, and skin blood flow compared with the measured data (X) of Nadel, Cafarelli, Roberts, and Wenger (1979) over time.


Ta=36 C, Ts=35.2 C, 40% VO2,max
Temperatures C
minutes


Skin Blood Flow Rate, Ta=36, 40% VO2max
Qs, (L/min)
minutes


Total Blood Flow Rate, Ta=36, 40% VO2max
Qb, (L/min)
minutes

cardiac output, however, consistently underestimates the measured values. This could be a result of inaccuracies in the experimental measurements of cardiac output since other experimental results have shown cardiac outputs lower than predicted here.

Limitations

The present limitations of this model most likely result from the simplicity of the predominantly linear control mechanisms which it employs. This appears to be especially true in the case of skin blood flow. Since there is no adequate means for measuring skin blood flow in vivo (Rowell, 1977), most of the data we find is the result of crude approximations which are inadequate to use as the basis for an empirical model. Because this is the case, we must base skin blood flow control mainly upon skin temperature measurements. These measurements can be subject to a great deal of variability, since skin temperature is highly inhomogeneous during exercise.

Many different resources must be consulted since no experiments have been performed to test all of the variables calculated by this model. This introduces various errors from differing basal conditions in both the environment and the subjects involved in a specific experiment. Also, most studies just include one measurement when the variable appears to be at steady-state, but do not show measurements at different times throughout their experiment. This makes it difficult to validate the dynamic changes of the process.

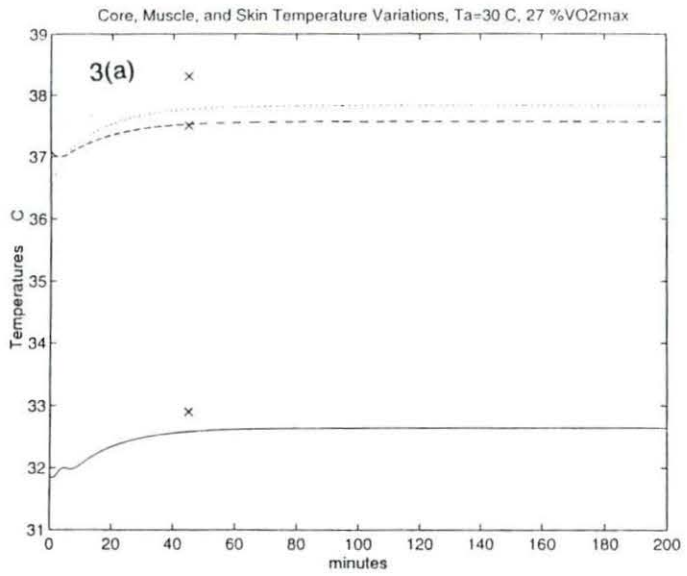
SENSITIVITY OF THE MODEL

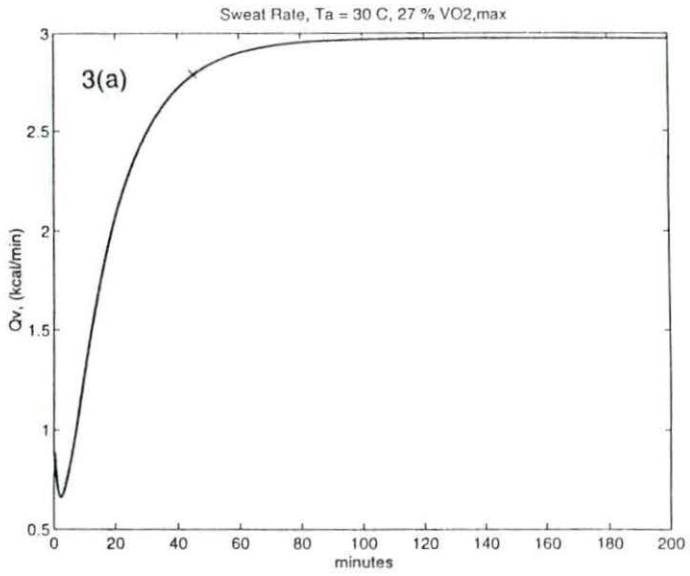
Maximum Oxygen Uptake

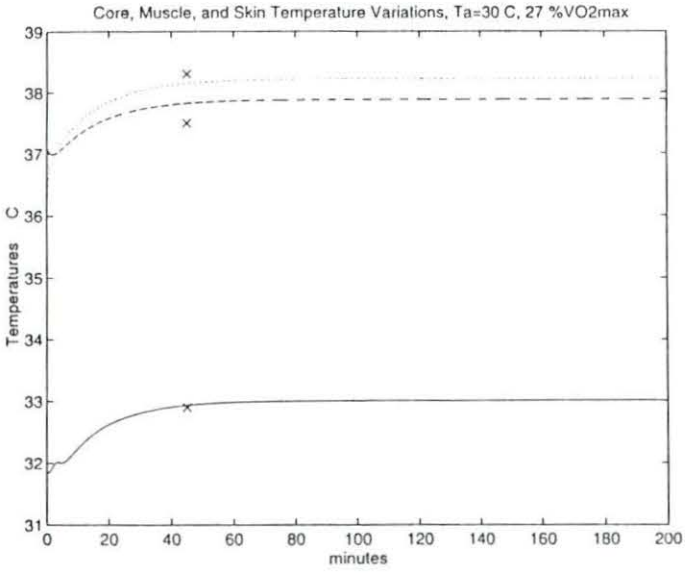
Maximum oxygen uptake is a factor which has been shown to vary greatly between different individuals. For the purposes of our model, setting the exercise level to make a comparison with literature values, we must set a value for maximum oxygen uptake and calculate the exercise level, ΔM, based on a percentage of that number. Two typical values for an average person which were discussed in Chapter 2 of 3.7 L/min and 2.66 L/min were used, keeping all other initially set parameters constant. The gain on muscle blood flow was reset to allow for the minimum oxygen concentration exiting the muscles to be obtained at the maximum oxygen uptake and the relationship between the respiratory quotient and metabolism level was recalculated to find a new slope.

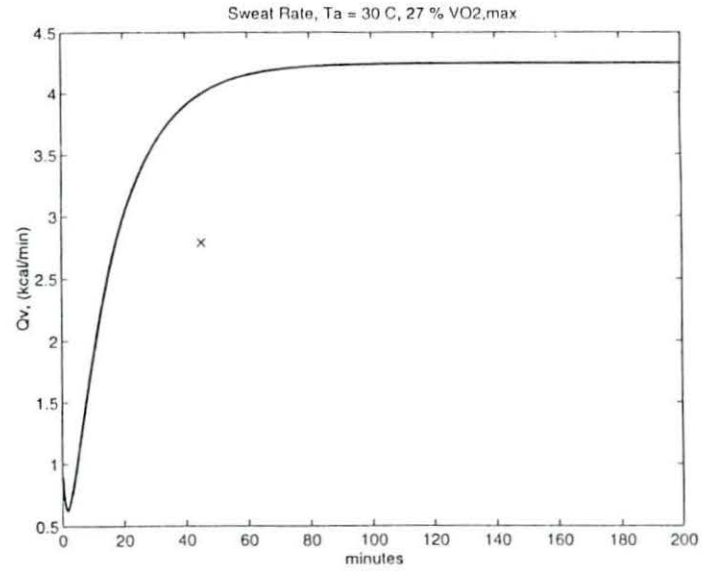
All of the previous predictions shown were made using a maximum oxygen uptake of 2.66 L/min except those in the Steady-State Comparisons section which were compared with data from Rowell et al. who use 3.7 L/min for their average maximum oxygen uptake. Figure 9 can be compared to Figure 3a, showing predicted values for core and muscle temperatures that are now closer to the measured muscle temperature. Sweating rate is now overestimated and the core temperature prediction is high. Other factors, such as an overestimation of muscle to core conduction, may contribute to the prediction of core and muscle temperatures being closer to the same

Figure 9: Results from Figure 3(a) for a maximum oxygen uptake of 2.66 L/min compared with results for a maximum oxygen uptake of 3.7 L/min. Data (X) from Saltin, Gagge, and Stolwijk (1968).


Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
3(a)
Temperatures C
minutes


Sweat Rate, Ta = 30 C, 27 % VO2,max
3(a)
Qv, (kcal/min)
minutes


Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
Temperatures C
minutes


Sweat Rate, Ta = 30 C, 27 % VO2,max
Qv, (kcal/min)
minutes

value than in reality. This example does show, though, that some elements of this model are highly sensitive to the choice of maximum oxygen uptake.

Volume Changes

One important physiological effect of exercise and ambient temperature changes which has not been accounted for in this model is the peripheral redistribution of water when blood flows, especially skin blood flow, are increased. While we assume complete water replacement for sweat losses, we do not increase skin blood volume and decrease core blood volume to account for the water redistribution that occurs when skin blood vessels dilate and skin blood flow increases. As is shown in Figure 10, this only affects the dynamics of our results slightly (the time it takes to reach steady state) and does not affect the final steady-state solution.

Resting Blood Flows

The resting blood flow rates were chosen based on estimates given in literature. Muscle blood flow was set at 1.1 L/min, according to Ganong (1993). This figure does vary considerably when it is approximated in literature. Ganong also gives a value equivalent to 0.55 L/min for blood flow to only active muscles at rest. To test the model sensitivity to changes in resting muscle blood flow rate, we reset $Q_{M,0}$ keeping $Q_{B,0}$ and $Q_{S,0}$ constant. Controllers were removed

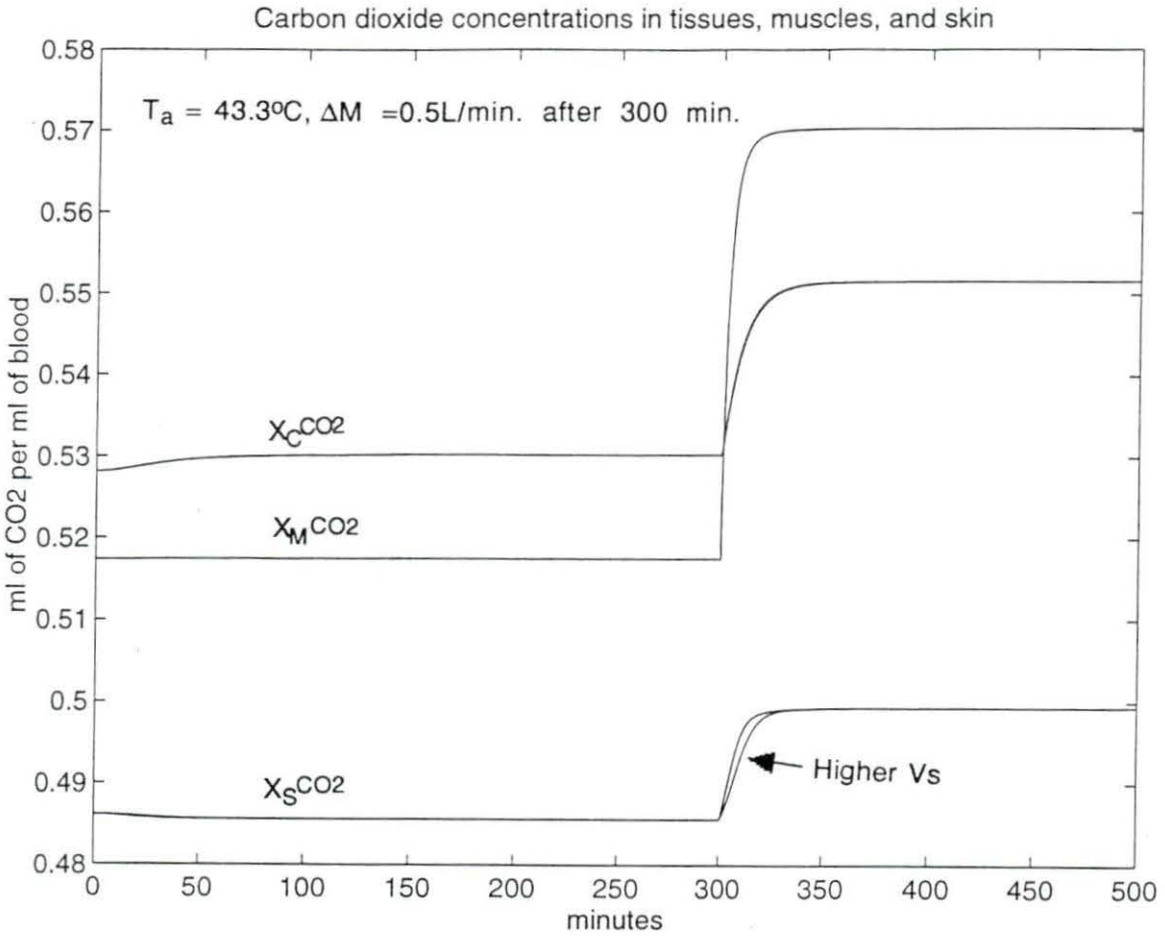


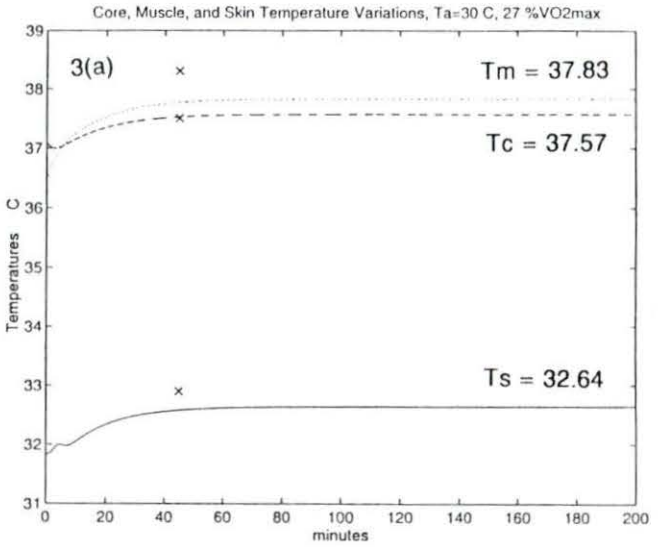
Figure 10: Comparisons of carbon dioxide concentration model predictions before and after doubling skin blood volume; increasing it from 2 to 4 liters and decreasing core blood volume by 2 liters to account for this redistribution. These were the variables most affected by the change.

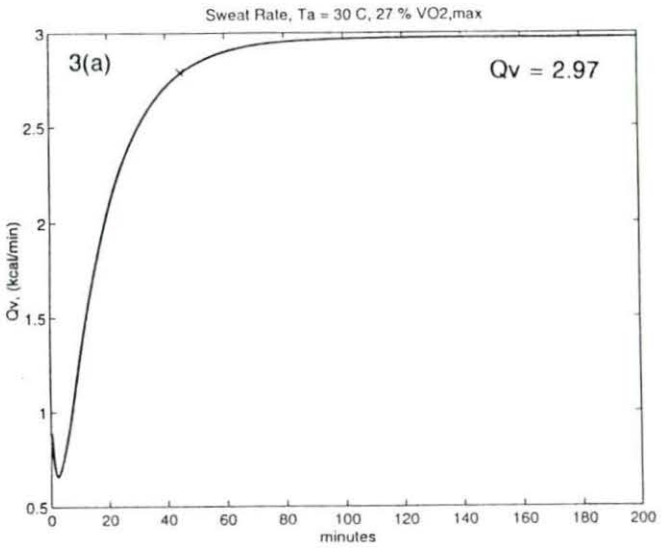
and the model was allowed to reach a steady state at T_a = 30°C. The setpoint for X_M^{O2} was reset to the new result of the mass balance in the Q_M control equation and the controllers were reconnected. When exercise was added, it was found that oxygen was removed from the blood stream to an unrealistic level ($X_M^{O2} < 0.044$), so the gain on the muscle blood flow equation was increased to obtain this value at maximum oxygen uptake.

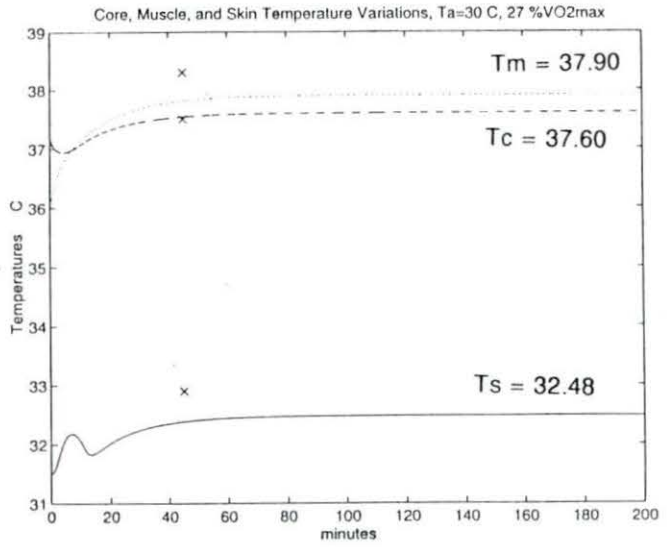
The plots in Figure 11 show a comparison between the result in Figure 3a and the result of our model with the lower $Q_{M,0}$. Figure 12 shows a comparison between these steady-state results at T_a= 43.3°C and ΔM = 1.486 L/min, the original model results for this case, and the data of Rowell, Marx, Bruce, Conn, and Kusumi (1966). The lowered $Q_{M,0}$ has little effect on the model results during exercise when the muscle blood flow gains are increased to prevent impossible mass balance results. The expected temperature results occur at rest and during exercise when core temperature is increased while skin temperature decreases to account for the lowered peripheral blood flow.

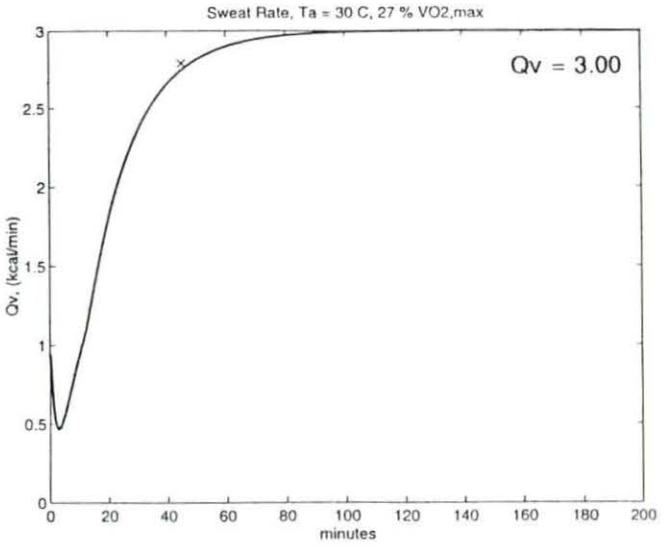
Resting skin blood flow was originally set at 0.05 L/min at 30°C ambient temperature to agree with experimental data. Resting skin blood flows at 0.425 L/min are reported by Ganong (1993), but this was presumably in a warmer environment. If we double the skin blood flow at rest while holding Q_M and Q_B constant and re-solving the steady-state equations at T_a = 30°C again, we find that core and muscle temperatures decrease while skin temperature increases. Evaporative heat loss, therefore, decreases while the mass balances remain

Figure 11: Figure 3(a) (top) compared with the case of resting muscle blood flow halved and muscle blood flow gain, consequently, increased. Data (X) from Saltin, Gagge, and Stolwijk (1968).


Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
3(a)
Tm = 37.83
Tc = 37.57
Ts = 32.64
Temperatures C
minutes


Sweat Rate, Ta = 30 C, 27 % VO2,max
3(a)
Qv = 2.97
Qv, (kcal/min)
minutes


Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
Tm = 37.90
Tc = 37.60
Ts = 32.48
Temperatures C
minutes


Sweat Rate, Ta = 30 C, 27 % VO2,max
Qv = 3.00
Qv, (kcal/min)
minutes

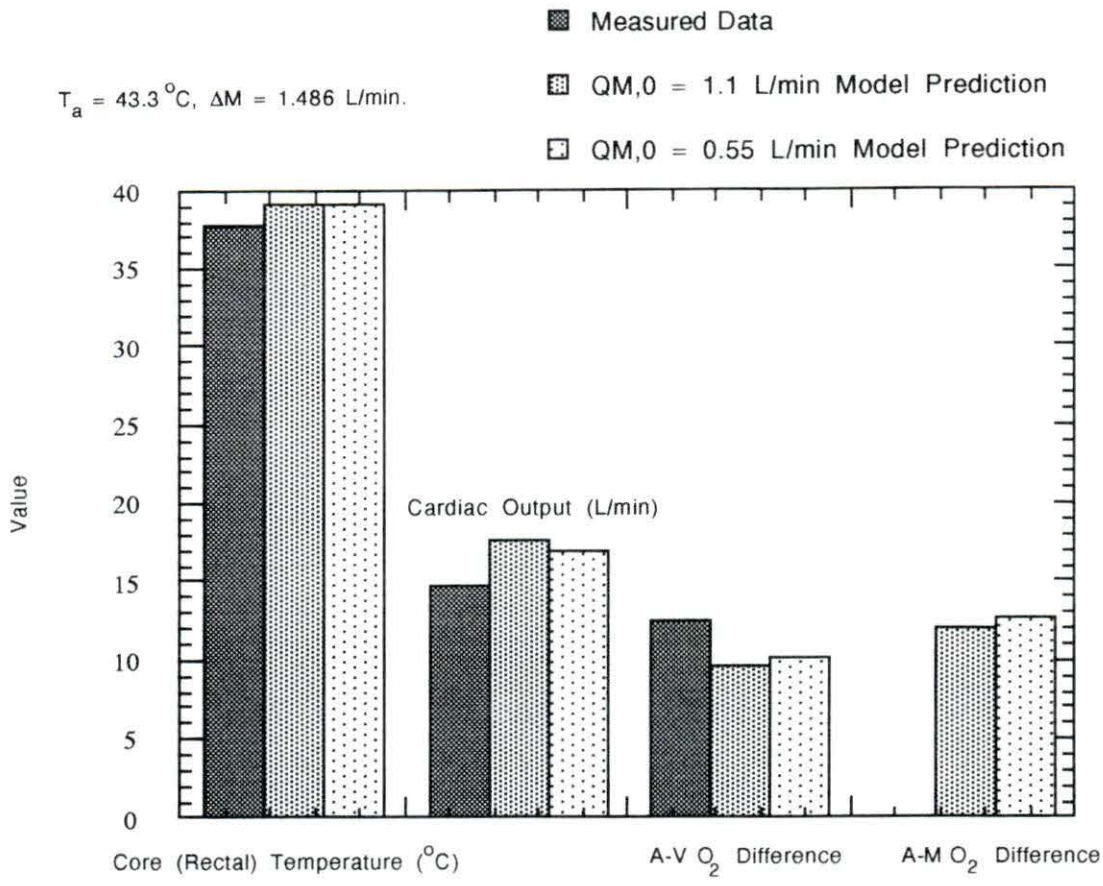
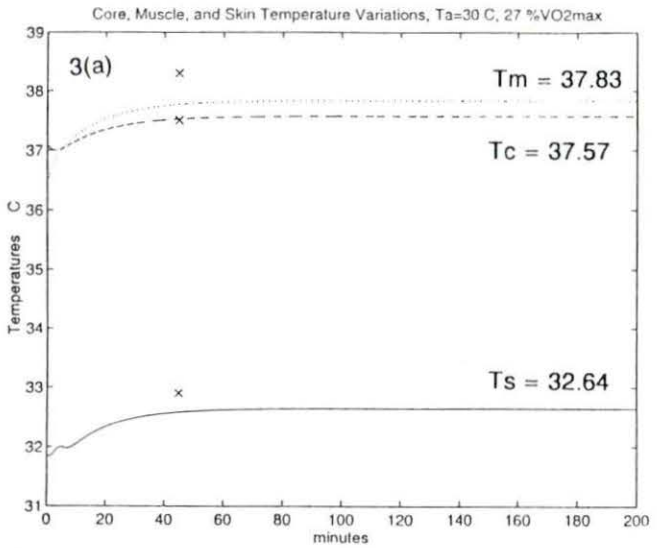


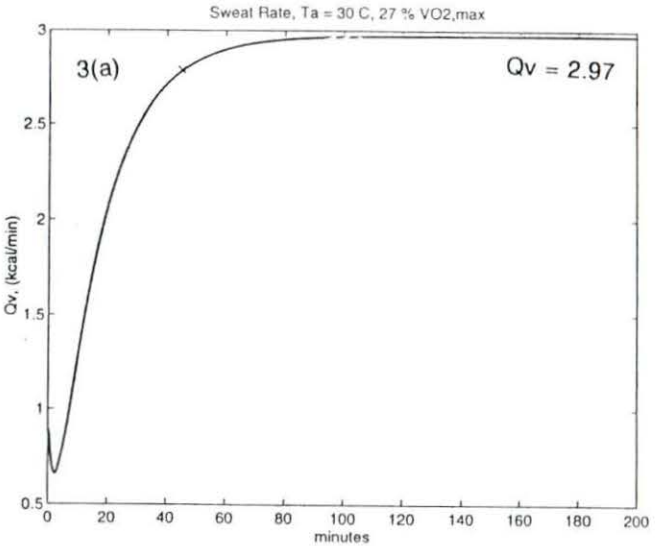
Figure 12: Comparisons between the data of Rowell, Marx, Bruce, Conn, and Kusumi (1966) and the results of our model with two different values for resting muscle blood flow.

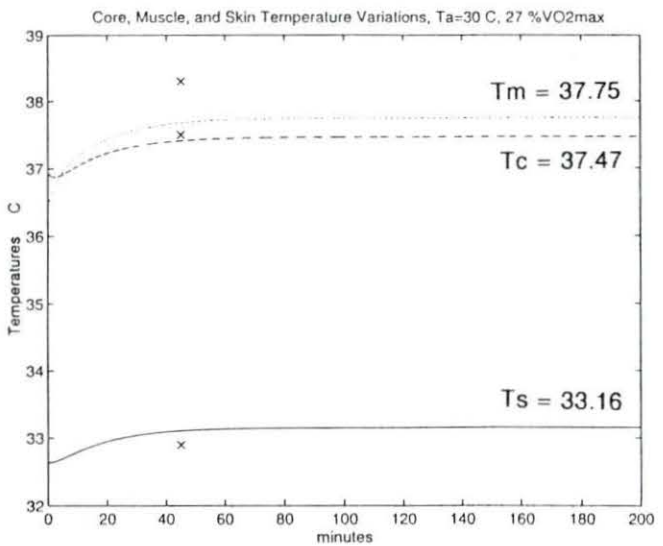
virtually unchanged. As shown in Figure 13, core temperature is now underestimated while skin temperature is overestimated, even at a low level of exercise.

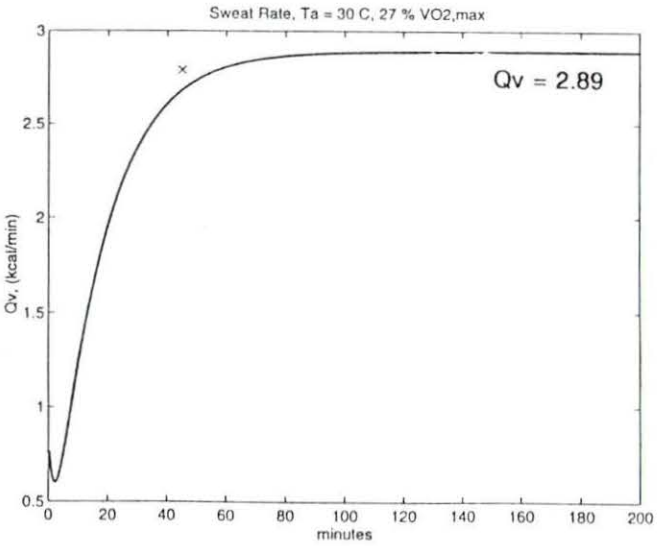
Resting cardiac output is set at 5 L/min for a standard man. In an attempt to study the effects of its variability upon the results of our model, it was set at 6 L/min with the increase reflected entirely in the core compartment since we have already studied changes in resting skin and muscle blood flows. In the resulting steady-state balances,

Figure 13: Comparison between model predictions with resting skin blood flow doubled (bottom) and Figure 3(a) conditions. Data (X) from Saltin, Gagge, and Stolwijk (1968).


Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
3(a)
Tm = 37.83
Tc = 37.57
Ts = 32.64
Temperatures C
minutes


Sweat Rate, Ta = 30 C, 27 % VO2,max
3(a)
Qv = 2.97
Qv, (kcal/min)
minutes


Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
Tm = 37.75
Tc = 37.47
Ts = 33.16
Temperatures C
minutes


Sweat Rate, Ta = 30 C, 27 % VO2,max
Qv = 2.89
Qv, (kcal/min)
minutes

X_C^{O2} (and, consequently, X_V^{O2}) were increased while X_C^{CO2} and X_V^{CO2} decreased. This is consistent with the increased blood flow through the tissue compartment which results. All other variables were the same as when the cardiac output was 5 L/min. Exercise addition to the increased cardiac output model yielded the same results as before, since tissue blood flow still decreases to the same minimum value. Resting cardiac output is a parameter which varies significantly with individual characteristics such as size, age, and fitness level, but its variation does not have a significant effect on our model.

Conduction

In most cylinder-type thermoregulatory models, the effective thermal conductivity is calculated as a combined function of conduction and convection. It is shown to increase during blood vessel dilation to simulate increases in skin blood flow during exercise or increasing ambient temperatures. It decreases to a minimum level in a cold, resting state when blood vessels are constricted.

In this model, since we are separating convection by blood flow from conduction, a value for conduction between the tissue beds had to be estimated. According to Coffey and Seagrave (1972), thermal conductivity approaches a constant value at temperatures lower than 18°C. Since convection should be near a minimum at this point, we used the thermal conductivity to calculate conduction, which can be approximated as remaining constant. Coffey and Seagrave also give estimations for the thickness of each layer (core, muscles, and skin)

which are used in this model. These are then used to calculate the values for K_{CM} and K_{MS} in kcal/min. K_{CM} is always twice K_{MS} due to the values assigned for the thicknesses of the layers.

If these K values are doubled, while holding skin and muscle blood flows constant, the effect is similar to increasing resting skin blood flow (see previous section) considerably. Core and muscle temperatures are underestimated while skin temperature is overestimated at a low level of exercise in neutral conditions, as shown in Figure 14(a). When the original K values are divided by two, the results show the opposite effect, which is also fairly extreme (see Figure 14(b)).

The value of K does appear to have a large effect upon these results, but it can be seen that if K is varied, skin blood flow can be adjusted to achieve agreement with experimental data. It is actually the ratio of conduction to convection (at rest and during exercise) which we are attempting to estimate. At rest, as the K values are increased, the distance between core and muscle temperatures also increases while the difference between muscle and skin temperatures decreases within this range. This observation can be used to check the K values against resting temperature measurements when skin blood flow is low and before shivering begins (near $T_a = 30^oC$), but most references give such a large range for resting muscle temperatures that it would be unrealistic to use one value as a basis for determining the value of conduction.

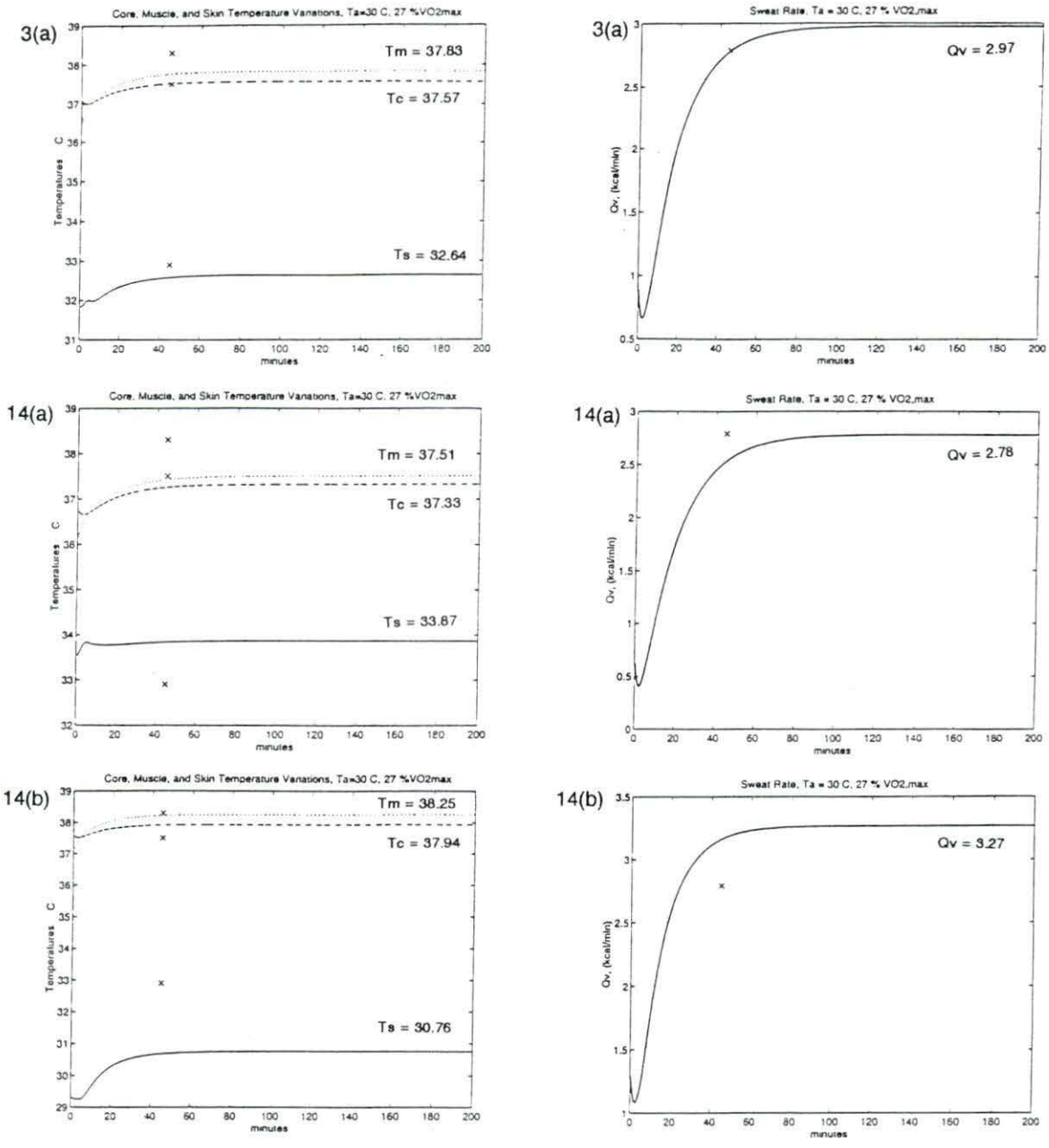


Figure 14: Effects of varying conduction (k). Figure 3(a) (top) is compared with Figure 14(a) (middle) where k is doubled and Figure 14(b) where k is reduced by a factor of two. Data (X) from Saltin, Gagge, and Stolwijk (1968).

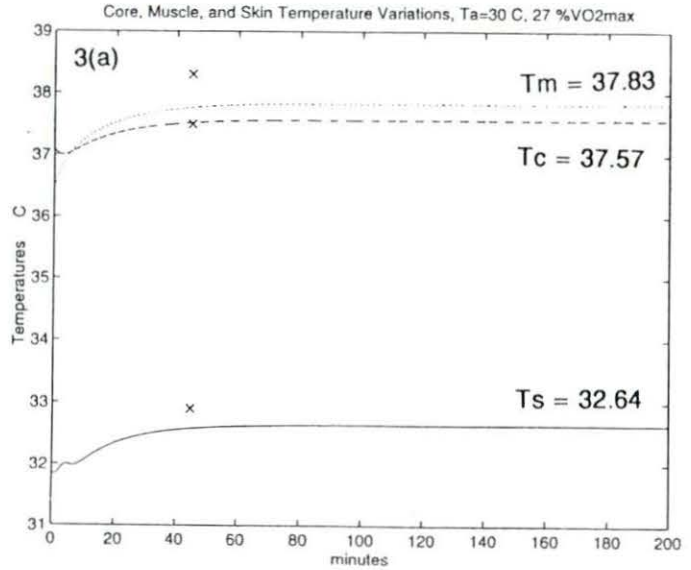
Controller Gains

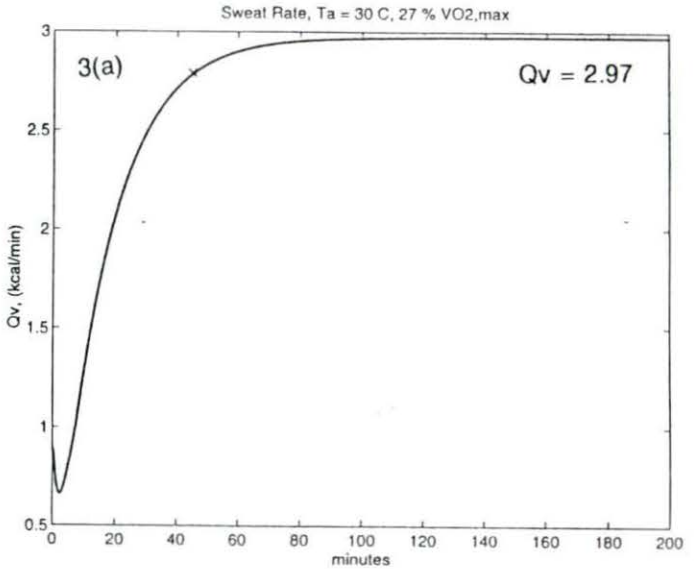
Variation of the controller gains can have significant effects on important variables. The skin blood flow gain, for example, was particularly difficult to determine to account for both ambient temperature changes and exercise. A much higher value is required to support evidence that skin blood flow can reach 7 L/min at rest in a 43.3°C environment. In fact, the gain should be set at 5.7, assuming that below an ambient temperature of 115°F, skin blood flow at rest can be increased by diverting blood flow from internal organs. Above this point, cardiac output must increase to provide more blood flow to the skin for cooling, as was discussed in Chapter 3.

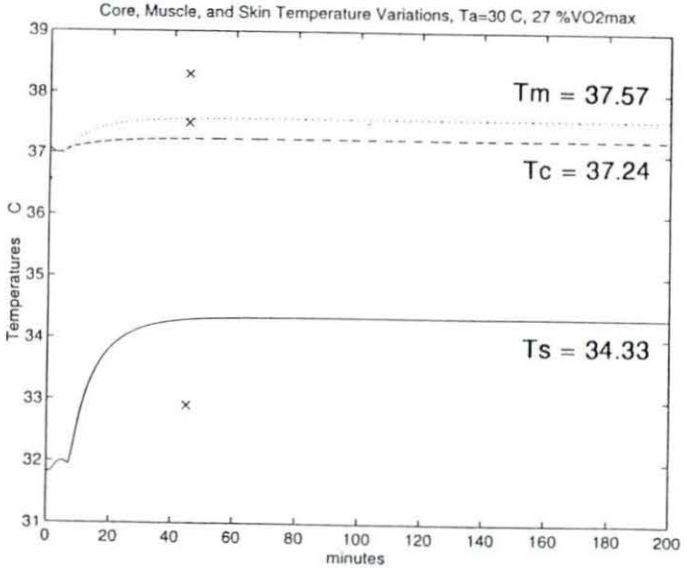
The value of 5.7 is obtained by assuming that Q_C can decrease by 2.2 L/min from the resting state in order to simulate the effects of repartitioning of blood flow from splanchnic and renal regions when their vessels are maximally constricted. This change occurs before cardiac output begins to increase. Figure 15 shows the effects of changing the gain from 0.9 to 5.7 for near neutral ambient conditions and a low level of exercise. Skin blood flow appears to be highly overestimated for this case. It is overestimated even more during higher exercise levels at the same ambient conditions. A value even lower than 0.9 is indicated in some examples of exercise, especially exercising in the cold where shivering was first present.

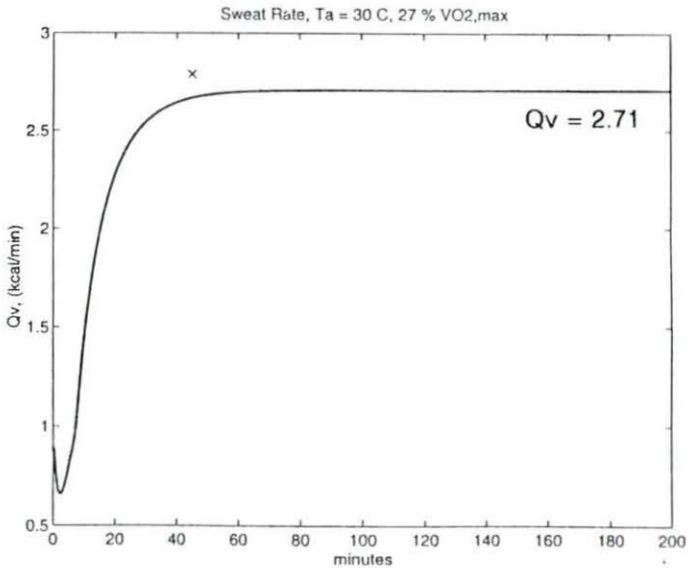
The controller for muscle blood flow does not have as significant an effect on temperature, but does provide the main factor in determining cardiac output. Increasing this gain alone increases the muscle blood

Figure 15: Figure 3(a) results compared to model predictions when the skin blood flow gain is set at 5.7. Data (X) from Saltin, Gagge, and Stolwijk (1968).


Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
3(a)
Tm = 37.83
Tc = 37.57
Ts = 32.64
Temperatures C
minutes


Sweat Rate, Ta = 30 C, 27 % VO2,max
3(a)
Qv = 2.97
Qv, (kcal/min)
minutes

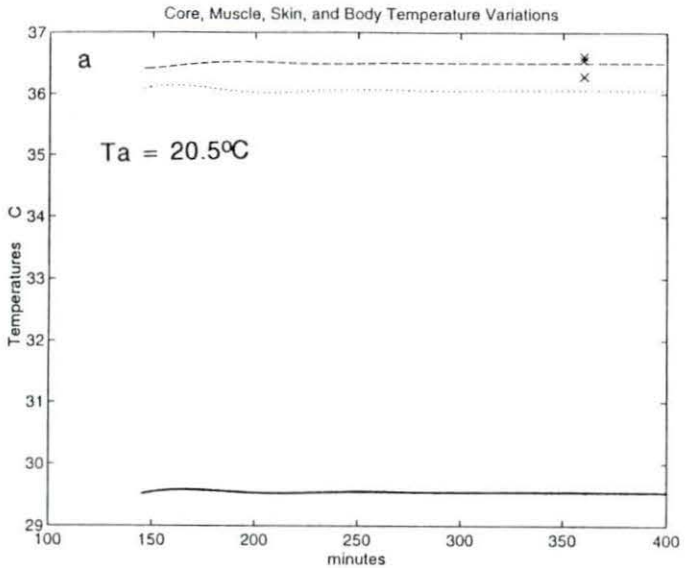

Core, Muscle, and Skin Temperature Variations, Ta=30 C, 27 %VO2max
Tm = 37.57
Tc = 37.24
Ts = 34.33
Temperatures C
minutes

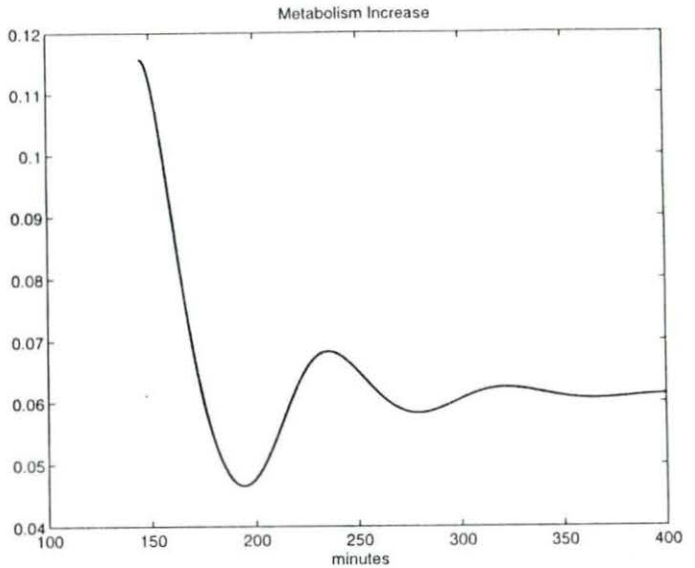

Sweat Rate, Ta = 30 C, 27 % VO2,max
Qv = 2.71
Qv, (kcal/min)
minutes

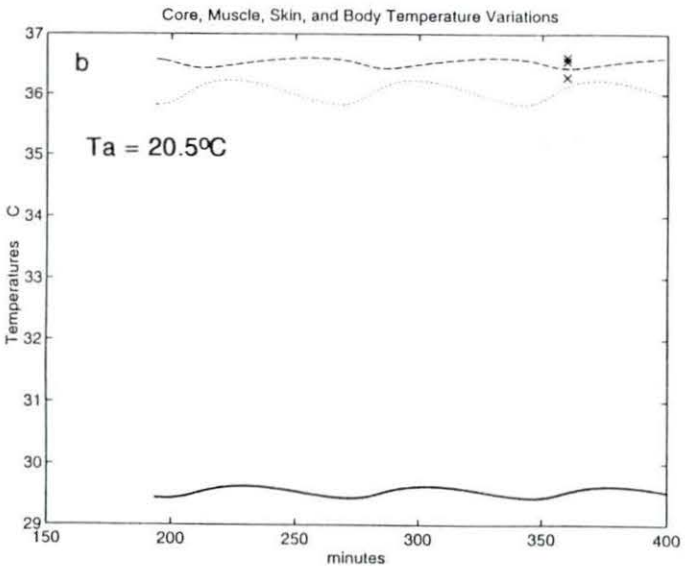
flow, but has very little effect on any other variables, besides the resulting mass balances. This gain cannot be decreased any further since it has been set to reach minimum oxygen concentration in the blood leaving the muscles at the maximum oxygen uptake.

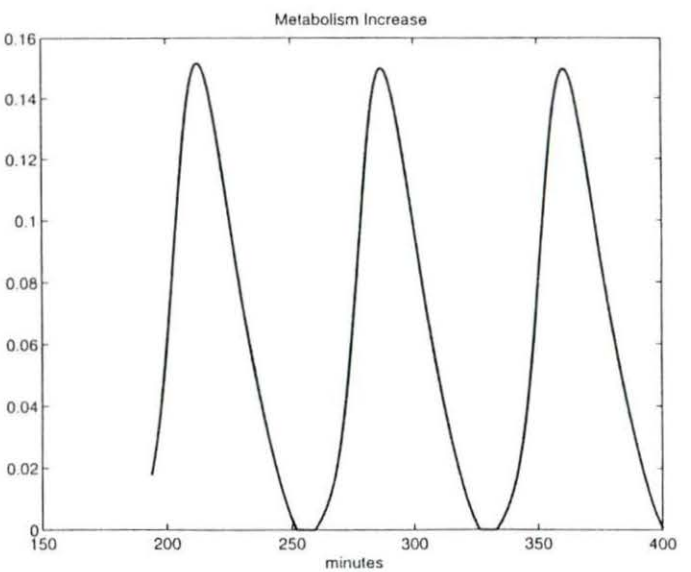
The controller gain for shivering is important in determining the magnitude of the oscillatory action of the metabolism changes associated with shivering. If the gain is large, metabolism will increase very fast when core temperature drops below 36.6°C. Core temperature will increase above this threshold and shivering will stop until the temperature decreases enough. A true steady-state is never reached, but if the gain is small enough, the oscillations become small and undetectable. With a gain of 0.3, as shown in Figure 4, no oscillations are detected for resting conditions at 20.5°C. When the gain is increased to 0.6, oscillations start out large, but quickly dampen out. When the gain is increased further, the oscillations in metabolism are large and lead to large, continued, temperature oscillations (see Figure 16).

Figure 16: Temperature oscillations (left) caused by metabolism oscillations (right) when the gain on shivering is (a) 0.6 and (b) 0.9. Data (X) from Saltin and Hermansen (1966).


Core, Muscle, Skin, and Body Temperature Variations
a
Ta = 20.5ºC
Temperatures C
minutes


Metabolism Increase
minutes


Core, Muscle, Skin, and Body Temperature Variations
b
Ta = 20.5ºC
Temperatures C
minutes


Metabolism Increase
minutes

CONCLUSIONS

A model which describes both the transport of oxygen and carbon dioxide and thermoregulation has been developed in this work. This model is unique in the fact that it separates convection and conduction in compartmentalized energy balances and that it provides a means for modeling the contest between skin and muscles in their needs for blood flow during exercise and heat stress.

A major difficulty is encountered in validating this model because most studies measure only a few of the variables we are concerned with here. Individual variations between subjects and variations in experimental conditions between different data sources have produced significant disagreement. Nevertheless, the trends that are shown here are clearly in agreement with those shown by experimental data.

Several physiological observations and theories are also supported by this model. Blood flow from the tissues to the skin has been included to show the repartitioning effect during exercise. The attainable skin blood flow rate has been limited at high rates of exercise and/or high ambient temperatures, showing that metabolic circulatory regulation is given precedence over thermoregulation at high exercise levels. The circulatory delivery of oxygen can be the limiting factor in the maximum oxygen uptake attainable. Temperature limitations may also be a factor in the peak oxygen uptake attainable under certain conditions, at least during exercise in the heat. In a cold environment, the subject will exhibit a shivering response to generate heat so that the core temperature does not fall too low.

The major limitations of this model have now been determined and it has been shown which of these can be modeled better (see Future Work) and which are due to individual variations between subjects. The sensitivity of the model to various parameters has been tested and it has been determined which are the most significant to produce changes in the model results.

FUTURE WORK

The development of this coupled model has demonstrated some important physiological concepts, but is by no means complete. The next steps in the modeling process should include:

1. Attempting to change the skin blood flow algorithm so that it is affected more by changes in ambient temperature than by changes in metabolism.
2. Making stroke volume vary, allowing for dehydration effects on the thermoregulatory system, and including water balances on the system.
3. Combining the model with more detailed models of the pulmonary and cardiovascular systems.
4. Expanding the model to include regional variation of flows with more compartments and sections, then modeling the effects of microgravity.
5. Exploring the possible methods to improve the control relations for skin and muscle blood flows.
6. Expanding on the ways in which changing environmental conditions affect the model. Including the effects of water immersion and swimming, which will have significant effects on the convective heat transfer coefficient.

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