THE THERMO-REGULATORY CONTROL SYSTEM IN MAN AND ITS STUDY BY DIGITAL COMPUTER SIMULATION.

a thesis submitted for the degree
of Doctor of Philosophy of
the University of London.

by

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ABSTRACT.

This thesis describes a study into the nature of the thermo-regulatory control system in man. The work has been advanced by collecting physiological information, which has been augmented by experimentation, and by devising and studying a digital computer simulation of the vasomotor activity associated with human thermal control. An analysis of the control system, led to the proposal that thermo-regulation in humans emanates from two basic control systems which influence each other: these control systems have been called the first and second lines of defence. The first line of defence, which has been of primary interest within this thesis, is a control system whose efferent activity is associated with adjustments in vaso-motor tone, and whose afferent information is derived from thermoreceptors in the skin. It has been shown that the incorporation of on-off control in the model, allows two key aspects of the control system associated with thermal vasomotor activity to be duplicated: a) the spontaneous fluctuations in digit blood flow b) the ability of a thermally induced disturbance to entrain these spontaneous fluctuations. It has also been possible to illustrate the driving frequency dependence of the entrainment phenomenon both in the physical system, by physiological experimentation, and in the computer model. It is noted that an on-off

element is believed to be important in the control of blood pressure, indicating that nonlinear elements of this type may be common to a wide variety of physiological control systems.

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CHAPTER I

THE PHYSIOLOGICAL BACKGROUND TO TEMPERATURE REGULATION.

1.1 INTRODUCTION.

In a series of lectures to the Royal College of France in 1865, Claude Bernard divided all life into three forms. First, life which is in a state of suspended animation, for example eels in ice. Secondly, plants and animals whose existence is dependent upon the environment; typically, cold blooded animals. Finally, the third, and highest, form of life, where to quote Bernard: "The perpetual changes of the cosmic environment do not penetrate the animal". Man is therefore a homeotherm, that is, his body temperature is maintained at a constant level regardless of the environmental conditions.

In 1958, Aschoff and Wever presented the core and shell hypothesis. It can be seen from figure 1.1 that the body is divided into a central region (core), the temperature of which varies within narrow limits, and the more peripheral tissues, where there are considerable gradients or variations in temperature. The inner core comprises the intra-abdominal, the intra-thoracic and the intra-cranial contents, as well as a variable amount of the deeper tissue of the limbs. The left hand diagram shows the body isotherms in a warm environment, while the right hand diagram illustrates the isotherms in a cold environment. These diagrams illustrate how the size of the warm core varies with environmental temperature.

Under conditions of high environmental temperature the region whose temperature is near to 37°C is relatively large, while in a colder environment the region of warm core diminishes by a marked amount.

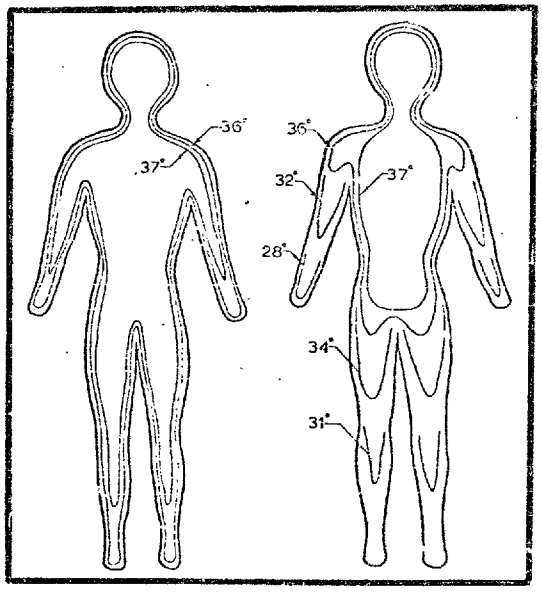


FIGURE 1.1

Although the relative proportions of core and shell temperature are subject to difficulties in measurement, physiologists (Hardy and Du Bois(1937); Burton and Bazett (1936)), have estimated the mean body temperature for normal conditions is represented by the equation:

$$U_{MB} = 0.3\ U_S + 0.7\ U_c$$

where U_S - the average skin temperature.

U_c - the core temperature.

For the condition of a cold environment, the skin temperature factor increases to about 0.4, while the core factor obviously decreases to 0.6. In warm environments the core expands, resulting in weighting factors of 0.2 and 0.8, for U_S and U_c respectively.

At first sight it appears that the parameter which is used as a reference in the maintenance of homeostasis is core temperature. However, it is interesting to note that the rate of change of body heat content, $\frac{dQ}{dt}$, is determined by the difference between the rates of body heat production and heat loss. A simple model of this phenomenon is the equation:

$$\text{Heat Produced} - \text{Heat Lost} = \frac{dQ}{dt} = cM \frac{dU_{MB}}{dt}$$

where:

M - body mass.

c - specific heat.

When the environmental thermal stress changes, heat production and heat loss are transiently imbalanced. As the body approaches a new state of thermal equilibrium, the rate of change of temperature decreases until $\frac{dU_{MB}}{dt} = 0$, and the

heat production and heat loss are again equal. Because of the high heat capacity of an adult human, heat production and heat loss may be in a state of imbalance for perhaps several hours with only slight alteration in body temperature.

This has two advantages. First, levels of motor responses need not be instantaneously in proportion to the severity of existing thermal stress. Secondly, the long latency provides time for the body to escape from highly stressful environments in which physiologic compensation is impossible.

Figure 1.2 shows how the body responds over a wide range of temperature. The bar diagram shows sharp boundaries between the various types of response, in the physical system there is however, a degree of overlapping. Another feature of the system is that each broad type of response is in fact made up of a number of smaller reflexes.

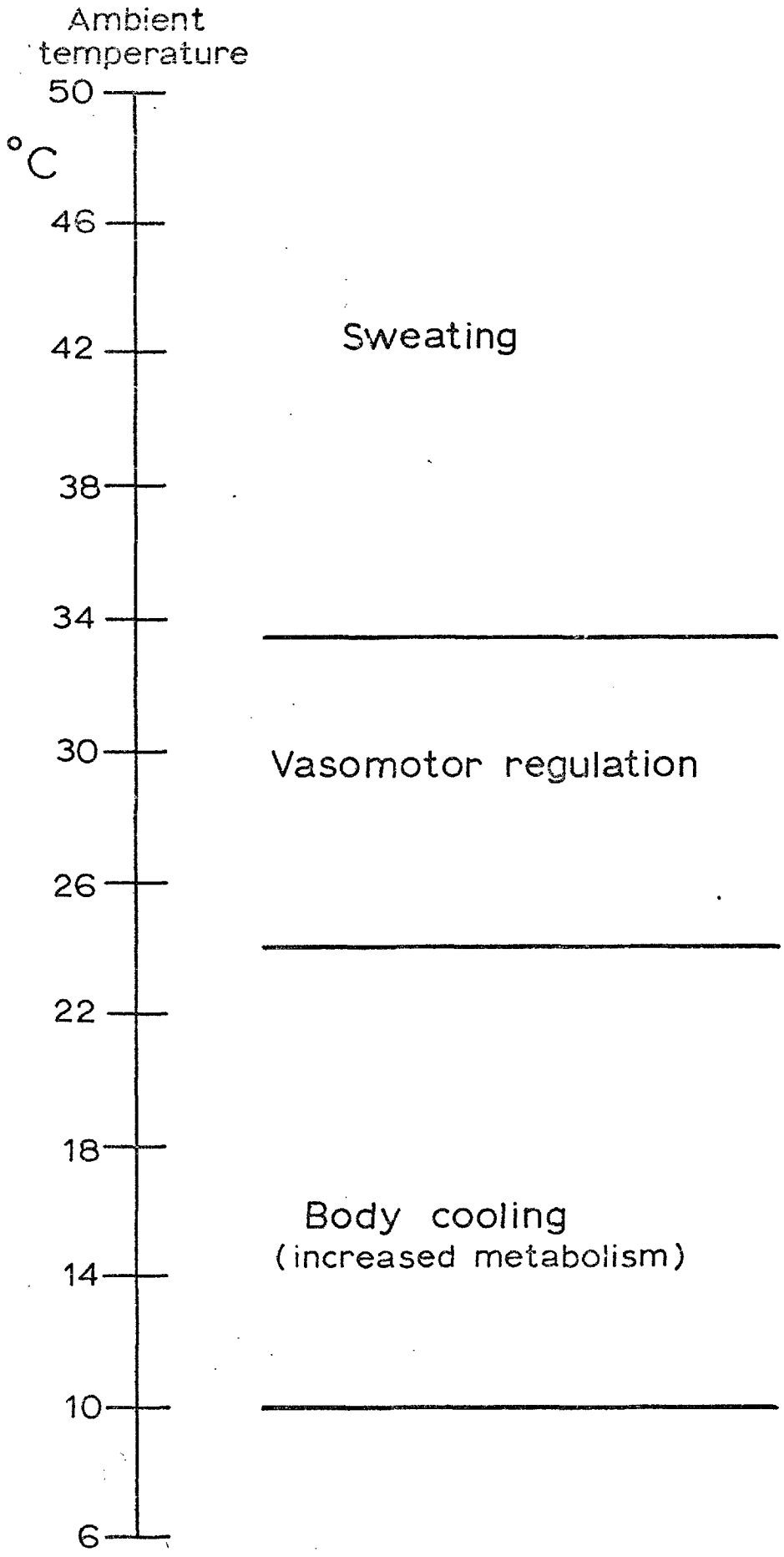


Fig. 1·2 The body's response to changes in the environmental temperature.

1.2 THE PHYSIOLOGICAL CONDITIONS OF HYPERTHERMIA AND HYPOTHERMIA.

The conditions of hyperthermia and hypothermia, are interesting because they define the upper and lower limits of thermal control, respectively.

Hyperthermia (Heat Death).

At high heat stresses, e.g. 40°C (core temperature), the demands upon the circulatory system may exceed its capacity. A number of studies have shown that increased heart rate is followed by increased venous pressure and a sudden fall in cardiac output. A stoppage or decrease in sweating coincides with these events. A loss of the increased sweating and circulation functions has an accumulative effect on body temperature regulation. As the body temperature rises, heat production in the tissues increases, this being the result of thermally forced increased chemical reaction rates. An avalance condition occurs in which the core temperature is increasingly heightened until the lethal temperature is reached. In man, the lethal temperature appears to be 43-45°C, (Burton and Edholm, 1955), although serious impairment occurs in some individuals below 40°C.

Hypothermia (Cold Death).

When the body is exposed to severe cold, the circulatory and metabolic mechanisms are rapidly exhausted.

This causes the body temperature to fall, resulting in the condition of hypothermia. As the body temperature falls, there is progressive depression of the nervous system; excitability, slowing of muscular movement, and eventual respiratory failure, followed by circulatory failure. This reduction in temperature also causes paralysis of the central nervous system which in turn supresses the hypothalamic control centres.

At about 33°C, consciousness is lost. Below 30°C central temperature regulation is almost completely lost and the subject becomes poikilothermic. At about 28°C, disco-ordination of the cardiac muscle frequently leads to cardiac fibrillation and death.

1.3 CARDIOVASCULAR CONTROL OF BODY TEMPERATURE

The physical regulation of body temperature during heat stress, depends mainly upon the physiological control of the peripheral circulation when the environmental temperature is below that required to fully activate the sweat glands. The thermal conductivity of tissue can be altered decisively by adjustment of the blood flow. Regulation of the average flow requirements of heat elimination is achieved by sympathetic control of the tone of the peripheral blood vessels. The activity of the cardiac sympathetic nerves, Bronk (1937), shows the interaction of several rhythms of various origins. Modification of the peripheral blood flow to meet the needs of temperature regulation is carried out by modifying the underlying sympathetic tone, which in itself has a complicated pattern of activity. An additional complication arises from the fact that blood flow must be adjusted simultaneously to meet the needs of other types of regulation. For example the supply of oxygen to meet the needs of metabolic activity. Most of the heat is brought to the skin by the circulation. When cutaneous vessels are dilated, the skin is red and warm. A large amount of blood is cooled at the air-skin interface, this blood then returns to the core and mixes with blood there, thus lowering the core temperature. Temperature receptors are present in the skin, these receptors send action potentials along the

afferent sympathetic nerves to the brain. This results in sympathetic vasomotor activity which causes vaso-constriction or vasodilation according to temperature. Hertzman (1959), records "Reflex activity of the vaso-constrictor centres regulated by the temperature sensitive nerves of the skin. Chilling one paw in the rabbit or dog, elicits blanching and a fall in temperature in the opposite paw. A similar effect has been observed in man."

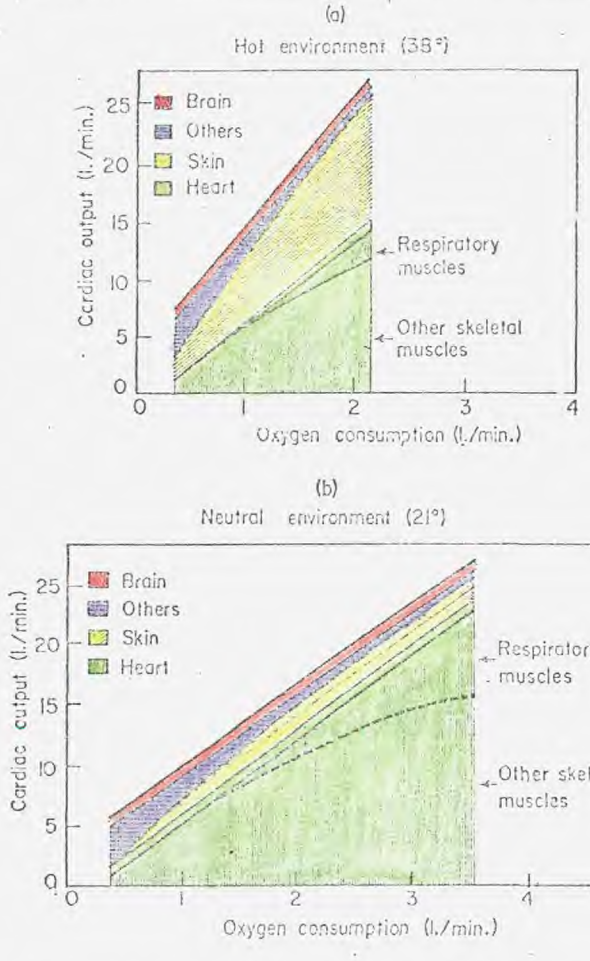
1.4 CIRCULATORY ADJUSTMENT TO HEAT

Cutaneous Conductivity and Cutaneous Blood Flow

The immediate result of cutaneous vasodilation is a rise in skin temperature. This increases the temperature gradient between the skin and the environment, which in turn facilitates the loss of metabolic heat by radiation and convection. One advantage of sweating is that it improves the efficiency of heat loss. A man at rest in a cool environment may lose as little as 16K cal/hr/^{o}C of the core/skin temperature gradient. In a hot environment, it may be as high as 60K cal/hr/^{o}C.

If it is assumed that the skin is 100% efficient heat exchanger, then 1 litre of blood flow would be required to remove 1K cal of heat per degree of core/skin temperature gradient. Kraning et al (1966) found that the flow was 2 l/min due to heat at rest, and 3 l/min at work. A schematic representation of the effects of heat on cardiac output and the distribution of blood flow is shown in figure 1.3.

The hands, and to some extent the feet, are ideally suited to serve as heat exchangers in that they have a large surface area and produce relatively little metabolic heat. Forster et al (1946), recorded flows of 80 m l/min for each hand in resting men which can be projected to give a rate of 4 l/min for the whole surface of an average nude man. The



Distribution of total cardiac output to various organs of the body as a function of oxygen consumption (metabolic cost), (a) under heat stress at 38° and (b) in a thermally neutral environment at 21°. The values quoted are approximate. Visceral blood flow, which is designated as "others", is markedly decreased with moderate to heavy exercise, and practically all of the increase in total blood flow goes to the muscles. Under hot conditions, the extra blood flow to the skin will decrease the work capacity achievable at maximum cardiac output. The data are adapted from Brouha and Radford (1960).

FIGURE 1.3

increase in blood pressure which accompanies exercise also favours increased cutaneous blood flow.

A number of advances have been made in recent years regarding cutaneous circulation and its regulation in response to heat. Hertzman (1959), found that the quantity of blood supplied to different skin areas was arranged in descending order as follows:- finger pad, ear lobe, toe pad, palm of hand, forehead, forearm, knee and fibia. Within the hand the rate of flow in the fingers is significantly greater than in the palm.

It is now known that the vasomotor regulation of flow to the hands and feet is radically different from that to the forearms and legs. Flow to hands and feet is increased in heat largely by graded release of these vascular beds from vasoconstrictor tone. Cutaneous flow to the forearm conversely is controlled by sympathetic vasodilatory action. Blocking the sympathetic supply to the hand results in maximum vasodilation even when the hand is placed in iced water. Vasodilation in the hand of a man begins at a room temperature of 22°C, although the critical environmental temperature at which over all heat conductance increases significantly is 28°C.

It has been known for a number of years that heating the skin in remote areas results in vasodilation of the digits. Kerslake and Cooper (1950), have shown that this reflex response to indirect heating must be due to

excitation of cutaneous temperature receptors by demonstrating that the latent period is only 10 to 15 seconds. It was also found that the response was proportional to the intensity of the stimulus.

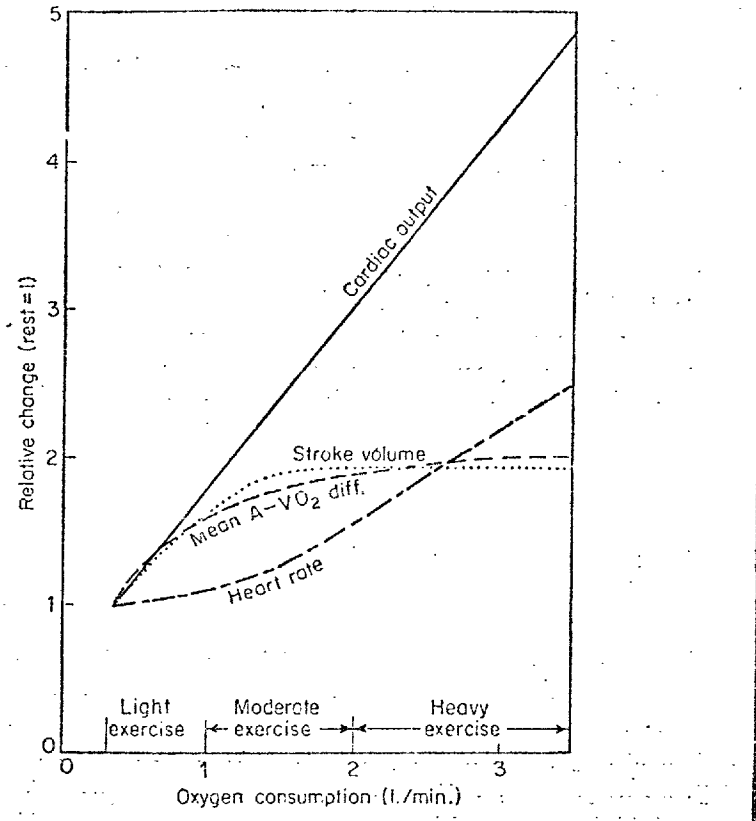
Evidence of active vasodilator control of blood flow to the periphery was presented by Grant and Holling in 1938 when they observed that intense heating of the legs caused marked vasodilation in the forearms. Active vasodilation is now known to participate in the regulation of flow to the skin of the forearm. Blocking the cutaneous nerves to the forearm prevented cutaneous vasodilation in response to body heating.

Circulatory Strain

It is clear that the increase in cutaneous circulation evoked by exposure to heat is accomplished at a cost of cardiac work. This sometimes occurs at the expense of vital circulation of blood to other body regions, e.g., the lack of blood to the brain during acclimatization to heat. Hatch (1963), regarded the circulatory responses as the primary strain of exposure to heat. In fact, under conditions where the sweating is limited, the circulatory demands may become greater than the capacity to deliver blood. The conflict arises from the body attempting to maintain its normal core temperature and the fact that the skin temperature is elevated by the external thermal

conditions. The resulting decrease in thermal gradient can only be compensated by increasing the blood flow to the skin, and to the extent that this is not possible, the body temperature must rise.

The demands of heat and work are competitive, more cutaneous blood is required for heat loss, while at the same time more blood is required to supply the muscles. These demands were investigated by Brouha and Radford (1960), shown in Figure 1.4. At rates of 100 beats/min and above, an increase in metabolic rate brings about an appropriate increase in cardiac output and heart rate. It would appear that when men are active, the circulatory strain of combinations of heat stress and work are manifested in heart rate. Simply to quote heart rates can prove misleading. A heart rate of 130 beats/min during work may be considered moderate, while at rest in heat, this may signify excessive strain. Under these conditions, the support obtained from the return flow of blood to the heart may be the critical factor. An acceleration of the heart rate without a proportionate rise in venous pressure may not increase cardiac output sufficiently to meet the needs of the system.



Relative changes in cardiovascular responses as a function of the intensity of work expressed by oxygen consumption. With light exercise, changes in the stroke volume of the heart account for most of the increase in cardiac output. With heavier exercise, the stroke volume becomes relatively constant and the cardiac output is proportional to the heart rate. These relative changes apply only after cardiovascular responses reach steady values. "A-V" indicates arteriovenous. Data reproduced from Brouha and Radford (1960).

FIGURE 1.4

1.5 CIRCULATORY ADJUSTMENT TO COLD

There are, essentially, two types of vascular control associated with body cooling, namely Vasoconstriction and A-V Anastomosis.

Cutaneous Vasoconstriction

Cutaneous vasoconstriction is really the reverse process to vasodilation which was discussed in detail in the section entitled "Cutaneous Conductivity and Cutaneous Blood Flow". To recapitulate: Flow to the hands and feet is increased in heat largely by graded release of the vascular beds from vasoconstrictor tone. Cutaneous flow to the forearm on the other hand, is controlled by sympathetic vasodilatory tone. When the body is cooled, the resulting reflexes control the blood flow in the manner shown in figure 1.5. The overall effect is that the vasodilatory tone is removed from the forearm, while the vasoconstrictor tone returns to the vascular beds of the hands.

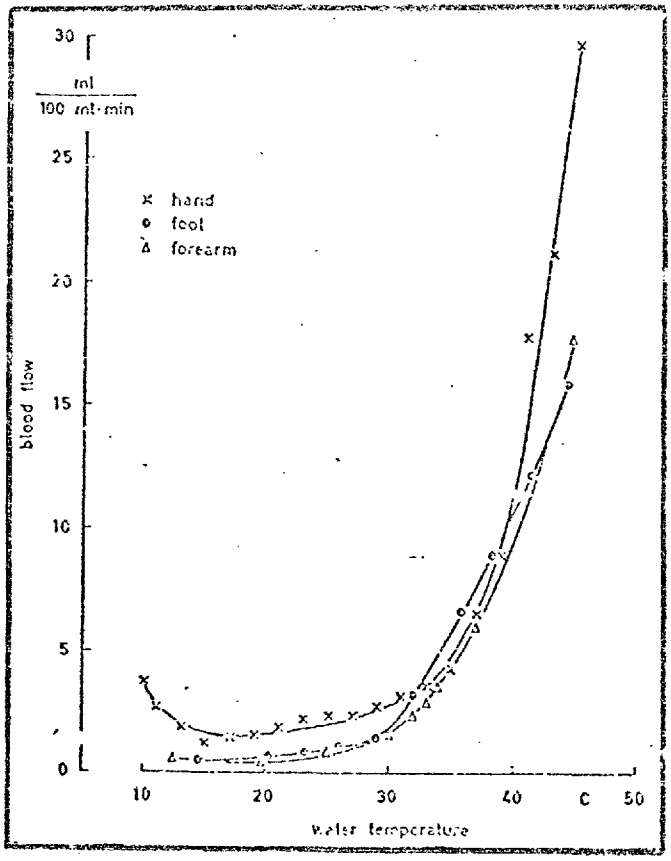
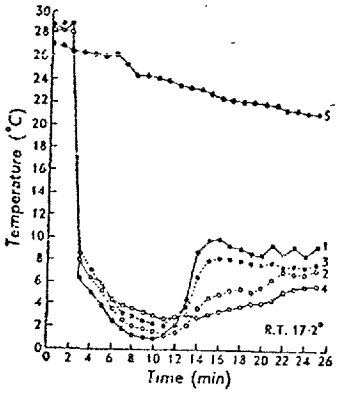


FIGURE 1.5

Arteriovenous Anastomosis

In 1930 Lewis described a phenomenon which has become known as "cold vasodilation" or "hunting reaction". Lewis's technique was to immerse the fingers in ice water. The result was that the finger temperature (skin) fell rapidly to almost zero (^{o}C) but 10 to 15 minutes later the skin temperature rose by some 5^{o} to $6^{o}C$. With continued immersion the finger temperature fluctuated slowly between $0^{o}C$ and 5-$6^{o}C$. Lewis concluded that the rise in temperature

was due to increased blood flow, and he called the fluctuations in skin temperature the 'hunting' phenomenon.



Skin temperature recorded with thermocouples on right index finger (1, 2, 3, 4) and temperature of dorsal surface, base of nail of left index finger. At time 2 minutes, right index finger immersed in crushed ice. Note the abrupt fall of skin temperature of this finger, followed by a rise of temperature after 10 minutes, which is more marked in the distal than in the middle phalanx. 1. Tip of right index finger. 2. Middle of ventral surface, middle phalanx. 3. Dorsal surface, base of nail. 4. Dorsal surface, middle phalanx. 5. Dorsal surface, base of nail, left index finger (control). Room temperature 17·2°C. (Redrawn from Grant and Bland, *Heart*, 15, 385, 1931.)

FIGURE 1.6

Grant and Bland (1931), undertook further studies involving microscopic observation of a rabbit's ear, and produced convincing evidence that the 'colddilation' was due to an increased flow through the arteriovenous anastomoses. Figure 1.7 shows arteriovenous anastomoses in the skin of the exposed part (e.g., ear, cheek, finger) through which warmer blood from deeper parts is conducted through the skin, just beneath the more superficial vessels. In 1, the arteriovenous anastomoses is closed, and, as at

ordinary environmental temperature, blood is directed through the subpapillary venous plexus. In 2, the blood, as at low temperatures, is shunted through the communicating vessel, a small proportion only passing through the more superficial vessels. The continuations of the arteriole into the subpapillary venous plexus and of the small vein leading therefrom are represented merely by double rows of dotted lines.

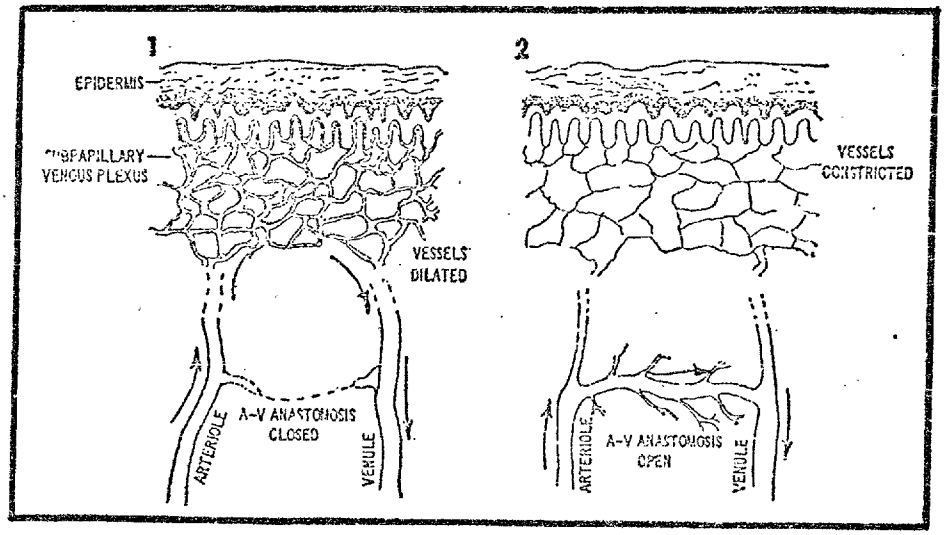


FIGURE 1.7

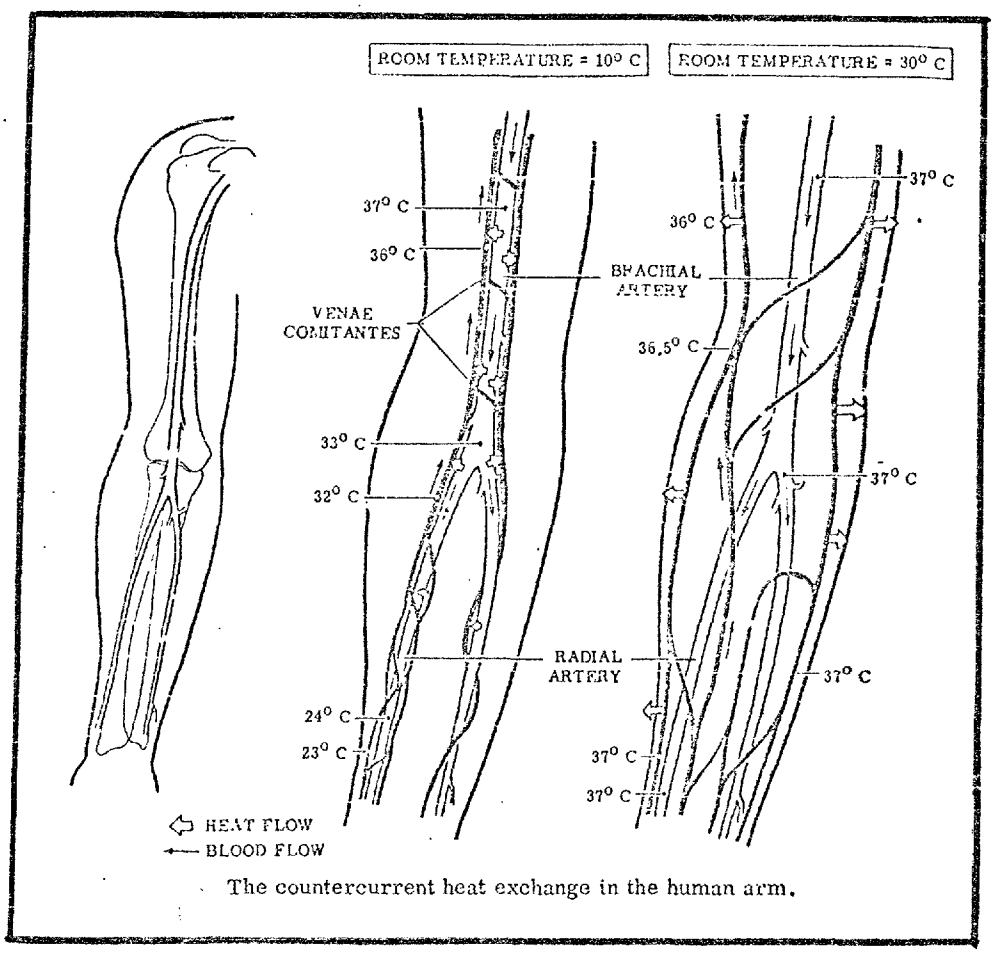
Lewis also showed that it was not possible to produce a cold vasodilation, when the peripheral nerve had degenerated and he concluded that an axon reflex was involved. Kramer and Schulze (1948), also considered that cold vasodilation was due to an axon reflex. They succeeded in preventing cold vasodilation by blocking the finger tip with novocaine.

In a series of papers, Aschoff (1944 a-g), described the factors influencing cold vasodilation. He used a constant flow calorimeter and measured the heat output of the whole hand. Using water at 10 to 13°C, the heat output was at the lowest, values obtained being 25 to 30 cal/min. When the water temperature was reduced below 6°C, the heat output increased abruptly after 10 to 15 minutes to values of 150 to 200 cal/min. Aschoff demonstrated fluctuations in heat output during cold vasodilation, corresponding to the fluctuation of skin temperature. In Aschoff's experiments the heat output of the finger-unit surface area was five times greater than that of the whole hand. This observation is reasonably explained by the distribution of arteriovenous anastomoses.

Spealman (1945), made direct measurements of the blood flow in the hand at different water bath temperatures. The local effects of temperature were considerably influenced by the general thermal state of the body, a finding which was later confirmed by several sources. If the subject was comfortably warm, the effects were as already described, but when the subject was uncomfortably hot the blood flow in the hand remained high even when it was in water at 10°C, so the local vasoconstriction effect of the cold water was suppressed. On the other hand, if the subject was chilled, the increased blood flow at low water temperatures was reduced, although some cold vasodilation was still observed.

Countercurrent Heat Exchange

Under conditions of cold the routes of venous return from the limbs may be shifted to set up a countercurrent heat exchanger. Venous blood is warmed as it returns to the deep core and arterial blood is cooled as it proceeds to the extremities. Prime examples of this type of exchanger are found in the legs of wading birds that stand in freezing water. Bazett (1948), suggested that this mechanism was effective in human subjects; some of his data is shown below.



The countercurrent heat exchange in the human arm.

FIGURE 1.8

He found that the temperature of arterial blood near the chest was about 37°C, but by the time this blood had reached the wrist it could be as low as 25°C. As a response to cold, venous flow shifts from the surface veins, to the deep venous plexus or venae comitantes where heat is gained from the arterial blood. As the cool venous blood flows towards the core and passes the warmer arterial blood in countercurrent fashion, heat passes through the vessel walls at a rate proportional to the arterial-venous temperature gradient and the contact area. It has been shown that when a hand is placed in cold water the arterial blood at the elbow may cool because of this countercurrent heat exchange mechanism. In this way, blood flow in the limbs can be maintained while heat loss is diminished, since heat is not carried from the core by this flow. The vasoconstriction and blood flow shifts are so effective that upon exposure to cold a rise in rectal temperature of as much as 0.5°C may ensue. It has been estimated that in a cool environment, heat loss from the hands and feet may be reduced by these mechanisms to 2% of the total heat loss, yet hand and foot surface area amount to 15% of the total body surface area.

1.6 THE GROSS MECHANISMS OF THERMAL CONTROL.

When the degree of heat stress exceeds the range of vasomotor control, the coarser mechanisms of thermal control are called into play, and either shivering or sweating occurs.

The Mechanism of Shivering.

Cooper (1969), states that there appears to be interplay between the central and peripheral stimuli involved in regulating the intensity of the shivering response. For example, the sudden exposure of a naked man to an air temperature of $0^{o}C$, with a high air movement, causes him to shiver; this starts within a minute or so and continues for a considerable time, resulting in a rise in core temperature. Cooper (1969), deducès that the initiation of shivering in this case is dependent on the peripheral afferent stimulus. Thauer (1961), argued that shivering was normally initiated by the peripheral receptors and the intensity of the response depends on the temperature of the central receptors. At the present time, this argument appears to be the most reasonable fit to the physiological facts.

The Control of Sweat Gland Activity.

There is a considerable amount of literature, (Kerslake, 1955; Benzinger, 1959 ; and Brebner and Kerslake, 1961), to support the theory that both central

and peripheral receptors are involved in the control of sweating. The sweat glands can be described as a second line of defence against heat stress, the first line being vasodilation. As the amount of heat stress increases, a point is reached where normal vasodilation becomes ineffectual. If this situation were to continue, the result would be circulatory shock i.e. rapid, weak pulse; low blood pressure, which would lead to heat exhaustion. In the normal body, these effects are offset by sweating. However, it should not be supposed that maximum cutaneous vasodilation is necessarily attained before the sweat glands begin to secrete. As the heat stress continues to increase, there occurs within a given area an increase in the number of active sweat glands, and additional glands are recruited in previously non-sweating areas. Randall and McClure (1949), have found that an even greater degree of heat stress leads to sweating on all skin surfaces, and that those glands which are already active show a larger rate of sweat secretion.

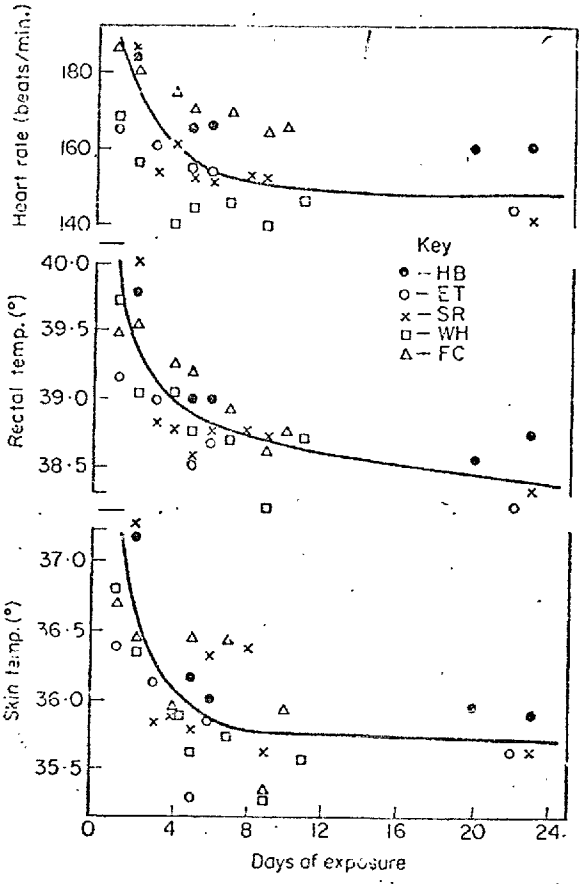
Sweating is not a continuous process, but rather a cyclic process, marked by high and low points in sweating activity, (Randall, 1946; Albert and Palmes, 1951). At threshold environmental temperatures, this cyclic activity results in the appearance and disappearance of sweating within a given area.

Hertzman (1957), found that when normal subjects were placed in a climatic chamber in such a way that only a portion of the body was heated, while the remainder was held at constant temperature or cooled, sweating always began in the feet whether the upper or lower portion of the body was heated. It seems that the topographic distribution of sweating is determined by the total thermal demand rather than the manner in which it develops.

Acclimatization to Heat.

It is well known that when subjects are exposed to heat, for example in a desert, a feeling of well being only occurs after several days. At one time it was thought that this was due to psychological reasons only. However Dreosti (1935), observed that for a set amount of work the rectal temperature and heart rate decreased over a period of days.

Robinson (1943), carried out similar experiments. He found that unacclimatized subjects reached a state of collapse in 1-1.5 hours, with rectal temperatures of 39.4 - 40.0°C, heart rates of 165-195 beats/minute, and skin temperatures of 36.4 - 37.3°. The graphs of Figure 1.9 show the overall effect of acclimatization on the rectal temperature, skin temperature and heart rate of five subjects. The graphs show that when those exposures were repeated daily, the final rectal temperatures were



Acclimatization to heat as shown by the lowering of body temperatures and heart rates of men in a standard work experiment (room temperature 40°; humidity 23%). On some of the days of exposure, the men wore clothing which differed from the standard costume, and the resulting data are omitted from this figure. The key refers to the initials of the subjects involved in the experiment. From Robinson *et al.* (1943).

FIGURE 1.9

down by 0.9 - 1.6°, heart rates by 25-50 beats/min., and skin temperatures by 1.1-1.6°C.

Eichna et al. (1950), discussed the role of increased sweat production in acclimatization. These workers measured heart rate, skin and rectal temperatures,

sweat rate, and oxygen consumption during acclimatization to work in a hot, dry environment. They found that after a suitable period of acclimatization, their working subjects produced 10% more sweat, had lower heart rates, lower skin temperatures, lower rectal temperatures, and consumed 4% less oxygen than on the first day in the hot environment.

Their results showed that the total body heat content on the first day, was appreciably higher than on the tenth day of acclimatization. Another important finding was that on the first day any additional heat was equally divided between the core and peripheral tissue; whereas, by the tenth day only about one sixth of the additional heat was contained in the core. This heat was also found to be equal to that added to the body core when the same amount of work was performed in a cool environment.

Eichna et. al. (1950), summarize what is achieved by acclimatization in the following terms: "Deep tissue temperature is returned to the normal level set by the metabolic rate of the task in a cool environment, but neither total body temperature nor skin temperature are returned to their levels in the cool environment. Mean skin temperature is adjusted to a level which permits thermal equilibrium between the body and the environment on the one hand, yet still maintains an internal thermal

gradient which permits the transport of the deep body heat to the surface without overtaxing the circulation. In the hot, dry environment of this study these conditions were attained almost wholly as a result of the increased evaporative cooling which an increased sweat secretion produced".

CHAPTER 2

THE ANALYSIS OF THE HUMAN THERMO-REGULATORY SYSTEM.

2.1 INTRODUCTION.

The discovery that over a wide range of thermal stress, from extreme heat to extreme cold, the core temperature varies by only a small amount, suggests the presence of a regulating system for human internal body temperature. To quote a recent review by Hammel (1968): "This means that internal temperature is compared in some way with a reference, and when a difference occurs an appropriate response is made tending to reduce the difference". Workers in the field of regulatory physiology have applied the concept of negative feedback control to human thermoregulation. The essential features of such a control system are shown in figure 2.1. The concept of a reference to which the internal temperature is compared, is discussed in detail by Hardy (1965). Hardy quotes from the American Standards Association (1963), who define a set point as: "a fixed or constant input, established by means external to, and independent of, the automatic control system which sets the ideal value of the controlled variable." Since regulation is achieved by a system, it is perhaps expedient to determine what constitutes a system.

Grodins (1963) and La Joy (1958), define such a system as a collection of components arranged and inter-

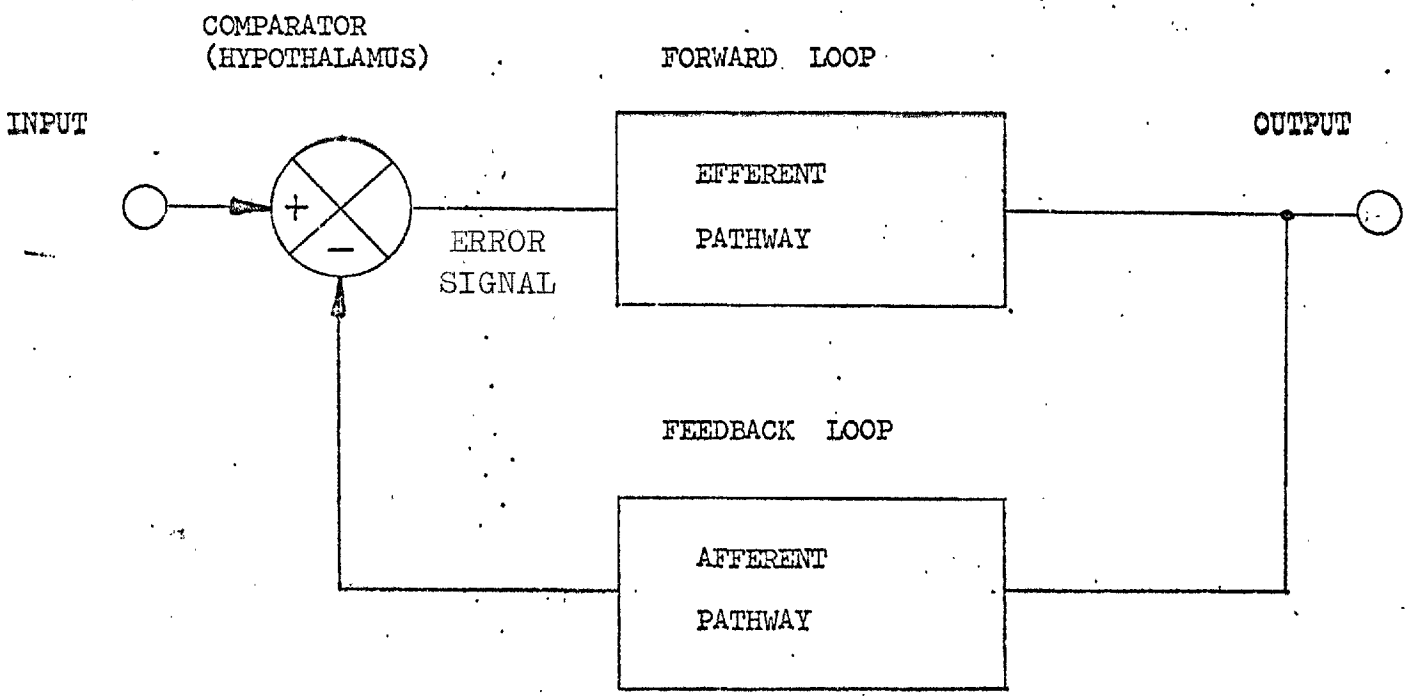


Figure 2.1

THE BASIC BLOCK DIAGRAM OF THE CONTROL SYSTEM UNDER INVESTIGATION.

connected in a definite way for which there can be identified an output which is related to a known input. In theory, the number and complexity of the components is unlimited and consequently may include chemical, mechanical, electrical, biological and other elements taken individually or in any combination. Many physiological studies begin by observing stimulus/response relationships which in control system terminology would be known as the transfer function.

In normal homeothermic mammals, under conditions of thermal stress, the central nervous system (CNS) intervenes by way of its thermal sensing elements, integrative components, and effector pathways, to activate responses which modify the rates of heat production and heat loss. The relationship linking thermal responses and body temperature have been well established in many reviews of the subject, for example: Bazett (1949), Hensel (1952), von Euler (1961), Hardy (1961), Hammel (1968) and Benzinger (1970). Each of these authors have recognised the sensing, integrative and effector roles of the nervous system.

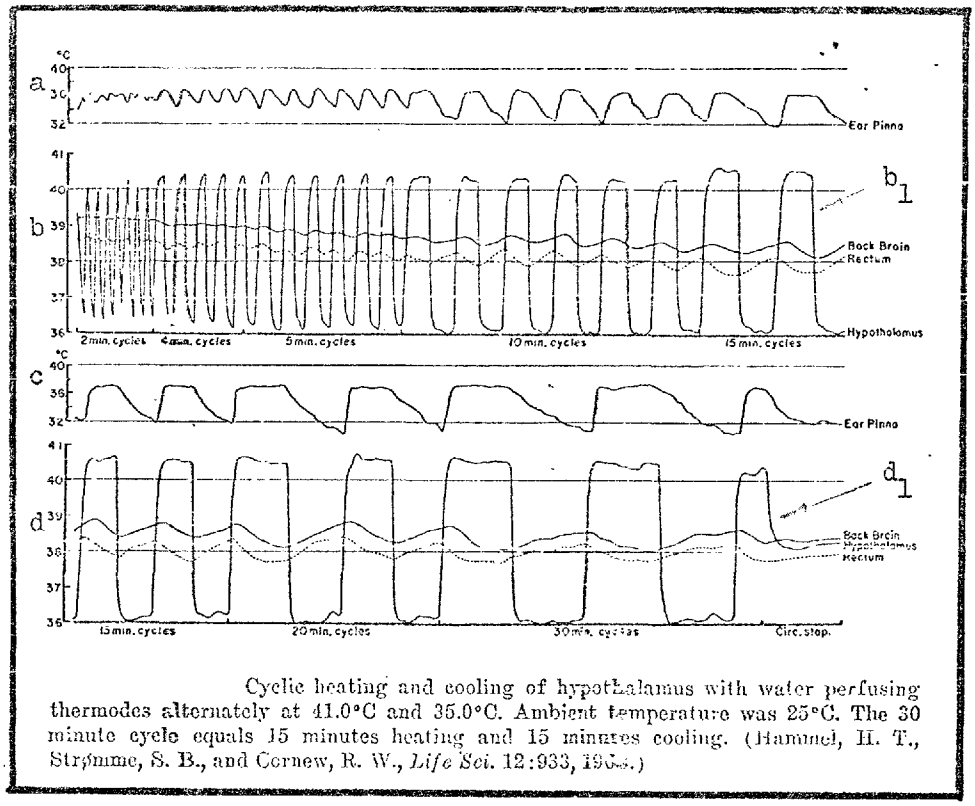
By using the information which is available, many workers have produced block diagrams which identify the inputs, outputs, and feedback loops, together with the important anatomical sites represented by the various

blocks. It should be noted however, that no one appears to have defined the properties and interconnections between neurons required to achieve the characteristics of the block diagram. Hammel (1968) states that this is because at the present time, little is known about the neurons in those parts of the CNS which are essential to the accomplishment of thermoregulation. Models which are constructed from the basic block diagrams of their authors, simply account for known relationships between thermo-regulatory responses, body temperatures and other inputs.

2.2 THE CONTROLLER AND COMPARATOR - THE HYPOTHALAMUS.

Hammel (1968), Benzinger et.al. (1963) and Bullard et. al. (1971), are examples of papers which illustrate the widely accepted view that the controlling system originates within the Hypothalamus in the pre-optic region. In terms of the basic block diagram of figure 2.1, the hypothalamus may be said to be equivalent to the comparator. There is a large amount of evidence, Hardy (1961), to suggest that the pre-optic region of un-anesthetised mammals responds to local heating by inducing panting and vaso-dilatation, and local cooling by producing shivering and vasoconstriction.

A good example of these studies is the paper by Hammel et. al. (1963).



Cyclic heating and cooling of hypothalamus with water perfusing thermodes alternately at 41.0°C and 35.0°C. Ambient temperature was 25°C. The 30 minute cycle equals 15 minutes heating and 15 minutes cooling. (Hammel, H. T., Strømme, S. B., and Cornew, R. W., *Life Sci.* 12:933, 1963.)

FIGURE 2.2

Figure 2.2 illustrates that the hypothalamus responds, and is sensitive to, small changes in its own temperature. Traces b_1 and d_1, correspond to the temperature of a thermocouple, situated in the centre of the anterior hypothalamus, being heated and cooled at various frequencies. The low amplitude records, which are labelled in the traces b and d as Back Brain, are said by Hammel et. al. to be those of the cerebellar.

The ear pinna temperatures are those of the dog in an ambient temperature of 25°C, with the hypothalamus

alternately heated and cooled. Hammel et. al. (1963), conclude that the anterior hypothalamus is responsive to both heating and cooling, with equal sensitivity to moderate heating and cooling. Other experiments, Andersonn et. al. (1965), have included the destruction of the entire pre-optic region of an un-anaesthetized goat by proton radiation. These experiments demonstrate that the goat's thermoregulation was much impaired. Similarly, Sah and Fulton (1940), were able to show that animals subjected to transection of the brain stem below the level of the hypothalamus become poikilothermic. Davidson (1940) and Zimmerman (1940), have described hyperthermia in man, and the inability to withstand warm environments following anterior hypothalamic lesions due to tumors.

Benzinger (1961), postulates that there are two central sites involved in thermo-regulation. These sites are basically different in that one is activated exclusively by heat stress, while the other responds solely to cold stress. Benzinger's findings agree with a series of experiments carried out by Fusco (1959). These experiments involved the local heating and cooling of the hypothalamus in connection with studies of heat loss and heat production in an un-anaesthetized dog exposed different environmental temperatures. In a

cool environment (14°C) there was a decrease in metabolic rate associated with a lack of shivering. Upon the termination of heating, violent shivering occurred, this increased the metabolic rate by as much as sixfold. In a neutral environment, minimal heating evoked vasodilatation and the average level of the metabolic rate was reduced to very low levels associated with lethargy, drowsiness and sleep. In a warm environment (29°C), there were marked vasodilator and panting responses, although the metabolic rate was somewhat elevated.

It was noted on a number of occasions by Fusco, that it was possible to artificially drive the temperature regulation system of the dog so as to make the animal pant and shiver at the same time. This being accomplished by heating the hypothalamic area and, by causing the dog to pant, lower its body temperature by 1° or 2°C. Upon terminating the heating, the animal began to shiver violently. If the hypothalamic heating were resumed, the animal would begin to salivate and to pant, even while continuing vigorous shivering. This observation indicates that the responses to heat do not always completely inhibit the responses to cold and vice versa. It would therefore seem that one could place the central site for the regulation of vasodilatation

and sweating in the anterior hypothalamus. This seems to act as a terminal sensory receptor for temperature, and acts independently from heat stimulation of the skin. Alternatively, the central site for regulating metabolism appears to be in the posterior hypothalamus. Benzinger states that there may be some degree of interaction between these sites; that is to say, that a warm anterior hypothalamus may diminish shivering by suppressing muscular activity.

The hypothalamus can therefore be considered as the controller or comparator in human thermo-regulation. Although there still appears to be some disagreement, it now seems to be generally accepted that there is a heat maintenance centre in the posterior hypothalamus, and a heat loss centre situated in the anterior hypothalamus.

2.3 THE CUTANEOUS THERMORECEPTORS.

Grant (1955), states that two types of thermo-receptors have been identified in the skin. Three pieces of evidence support this statement:

(i). The skin contains receptors which fire more rapidly as the temperature increases, and others which fire more rapidly when the temperature decreases.

(ii). There is a clear subjective difference between warmth and cold.

(iii). Temperature sensibility is distributed in a punctate or spotty fashion. Small areas of skin were explored millimeter by millimeter by Jenkins (1941). Jenkins observed that there are small areas which only respond to the sensation of cold. While other spots, fewer in number, respond solely to warmth. The intervening areas are sensitive to neither stimulus. Burton (1963), states that the warm receptors have been identified with the endings of Ruffini, and the cold receptors similarly identified with the end bulbs of Krause. Other authors (Kenshalo and Nafe, 1963), seem to doubt the evidence for a specialized nerve ending. Hensel and Boman (1960), have shown that some skin receptors are served by myelinated fibres which are sensitive only to cooling. Such receptors in man respond to a lowered temperature with a large increase in the firing rate.

Zotterman and Dodt (1952a, 1952b), produced two classic papers in which they investigated the cold and hot receptors in the tongue of the cat. These authors discovered that warm receptors respond with a fairly steady discharge at any tissue temperature between 20 and 47°C. Figure 2.3 illustrates that the maximum frequency of discharge is generally at a tissue temperature of 38 - 43°C, but even then at a rate of only

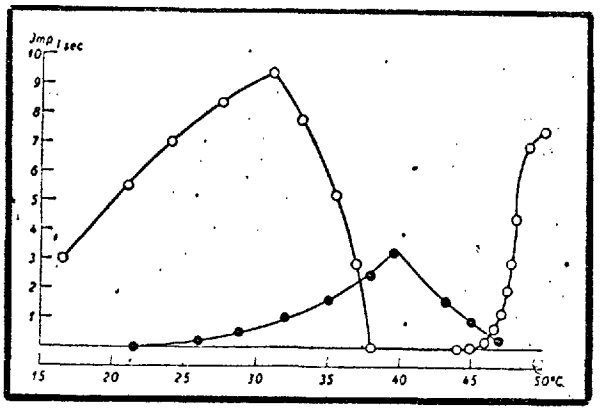


Figure 2.3 After Dodt and Zotterman 1952. Responses of the warm and cold receptors in the lingual nerve of the cat(open circles -cold fibres, filled circles-warm fibres).

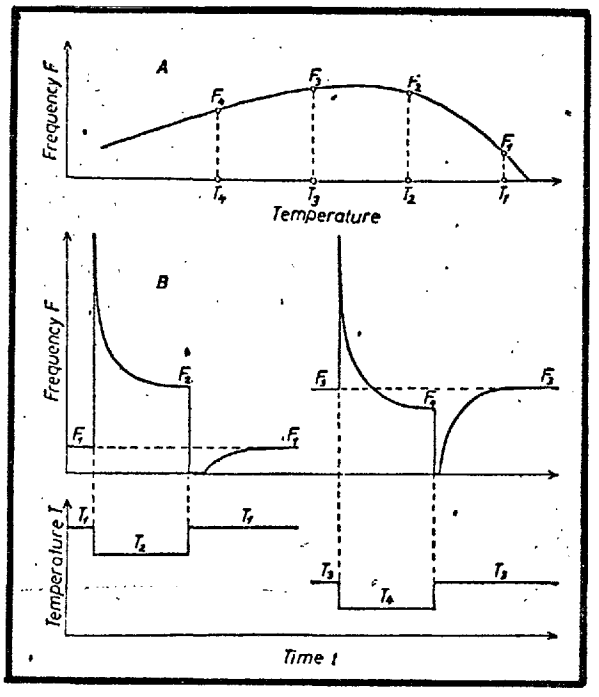


Figure 2.4 After Hensel 1952.
The diagram shows the impulse frequency of a single cold fiber. a) with constant temperatures. b) with rectangular temperature jumps.

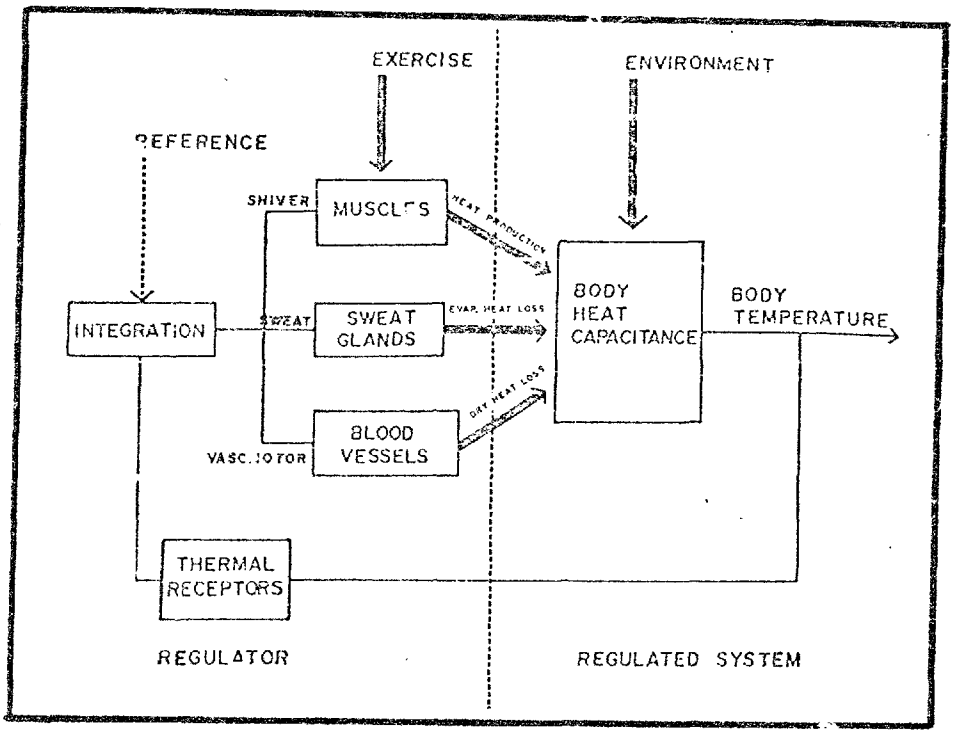
three or four impulses per second. Cold receptors fire with a steady discharge at any one tissue temperature between 10 and 35°C. The maximal frequency of discharge is at a tissue temperature of 25 - 30°C, and is of the order of 10 impulses per second.

Both groups of cutaneous receptors exhibit rapid adaptation. As shown by Hensel (1963), the cutaneous thermo-receptor discharge is dependent on the absolute temperature U, as well as the temporal gradient $\frac{dU}{dt}$ of temperature changes. Ruch and Patton (1966), indicate that the thermal sense organs record the temperature of the tissue at the depth at which they are situated. Hence they are affected by internal body heat as well as by the heat of the environment.

2.4 THE THERMAL CONTROLLING SYSTEM.

A variety of models have been proposed to represent the human thermal system. These models, whether empirical or mathematical, have been designed to predict the thermal behaviour of all or part of the human body. Examples of such models are: Stolwijk (1970), Crosbie et. al. (1963), and Wissler (1963).

Common to nearly all these simulations, is the initial step whereby the thermal system is represented by a block diagram of the type used by Stolwijk (1970), which is illustrated in figure 2.5.



A Simplified Block Diagram of Human Thermoregulation.

After Stolwijk 1970.

FIGURE 2.5

Here the effector section of the controlled system is represented by three sectors, namely: shivering, sweating, and vasomotor activity. Cornew et. al (1967) state that recent work by Benzinger (1959,1961) and Benzinger et. al (1961), demonstrates quantitatively that a key reference of the system is located in the hypothalamus. Cornew et. al. (1967) comment that the controlled variable of the system is the inner core temperature as attained from the blood supply, which is largely derived from the Circle of Willis, the arterial ring located beneath the hypothalamus.

The three regions of efferent activity due to thermal control, which were described by Stolwijk (1970), can be summarised as follows:

(a) The Low Temperature Region (Shivering).

The reaction of the body to low temperatures is to create more heat by increased muscular tone and shivering. The heat generated by these factors is related to the error signal by Benzinger et. al. (1961) as illustrated in figure 2.6. The data shown here comprises a family of characteristics which have skin temperature as a parameter.

(b) The High Temperature Region. (Sweating)

In this region of efferent activity, the body loses heat by sweating. The relation between heat loss and error signal,* as shown by Benzinger (1961), is illustrated in figure 2.7. An interesting feature, is that these curves indicate a shift in the, so called, set point with skin temperature.

(c) The Neutral Temperature Region (Vasomotor Control)

It was established in the initial chapter of this dissertation, that a substantial amount of heat is carried from the core to the skin via blood flow. Fine control of the thermal state of the body can be achieved by adjustment of the size of the peripheral blood vessels. Benzinger (1959), approximated this vasomotor activity by a piecewise linear curve. The importance of skin temperature as a factor in determining vascular responses has been discussed by Rawson and and Randall (1961), and Randall et. al. (1963). Recent models, for example Hardy and Hammel (1963), and Stolwijk and Hardy (1966), have considered thermal mediation to be primarily within the hypothalamus, with temperature deviations in the brain and skin temperature, being feed to this hypothalamic regulator.

Figure 2.5 illustrated the essential factors involved in dynamic thermo-regulation. However, for a

* Refer to Figure 2.1

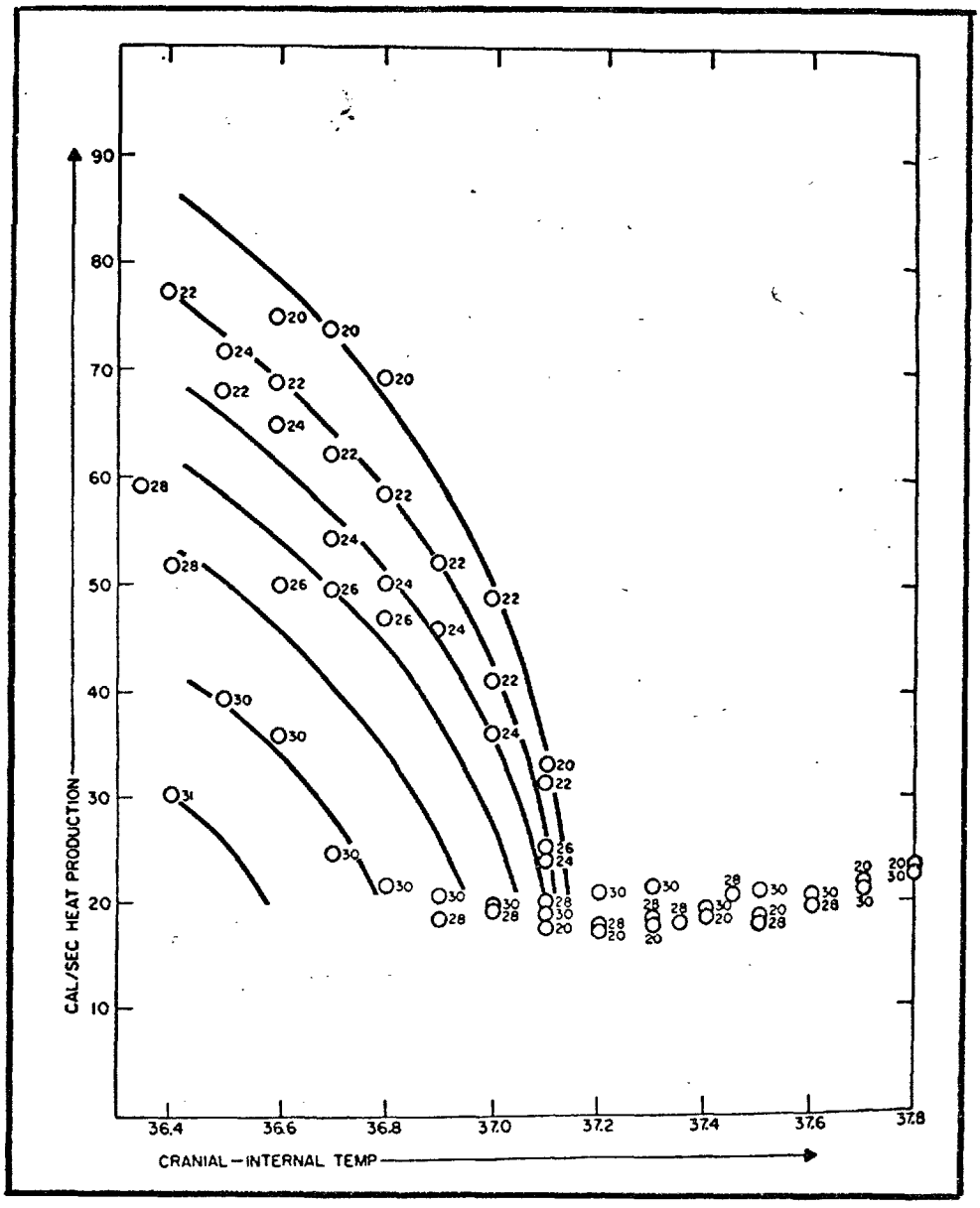


Figure 2.6 After Benzinger et.al 1961.
This figure illustrates the relationship between skin temperature, core temperature, and the metabolic rate.

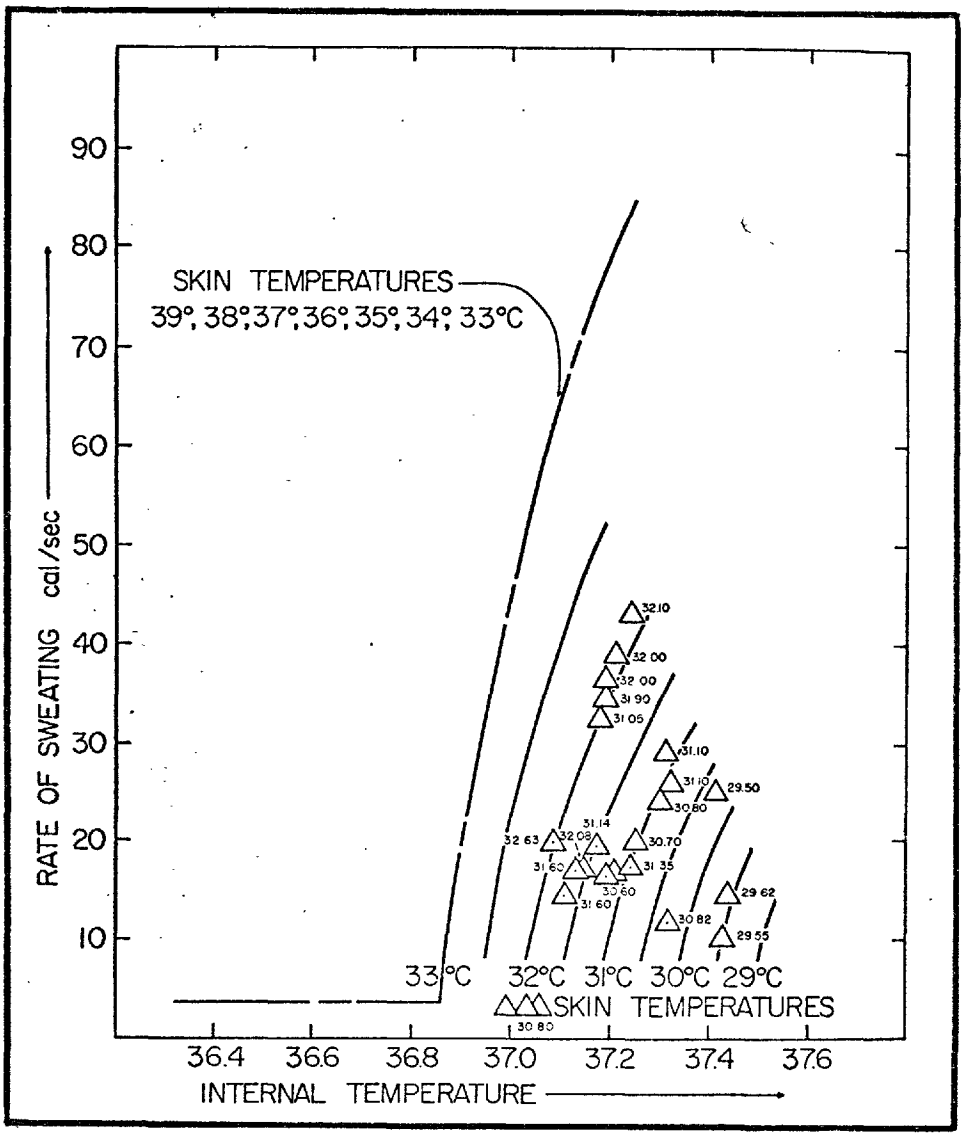


Figure 2.7 After Benzinger 1961.
This figure illustrates the relationship between the skin temperature, core temperature, and the sweat gland activity.

more detailed study, a more detailed block diagram is prerequisite. As Hammel (1968) indicates, it is doubtful whether any two modellers or, for that matter reviewers, would produce the same block diagram of the controlling and controlled system. Examples of such block diagrams can be found in the following papers: Hammel (1968), Stolwijk (1970), Stolwijk and Hardy (1966).

Such diagrams therefore only outline a particular point of view. Figure 2.8 illustrates the block diagram which has been developed for this particular study. The system consists, essentially, of seven forward loops and four feedback loops. Four inputs are shown between the forward loops node and the skin temperature output, these enable the environmental conditions to influence the system.

The gross operation of the system is as follows: an input temperature U_B is presumed to be set in the brain, this set point is really a physiological concept rather than an actual temperature. Under conditions of health the value of U_B, in the average man, is $37^{o}C$.

The response of the system is dependent on the magnitude and sign of the error signal. For example if the afferent temperature is U_{AFF}, then for $U_B < U_{AFF}$ there will be one response, while for $U_B > U_{AFF}$ there

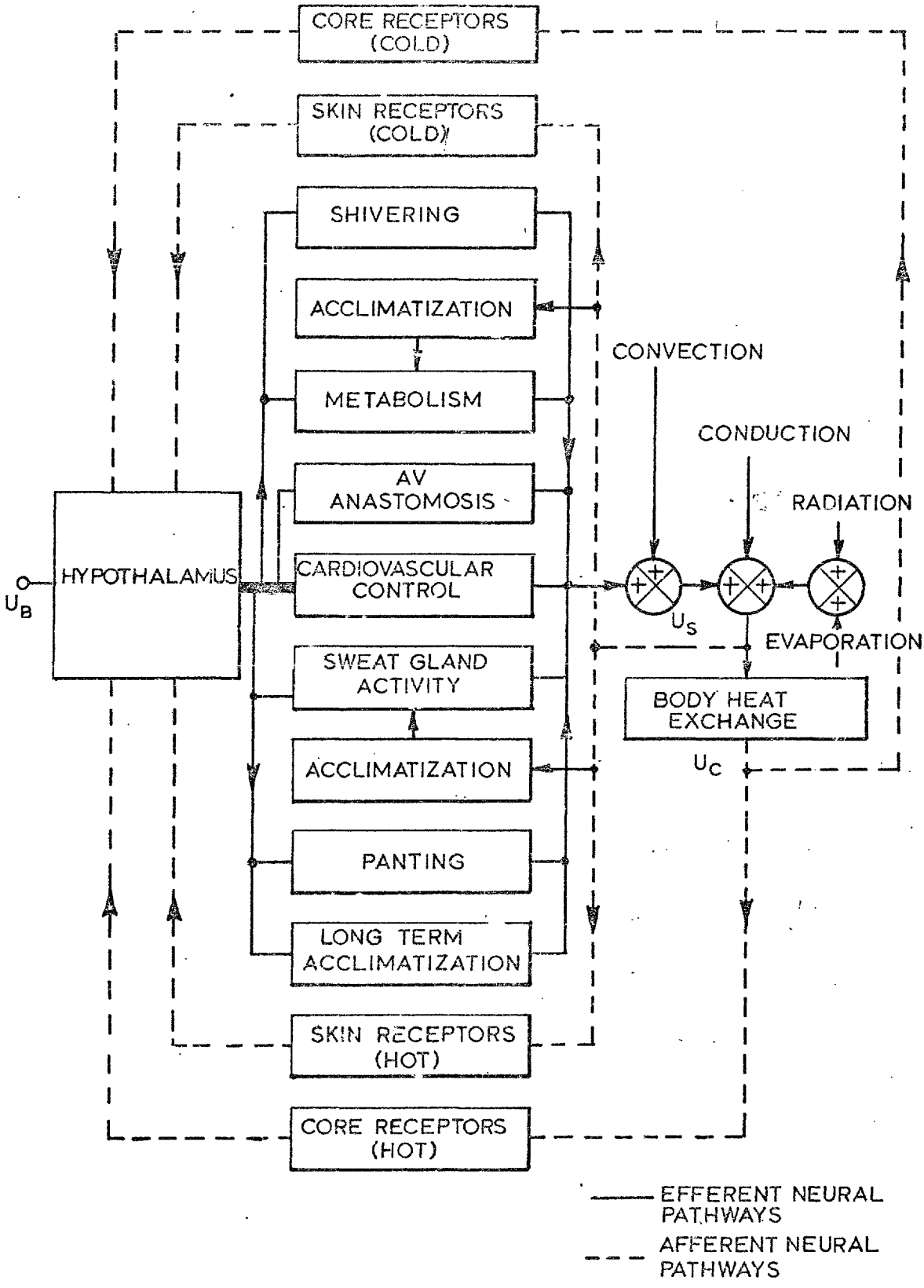


Fig. 2·8 Block diagram of the thermo-regulatory system.

will be a totally different response.

$U_B > U_{AFF}$.

When $U_B > U_{AFF}$ the environmental or metabolic conditions are such as to enable the flow of heat from the core to the extremities in the uncontrolled system. If there is only a slight amount of error, the system will respond by applying cutaneous vasoconstriction to the hands, feet and other exposed parts. As the error increases, vasoconstriction of the limbs occurs and the blood returns to the core via the deep veins. Large error signals of this type result in metabolic responses which normally take the form of shivering.

It would appear, referring to figure 2.9, that under conditions of extreme cold, the body strives to keep elements 5 and 6 at 37°C, this is essential if the vital life functions are to be maintained. As the environmental temperature falls the error signal becomes large, occluding blood from elements 1-4. Only small quantities of blood flow through these regions to supply enough oxygen to stop tissue deterioration.

$U_B < U_{AFF}$

When $U_B < U_{AFF}$, the environmental conditions force the quantity of heat within the human body to increase in

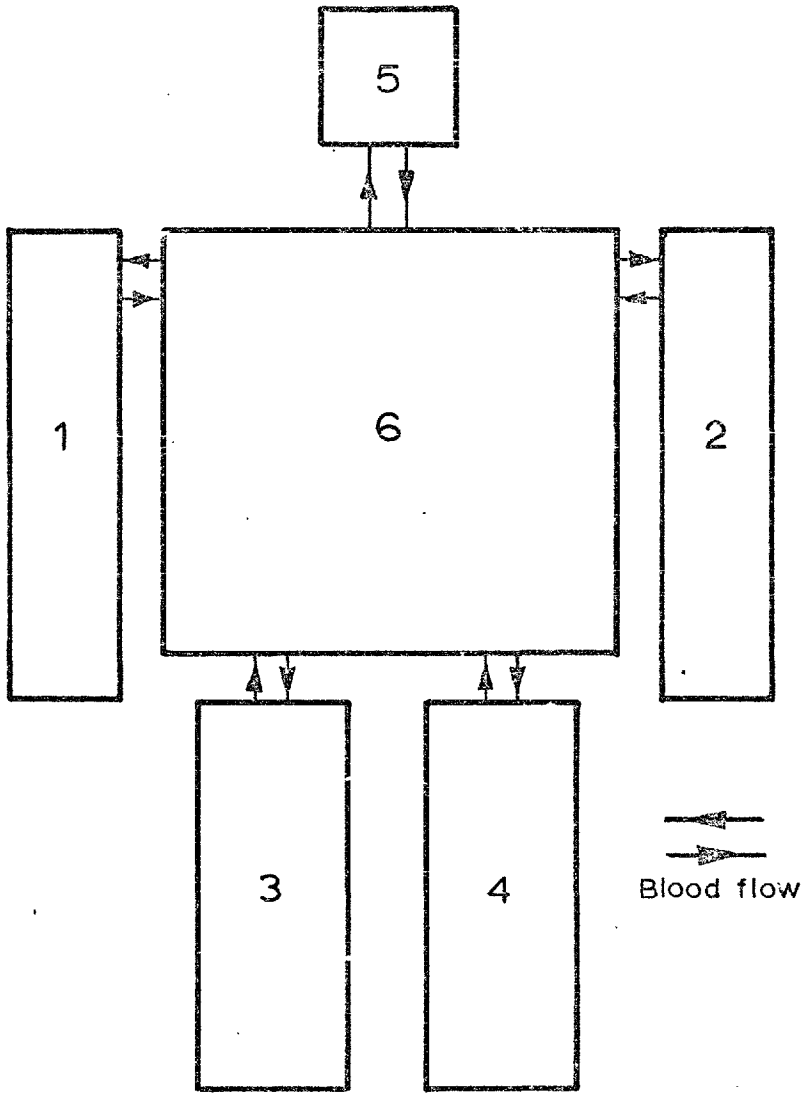


Fig. 2·9 A symbolic representation of the thermal sections of the human body.

the case of the uncontrolled system. A slight variation from U_B by U_{AFF} can be compensated by cutaneous vasodilitation, first in the hands and feet, and then in the rest of the limbs, for example the forearms. A more serious discrepancy would cause the sweat glands to become activated. Blood flow through the Venae Comitantes would be reduced to a minimum in order to prevent countercurrent heat exchange. Under conditions of extreme heat the prime reflex appears to be the supply of blood for the reduction of body temperature, this overrides the supply of blood to the muscles and even the brain; however, such blood deficiencies are thought to result from a lack of heat acclimatization.

2.5 THE PHILOSOPHY OF HUMAN THERMAL CONTROL.

Understanding of the role of the controller of body temperature has evolved rapidly with knowledge gained from neuro-physiological studies, and from thermal and calorimetric measurements. It has become apparent, that the brain temperature and skin temperature somehow combine to produce temperature regulation. One of the first attempts to treat the thermoregulatory system as a controller operating with reference to a set point was made by Hardy (1953). He suggested that the thermal responses of homotherms could be considered as:

$$F(U) = f\left[\sum U_w + \sum U_c\right] \qquad 2.1.$$

where: U_w represents tissue temperatures above the set point.

U_c represents tissue temperatures below the set point.

$F(U)$ the thermal response.

However, no systematic relationship was offered between specific temperatures and the thermo-regulatory responses, apart from indicating the involvement of the skin and core temperatures. More recent analysis of the physiological data, Crosbie et. al. (1963), Hardy (1961), have

included controller equations.

Burton (1963), developed this type of control equation further by predicting that the efferent response R, of the thermo-regulatory system is described by the equation:

$$R = a\ U_H + b\ U_S \qquad 2.2.$$

where

U_H – the temperature of the hypothalamic centres.

U_S – the weighted average of the skin temperatures.

a and b – parameters or coefficients which denote the sensitivity of the co-ordinating centres to their own temperature and to the integrated afferent information as to the skin temperatures, and thus to the environmental temperature.

It has been a contention of these authors, that proportional control is one of the more likely control actions, in which the responses are a linear function of load error, or deviation from the set point. A typical control equation of this type would be:

$$R = \alpha (U_C - U_{CO}) + \beta (U_S - U_{SO}) \qquad 2.3.$$

where: Hammel et. al. 1963.

α and β are proportionality constants for the efferent activity which results from a suitable error signal.

U_C – the hypothalamic (core) temperature.

U_{CO} – the set temperature in the hypothalamus, normally 37°C in humans.

U_S – the average skin temperature.

U_{SO} – the set point of skin temperature, approximately 33°C in humans.

Hammel et. al. (1963) have also assumed a somewhat different law for the controlling system, namely:

$$R-R_O = - \alpha_R (U_{hypo} - U_{set_R}) \qquad 2.4.$$

where:

$R-R_O$ is the thermoregulatory response (metabolism, vasomotor activity, sweating, panting and so forth).
R_O is the basal level when $U_{hypo} = U_{set_R}$.
U_{hypo} is the actual temperature of the hypothalamus, while U_{set_R} is the effective setpoint temperature for a particular response R; α_R is the proportionality constant for the response $(R-R_O)$. Hammel et. al. (1963), in their hypothetical statement of the law of the system, suggest that the reference input signal U_{set_R} may be adjusted by

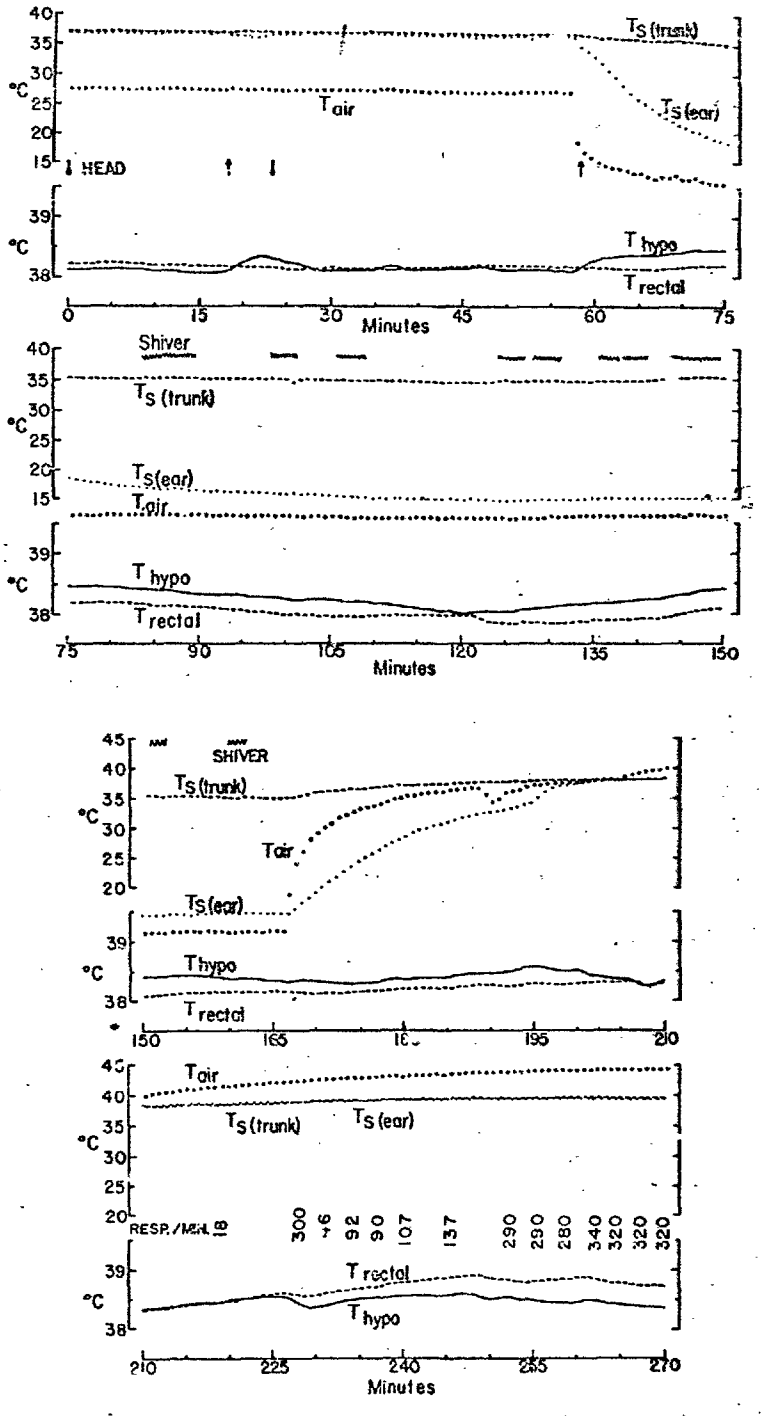
a variety of factors in which they include skin temperature, core temperature, exercise, sleep, pyrogens, together with a number of other factors.

In the same paper the authors describe the hypothalamic temperature changes which occur when an experimental animal is placed in a hot, neutral, or cold environment. The authors observed from the results, which are shown in figure 2.10, that the hypothalamic temperature changes by a very small amount when the environmental temperature was changed from 27°C (neutral), to 12°C to 44°C. Since the hypothalamic temperature did not change in response to the external thermal stress, then according to Hammel et. al. (1963), there are two alternative explanations.

(a). The hypothalamus is over sensitive to changes in its own temperature and the entire thermo-regulatory response is initiated by, and regulated by, a signal derived from the skin temperature.

(b). The actuating signal for driving the thermo-regulatory response may be achieved by offsetting the setpoint according to the thermal needs of the animal.

The authors give preference to the latter explanation. When the skin temperature falls in a cold environment, the steady state and phasic firing rates



A continuous record of hypothalamic temperature, T_{hypo}, and other temperatures of a resting, fasting dog exposed to neutral, cold, and hot environments. Shivering and respiration rates are noted. (Hammel, H. T., Jackson, D. C., Stolwijk, J. A. J., Hardy, J. D., and Strømme, S. B., *J. Appl. Physiol.* 18:1146, 1963.)

Figure 2.10

of cold receptors in the skin increase and elevate the setpoint so that the hypothalamic temperature, without changing, is below the setpoint and drives the heat conservation mechanisms or increases heat production.

Alternatively, when the skin temperature rises in a hot environment, the steady state firing from the cold receptors declines to zero, and the steady state and phasic firing rates from the warm receptors increase. If therefore, their hypothesis is correct, the effect is to lower the setpoint below the hypothalamic temperature and hence activate the heat loss mechanisms. Hammel et. al. (1963), state that even though the hypothalamic temperature may change by only a small amount in response to environmental change, nevertheless the hypothalamus is responsive to changes in its own temperature. The controlling system which Hammel et. al. envisage is illustrated in figure 2.11. The conclusion is that both the hypothalamic receptors, and the skin receptors are involved in the control of human body temperature.

2.6 THE PHILOSOPHY OF THE OVERALL SYSTEM.

Although the authors of papers which discuss the laws of human thermoregulation describe their work as gross simplifications of the true situation, equally, they are aware that the understanding of human thermo-regulation can only be enhanced by the development of a suitable system philosophy. It was therefore considered worthwhile to define a system philosophy in the light of our own experience.

To recapitulate, Stolwijk (1970) and other authors, divide the efferent activity due to thermal control into three regions: the low temperature region (shivering), the high temperature region (sweating) and a neutral temperature region (vasomotor activity). The afferent activity, associated with thermo-regulation is alternatively, divided into two sources: cutaneous thermoreceptors and hypothalamic thermoreceptors. As we have seen, the authors of current papers investigating the control philosophy of thermo-regulation feel that both sources of afferent information are involved in human thermal control. It is therefore proposed that thermo-regulation in humans, eminates from two basic control systems which influence each other.

The First Line of Defence.

The first line of defence, refers to the body's

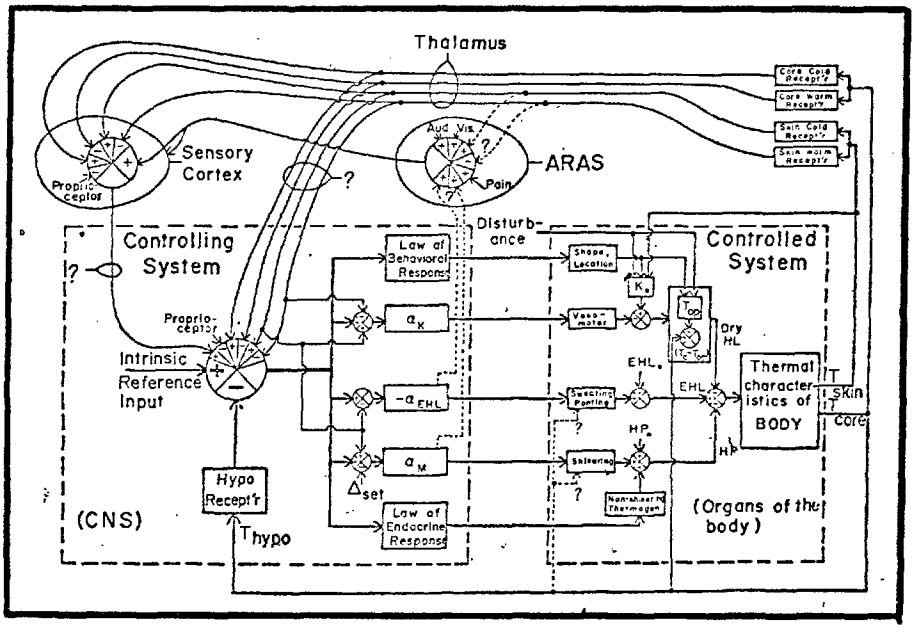


Figure 2.11. A block diagram of the human thermal system and its control. After Hammel 1968.

initial response in the face of temperature change. The overriding algorithm of thermal control seems to be: always preserve heat in the core. Because of its role as a first line of defence, the efferent activity associated with this control system is primarily vasomotor activity. Similarly, the prime source of afferent information is obtained from the skin receptors. When a change in the environmental conditions occurs, the skin receptors will detect this change and the thermal control system will respond by producing vasoconstriction or vasodilatation, whichever is applicable. If these measures are effective, homeostasis will be maintained and the core temperature will remain in steady state. However, if such vasomotor adjustments prove to be inadequate, the thermal equilibrium of the core will be upset and the receptors in the hypothalamus will detect a change in temperature.

The Second Line of Defence.

When the receptors in the hypothalamus detect a change in temperature, the so called second line of defence is activated. By virtue of the fact that the thermal equilibrium of the hypothalamus has been upset at all, the degree of thermal stress must be significant. The resulting efferent activity would therefore be likely

to produce gross control, which would constitute shivering or sweating in cases of severe disparity from the appropriate set value, and perhaps a more extreme vasomotor response when the degree of deviation from the set value is of a more minor nature.

The control system which has been described as the first line of defence, would seem to be primarily involved in the minimization of the effects of environmental changes. The physiological data alone, illustrates that human thermo-regulation is, to say the least, complex. Nevertheless the operation of the entire system can only be understood by dissociating and analysing, where possible, the function and range of the constituent parts.

In addition to Benzinger and Hammel, Houk et. al. (1967), recognise the existence of a neutral temperature region where the vasomotor mechanism acts alone. Randall et. al. (1963), also discuss the importance of skin temperature in the neutral temperature region. Similarly Yamamoto et. al. (1969), have shown that within the range of vasomotor control, blood circulation in the periphery is related to environmental temperature by an almost linear relationship. Milsum (1966), discusses the existence of fine control in human thermo-regulation

which acts as a feed forward mechanism which takes effect before the internal temperature has had time to change. Other authors, for example Hertzman (1963) and Robinson (1963) also emphasize the importance of the skin receptors in vasomotor control.

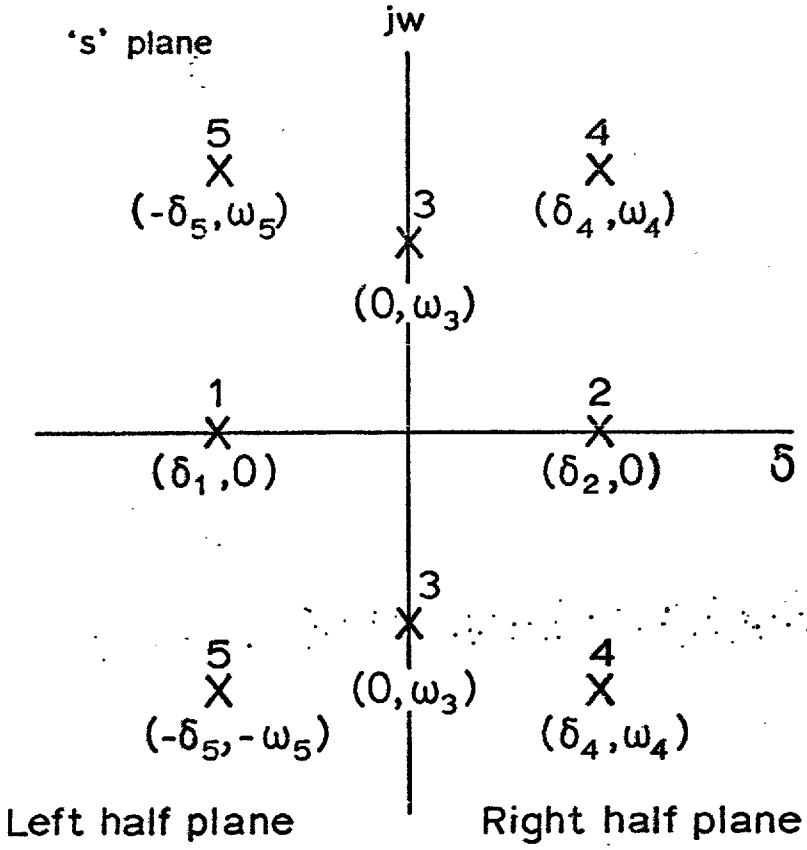
CHAPTER 3

THE ENTRAINMENT OF THE THERMO-REGULATORY SYSTEM.

3.1 INTRODUCTION.

It has been known for a considerable time that digit blood flow consists of a large number of spectral components which combine to produce a complex waveform. Burton (1939), and Burton and Taylor (1940), have investigated these waveforms in some detail and have managed to isolate certain spontaneous components which they attribute to thermo-regulation. These authors state that the comporent associated with temperature regulation varies in period from 15 seconds to 120 seconds. Careful studies by Taylor show that the commonest periodicity lies in the range 30-50 seconds. The question of attributing a particular set of spectral components to temperature regulation was a subject which was fully discussed by these authors. Their conclusion, based on a number of experiments, was that the components they were investigating resulted solely from thermo-regulatory control.

The evidence presented in chapter two led to the conclusion that the temperature of the human body is controlled by some form of negative feedback system. The issue to be resolved is therefore, what type of control system would produce the type of spontaneous activity described by Burton and Taylor? For linear systems, oscillations of the type under consideration



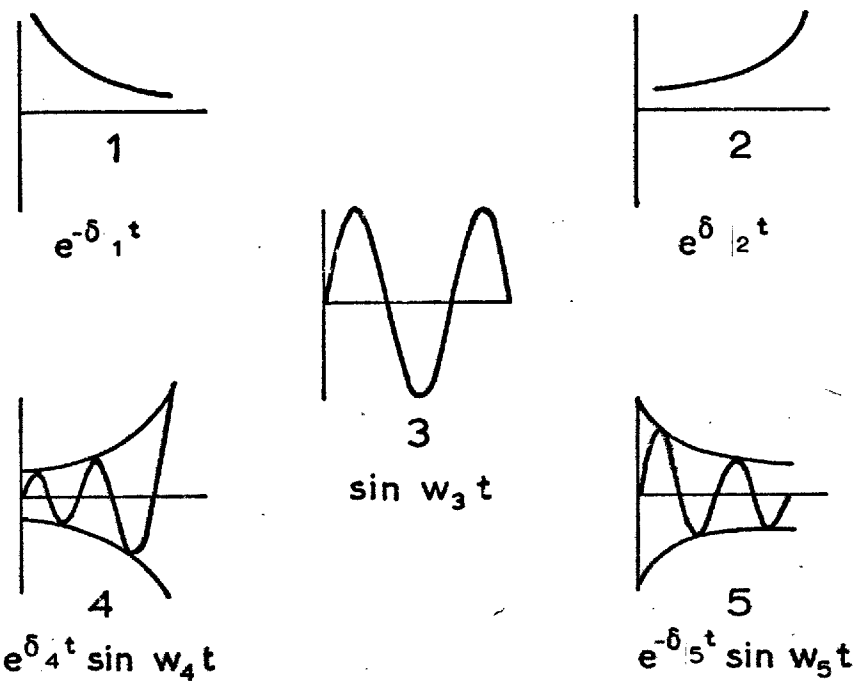


Fig. 3·1 The types of response and their equations, in the 's' plane.

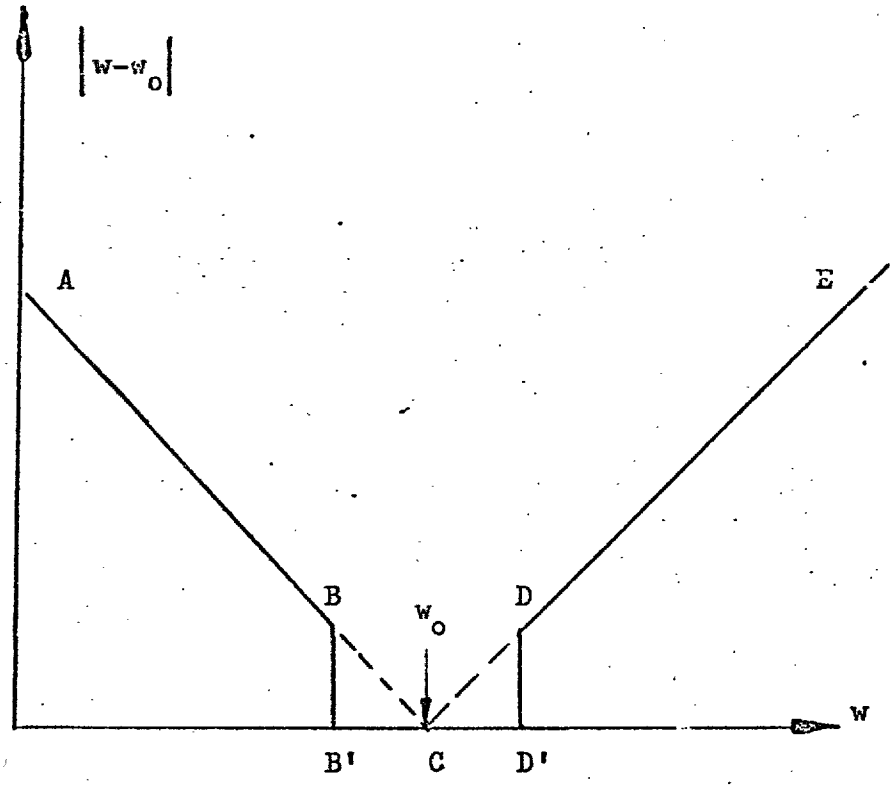


FIGURE 3.2

This figure illustrates the principle of entrainment described by Minorsky.

The region between B' and D' on the w axis is known as the range of entrainment.

occur when the system is operating on the jw axis (figure 3.1). Due to the anatomical structure of the physiological system, the neural time delays and other factors, this mode of operation is highly improbable. Therefore, to produce this type of stable oscillatory mode, the control system must be nonlinear.

Nonlinear control systems can be divided into two types: first, a system where the non-linearity is, in essence, purely due to the limitations of the dynamics of the physiological system. This type of system would be described as operating in the right half s-plane and has an impulse response which consists of a positive exponential term and sine function. Positive exponential terms cause the system output to increase until it is limited by the physical structure of the system. The second type of nonlinear system is one which is working within the limits of its response, but has within its structure discrete nonlinear elements.

Minorsky (1962), discusses this second type of nonlinear oscillatory system in some detail, with particular reference to the entrainment of such a system by an external stimulus. If the natural frequency of oscillation of the system is w_o, and an external perturbation of frequency w is applied, the system output exhibits a number of components which arise from the interaction of the natural oscillation and

the external stimulus. When the frequency of the stimulus (w), approaches the frequency w_o, the degree of interaction decreases up to a certain value of $|w-w_o|$. At this point the system output comprises a dominant component at the stimulus frequency (w), and the system is therefore said to have been entrained by the stimulus. The region over which the nonlinear oscillatory system output is of the entrained type is called (Minorsky (1962)), the range of entrainment.

This principle can be extended to any oscillatory system which has discrete nonlinear components. It was therefore proposed to perform experiments to establish if the peripheral thermo-regulatory system could be entrained by an external stimulus. Evidence of entrainment would confirm that the system is of the second nonlinear type.

3.2 ENTRAINMENT EXPERIMENTS- SERIES 1

The Experimental Procedure.

With the core at 37°C, thermal variations in the extremities have been postulated to be dealt with solely by the peripheral system. The relevant innervation is of two types: first, vasodilator nerves in the arm and secondly vasoconstrictor nerves in the hand. In the experiment, the digit blood flow was measured by a photocell attached to the small finger of the right hand. The justification for this procedure is as follows.

There have been a number of papers which compare the response of the hands to heating. Pickering (1936), was able to show that there were equal rates of heat elimination from the two hands. Arnott and Macfie (1948), discovered that there was also equal heat elimination from the five fingers of one hand. These papers indicate that monitoring the blood flow in one finger is an accurate representation of the state of the thermo-regulatory system. The hands and feet form the main vehicle of heat loss when the system is operating within the comfort zone. Under such conditions the blood flow in the hand gives a good indication of the state of the overall system. Because the hand is a good heat sink, it is also amply endowed with temperature receptors (Burton (1963); therefore within the comfort zone, any thermal stimulus should

have a noticeable effect.

The ideal thermal stimulus would be a sinusoidal disturbance; however, due to practical difficulties this type of input is very difficult to achieve. Fortunately a solution is available. If the input disturbance applied to the skin is a square-wave, the heat flow will have been filtered (low pass) by the time it reaches the thermal receptors. The squarewave thermal input U_{in} can be represented in time series form:

$$U_{in} = \sin wt + \tfrac{1}{3} \sin 3wt + {}^{1}/_{5} \sin 5wt + \qquad 3.1.$$

It is clear that approximate low pass filtering of the signal represented in equation 3.1. would produce an approximately sinusoidal input due to the fundamental term.

Spontaneous Digit Blood Flow.

At the commencement of the experiment, the subject was seated in a room at an ambient temperature of 18°C. With the subject relaxed and quiet, the spontaneous digit blood flow was recorded for a period of thirty minutes on to magnetic tape.

The Digit Blood Flow Control Experiment.

In order to produce a squarewave thermal stimulus, the left hand has to be transferred between two vessels. Therefore observations of the effects of a thermal stimulus have to be separated from the effects produced by changes in blood pressure due to the movement of the hand. The control experiment consists of transferring the hand from one vessel to the other every ten seconds, but with the water removed.

Digit Blood Flow With a Squarewave Thermal Input.

Thermal Stimulus of 20 Second Periodicity.

For this part of the experiment, the subject was seated in the same position and under similar ambient conditions as for the case of the spontaneous response. The subject placed his left hand alternately in water baths at 16°C and 46°C; the hand being placed in the other bath after ten seconds. The digit blood flow was recorded simultaneously on magnetic tape. This procedure was continued for a period of fifteen minutes.

Thermal Stimulus of Two Minute Periodicity.

During this phase of the experiment the same procedure was adopted as for the 20 second periodicity stimulus; however, on this occasion the hand was alternated between the two water baths at intervals of one minute.

The Analysis of the Experimental Data.

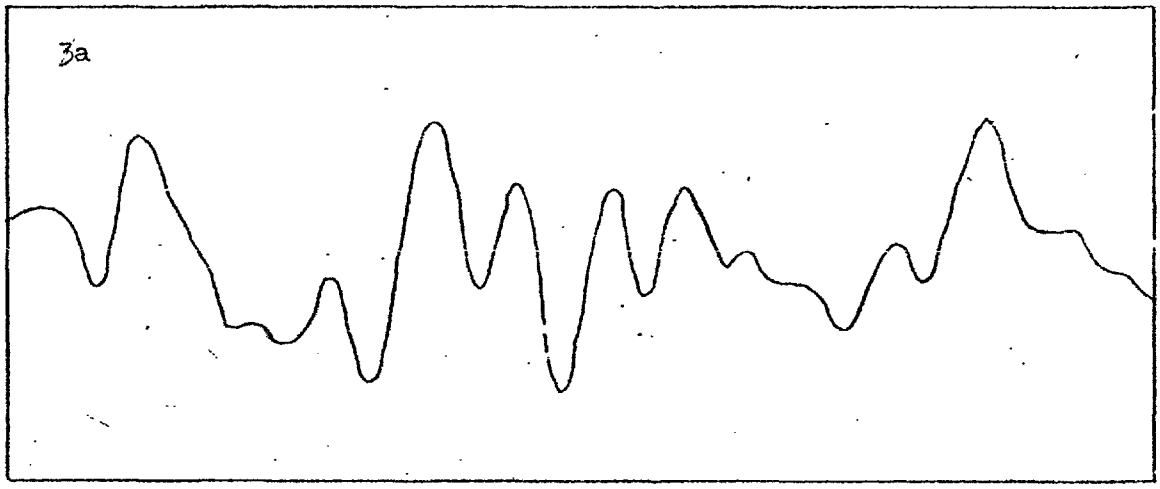
The initial step in the analysis of the experimental data was analogue filtering; low pass filtering of the data is effected with a corner frequency of 0.2 Hz. The filtered version of the data is illustrated in figure 3.3. A great deal more information can however be extracted from the data by digital filtering techniques. All the meaningful information related to temperature is contained within the frequency range 0-1 Hz, so that prior to Analogue to Digital Conversion (ADC), the original unfiltered data is low pass filtered at a corner frequency of 2 Hz.

Digital filtering of the data using an algorithm based on the fast Fourier transform (FFT), reveals fluctations presumed to be associated with thermo-regulation (and similar to those discussed by Burton 1939, 1940). Figure 3.4 illustrates the results as follows: diagram a, shows the digit plethysmogram signal obtained from the small finger of a normal resting adjust (subject RK), seated in a room at 18°C; while diagram b, is the plot of this information transferred to the frequency domain. It is apparent from figure 3.4b that the spontaneous digit blood flow comprises a large number of components spread throughout the frequency range 0-01 Hz; consequently plot c, shows

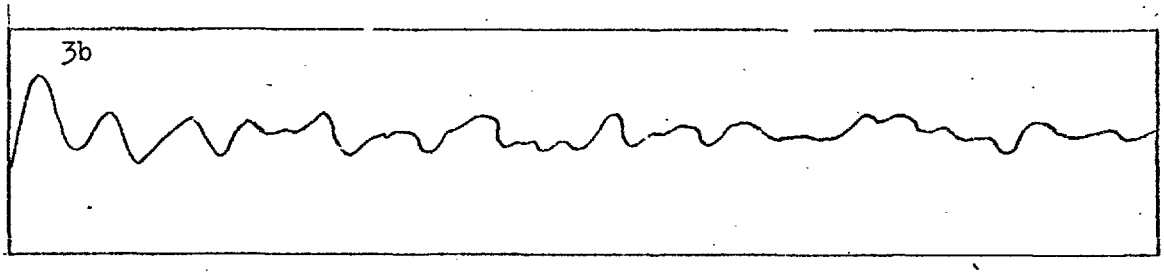
FIGURE 3.3 FILTERED (LOW PASS) f_c = 0.2 Hz

TIME SCALE 1 INCH = 100 SECONDS

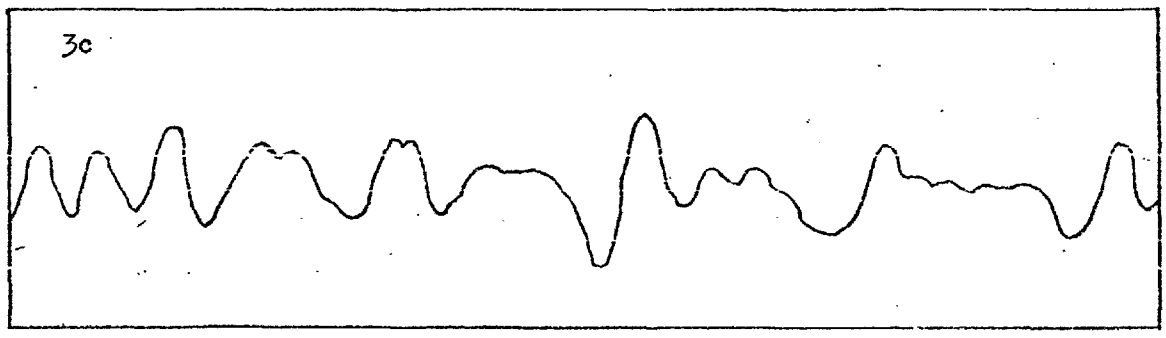
DIAGRAMS OF DIGIT BLOOD FLOW(FIG 3b and 3c are for the condition of a thermal stimulus applied to the contralateral hand).



SPONTANEOUS DIGIT BLOOD FLOW



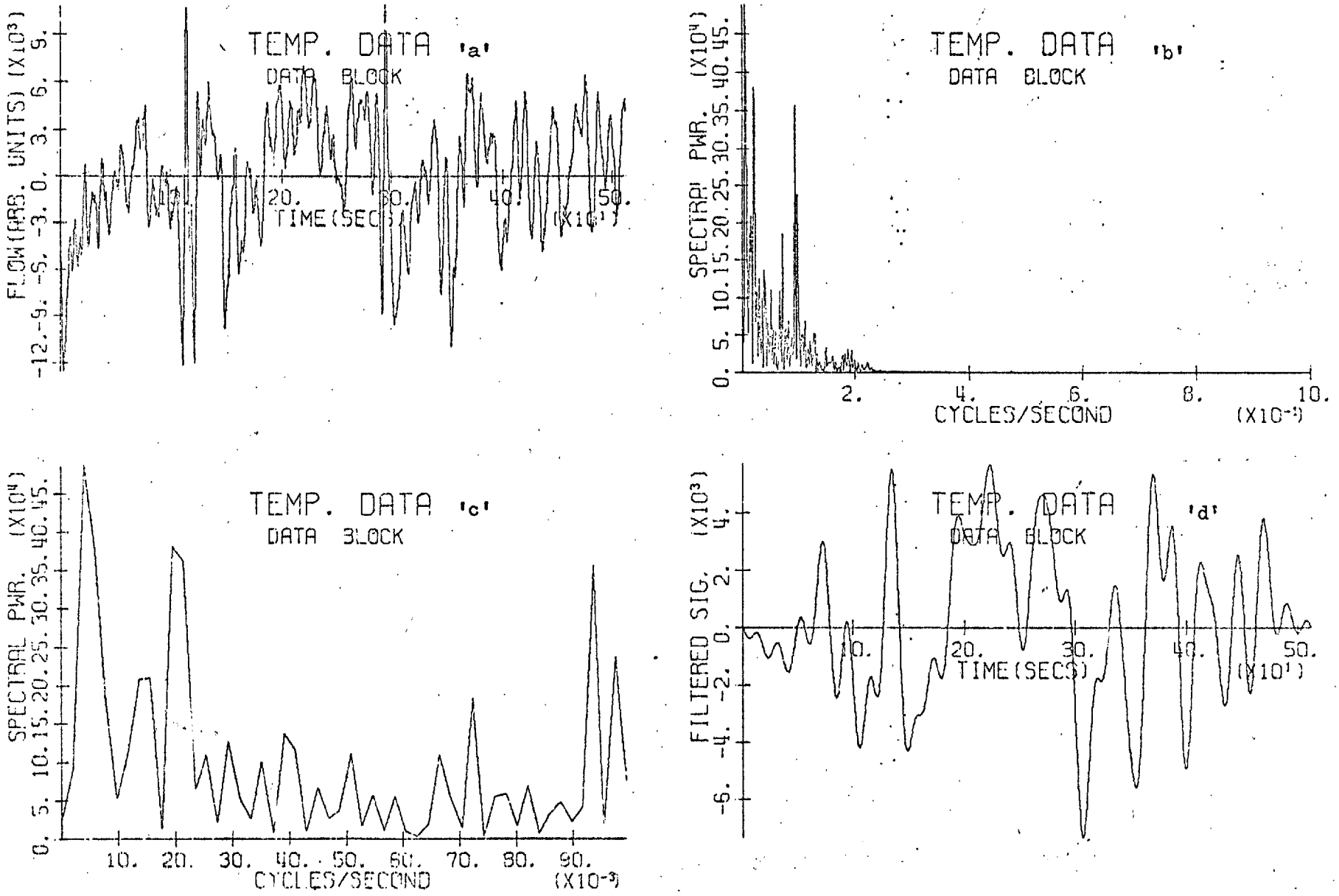
SQUAREWAVE INPUT-PERIOD 20 SECONDS



SQUAREWAVE INPUT-PERIOD TWO MINUTES

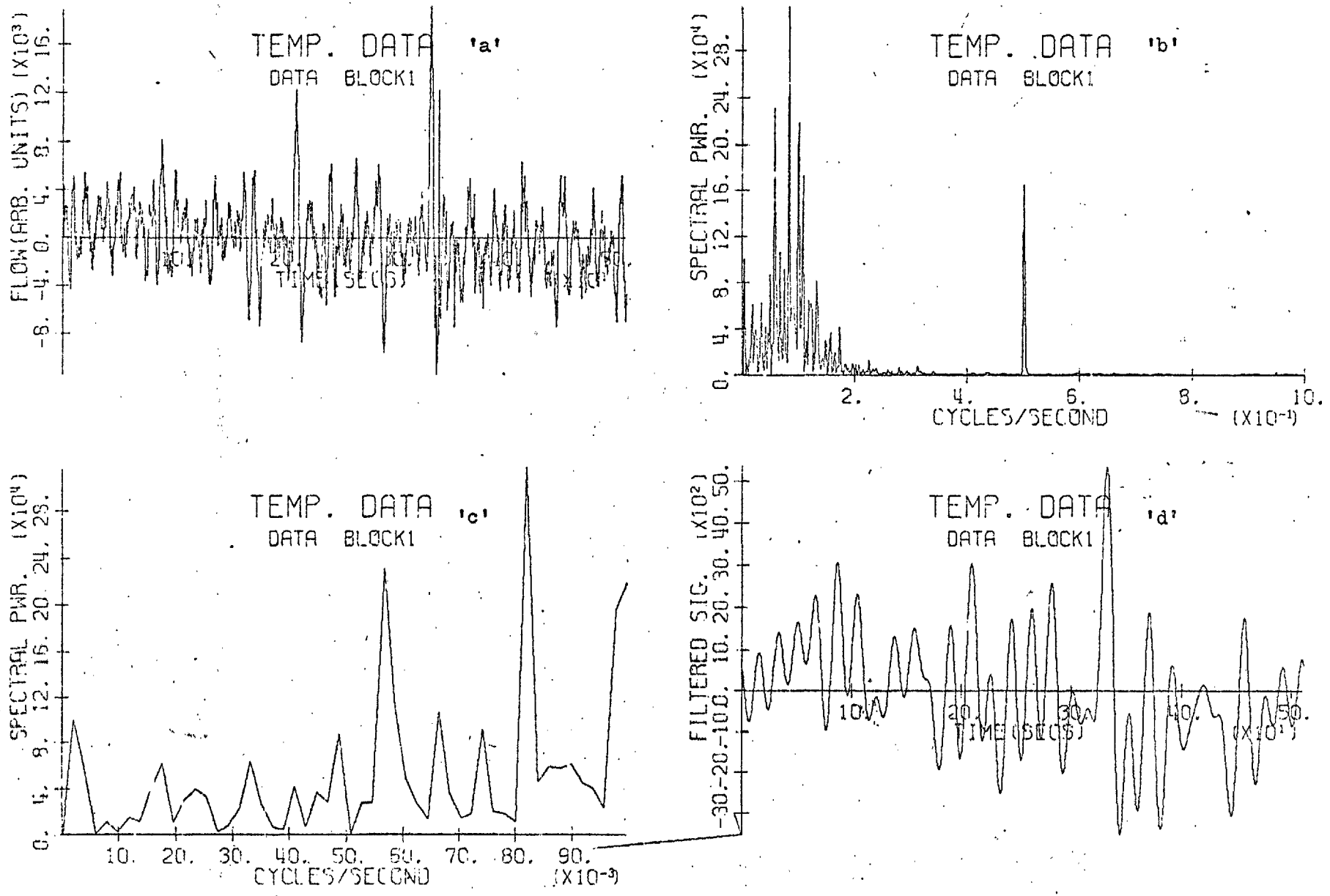
SUBJECT RK-SPONTANEOUS DIGIT BLOOD FLOW.

FIGURE 3.4



SUBJECT RC-SPONTANEOUS DIGIT BLOOD FLOW.

FIGURE 3.5

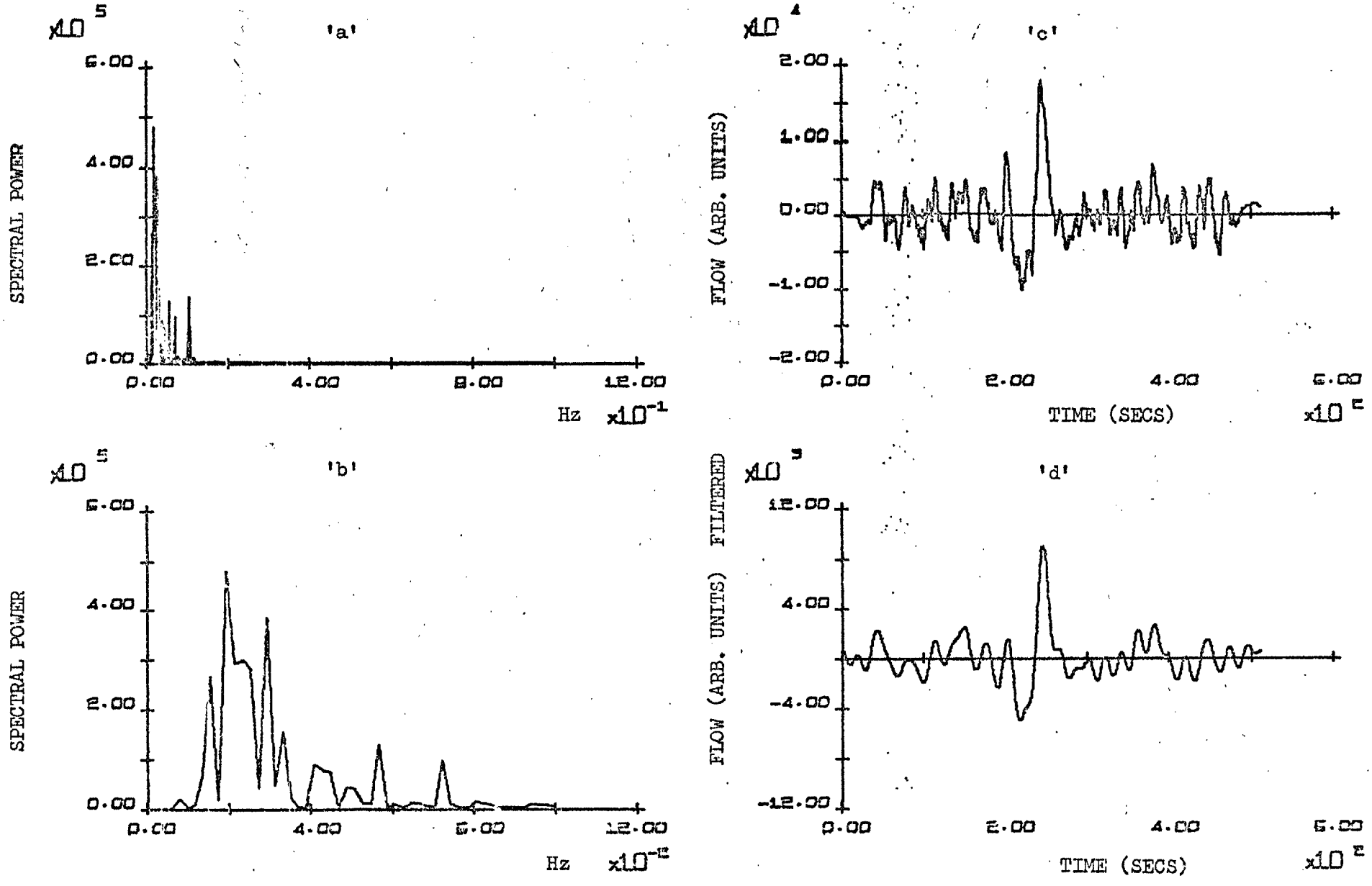


only the components in this range. Finally, in diagram d, all components of period less than seventeen seconds have been removed from the original waveform. The resultant signal consists solely of slow fluctuations thought to represent the activity of the thermo-regulatory system. Figure 3.5 represents equivalent experimental data to that of figure 3.4, but for subject RC.

The control experiment was designed to investigate the variations in digit blood flow produced by movement of the contralateral hand. The most interesting diagrams of figure 3.6 (which relates to the control experiment), are a and b, these show the power spectrum of the digit blood flow. It is apparent that most of the components lie in the frequency range 0-0.1 Hz. Consequently, to ease understanding of the data of figure 3.6a, figure 3.6b illustrates this power spectrum expanded over the frequency range 0-0.1 Hz. Figures 3.6c and 3.6d are the time domain equivalents of 3.6a and 3.6b. Figure 3.7 consists of two plots; the right hand diagram shows the power spectrum of the resultant digit blood flow when a twenty second period thermal stimulus is applied, while the left hand diagram is of the data obtained from the control experiment. By comparing these two diagrams, the effect of the thermal stimulus on blood flow,

THE RESULTS OF THE CONTROL EXPERIMENT.

FIGURE 3.6



DIGIT BLOOD FLOW-CONTROL EXPERIMENT FIGURE 3.7 DIGIT BLOOD FLOW-20 SECOND PERIOD STIMULUS.

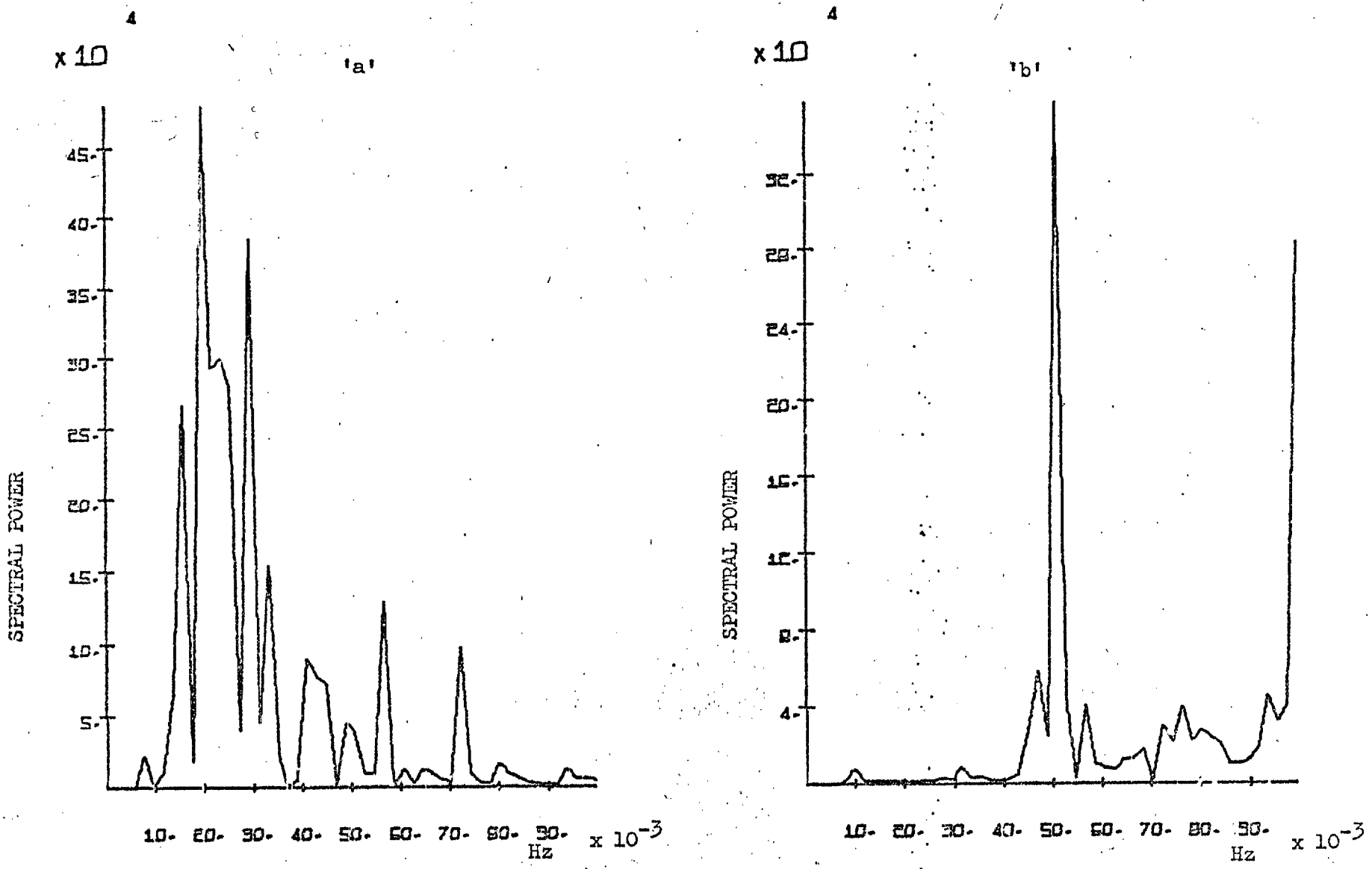
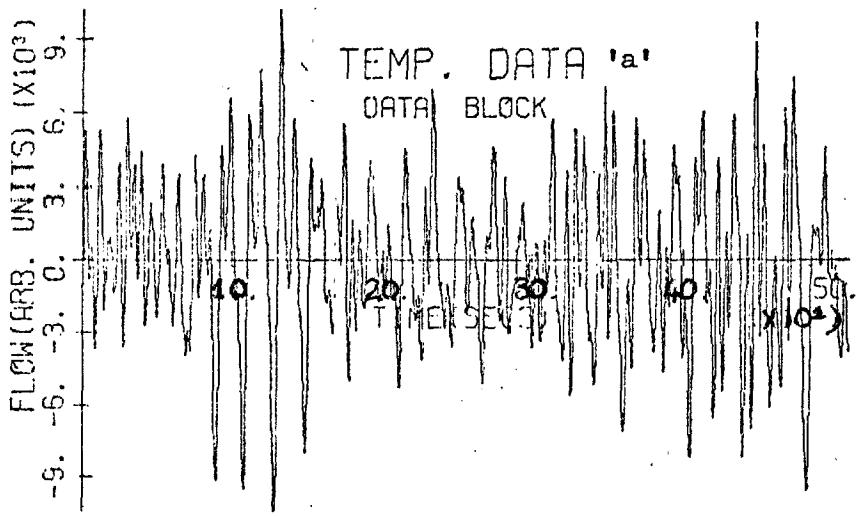


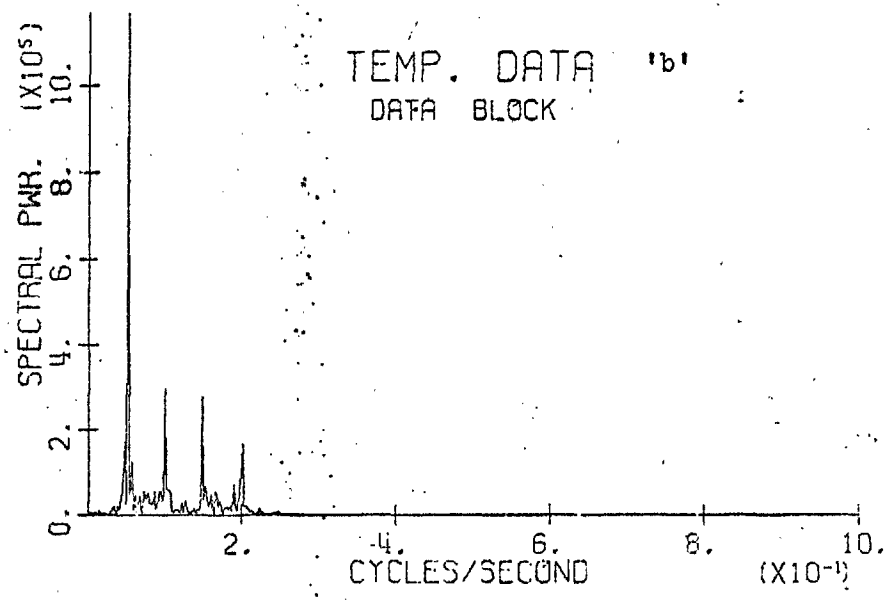
figure 3.7a, can be seen to apply throughout the entire frequency range. In the presence of the stimulus (fig. 3.7b), there is one dominant component which occurs at the stimulus frequency. It is therefore concluded that the phenomenon illustrated in figure 3.7b, is solely due to the effect of the thermal stimulus, and not due to movement. The entrainment experiment can now be discussed.

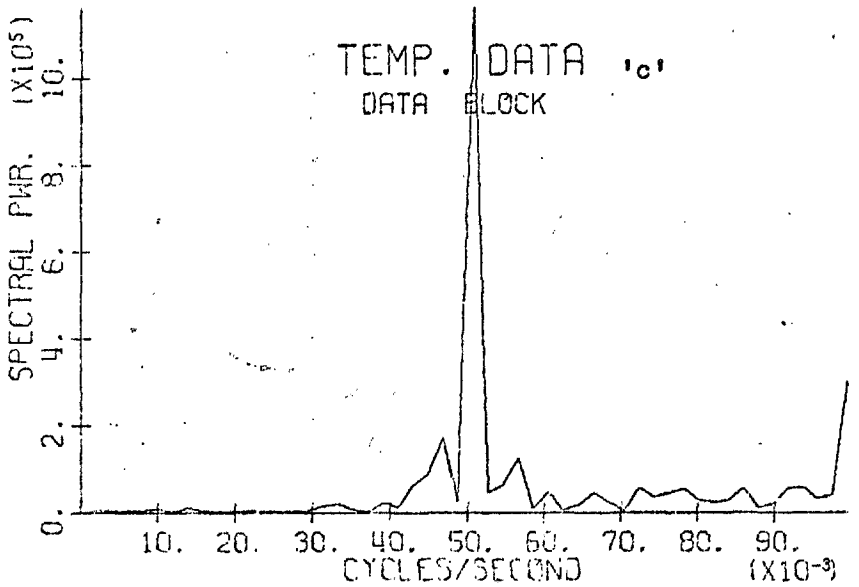
An external disturbance of twenty seconds periodicity (less than the period of the dominant spontaneous component of presumed thermal origin), was applied to one hand. The digit blood flow signal was recorded and the low pass filtered version is shown in figure 3.8. The waveform is quite different from the spontaneous signal; it comprises, when filtered, only a substantial component which has the same period as the stimulus. The expanded version of the response in the frequency domain shows this quite clearly; here the component at 5×10^{-2} Hz (20 seconds periodicity) is totally dominant. The implication is that entrainment of the system by the external stimulus has occurred. Figure 3.9 illustrates the equivalent data for subject RC; here also entrainment has occurred.

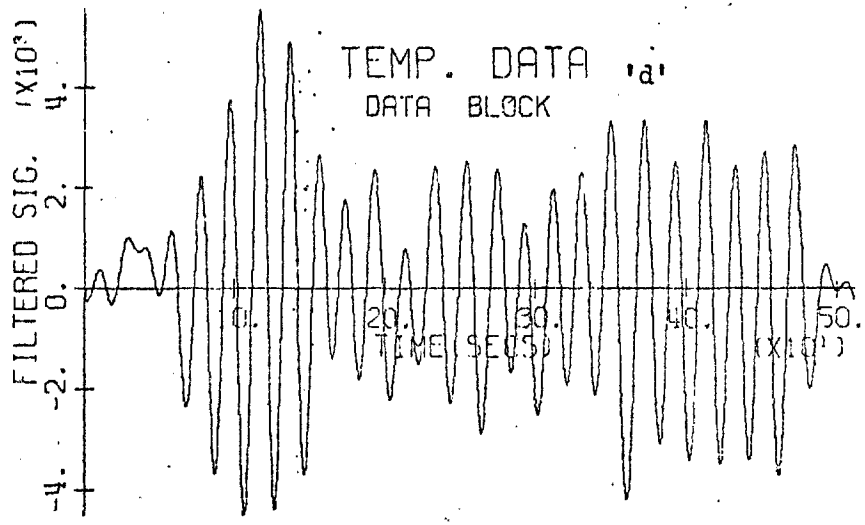
SUBJECT RK-DIGIT BLOOD FLOW WITH A 20 SECOND PERIOD STIMULUS.

FIGURE 3.8



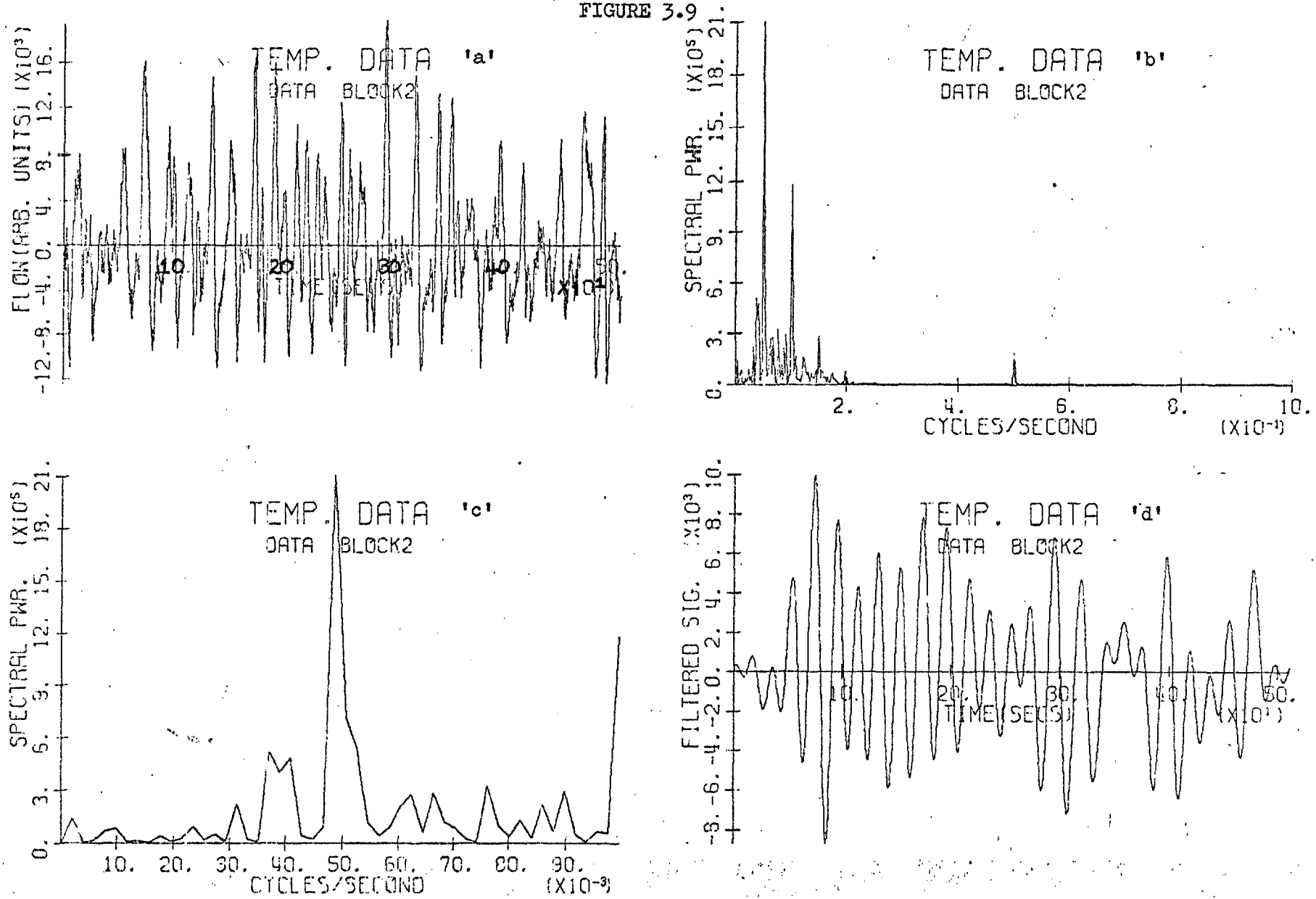






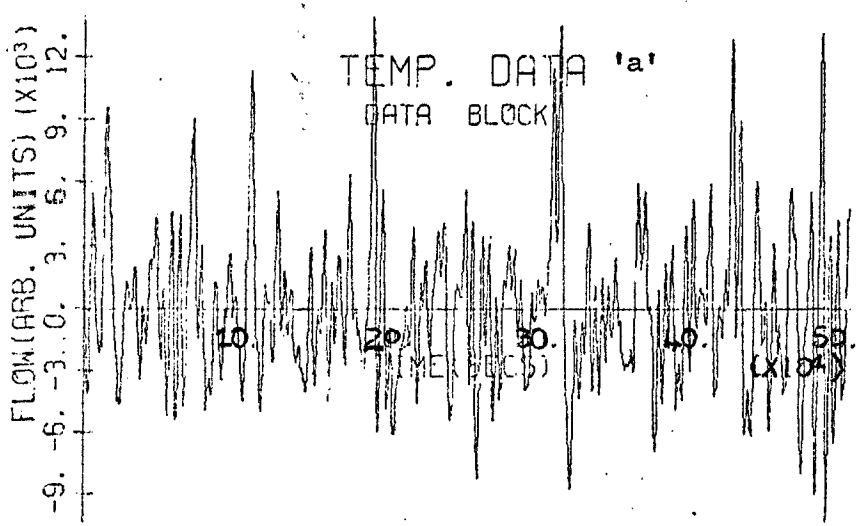
SUBJECT RC-DIGIT BLOOD FLOW WITH A 20 SECOND PERIOD STIMULUS.

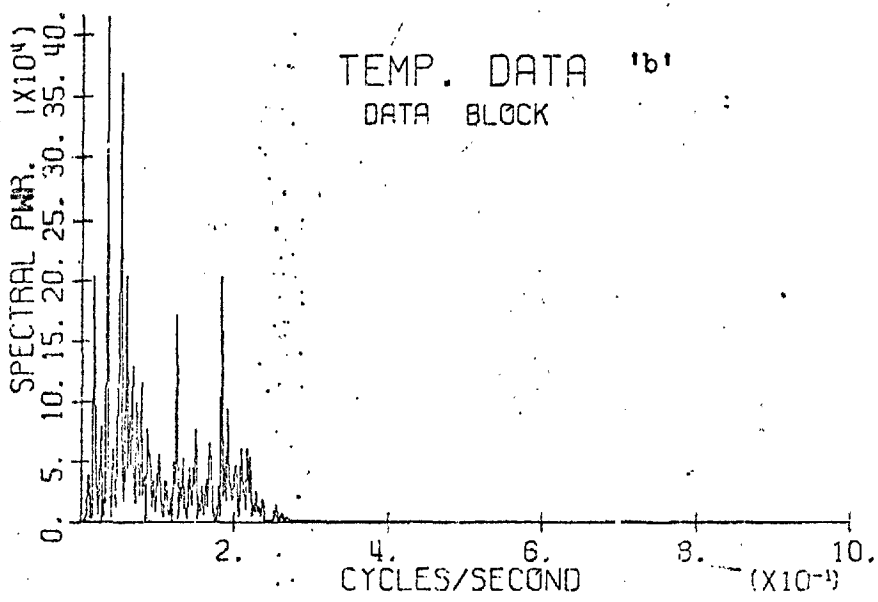
FIGURE 3.9

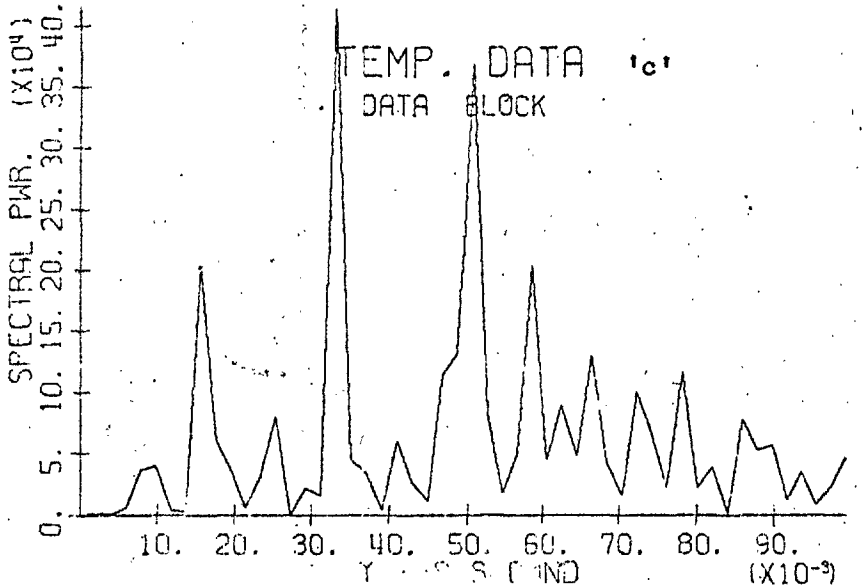


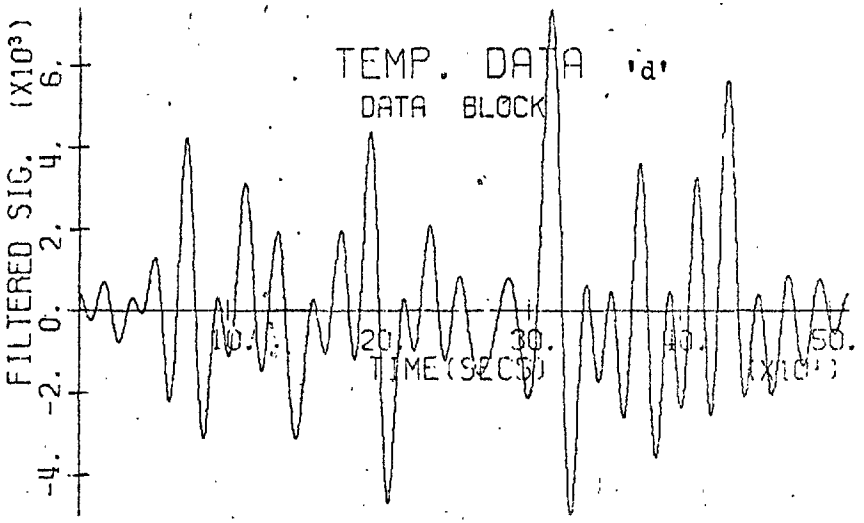
SUBJECT RK-DIGIT BLOOD FLOW WITH A 120 SECOND PERIOD STIMULUS.

FIGURE 3.10



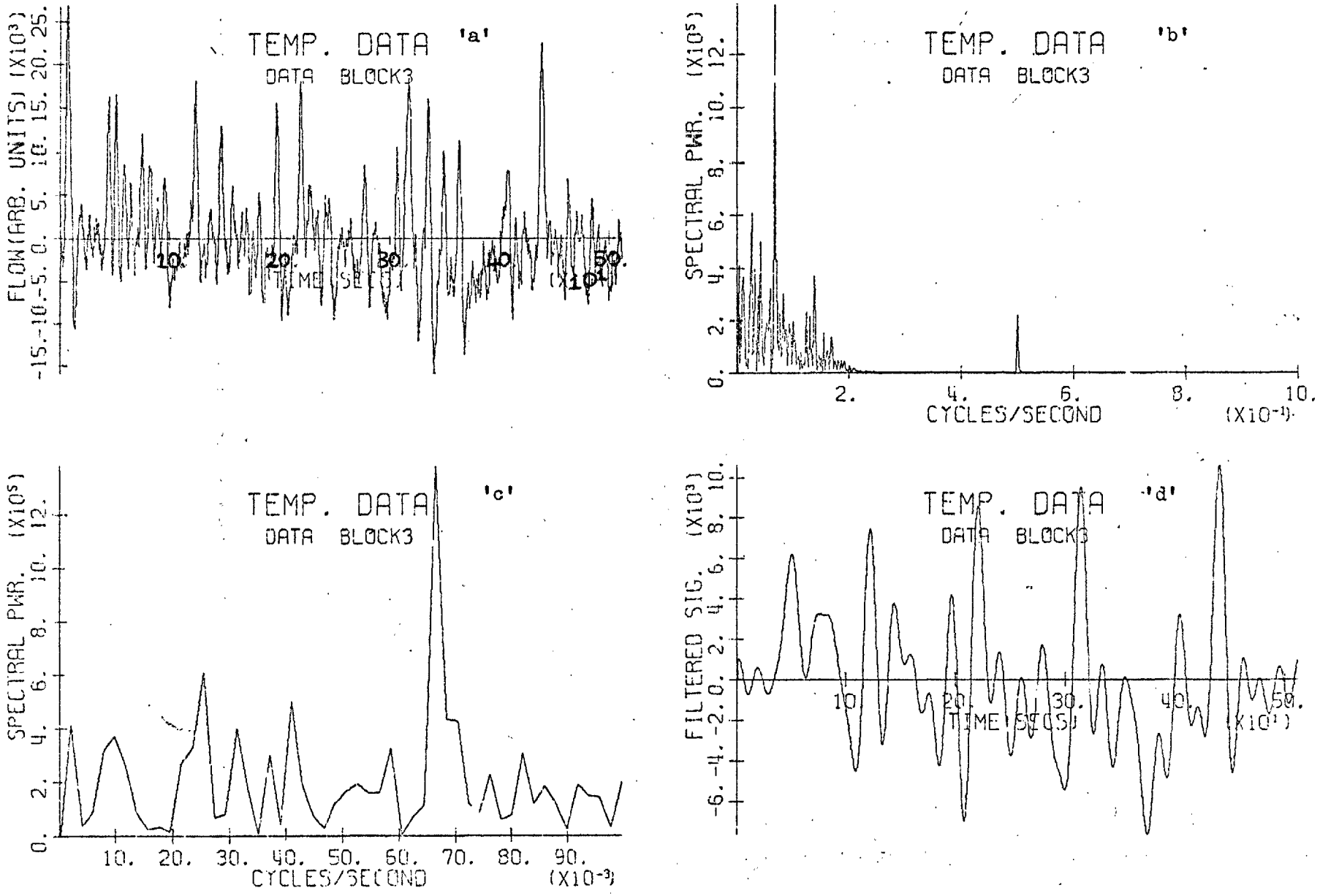






SUBJECT RC-DIGIT BLOOD FLOW WITH A 120 SECOND PERIOD STIMULUS.

FIGURE 3.11



An external stimulus having the same amplitude as the previous perturbation, but of two minute periodicity (greater than the most dominant presumed temperature component), produces a different effect. Figures 3.10 and 3.11, which are the graphical representations of the data obtained from the two subjects, illustrate that spontaneous activity remains and while a component at the stimulus frequency may be present in the digit blood flow this has certainly not entrained the system. It can be concluded therefore, that the two minute stimulus lies outside the range of entrainment described by Minorsky (1962). Hence the entrainment is frequency selective as far as the disturbance is concerned and the effect can be identified as selective entrainment.

The experiments which have been discussed here for subjects RK and RC, were also performed on a third subject DZ. Because of the similarity of the results (DZ), with the data obtained from the first two subjects, this experimental data is not illustrated in the text.

3.3 ENTRAINMENT EXPERIMENTS - SERIES TWO.

The first set of entrainment experiments investigated the entrainment of the peripheral thermo-regulatory system by an external stimulus at two frequencies; namely, twenty seconds and two minutes periodicity. These experiments established that the thermal system could be entrained by the twenty second stimulus, while the two minute stimulus did not entrain the system.

It was therefore considered worthwhile to perform a second series of experiments to test the systems behaviour between these limits. The experimental procedure was identical to that used for the first series, except that here the stimulus frequencies were of forty, sixty and eighty, seconds periodicity.

The Analysis of the Experimental Data.

The second series of experiments were performed on subjects RK and DZ, and the data sampled at 2Hz during analog to digital conversion.

Figure 3.12 (subject RK) shows the time domain plot of digit blood flow with a forty second periodicity stimulus, while figure 3.13 illustrates the corresponding power spectrum. Figure 3.13b shows the frequency range 0-0.1 Hz on an expanded scale. Figures 3.14 and 3.15 are

FIGURE 3.12 - SUBJECT RK - 40 SECOND STIMULUS

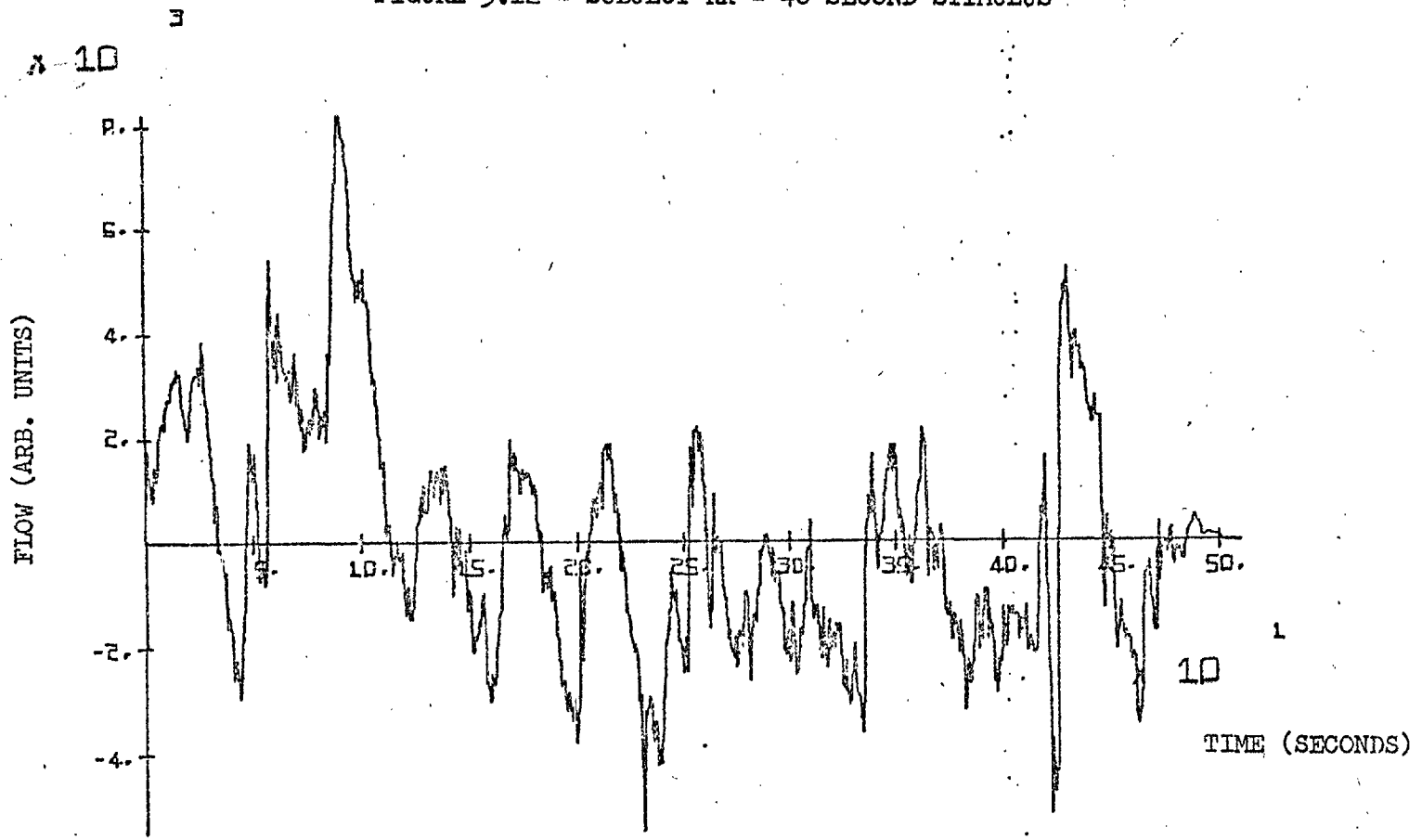
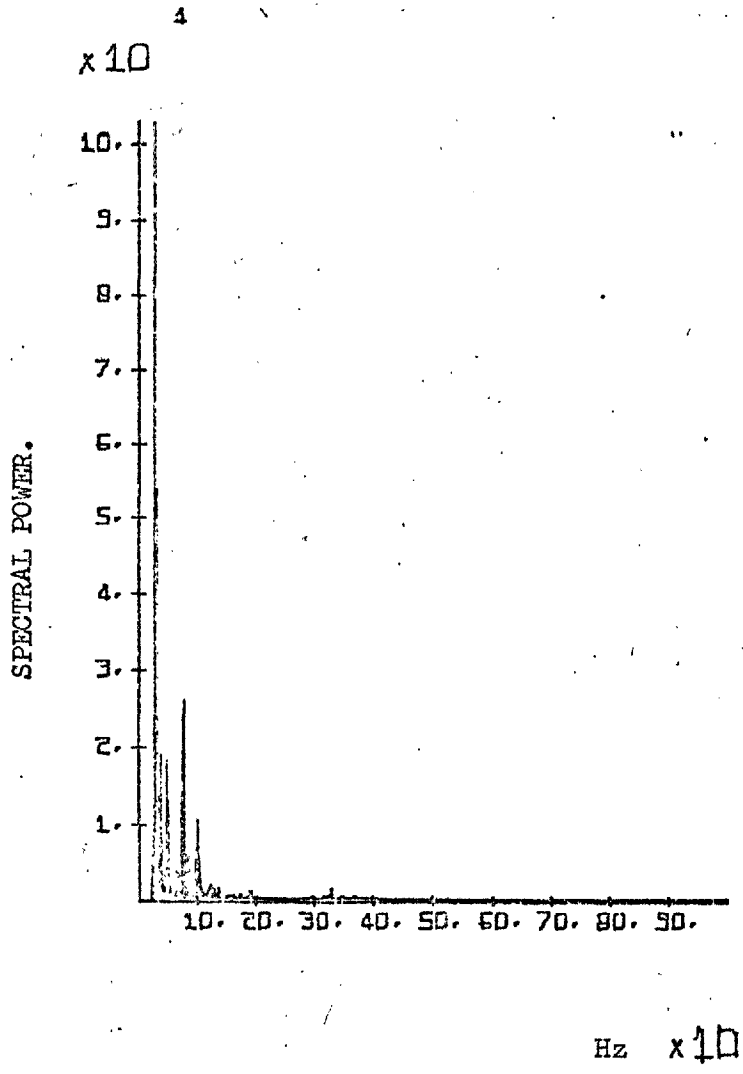


FIGURE 3.13 - SUBJECT RK - 40 SECOND STIMULUS



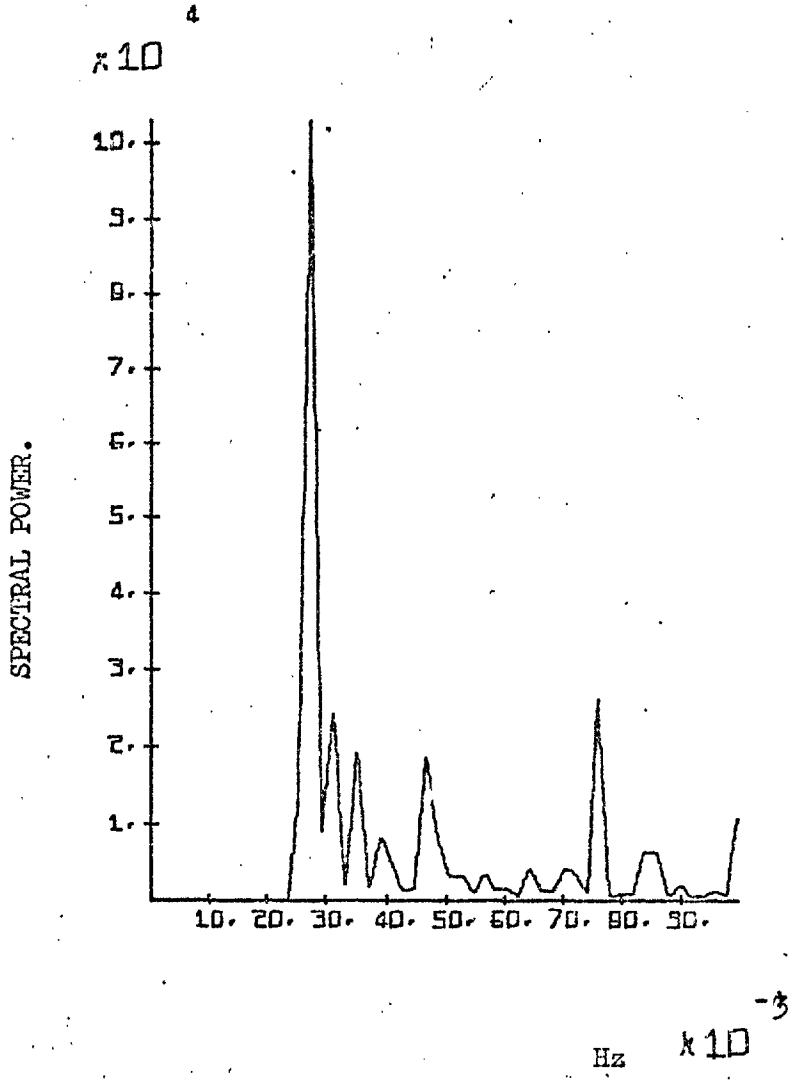


FIGURE 3.14 - SUBJECT DZ - 40 SECOND STIMULUS

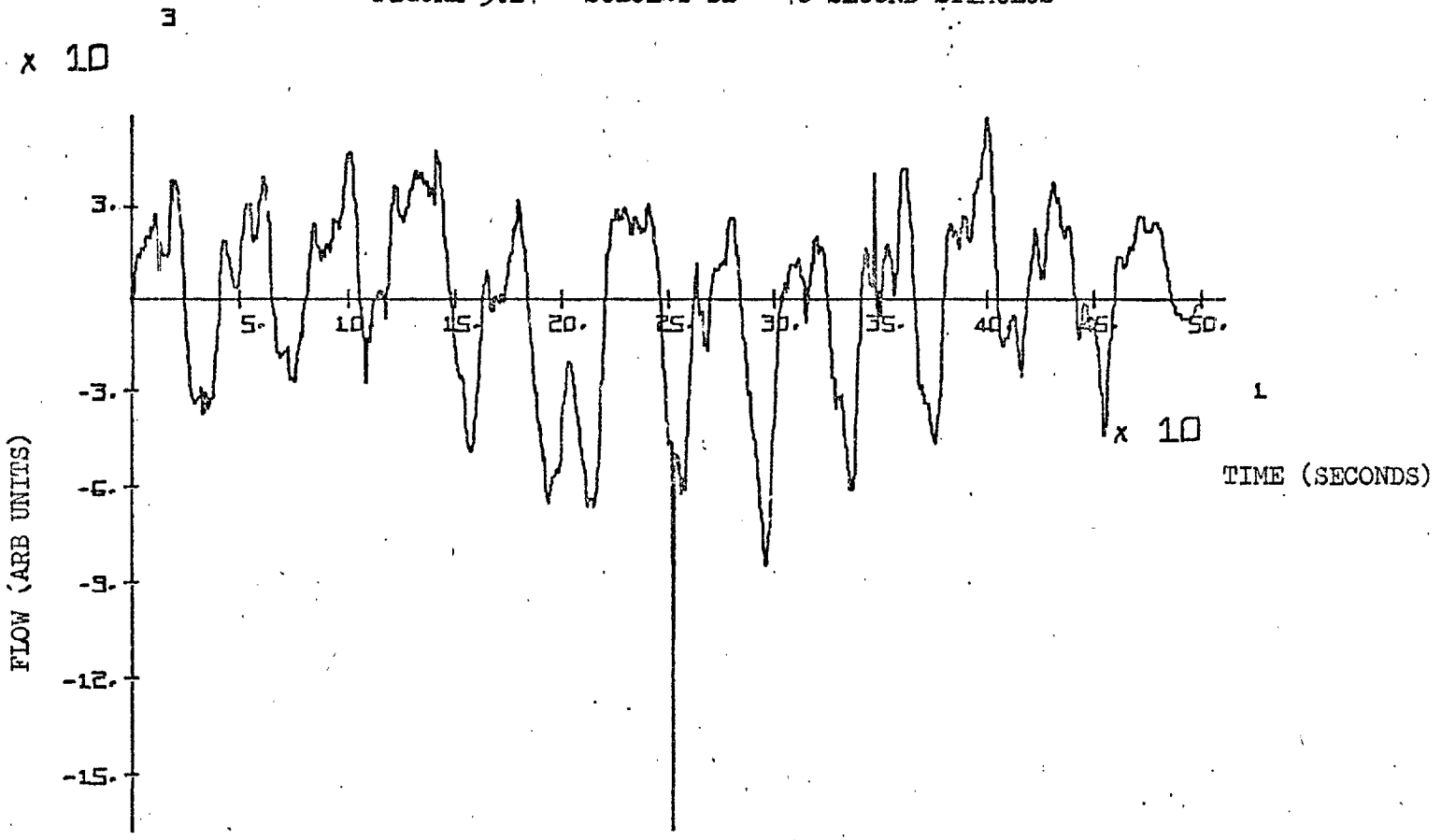
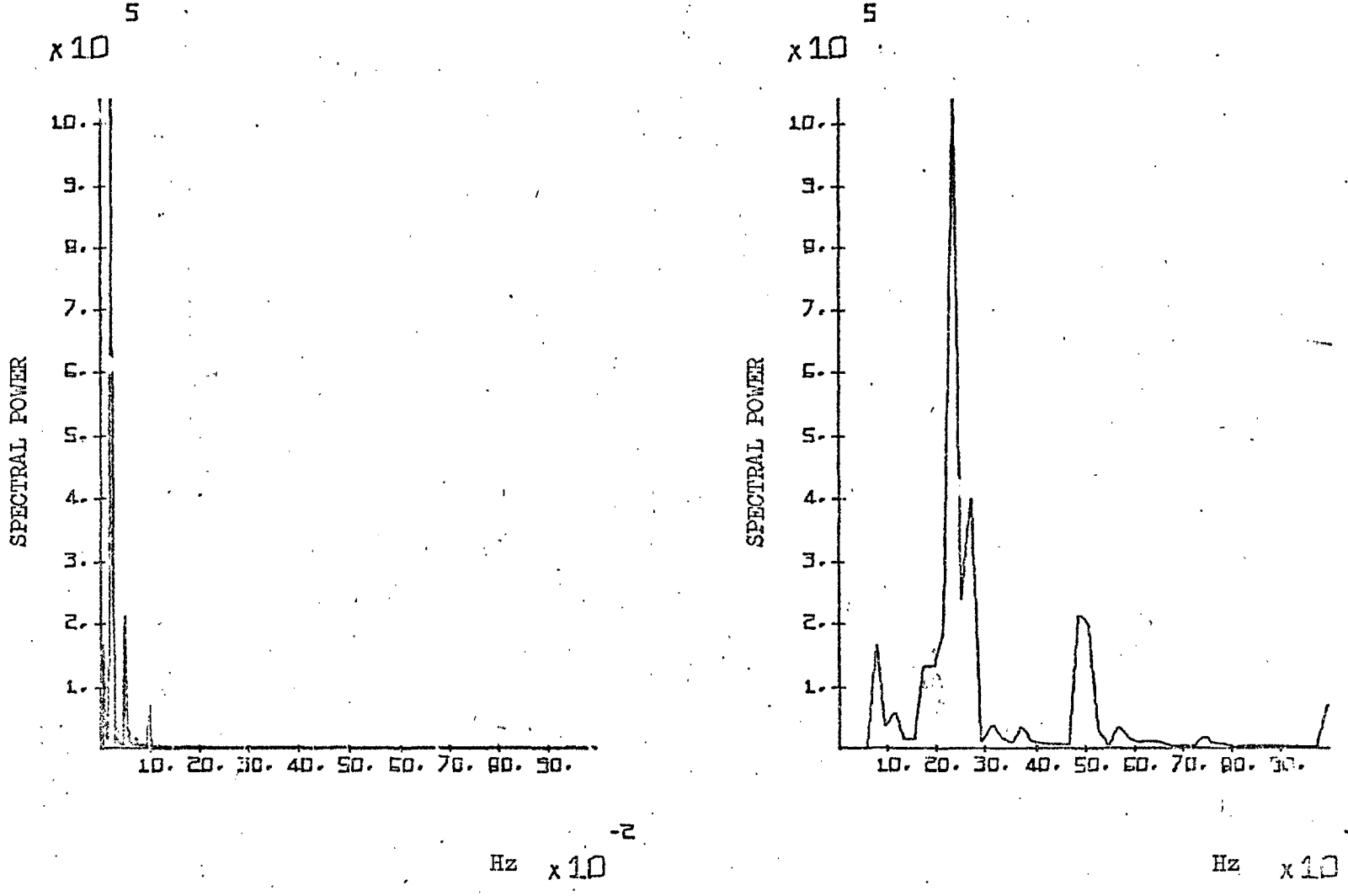


FIGURE 3.15 - SUBJECT DZ - 40 SECOND STIMULUS



the corresponding time domain and frequency domain plots for subject DZ. If one looks at the power spectra for the two subjects, it is apparent that there is a dominant frequency component at the stimulus frequency. This indicates that the thermal system has been entrained by the stimulus.

The experimental data for subject RK, with a sixty second stimulus applied, is interesting because the time domain waveform contains a section of data which is inconsistent with that which immediately preceeds and follows it. The region in question is approximately between 165 and 180 seconds (figure 3.16). This large component is thought to eminate from a source external to the system under consideration. If one applies a nonlinear filter to this region of the data (see appendix 1.1), it is apparent that the area under investigation becomes similar to the rest of the data in that region. Figure 3.17 illustrates the time domain waveform after the filter has been applied. The corresponding pre and post, filter spectra are shown in figures 3.18 and 3.19 and it can be seen that the effect of the filter is to reduce the power of the component at approximately 0.023Hz.

Figures 3.20 and 3.21, illustrate the data in the time domain and the power spectrum, for the sixty second stimulus applied to subject DZ. If the power spectra of

FIGURE 3.16 - SUBJECT RK - 60 SECOND STIMULUS
UNFILTERED WAVEFORM.

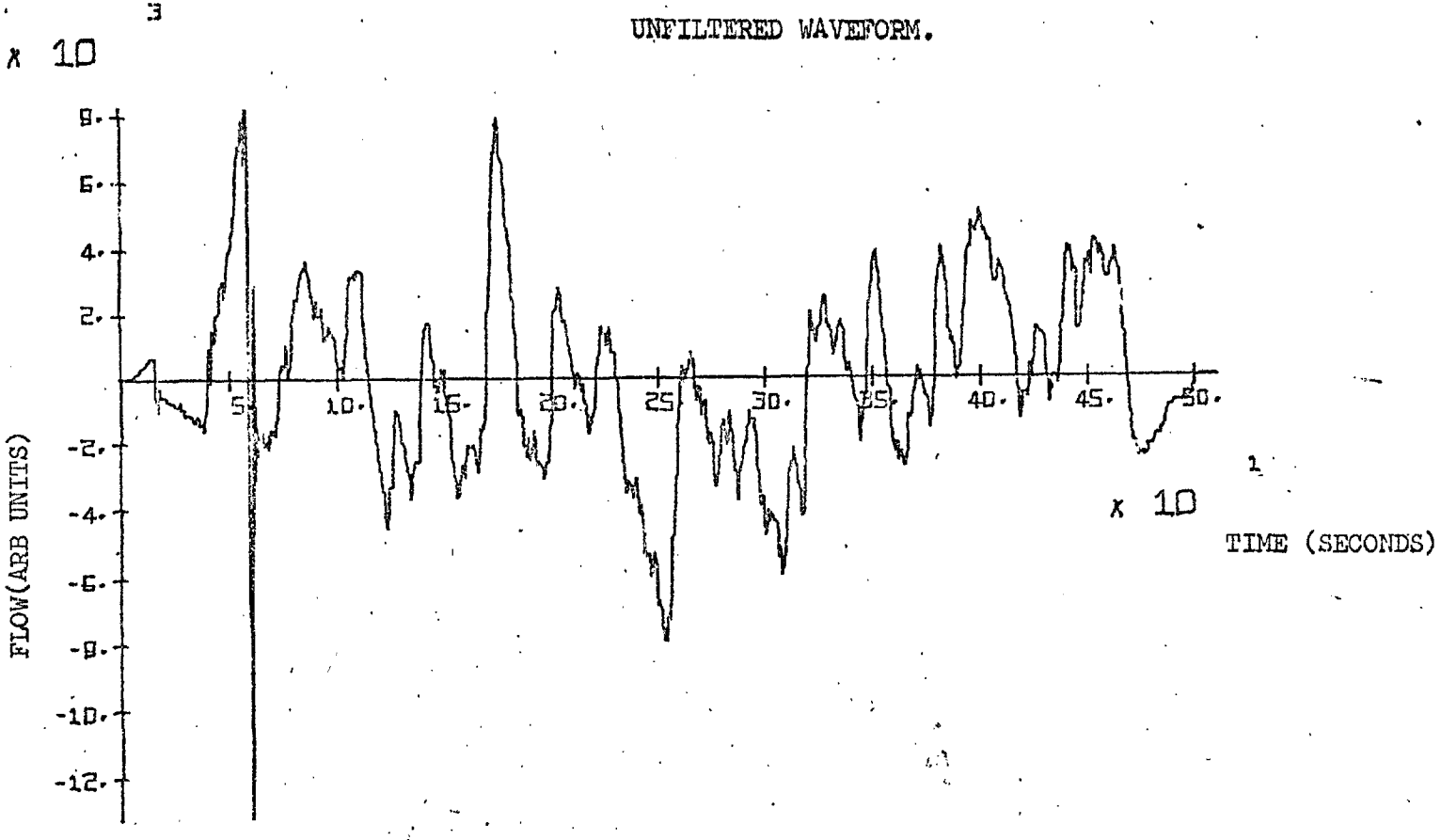


FIGURE 3.17 - SUBJECT RK - 60 SECOND STIMULUS FILTERED WAVEFORM.

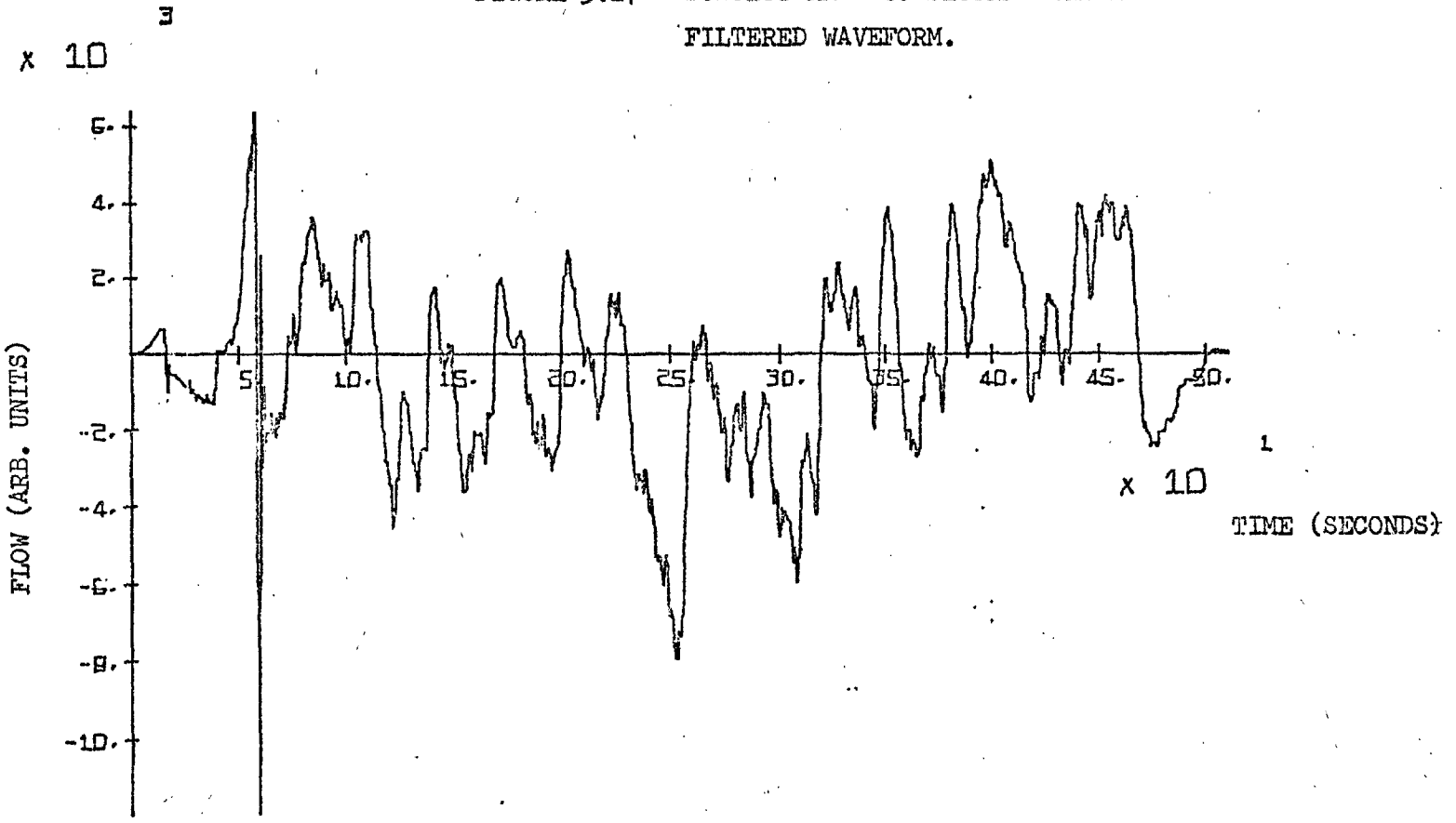


FIGURE 3.18 - SUBJECT PK - 60 SECOND STIMULUS UNFILTERED.

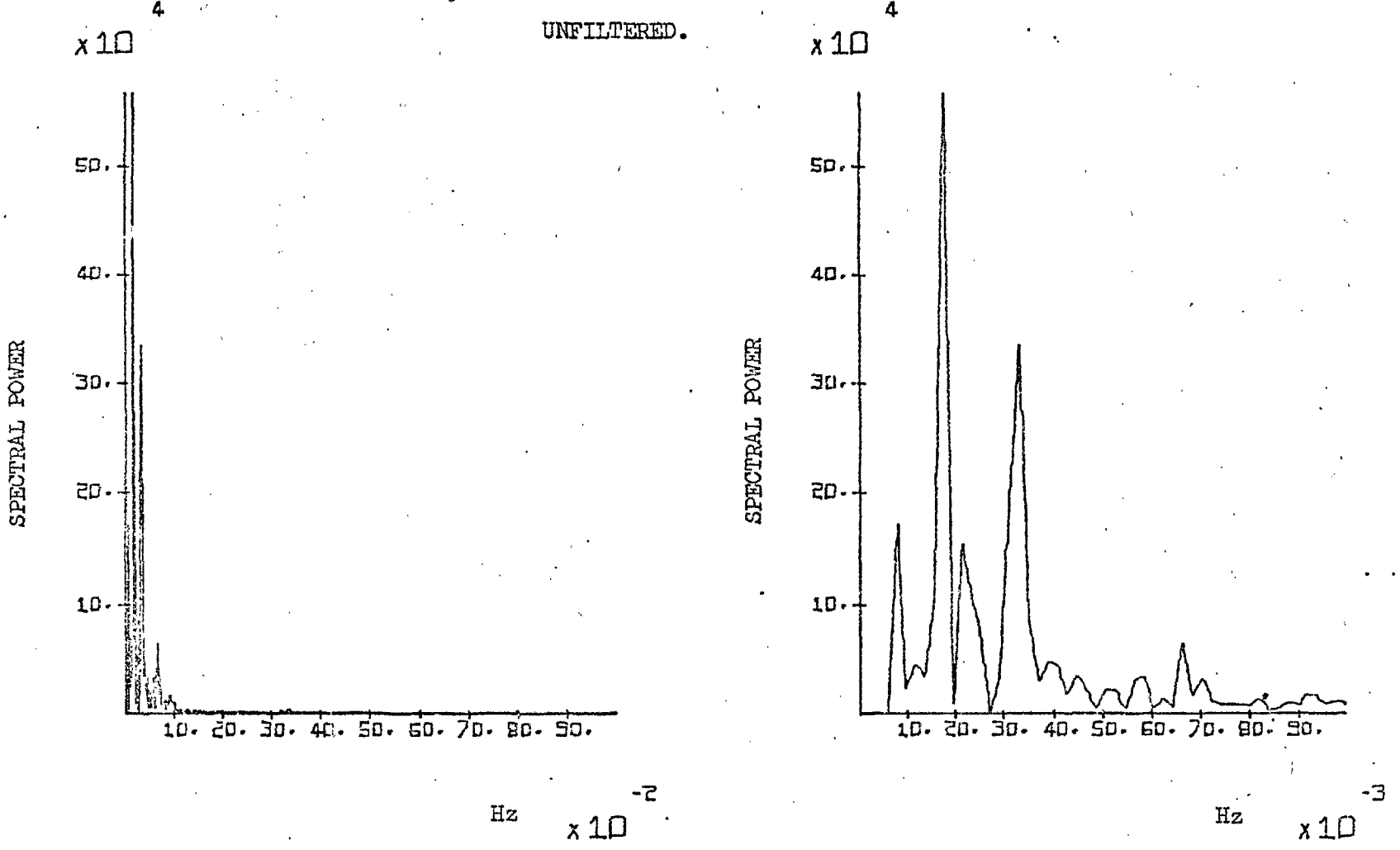
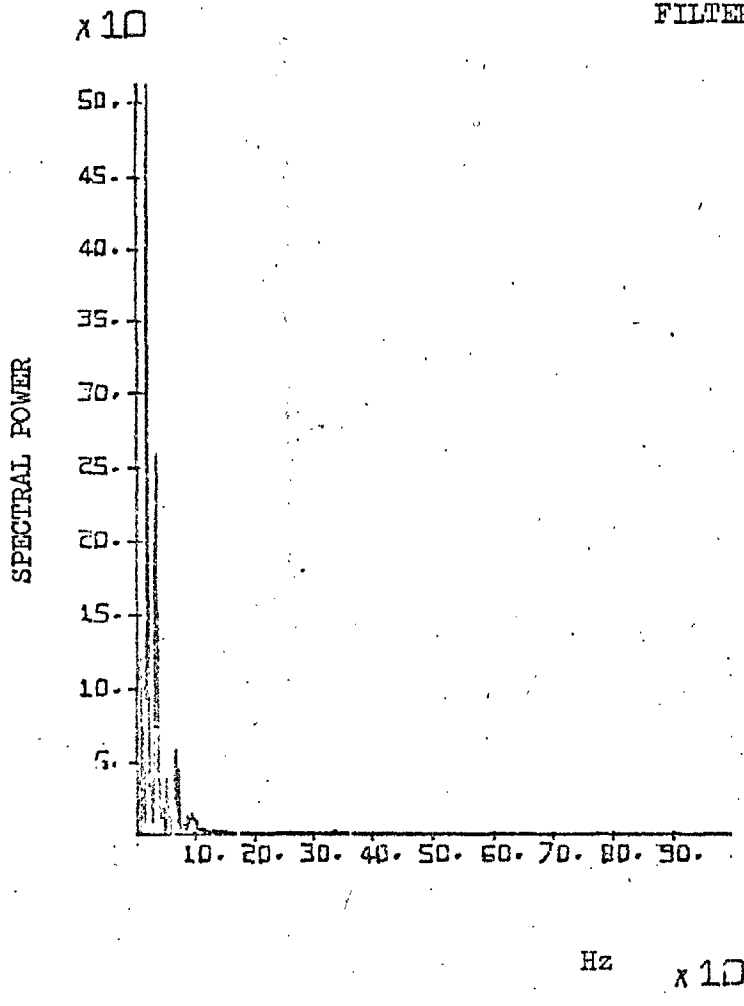


FIGURE 3.19 - SUBJECT RK - 60 SECOND STIMULUS FILTERED.



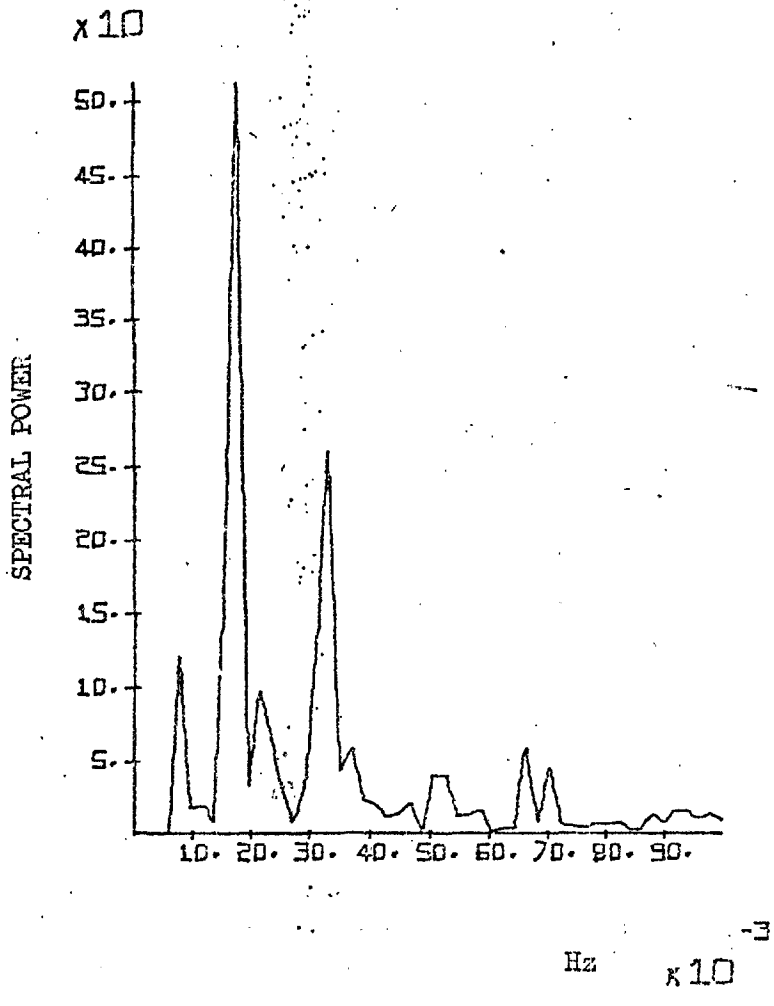


FIGURE 3.20 - SUBJECT DZ - 60 SECOND STIMULUS

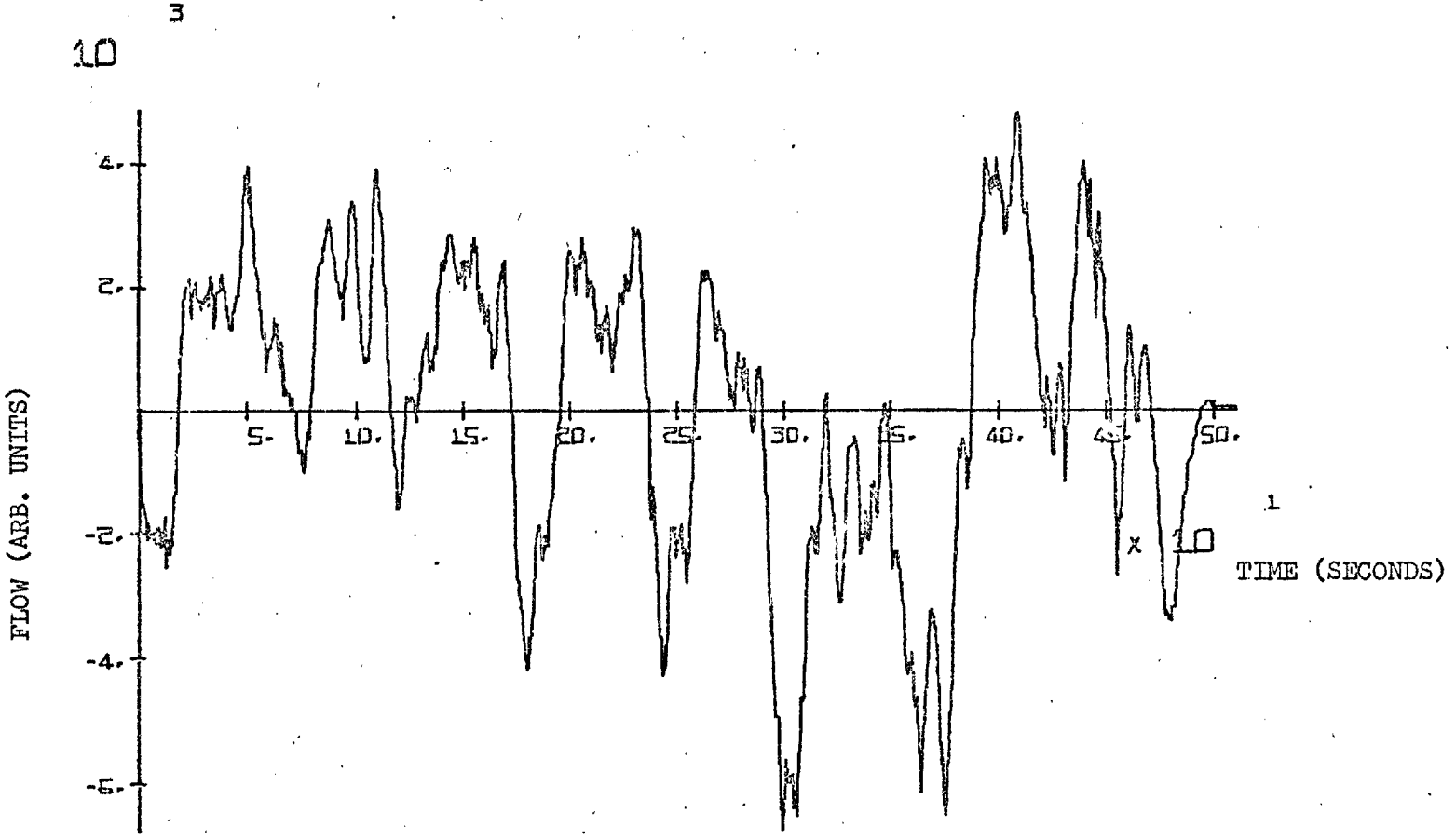
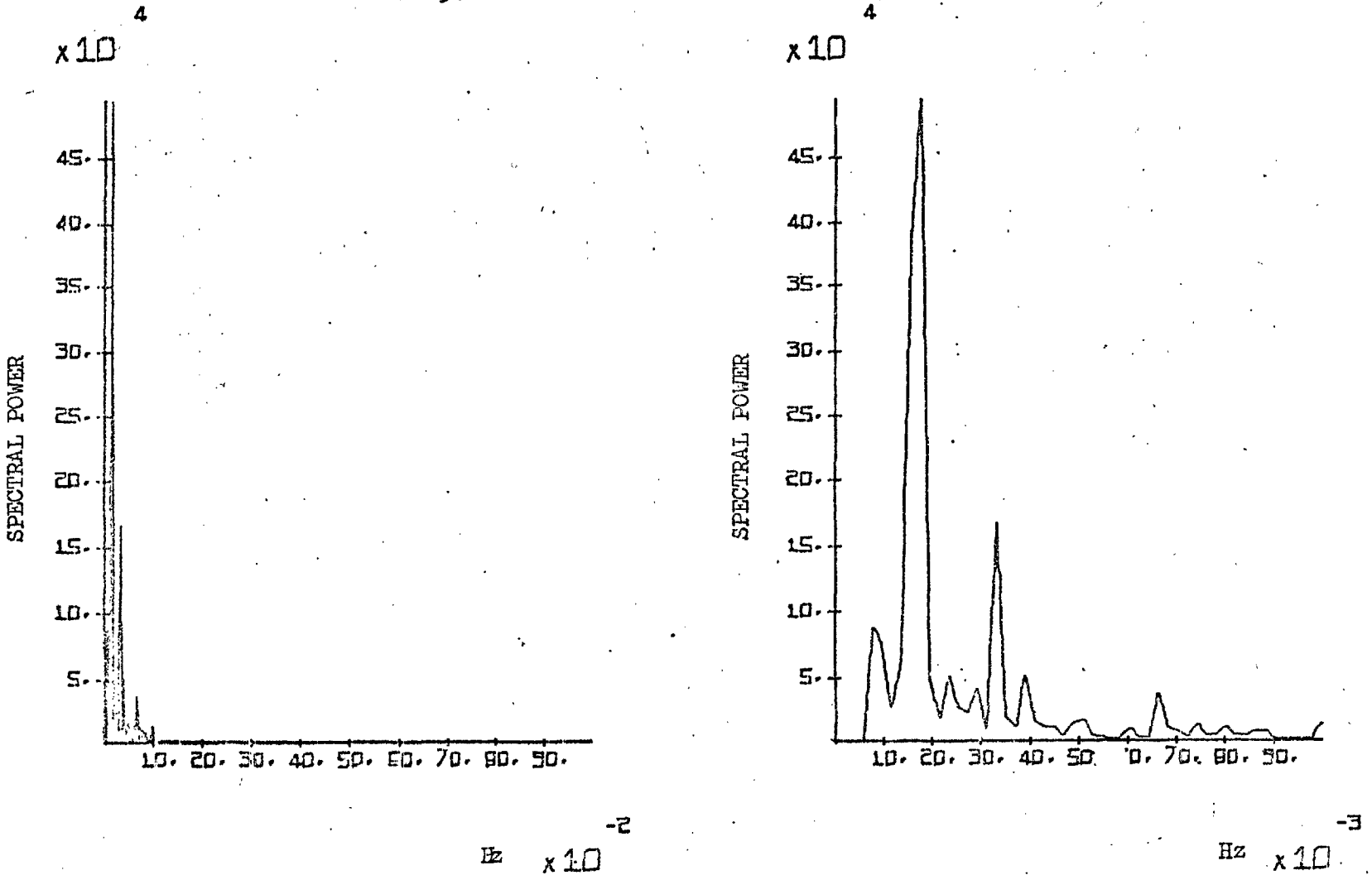


FIGURE 3.21 - SUBJECT DZ - 60 SECOND STIMULUS



the two subjects is compared (figures 3.19 and 3.21), it is apparent that in both cases there is a dominant component at the stimulus frequency (0.016 Hz) and another smaller component at twice the stimulus frequency. The system has still been entrained by the external stimulus, but also exhibits a degree of higher harmonic entrainment (Hayashi et. al. 1960).

The eighty second periodicity stimulus for subject RK, contains a component at around 350 seconds (figure 3.22) which again is thought to arise from a source outside the activity of the control system under investigation. A suitable nonlinear filter was therefore applied to the data in the time domain. Figures 3.22 and 3.23 illustrate the time domain waveforms before and after the application of the filter, respectively. However, it is probably more informative to observe the effect of the filter in the frequency domain (figures 3.24 and 3.25). These plots indicate a marked reduction in the component at a frequency of about 0.023 Hz. The corresponding data for subject DZ is illustrated in figure 3.26 (time domain), and 3.27 (frequency domain). The effect of the eighty second stimulus on the thermal systems of both subjects is to entrain the system. However, as with the sixty

FIGURE 3.22 - SUBJECT RK - 80 SECOND STIMULUS
UNFILTERED WAVEFORM.

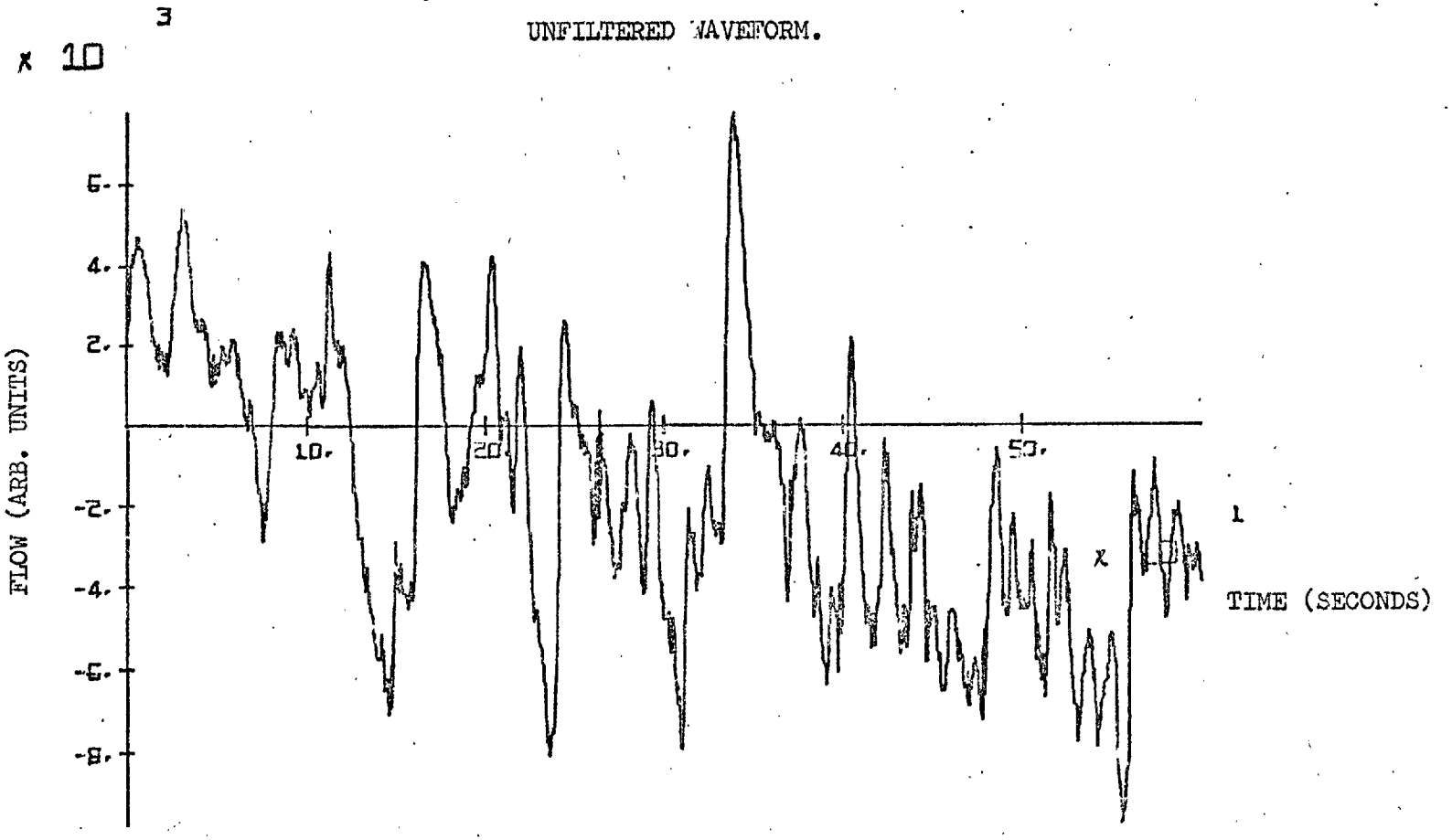


FIGURE 3.23 - SUBJECT RK - 80 SECOND STIMULUS FILTERED WAVEFORM.

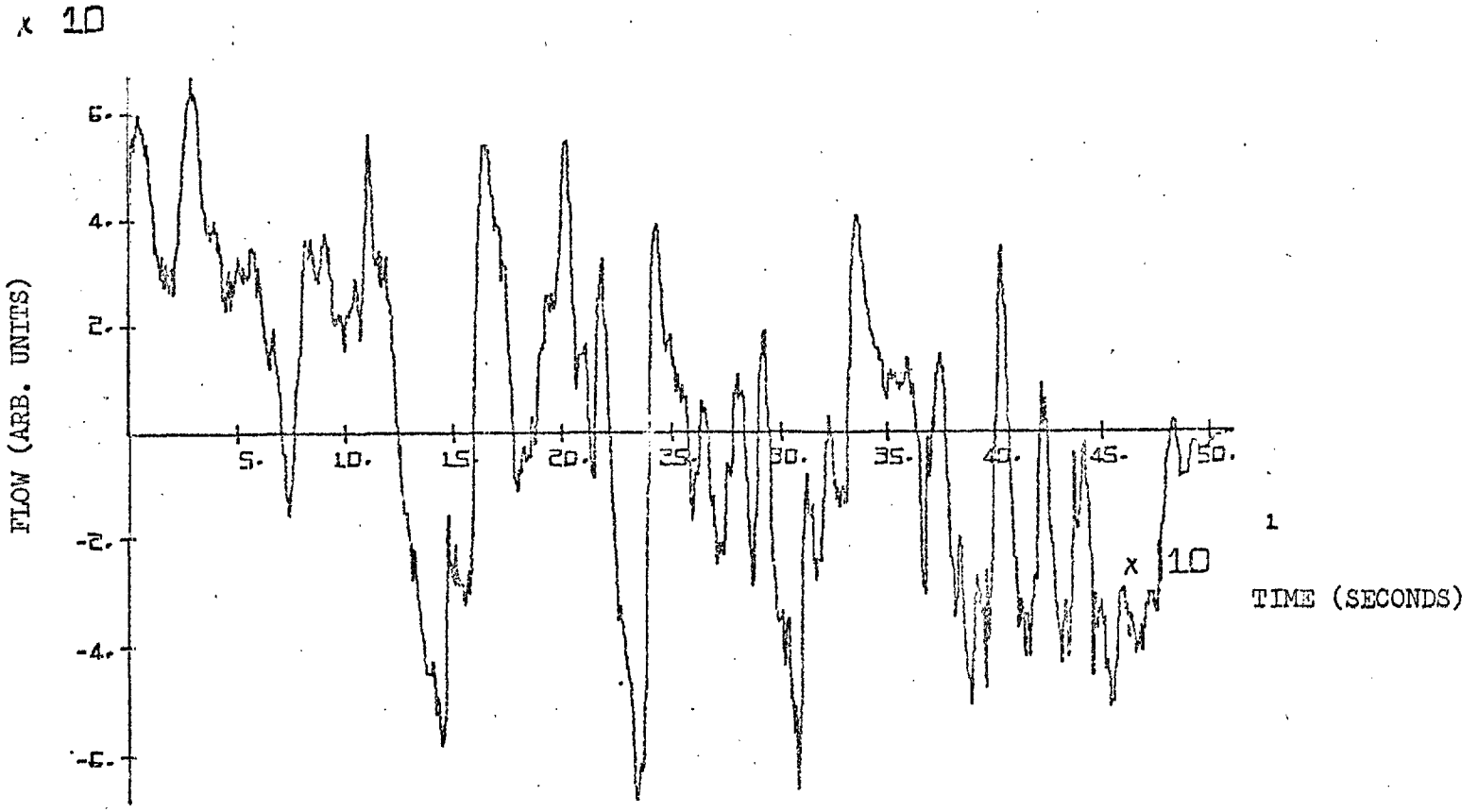


FIGURE 3.24 - SUBJECT RK - 80 SECOND STIMULUS UNFILTERED.

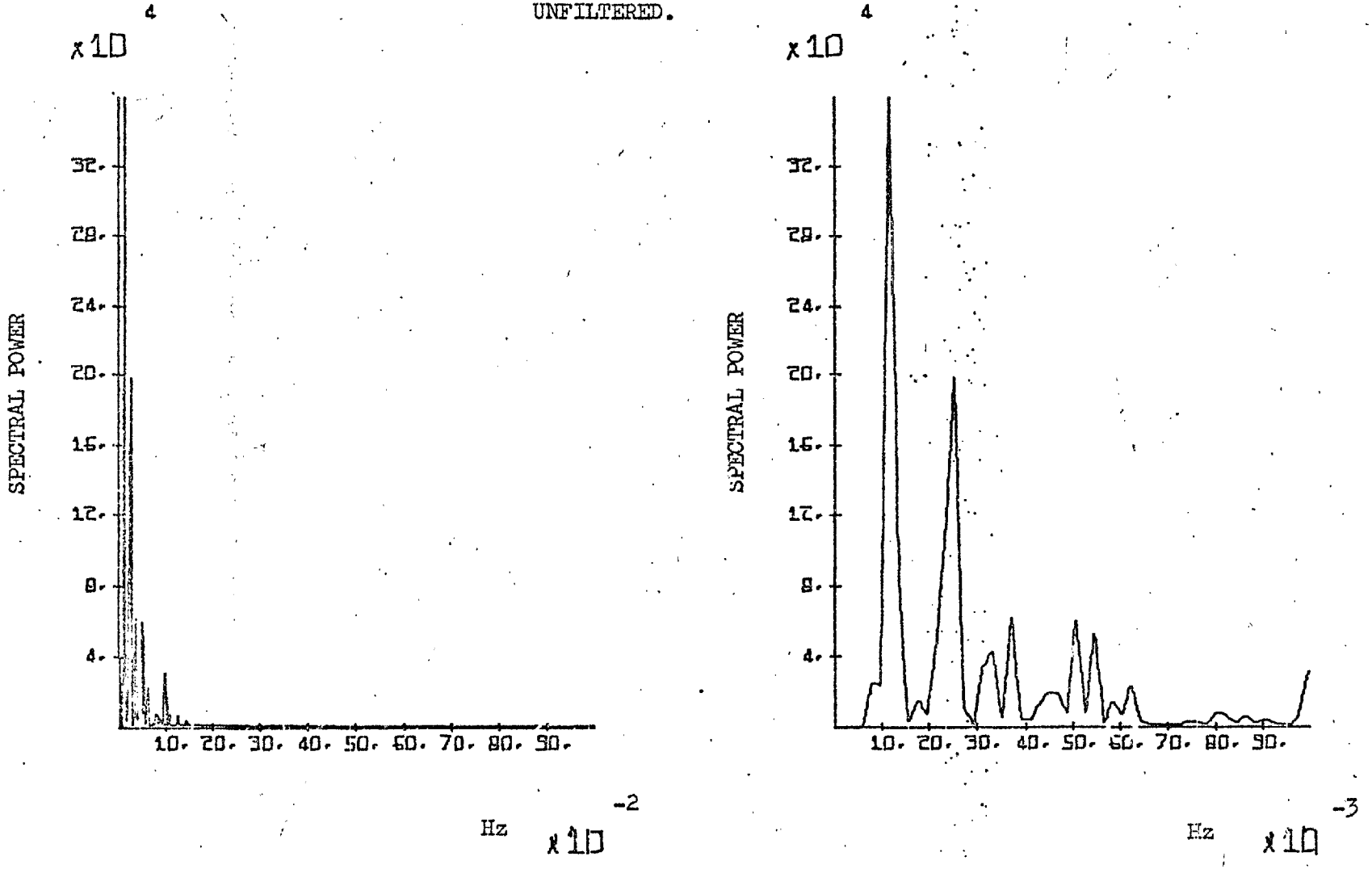


FIGURE 3.25 - SUBJECT RK - 80 SECOND STIMULUS FILTERED

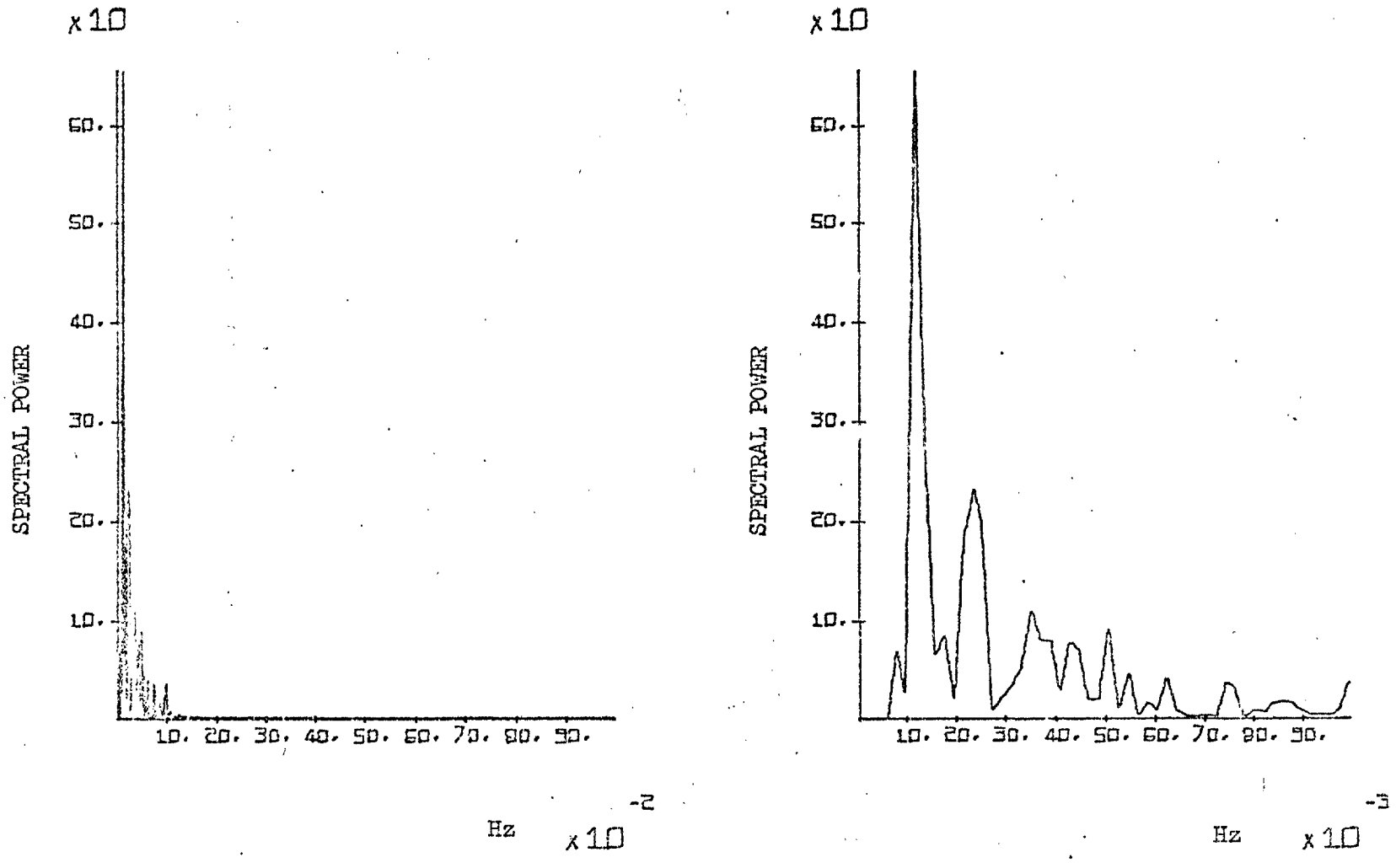


FIGURE 3.26 - SUBJECT DZ - 80 SECOND STIMULUS.

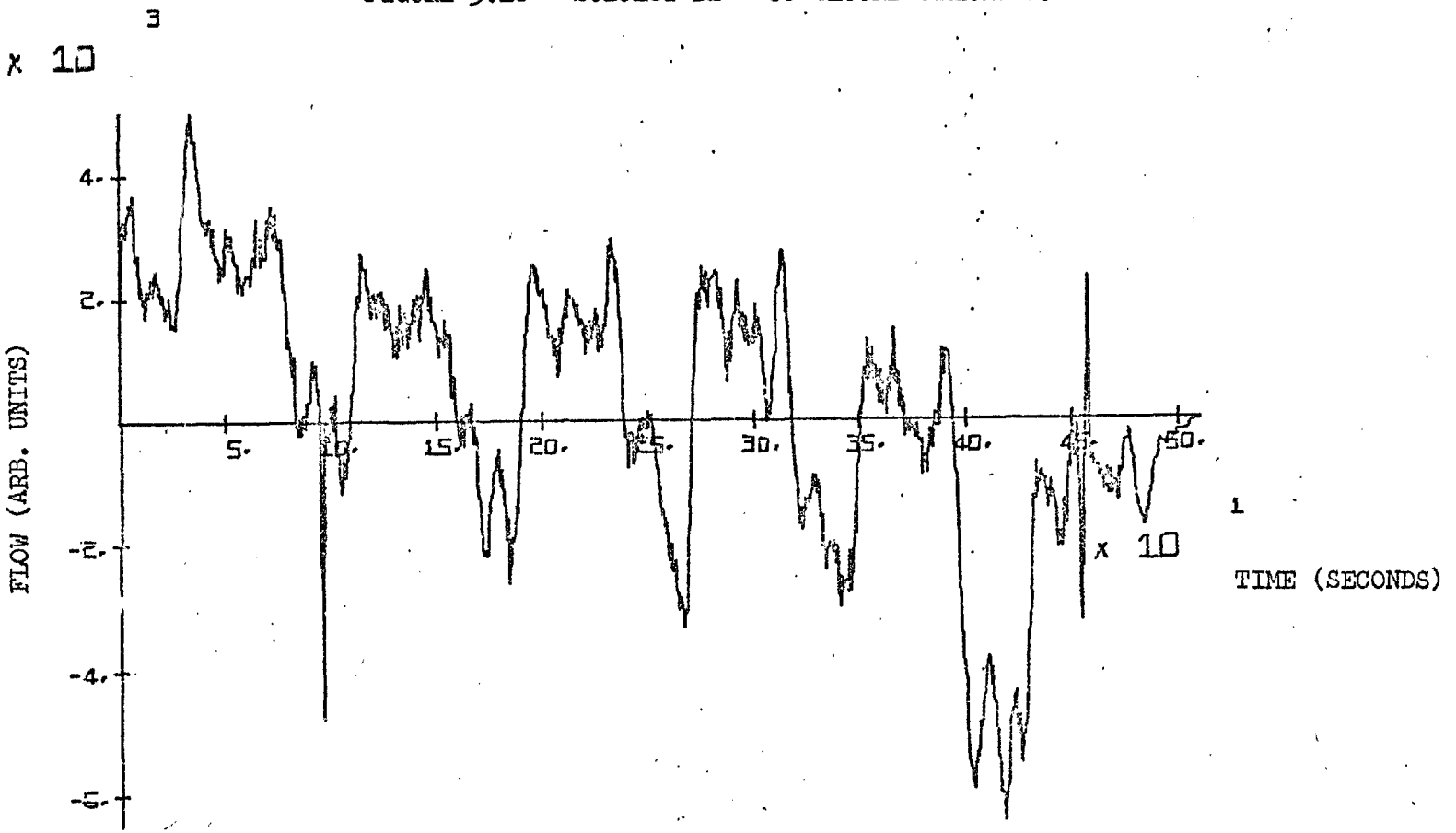
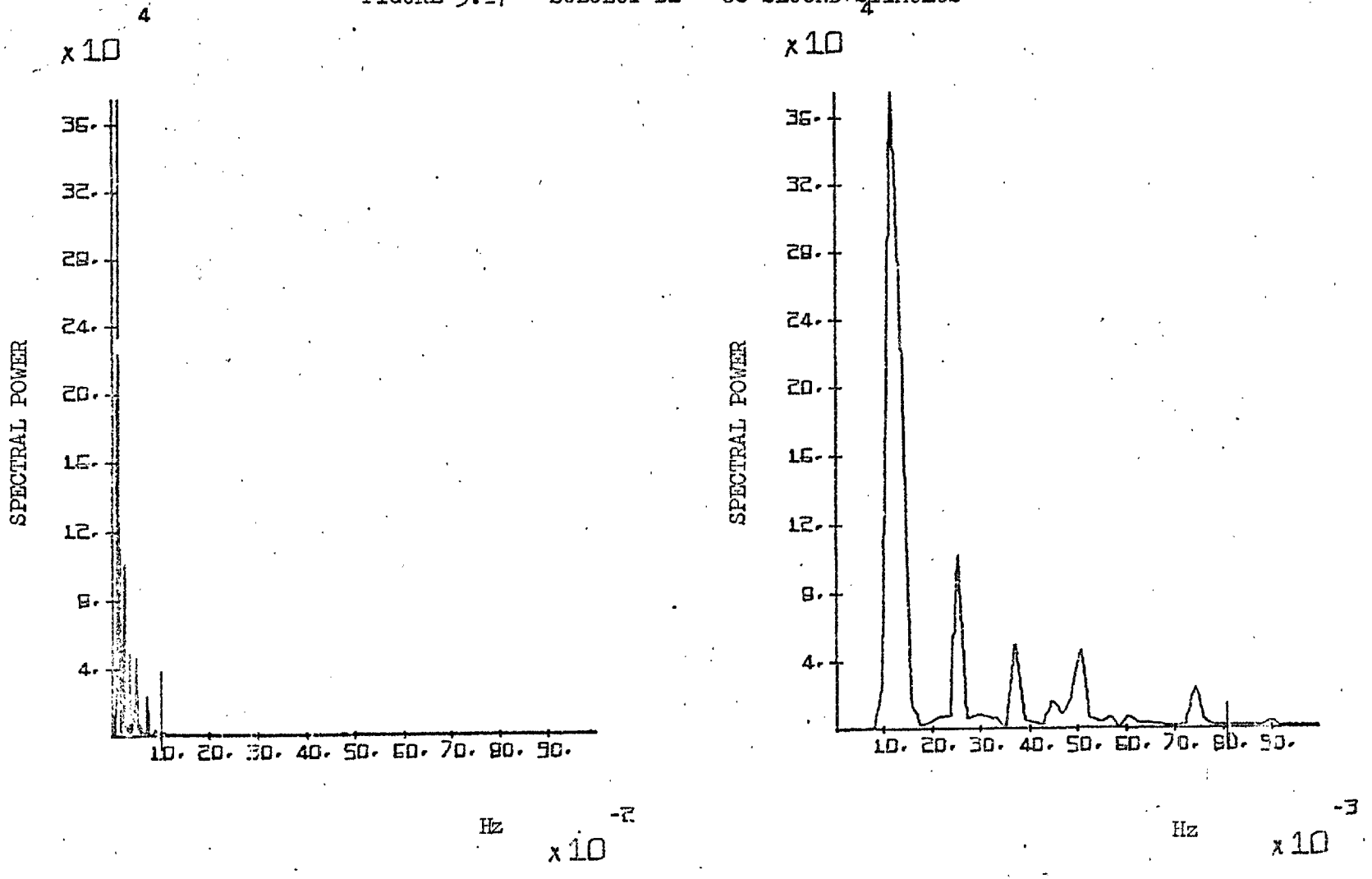


FIGURE 3.27 - SUBJECT DZ - 80 SECOND STIMULUS



second stimulus, there is evidence of higher harmonic entrainment at the second harmonic frequency.

The second series of entrainment experiments clearly show that it is possible to entrain the peripheral thermal system with a suitable stimuli at forty, sixty and eighty, seconds periodicity. For each stimulus frequency (both subjects), the large number of components shown in the power spectrum of digit blood flow for spontaneous conditions, was replaced by a single dominant component at the stimulus frequency.

3.4 ENTRAINMENT EXPERIMENTS-SERIES THREE.

The first and second series of experiments were designed to investigate the effect of an external stimulus on digit blood flow. All these experiments were performed under the condition that the core temperature remained within the comfort zone. The parameter varied during these experiments being the frequency of the external stimulus, and it was shown that selective entrainment could be identified.

The analysis of the system suggests that human thermo-regulation results from two basic control systems which co-operate. The first line of defence is thought to comprise a peripheral control system having vasomotor control in the forward path and skin receptors in the feedback path. If the measures of stabilization due to these mechanisms are sufficiently effective, the thermal conditions of the core will remain in steady state. However, if the vasomotor adjustments are inadequate, the thermal equilibrium of the core will be upset. This can be presumed to cause activation of the "core system". It would seem that the basic criterion of the system as a whole is to always preserve heat in the core. Hence, according to this proposition heating and cooling of an upper limb, with an elevated core temperature, would not result in comparable vasomotor

control; in other words the control resulting from the core system will override that of the peripheral system. As we have seen it is possible to entrain the peripheral system when the core temperature is within the comfort zone. If the system definition is accurate then the possibility of entrainment will be lost when the core temperature is elevated.

The Experimental Procedure.

Controlled elevation of the core temperature was achieved by using a specially designed thermal suit (Fox et. al. 1967). The complete suit consists of three PVC plastic suits; the outer garment provides insulation, inside this is an air distribution garment and finally an inner suit the function of which is to collect sweat. The middle suit is ventilated by an air conditioning system which can supply air over a wide range of temperatures. The core temperature is measured at the tympanic membrane in both ears following the technique described by Bradbury et. al. (1964). The skin temperature is the unweighted mean recorded from a number of sites. The purpose of the present series of experiments was to investigate the response of the thermal control system to an elevated core temperature. This was accomplished by holding the core temperature approximately constant at three levels namely: 37, 37.5 and 38°C. Having achieved

a particular constant level of core temperature, the left hand was then independently stimulated. This stimulation being identical to that used in the first series of experiments, where a squarewave thermal stimulus of 20 second periodicity was applied to the left hand.

Although the experiment is divided into three phases, the monitoring of the core and skin temperatures is a continuous process. Hence, when reference is made to the value of a particular variable at the 56^{th} minute say, this means fifty six minutes after the beginning of the entire experiment and not fifty six minutes after the start of a particular phase. Similarly, the graphs illustrated in figures 3.28 to 3.31 are all plotted to a common time scale with variations between graphs being confined to the ordinate scale.

PHASE 1.

With the subject lying in the horizontal position on the experimental bed, the air flow to the middle garment was set to produce as near a constant $37^{o}C$ core temperature as could be achieved. Referring to figure 3.28 it can be seen that in order to produce this constant core temperature, the air temperature had to be varied over the range $30-38^{o}C$. Having attained steady state, a thermal stimulus of 20 second periodicity, identical to that used in the first series, was applied to the left hand and the digit

blood flow in the contralateral hand monitored for the duration of the experiment. The thermal stimulus was applied to the left hand for a period of sixteen minutes. Other physiological measurements made during the experiment were those of skin temperature, core temperature and the temperature of the air in the middle suit.

PHASE 2.

The second phase of the experiment necessitates a core temperature of 37.5°C. To attain this core temperature, the air in the middle garment has to be held at 55°C for a period of 35 minutes, then decreased to around 33°C; this sudden decrease in suit temperature limits the overshoot, if any, in the core temperature. By the 56th minute the core temperature stabilized at 37.5°C allowing the second phase of the experiment to commence. With the core temperature held constant over the duration of the experiment, the subject's left hand was stimulated thermally by a perturbation of 20 seconds periodicity for 16 minutes and the digit blood flow, skin temperature, suit air temperature, and core temperature were recorded during the course of the experiment.

PHASE 3.

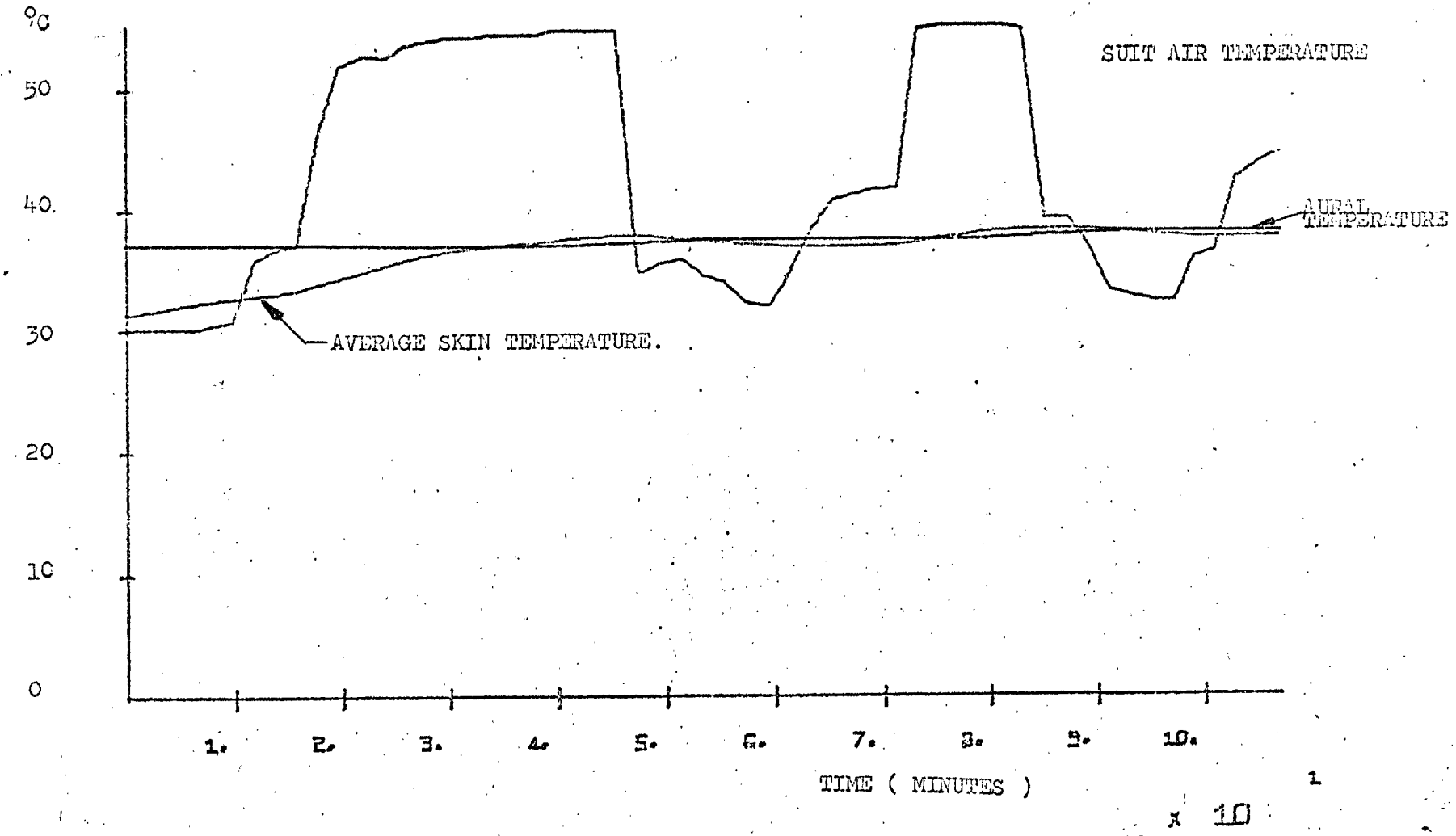
This final stage requires that the core temperature of the subject be at 38°C. To reach this core temperature

the air in the suit has to be at about 55°C for fourteen minutes and then reduced to roughly 32°C over the course of the subsequent ten minutes. By the 94th minute the core temperature had reached 38°C. With the core held at 38°C, the subject's left hand was stimulated by a perturbation of twenty second periodicity. During the sixteen minutes of this third phase the skin temperature and digit blood flow, together with core and suit air temperature were monitored simultaneously.

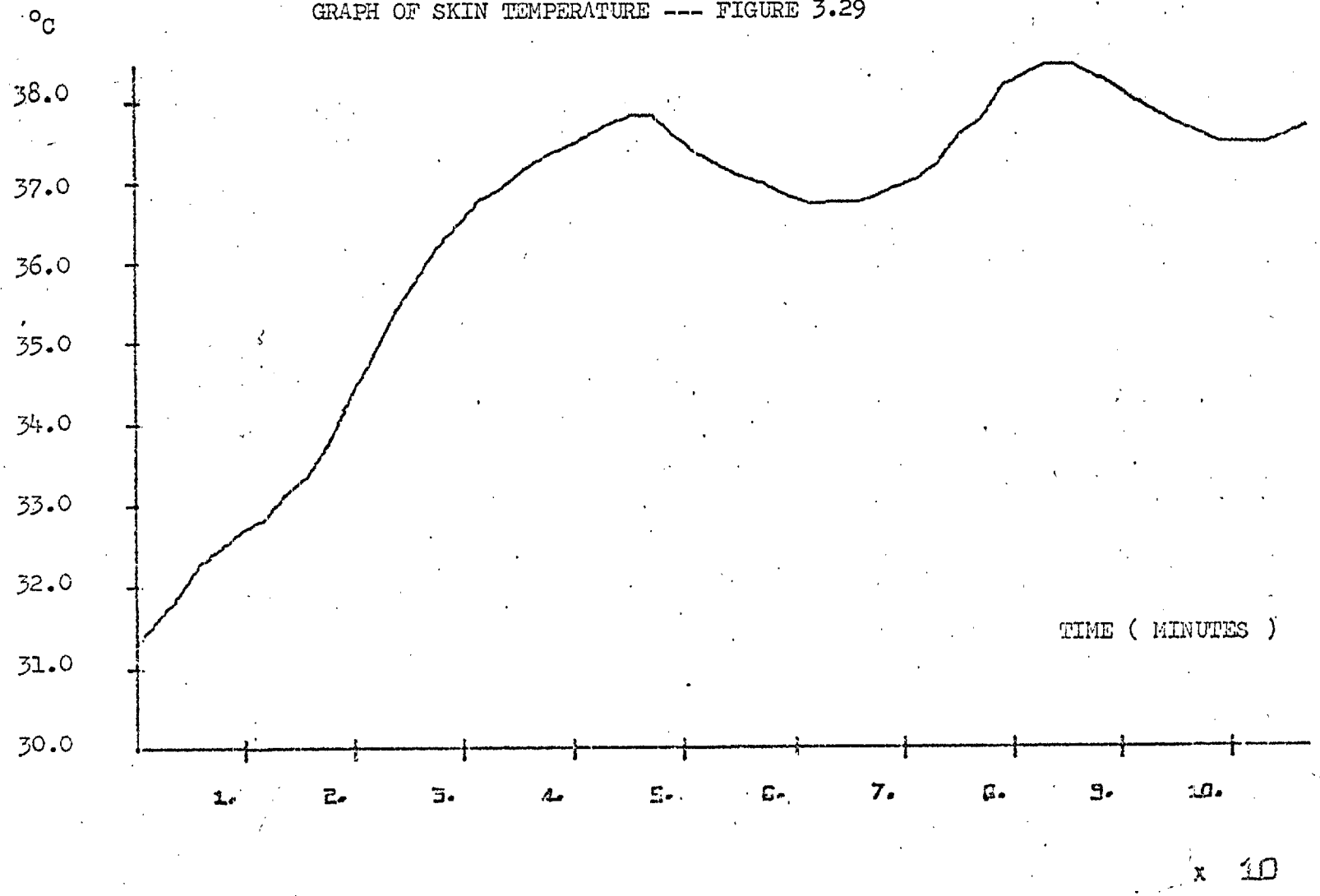
The Analysis and Discussion of the Experimental Results.

The procedure for the analysis of the experimental results can be divided into two sections. First an examination of the interactive effects of the various environmental and physiological temperatures, and secondly the changes in digit blood flow with temperature. Figure 3.28 illustrates on a common scale the monitored temperature variations. During the experiment the core temperature was held approximately constant at three levels. By far the most interesting relationship is between the aural (core temperature) and the average skin temperature (AST). Figure 3.29 illustrates that the AST increases over the first forty seven minutes of the experiment from an initial 31.3°C, to 37.9°C. Beyond this point the AST characteristic takes on a totally different form and begins

FIGURE 3.28


°C
50
40.
30
20
10
0
SUIT AIR TEMPERATURE
AURAL TEMPERATURE
AVERAGE SKIN TEMPERATURE.
1.
2.
3.
4.
5.
6.
7.
8.
9.
10.
TIME (MINUTES)
x 10

GRAPH OF SKIN TEMPERATURE --- FIGURE 3.29



GRAPH OF LEFT AND RIGHT AURAL TEMPERATURES.---- FIGURE 3.30

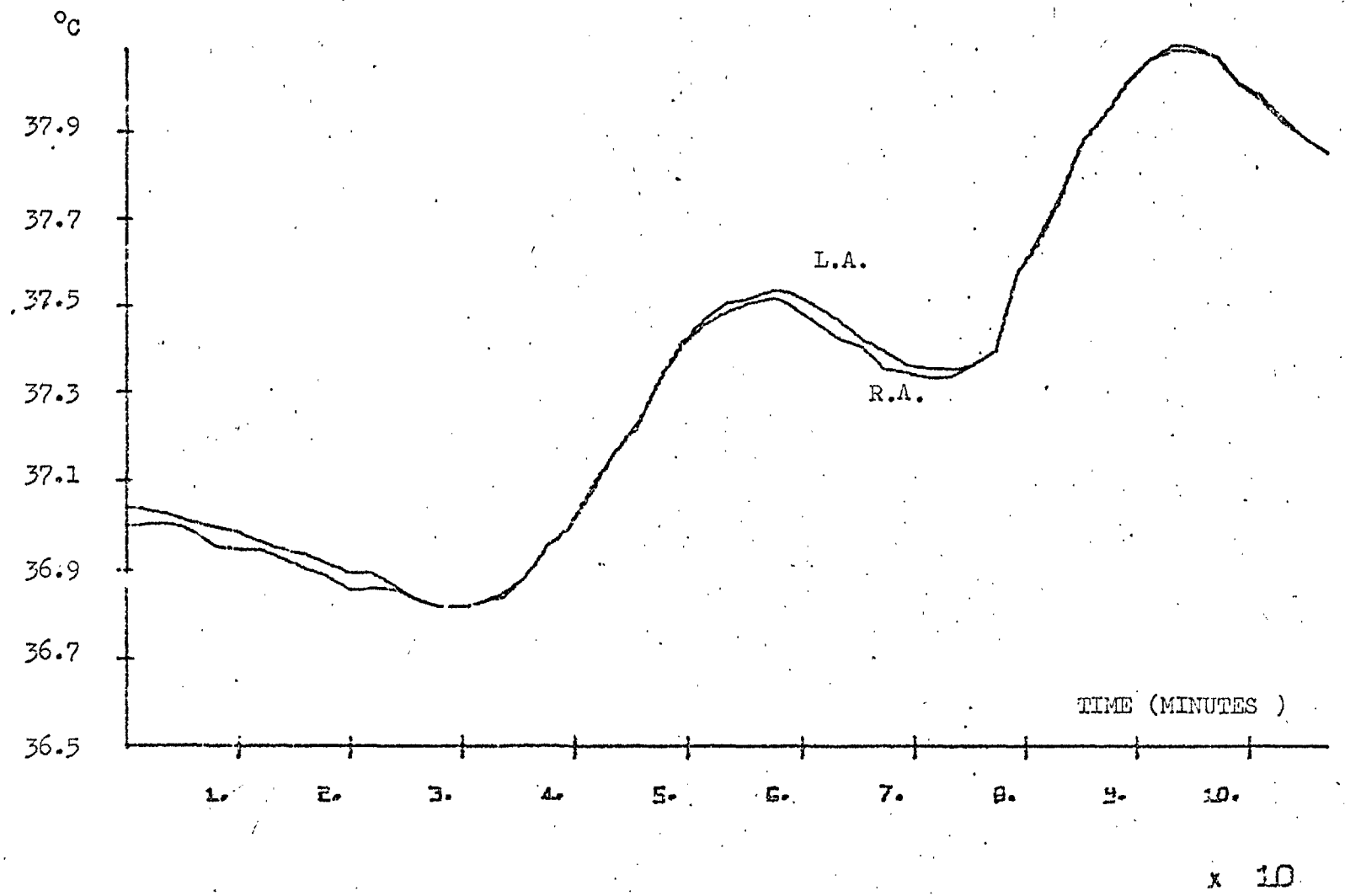
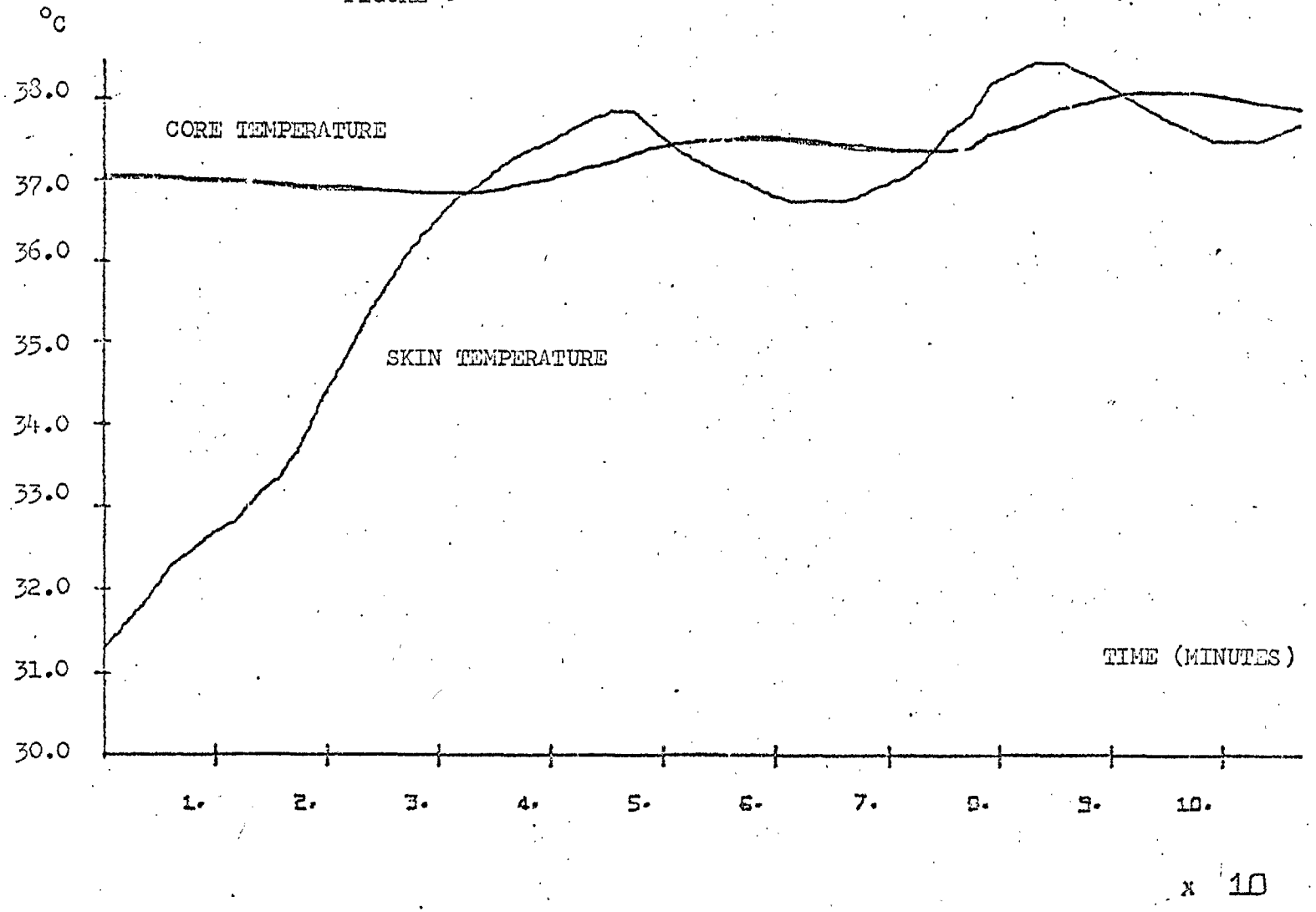


FIGURE 3.31


°C
38.0
37.0
36.0
35.0
34.0
33.0
32.0
31.0
30.0
CORE TEMPERATURE
SKIN TEMPERATURE
TIME (MINUTES)
1.
2.
3.
4.
5.
6.
7.
8.
9.
10.
x 10

to fluctuate about some mean. Plotting the core temperature and the AST to the same temperature scale clarifies this fluctuation of skin temperature. Figure 3.31 shows that the oscillatory phase begins when the AST exceeds the core temperature. After this time, the skin temperature continues to oscillate about the aural temperature. One naturally asks if and how the aural temperature characteristic could be explained in terms of the system philosophy?

We have presented in the hypothesis related to the human thermo-regulatory system, the idea that there are two control systems present which may be activated. It is presumed that the overriding algorithm is always to preserve heat in the core. The initial response to thermal stress is thus judged to be the activation of the peripheral system (which uses vasomotor activity to control temperature). Also in this picture, when the peripheral system proves ineffective the core system is then activated; the efferent response of this control system under the conditions of heat stress we are considering would then culminate in sweat gland activity. The detailed argument now follows.

The other quantity which was measured during the experiment was digit blood flow, or to be more precise the blood flow in the small finger of the right hand. The digit blood flow was monitored during the three phases of

the experiment; phase one, with the core temperature at 37°C, phase two at 37.5°C, and the third phase where the core was at a temperature of 38°C. The most obvious effect of the elevation of core temperature was the mean increase in the cutaneous blood flow, this has been well known as a physiological fact for a considerable period of time. The increased blood flow results from a combination of vasodilatation and possibly an increase in cardiac output. The time domain plots of the digit blood flow during the three experimental phases are illustrated in figures 3.32, 3.33 and 3.34.

Figure 3.32 shows the waveform of digit blood flow for phase 1 of the experiment. During the sixteen minutes of this phase, the skin temperature increased steadily from an initial value of 31.3°C to a final value of 36.5°C. It is apparent from figure 3.32 that there is a dominant component of about 20 second periodicity, this corresponds to the input stimulus. Taking the Fourier Transform of the data enables analysis of the experimental results in the frequency domain. Figure 3.35 is the power spectrum for phase 1. It is apparent from the spectrum, that the dominant component is that of the stimulus, of frequency 0.05 Hz. The right hand diagram shows the digit blood flow for the range 0-0.1 Hz. If one compares this power spectrum with

FIGURE 3.32

CORE TEMPERATURE 37°C

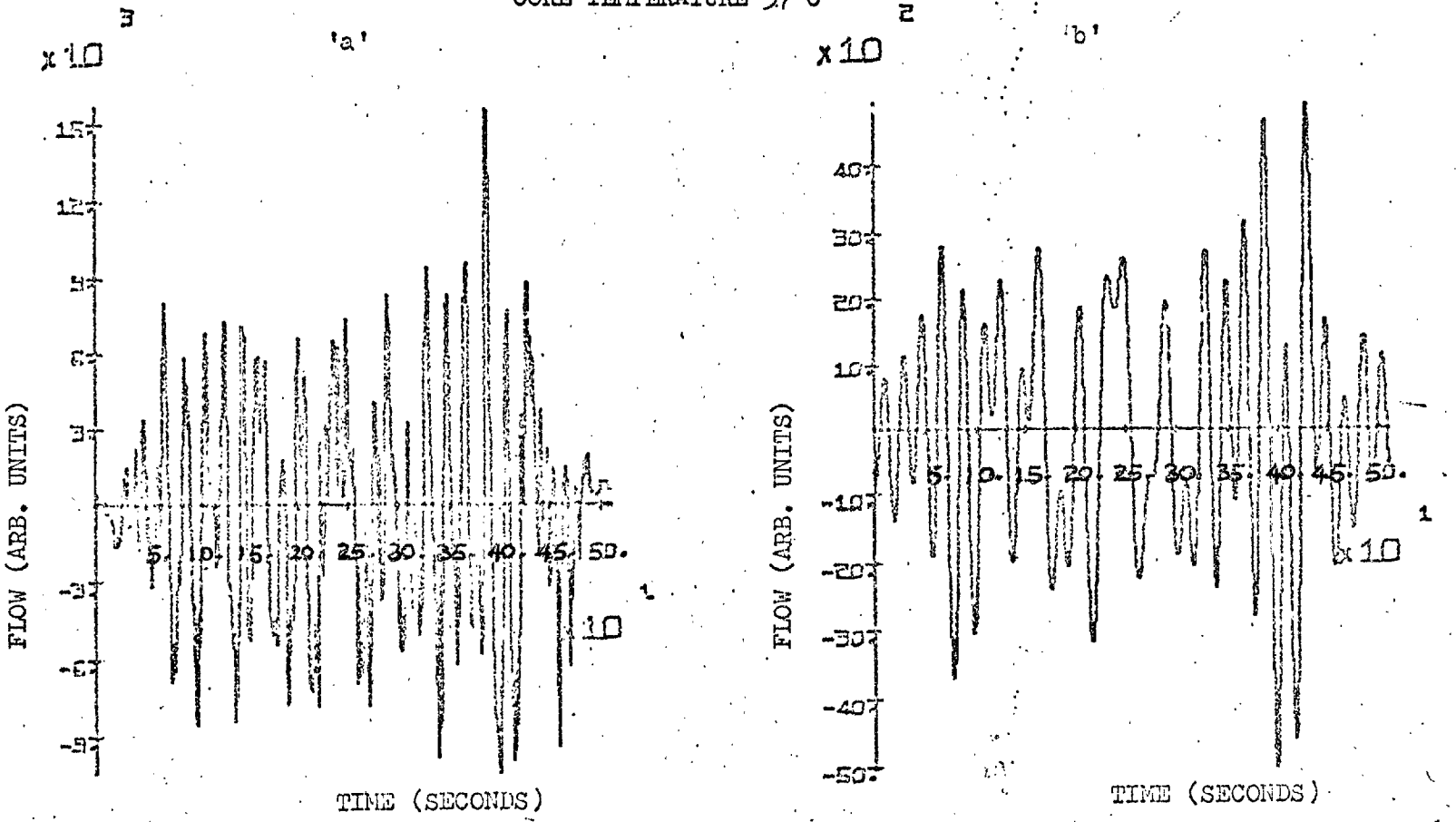


FIGURE 3.33

CORE TEMPERATURE 37.5°C

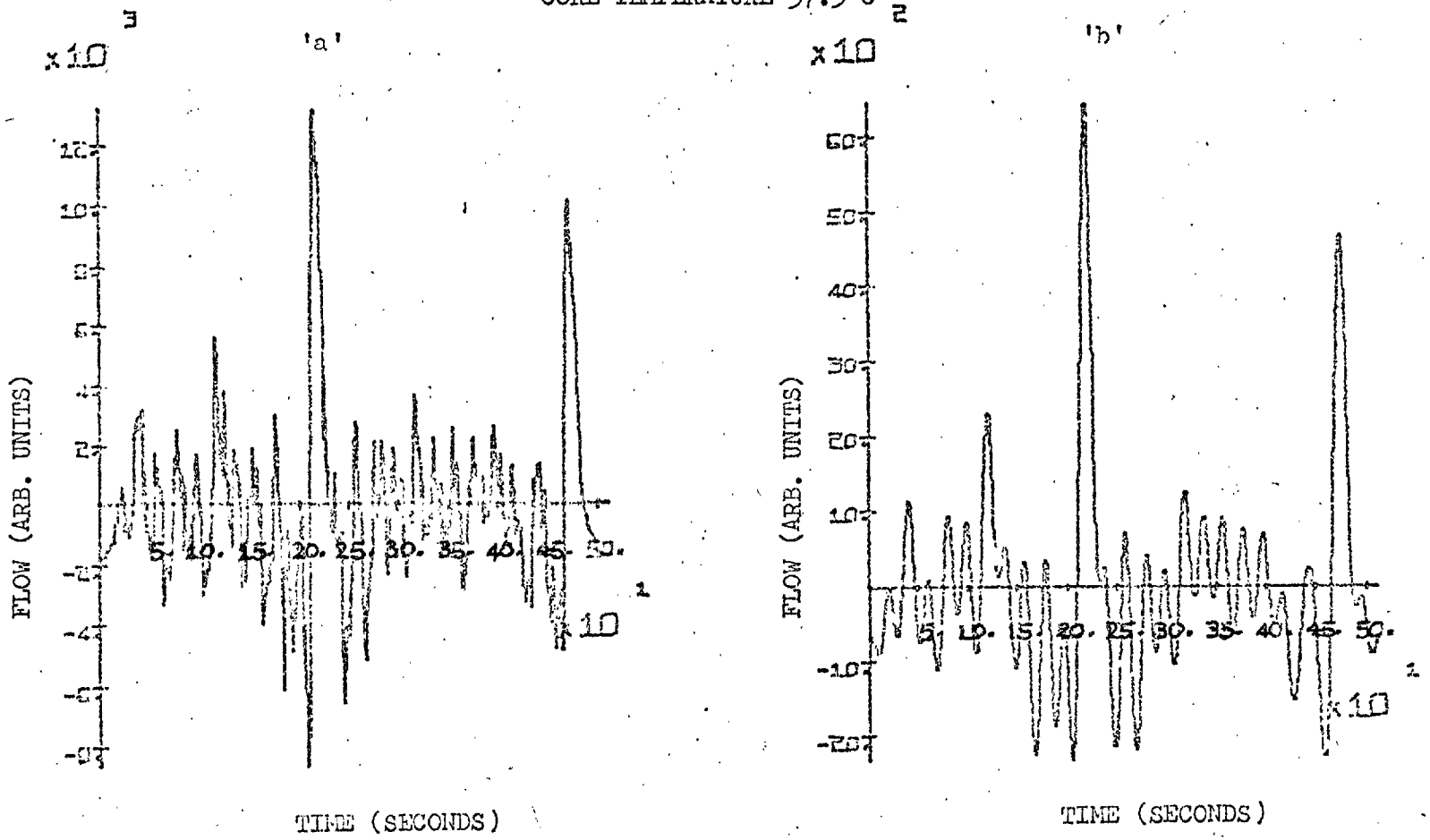


FIGURE 3.34
CORE TEMPERATURE 38°C

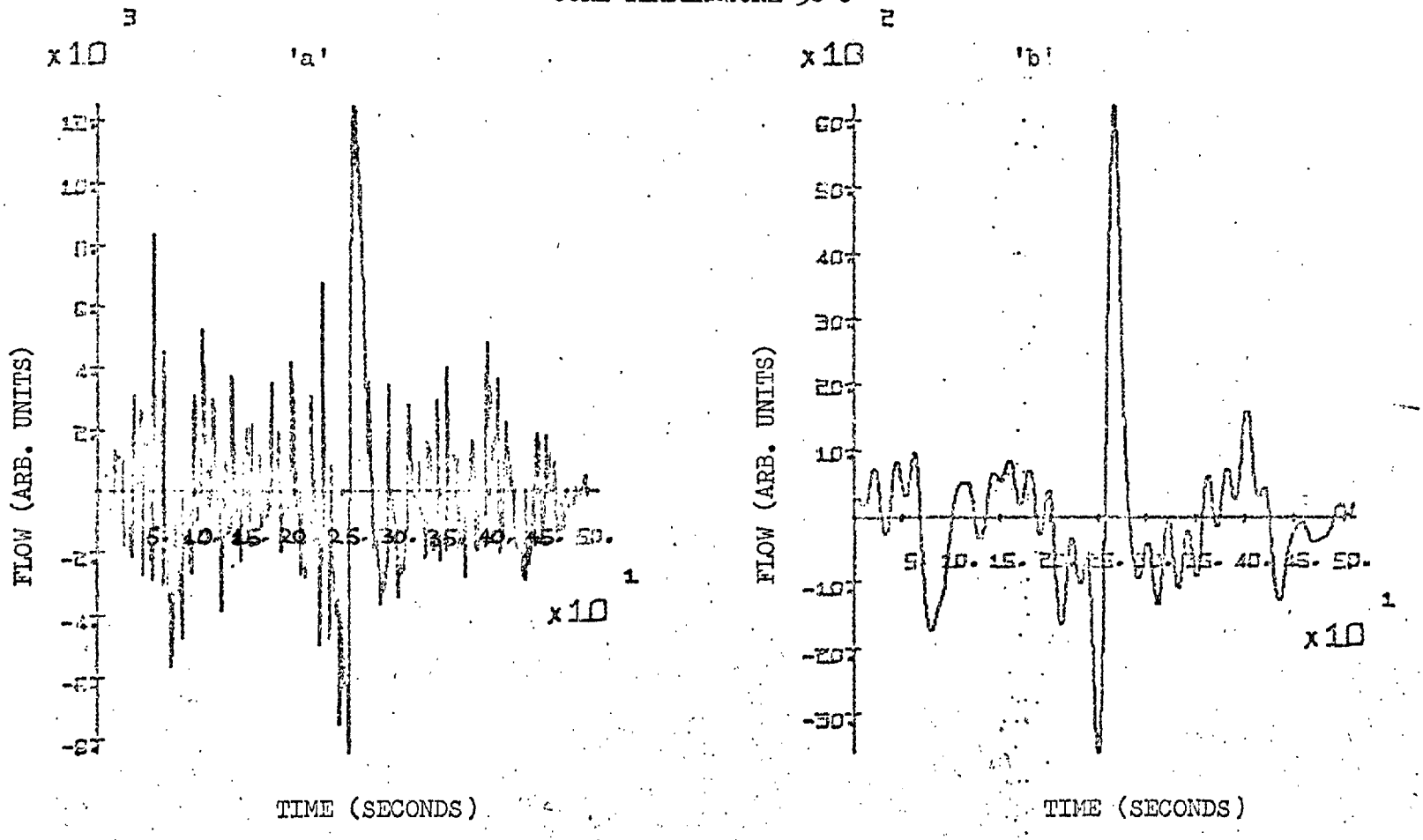


FIGURE 3.35

CORE TEMPERATURE 37°C

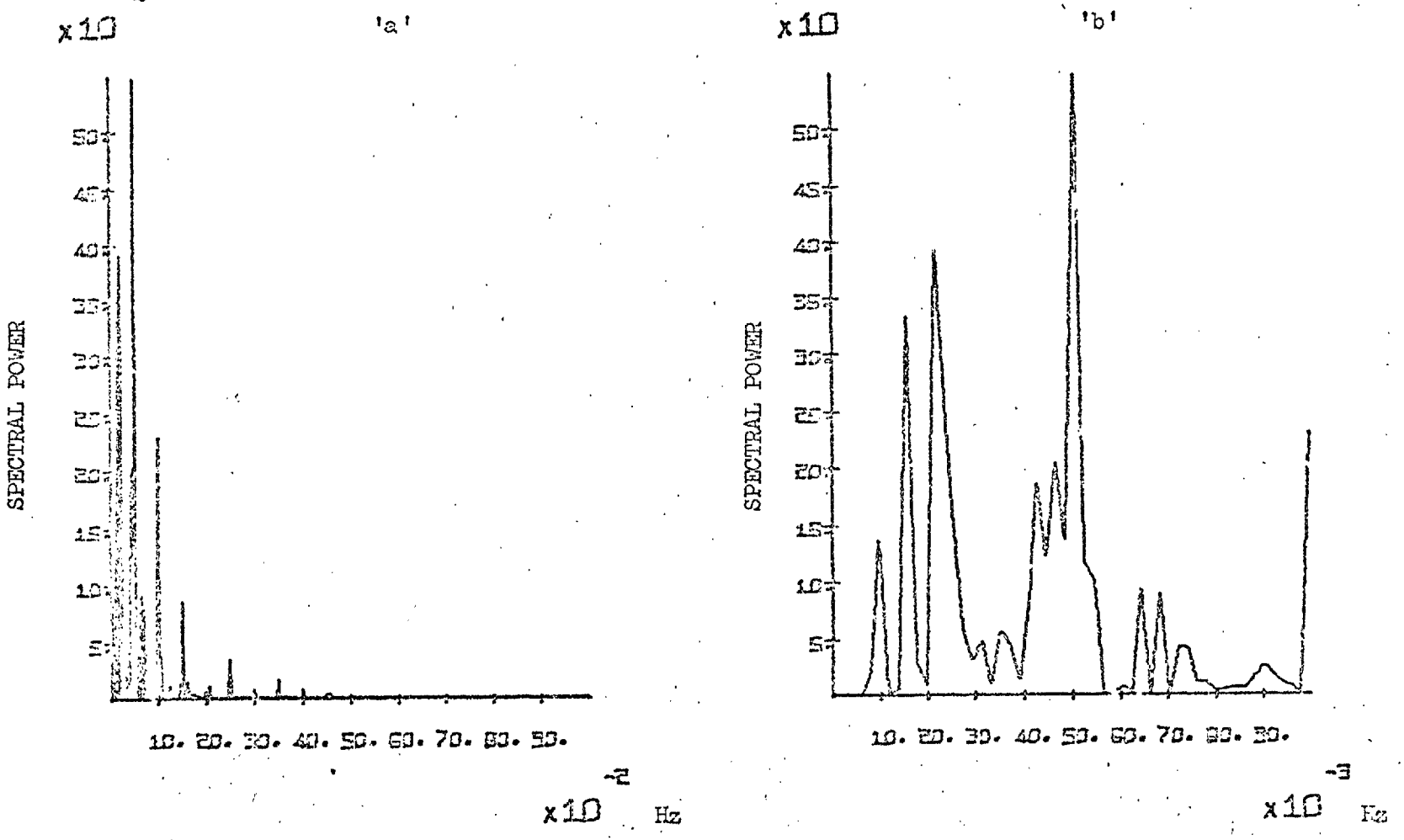


FIGURE 3.36

CORE TEMPERATURE 37.7°C

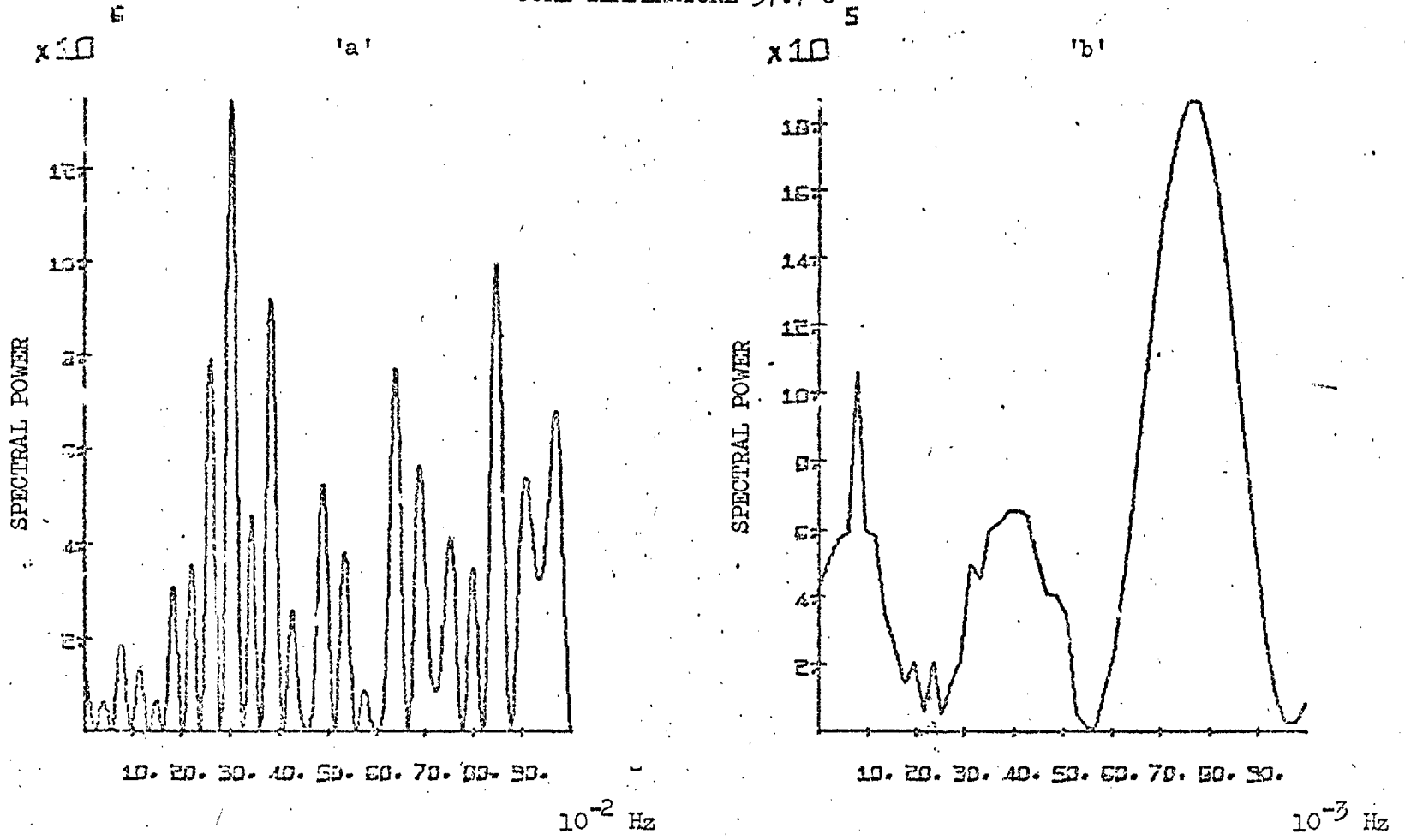
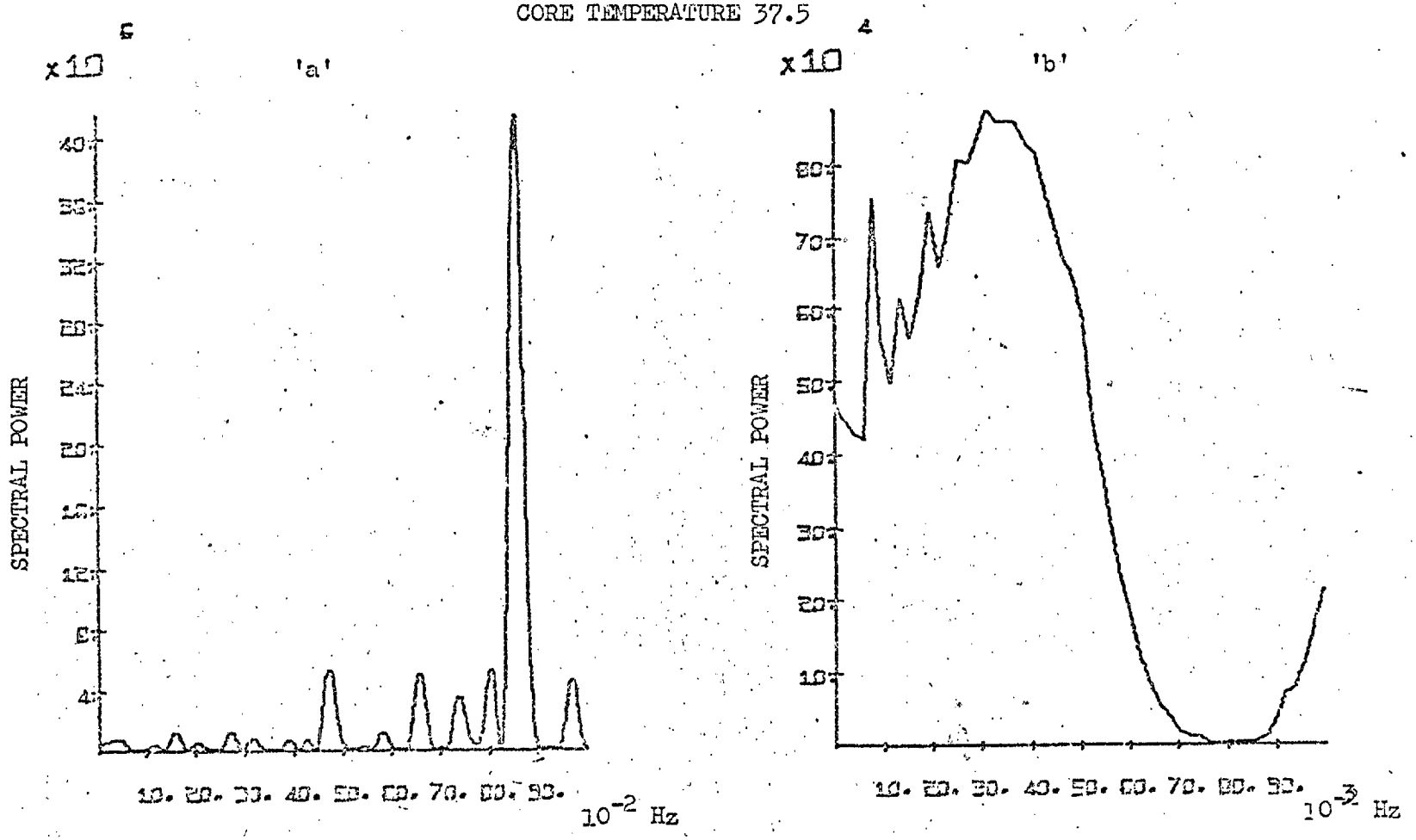


FIGURE 3.37

CORE TEMPERATURE 37.5



that of the first series of entrainment experiments, where a twenty second periodicity thermal stimulus was applied (figure 3.8c), it is apparent that there is evidence of entrainment (figure 3.35b exhibits a dominant component at the stimulus frequency).

As the core temperature is increased to 37.5°C, any evidence of entrainment disappears; figure 3.36b shows no evidence of a component at the stimulus frequency. Here the component related to the stimulus has been replaced by three, large bandwith components. Similarly, when the core temperature is elevated to 38°C, it is no longer possible to discern individual frequency components (figure 3.37b), indicating that no entrainment has occurred.

Returning to figure 3.31, one can therefore say that during phase 1, and up until the time when the average skin temperature exceeds the core temperature, thermal control is achieved and mediated through the peripheral system (this follows from the characteristics of the digit blood flow waveform). The peripheral system acts independently and controls the vasomotor tone for at least some of the range of heat stress. However, as the degree of heat stress continues to increase, a point is reached where the cutaneous vessels are in a state of maximal vasodilatation. Figure 3.30 indicates that the initial effect of heat stress is a

reduction in the core temperature this may be due to the response of the control system, which increases the degree of blood flow in the periphery. When the cutaneous vessels are completely vasodilated, the peripheral control system is saturated and hence ceases to control. The result is a subsequent increase in core temperature. Due to the physiological limitations of the peripheral system, the increase in core temperature may be presumed to activate the core control system. Nevertheless the core (aural) temperature soon starts to fluctuate, and it can be seen from figure 3.31 that these fluctuations occur after about thirty two minutes. The question one naturally asks is then, could there be any connection between the aural and skin temperatures in this region of the average skin temperature characteristic?

Cross Spectral Analysis of the Temperature Data.

As we have seen from the data illustrated in figure 3.31, after about thirty two minutes the skin temperature exceeds the core temperature and after this point in the experiment both these temperatures fluctuate. The question was raised whether these quantities were related in some way during this part of the experiment. One technique which can be used to establish the presence of any linear relationship between these two functions is

cross spectral analysis. The power spectrum $S_{xx}(t,f)$ of a process as a function of time and frequency is defined by:

$$S_{xx}(t,f) = \int_{-\infty}^{\infty} R_{xx}(t,\tau)\, e^{-j2\Pi f\tau}\, d\tau \qquad 3.2.$$

where: $R_{xx}(t,f)$ is the autocovariance function of the process. Similarly the cross spectrum between two processes $x(t),y(t)$ is defined as:

$$S_{xy}(t,f) = \int_{-\infty}^{\infty} R_{xy}(t,\tau)\, e^{-2\Pi jf\tau}\, d\tau \qquad 3.3.$$

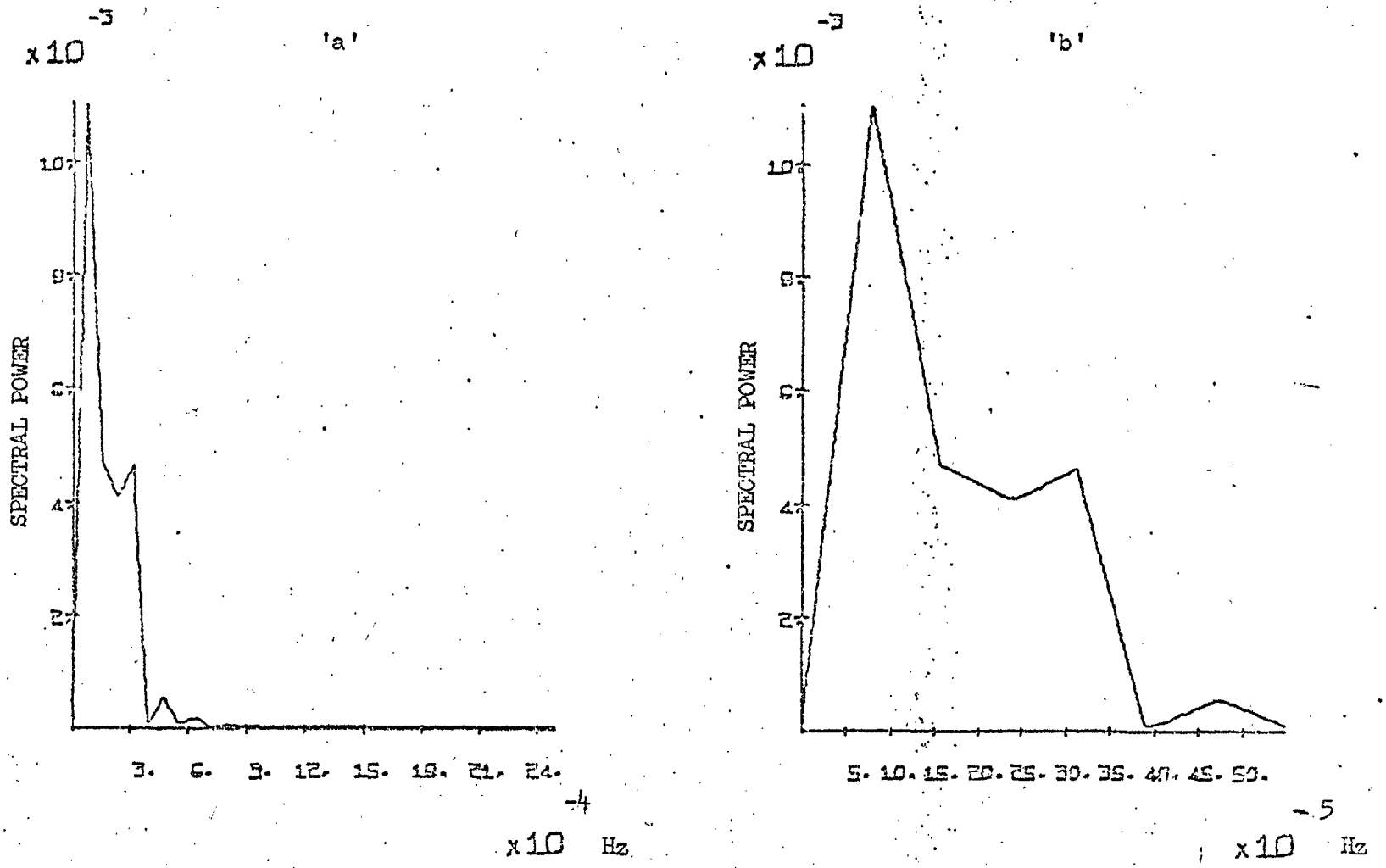
for a stationary process $R_{xy}(t,\tau)$ is given by:

$$R_{xy}(t,\tau) = R_{xy}(\tau) = \lim_{T\to\infty} {}^{1}/_{2T} \int_{-T}^{T} x(t)\,y(t+\tau)\,dt \qquad 3.$$

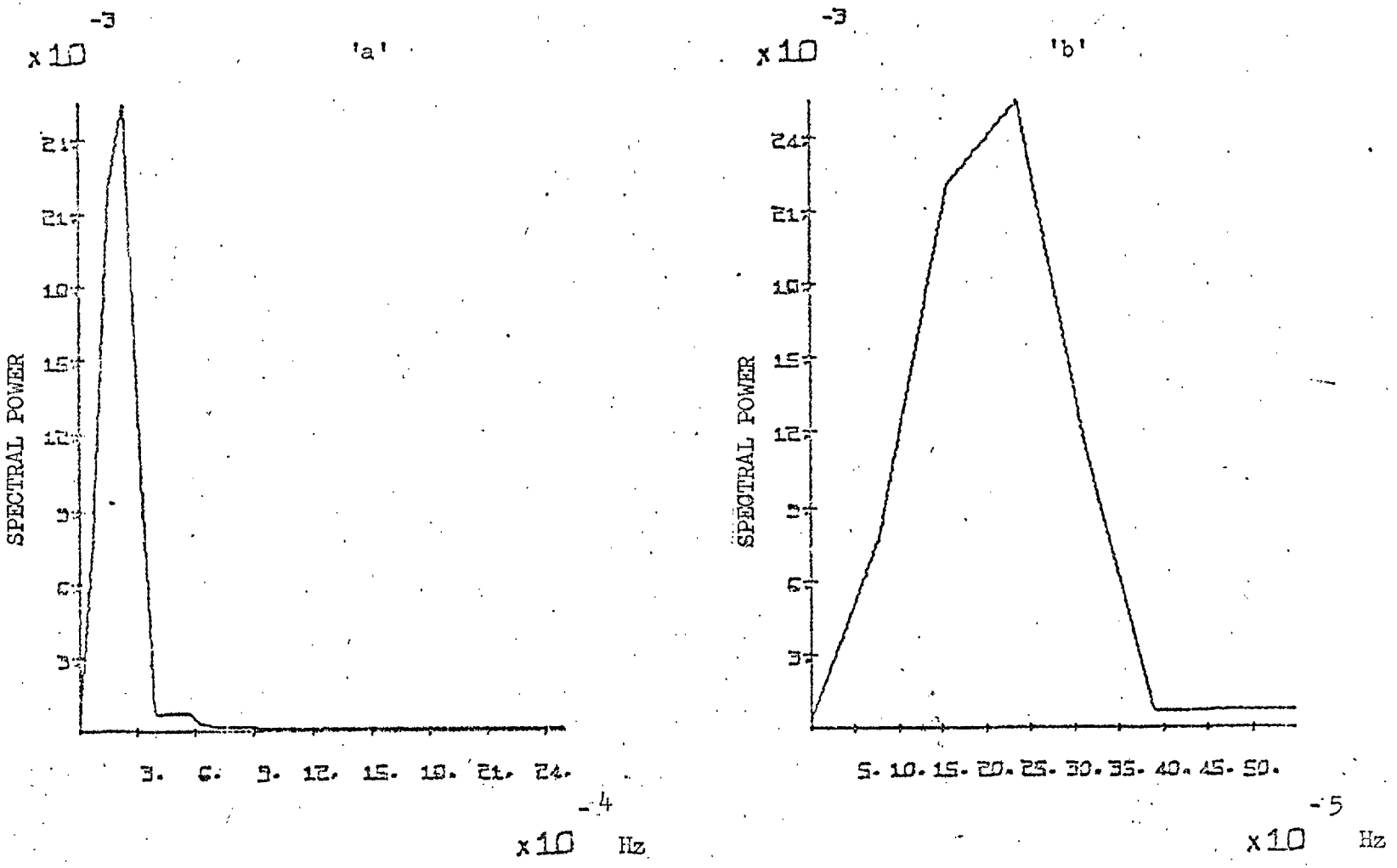
$S_{xx}(t,f)$ and $S_{xy}(t,f)$, for a stationary process, become simply: $S_{xx}(f)$ and $S_{xy}(f)$ respectively. The most practical route to the estimation of the power spectra and cross spectra is via the Fast Fourier Transform (FFT).

If we consider the experimental data for the aural temperature, the data is expressed in terms of a set of temperature values taken at two minute intervals. These values can be considered as sampled data taken at a sampling frequency of 0.0084 Hz; this implies that

THE POWER SPECTRUM OF CORE TEMPERATURE --- FIGURE 3.38



THE POWER SPECTRUM OF SKIN TEMPERATURE --- FIGURE 3.39



the highest frequency present in the power spectrum is 0.0042 Hz. The Fourier transformation produces discrete complex data which is defined as X(f), where:

$$X(f) = a+jb \qquad 3.5.$$

The power spectrum (S_{XX}) of the core temperature is found from the relationship:

$$S_{XX}(f) = X(f)X^{*}(f) \qquad 3.6.$$

substituting from equation 3.5.

$$S_{XX}(f) = (a+jb)(a-jb) = a^2 + b^2 \qquad 3.7.$$

Figure 3.38a illustrates the spectrum (core), for the frequency range 0-2.4 x 10^{-3} Hz. The majority of the power resides in the range 0-6 x 10^{-4} Hz, which is the frequency spectrum which is covered in figure 3.38b. If a similar technique is adopted with the data of skin temperature, the result is illustrated by the power spectrum (figure 3.29), the majority of the power is again seen to lie in the range 0-6 x 10^{-4} Hz.

If the core temperature and skin temperature are linearly related during the part of the experiment we are considering, there should be common frequency components in the two temperatures. The cross spectrum is a measure of the linear dependence of the output of a system upon its input, and is defined as:

$$S_{xy}(f) = X^{*}(f)Y(f) \qquad 3.8.$$

A discrete component of X(f) is expressed as a+jb, while a similar component of Y(f) is c+jd.

Hence:

$$S_{xy}(f)=(a-jb)(c+jd) = (ac+bd)+j(ad-bc) \qquad 3.9.$$

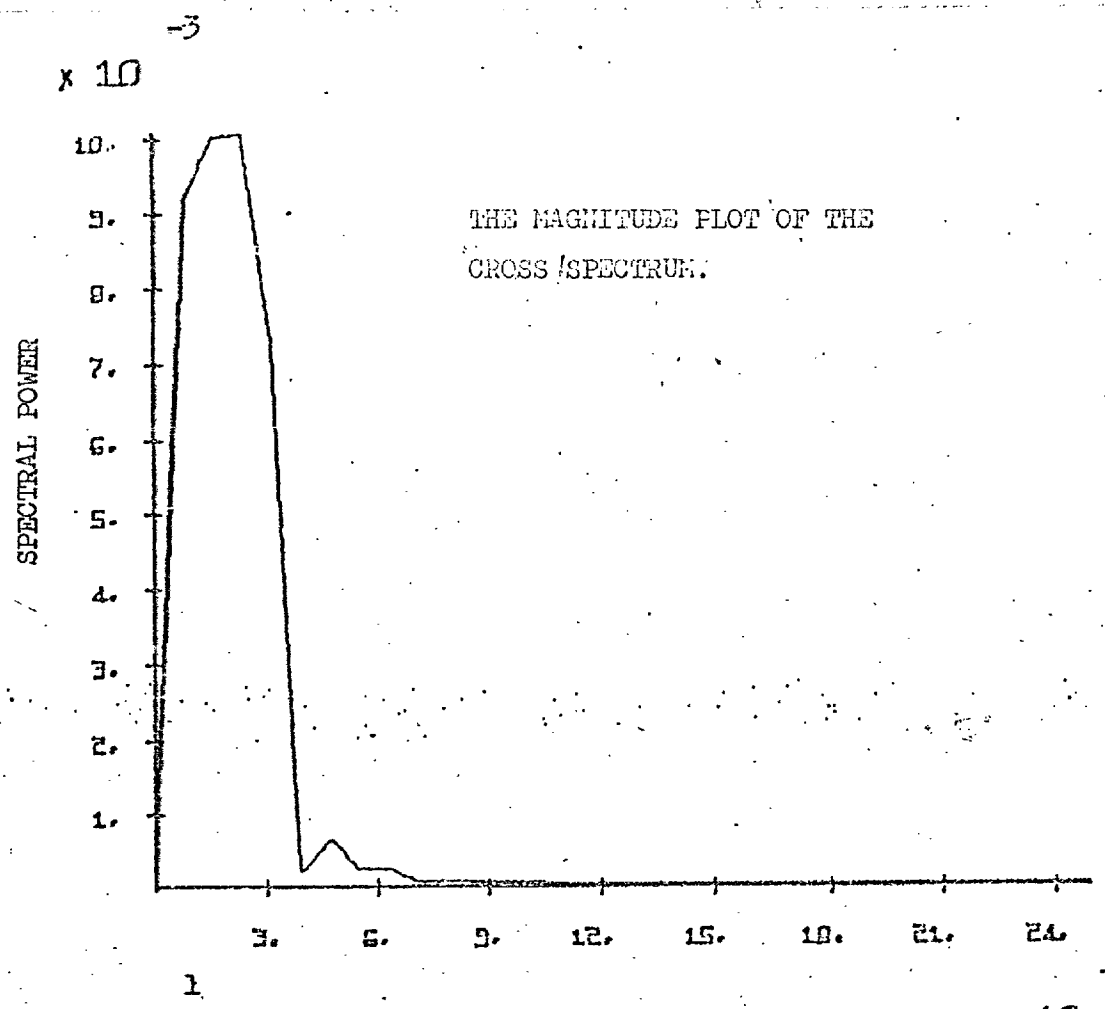
The cross spectrum is expressed in terms of its magnitude $|S_{xy}|$ and its phase ϕ_{xy} (degrees) where:

$$S_{xy} = \sqrt{\left\{(ac+bd)^2 + (ad-bc)^2\right\}} \qquad 3.10.$$

and

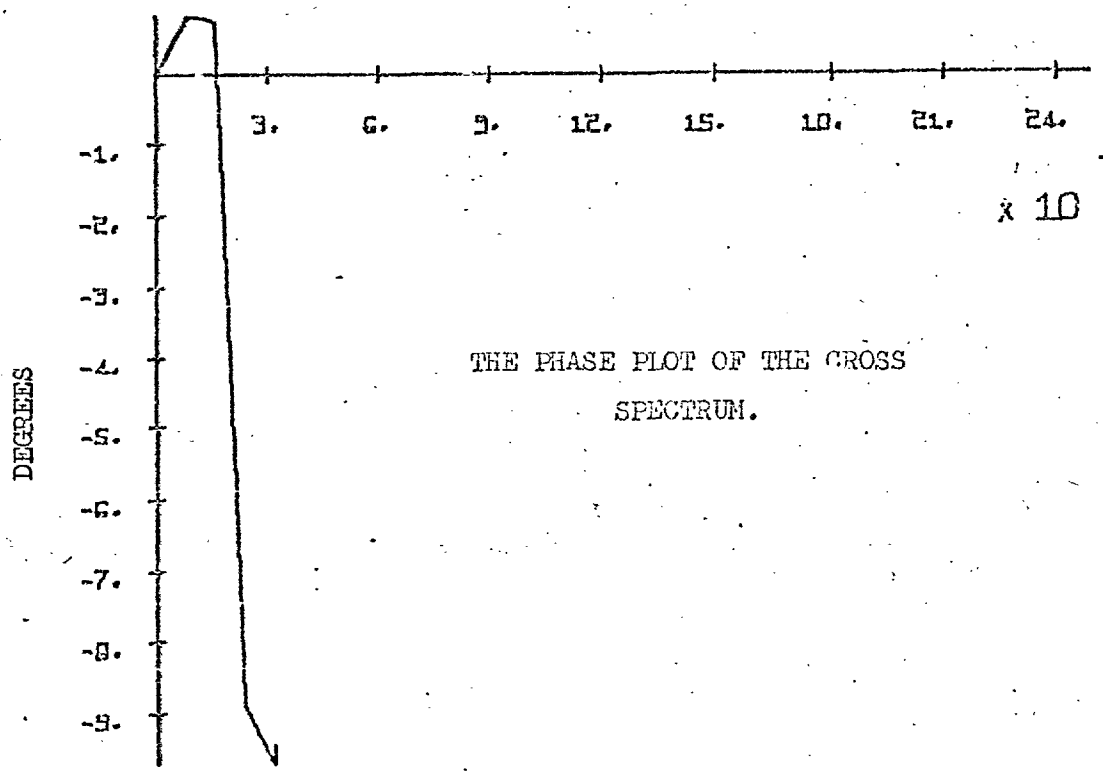
$$\phi_{xy} = \frac{180}{\Pi} \tan^{-1} \left\{\frac{ad-bc}{ac+bd}\right\} \qquad 3.11.$$

Figures 3.40 a & b, are the plots of the magnitude and phase relationships present in the cross spectrum and both exhibit evidence that the core temperature is related to the skin temperature by a simple lag transfer function. The implication is that the suit air temperature drives the skin and core temperatures during phase two and three of the experiment because even the core control system cannot reach the required level of heat loss. Due to the severity of the external stimulus, thermal control is swamped and the state of the body is solely dependent upon the heat diffusion properties of the tissue and the heat convection properties of blood. The block diagram



THE MAGNITUDE PLOT OF THE CROSS SPECTRUM.

FIGURE 3.40



THE PHASE PLOT OF THE CROSS SPECTRUM.

below illustrates this process.

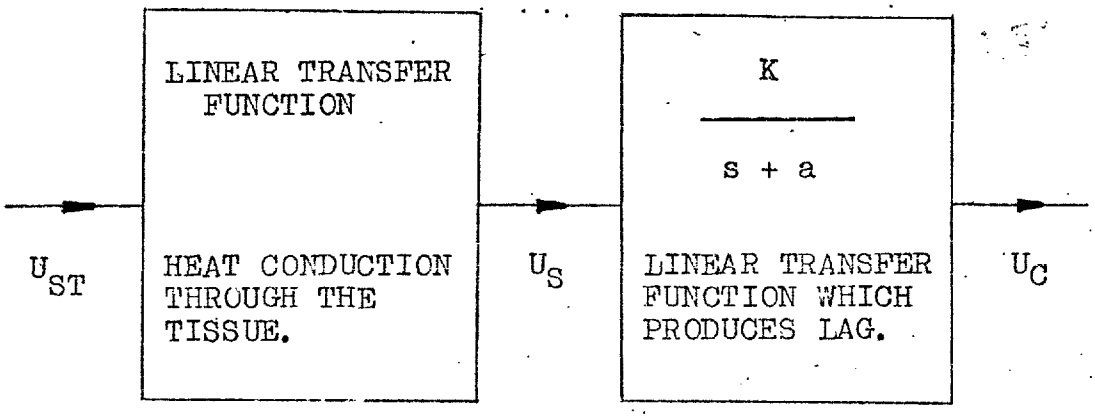


FIGURE 3.41.

U_{ST} - Suit temperature

U_S - Skin temperature

U_C - Core temperature

CHAPTER 4

THE THEORETICAL ANALYSIS OF ENTRAINMENT.

4.1 INTRODUCTION.

It has been established in chapter three, that the peripheral thermo-regulatory system, which we have been discussing, exhibits spontaneous fluctuations which are attributed to the action of an oscillatory system containing non-linear elements. The problem as yet unresolved is the exact definition of such an element, or elements, within the system.

The experimental results and the work of Minorsky (1962), clearly indicate that the phenomenon of frequency entrainment occurs when a periodic stimulus is applied to a system whose free oscillation is of the self excited type. Seifert and Steeg (1960), discuss self excited systems of this type, stating that the oscillations arise from changes in the internal equilibrium of the system. Seifert and Steeg, together with Pipes (1958), describe this type of nonlinear oscillatory behaviour as relaxation oscillations. According to Pipes, in a fundamental paper published in 1926 van der Pol presented a generalized equation to describe self excited nonlinear oscillatory systems, namely:

$$\ddot{x} + \epsilon(x^2 - 1)\dot{x} + x = 0 \qquad (4.1.)$$

By a suitable change in the ϵ parameter, the oscillation phenomenon for a particular system can be described by the van der Pol equation (4.1.). The approximate solution to the equation (4.1.), has been studied by Kryloff and Bogoliuboff (1943). These authors found that for small values of ϵ ($0 < \epsilon \ll 1$), the solution is a sustained, near, sinusoidal oscillation, and in this case equation (4.1.) is a quasi-linear differential equation. Alternatively, if ϵ is large ($\epsilon \gg 1$), the initial damping is large and negative, this makes the system highly aperiodic. Kryloff and Bogoliuboff found that in such a system as soon as the momentary value of x^2 becomes larger than unity, the negative character of the damping ceases to exist, and the damping becomes positive. Which in turn, they state, makes the amplitude of x decrease aperiodically. It is therefore apparent that for large values of ϵ the system has the tendency initially to jump away from zero to a position value of x, decreasing afterward gradually, until suddenly it jumps to a negative value of x, etc. The variation of x with time is therefore a relaxation oscillation.

In his paper (1926), van der Pol plotted the time domain waveforms for three different values of the parameter ($\epsilon=0.1$, $\epsilon=1.0$, $\epsilon=10.0$), these are

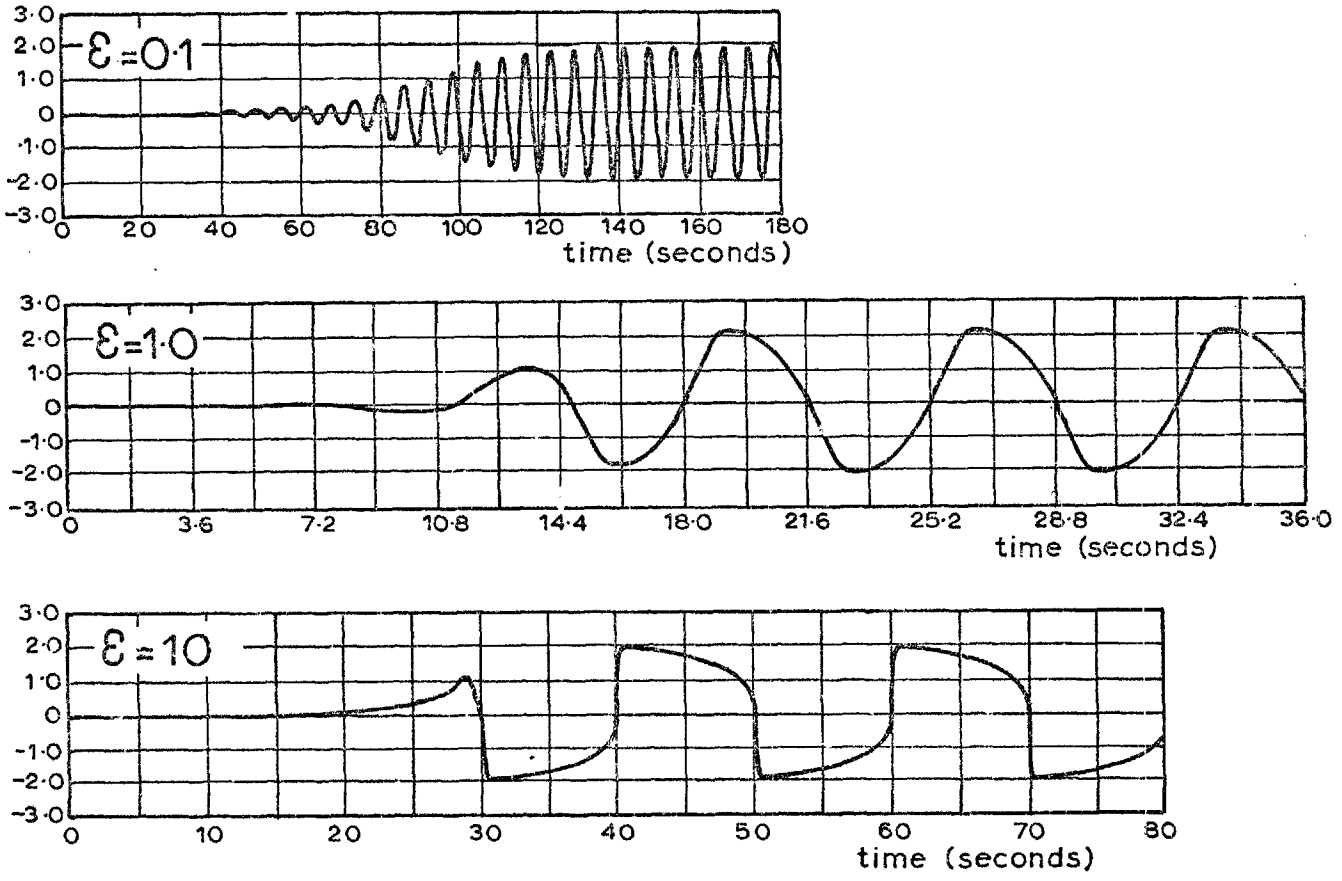


Fig. 4·1 Solutions of van der Pol's Equation

illustrated in figure 4.1. The graph of the oscillation for $\epsilon=10$ is a typical relaxation oscillation; it differs radically from the sinusoidal oscillation for $\epsilon=0.1$. The peripheral control of human body temperature is of the non-linear oscillatory type and the phenomenon is therefore described by the generalized van der Pol equation with the appropriate value of ϵ.

4.2 THE REPRESENTATION OF THE ENTRAINED SYSTEM BY A VAN DER POL OSCILLATOR.

Thaler and Pastel (1962), describe frequency entrainment in terms of the van der Pol equation, and it is clear from the experimental results of chapter three that the system under consideration is entrained by a suitable external stimulus. The frequency of the self excited oscillation in a van der Pol system, falls into synchronism with an applied driving frequency provided the two frequencies are not widely dissimilar; this is the phenomenon of entrainment. If their difference is large enough, one may expect the occurrence of an almost periodic oscillation; in other words, a beat oscillation may result. However, entrainment still occurs when the ratio (or its reciprocal), of the natural frequency of oscillation to the driving frequency, is in the neighbourhood of an integer other than unity. Under these conditions, the natural frequency of the system

is entrained by a frequency which is an integral multiple or sub-multiple of the driving frequency. Such entrainments are normally termed higher harmonic or sub-harmonic, respectively. Similarly, the phenomenon of synchronization is known as harmonic entrainment.

The spontaneous activity of the thermo-regulatory system is illustrated in figures 3.4 and 3.5. The frequency domain plots contained within these figures show that the output waveform consists of a number of frequency components of varying amplitude. Alternatively, when the system has been entrained, the output waveform has one dominant component at the frequency of the external stimulus. The system must therefore be of a nonlinear type which when functioning generates a number of frequency components.

The oscillation frequency of the van der Pol system is defined by the parameter ϵ. Dorodnicyn (1947), published a paper in which he presents an expression for the period of oscillation w, described in terms of the parameter ϵ :

$$w=(3-2\log 2)\epsilon+3a\epsilon^{-\frac{1}{3}}-\frac{22}{9}\frac{\log\epsilon}{\epsilon}+(3\log 2-\log 3-1/6+b_0-2d)/\epsilon \qquad (4.2.$$

where a, b_0 and d are constants. A later paper by Ponzo and Wax (1965), describes minor errors in the calculations leading to Dorodnicyns equation. These authors describe a corrected version:

$$w=(3-2\log 2)\epsilon + 3a\epsilon^{-\frac{1}{3}} - \frac{2}{3}\frac{\log\epsilon}{\epsilon} + (3\log 2-\log 3-\frac{3}{2}+b_0-2d)/\epsilon \qquad (4.3.)$$

in both equation (4.2.) and equation (4.3.), $a=2.338107$, $b_0=0.1723$, and $d=0.4889$.

The results of the first series of entrainment experiments show that when the peripheral temperature control system is entrained, there is only one frequency component of twenty seconds periodicity. By choosing a suitable value of ϵ, it is possible to select the correct van der Pol equation to match the physical system under these conditions. The output waveforms for the van der Pol equation (4.1.), with various values of ϵ are illustrated in figures 4.2 and 4.3. The value of ϵ which results in an oscillation frequency of 0.05 Hz is 10.5, and the corresponding waveform is shown in figure 4.4.

The relevant van der Pol waveform is synthesized on the computer by a series of solutions at intervals of 0.1 seconds. With the data in this form, the information can be transformed from the time domain to the frequency domain.

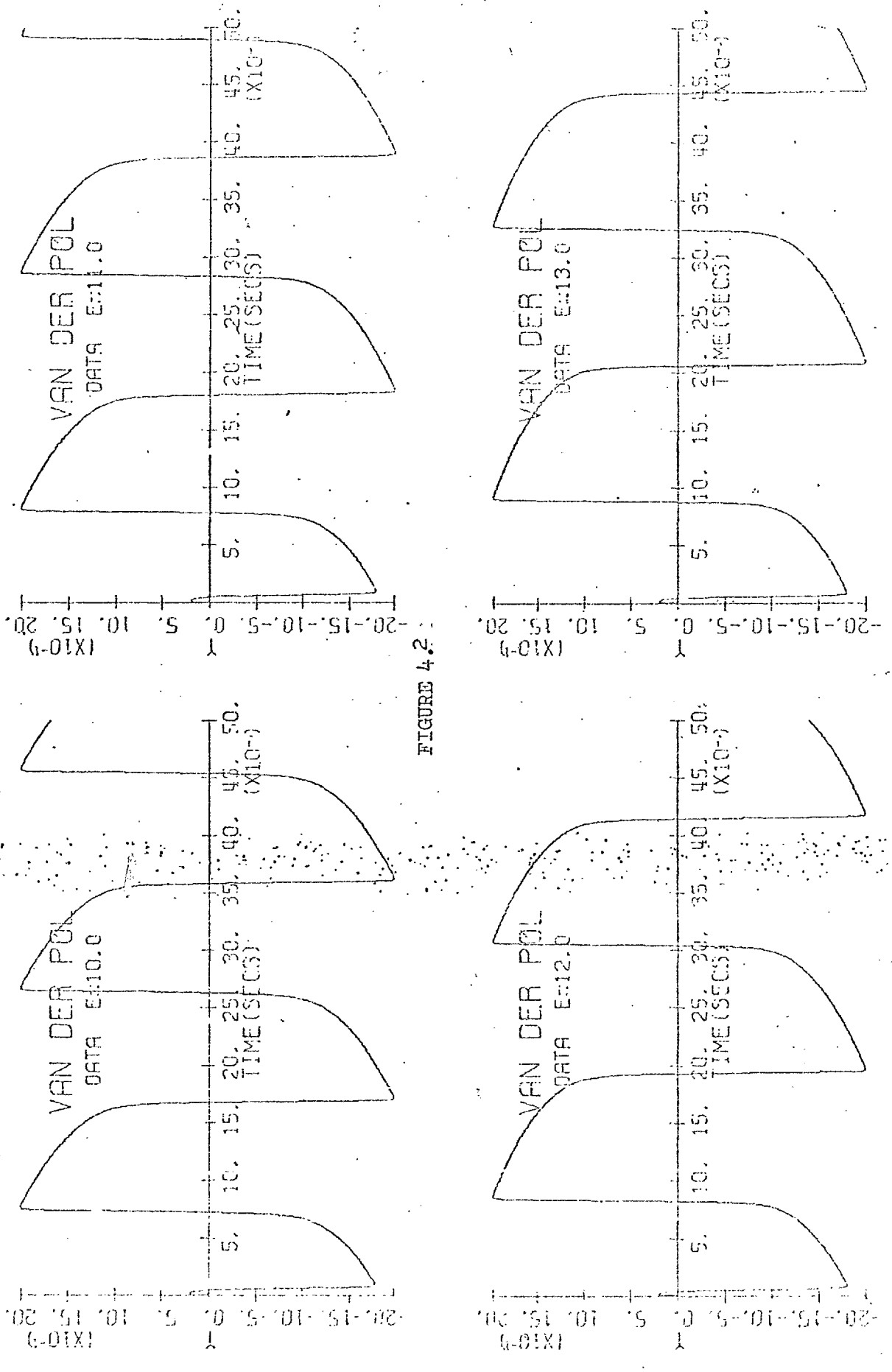
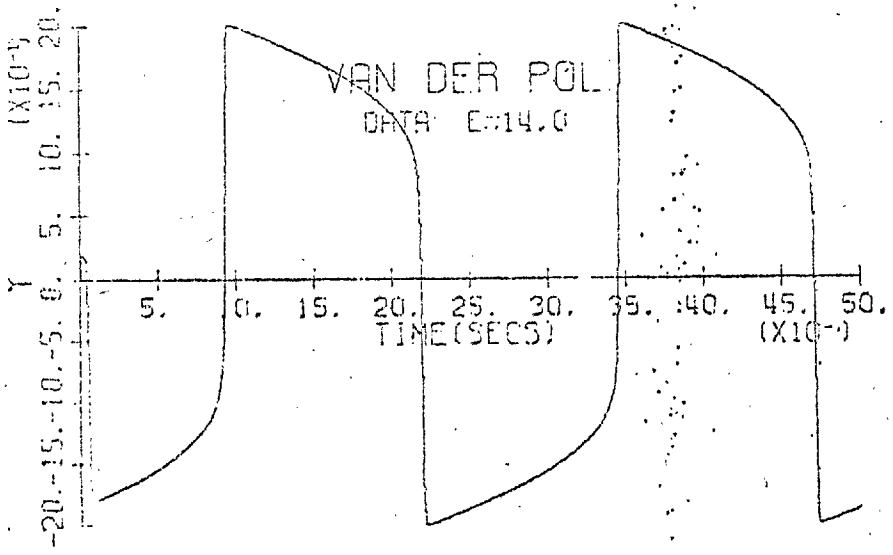

VAN DER POL
DATA E=11.0
VAN DER POL
DATA E=13.0
VAN DER POL
DATA E=10.0
VAN DER POL
DATA E=12.0
TIME(SECS)
(X10-3)
Y

FIGURE 4.2


VAN DER POL
DATA E=14.0
Y (X10⁻¹)
-20. -15. -10. -5. 0. 5. 10. 15. 20.
5. 10. 15. 20. 25. 30. 35. 40. 45. 50.
TIME(SECS) (X10⁻¹)

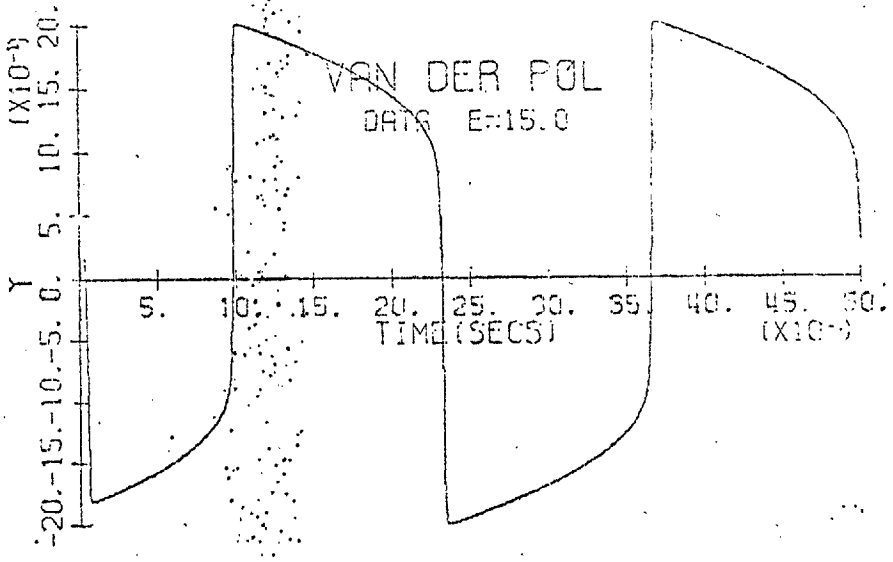
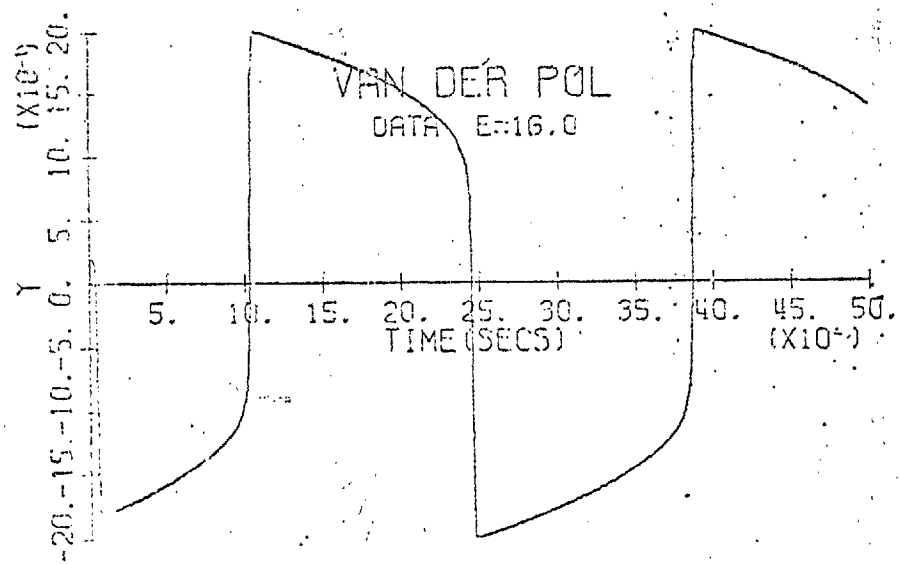

VAN DER POL
DATA E=15.0
Y (X10⁻¹)
-20. -15. -10. -5. 0. 5. 10. 15. 20.
5. 10. 15. 20. 25. 30. 35. 40. 45. 50.
TIME(SECS) (X10⁻¹)

FIGURE 4.3


VAN DER POL
DATA E=16.0
Y (X10⁻¹)
-20. -15. -10. -5. 0. 5. 10. 15. 20.
5. 10. 15. 20. 25. 30. 35. 40. 45. 50.
TIME(SECS) (X10⁻¹)

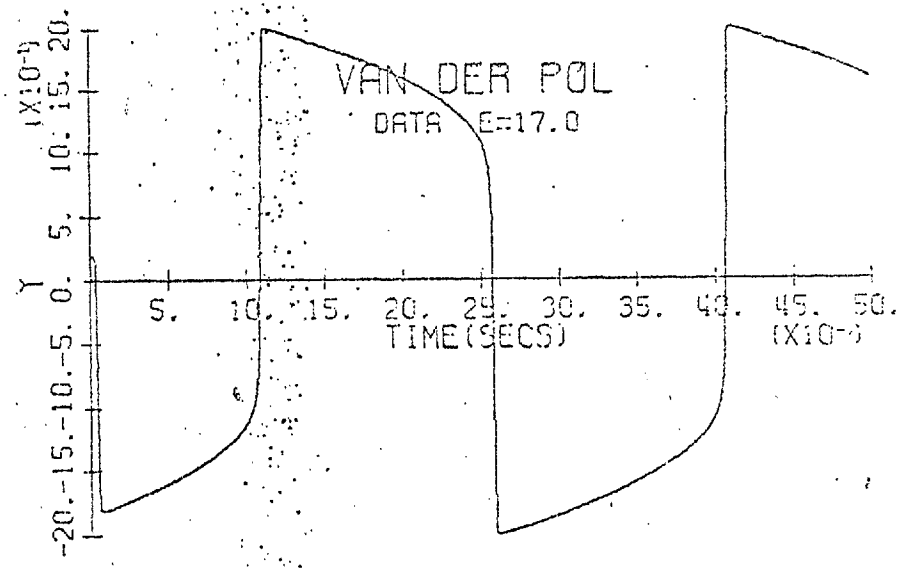
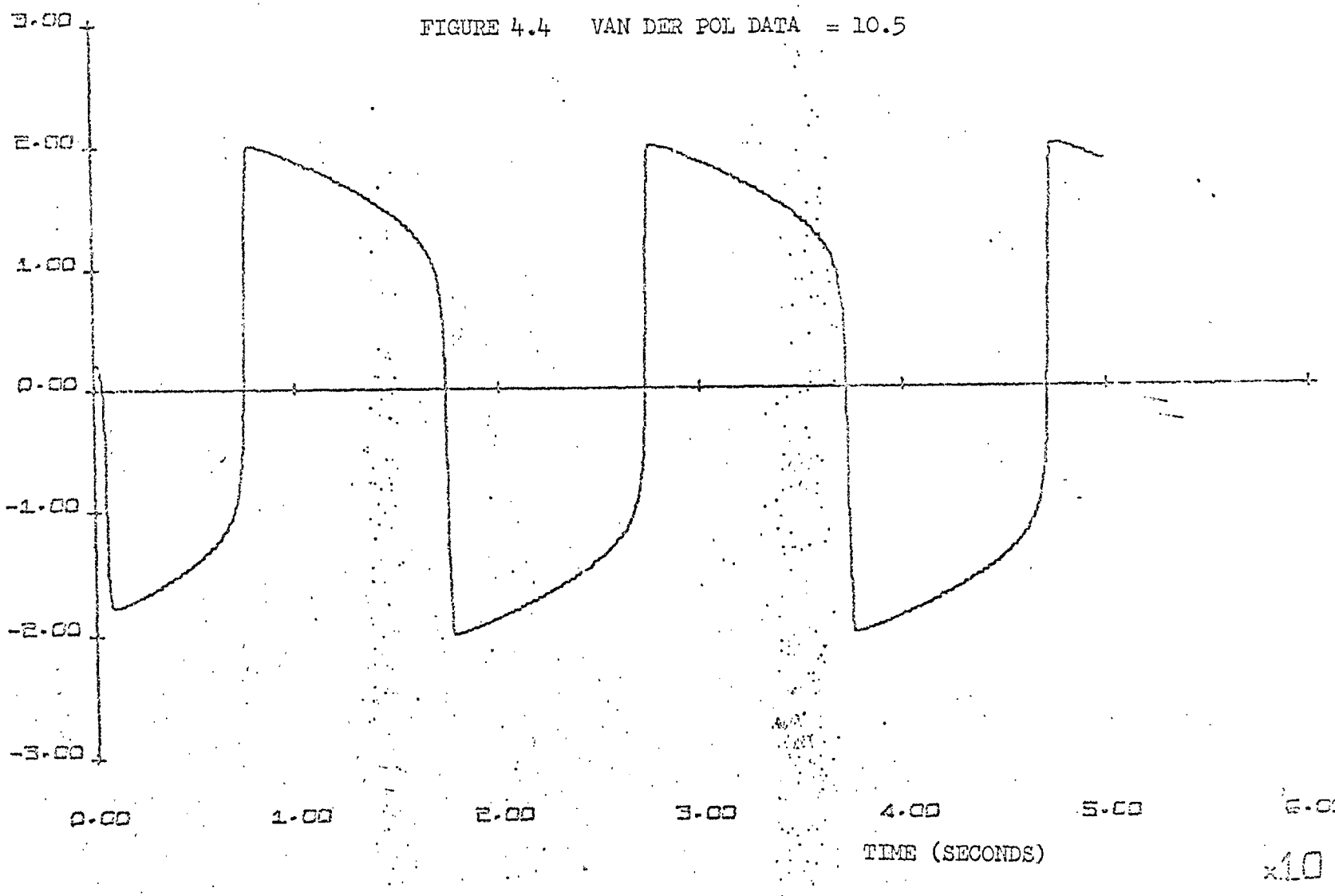

VAN DER POL
DATA E=17.0
Y (X10⁻¹)
-20. -15. -10. -5. 0. 5. 10. 15. 20.
5. 10. 15. 20. 25. 30. 35. 40. 45. 50.
TIME(SECS) (X10⁻¹)

FIGURE 4.4 VAN DER POL DATA = 10.5



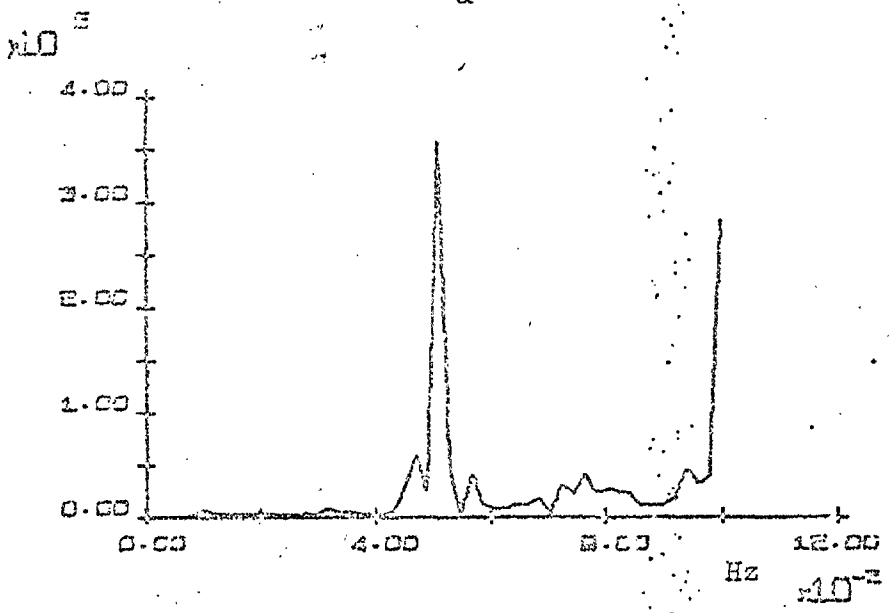
The power spectrum of the van der Pol system which describes the peripheral thermal system when it is entrained by a twenty second stimulus, is illustrated in figure 4.5. The left hand diagram is the spectrum of the entrained human system, whereas that on the right is of the van der Pol system. A simple sine function generator oscillating at the entrainment frequency would produce an ordinate at 0.05 Hz; whereas, the spectrum of the (human digit) blood flow waveform is much more complex than a simple sine component. The shape of the two spectra (figures 4.5a and 4.5b), are very similar, thus illustrating that the particular value of ϵ which was used defines a van der Pol system which is a close approximation to the natural system, when it has been entrained by a twenty second stimulus.

4.3 THE SPONTANEOUS ACTIVITY OF THE SYSTEM.

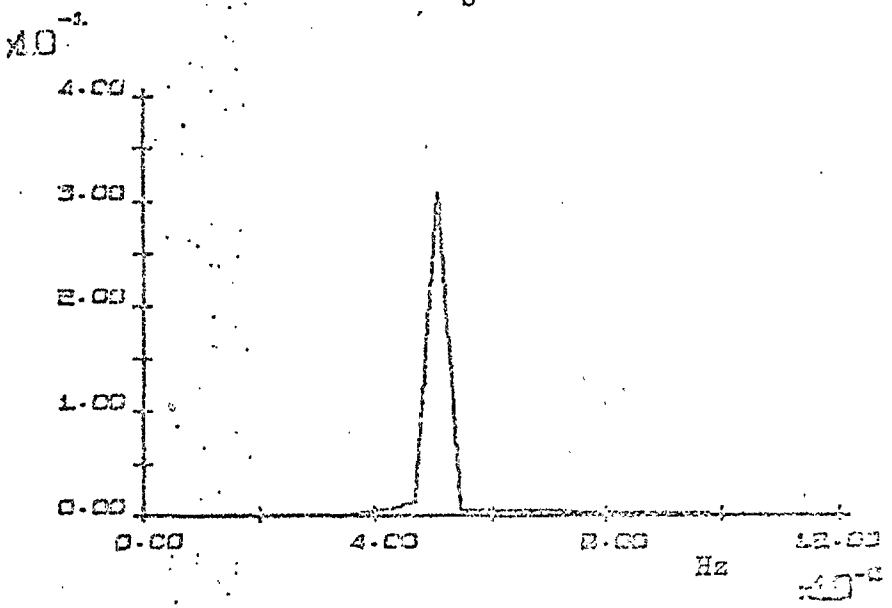
Although the entrained thermal system can be described by a suitable van der Pol oscillator, the factors involved in the production of the power spectra associated with the spontaneous activity, for example the spectrum of figure 3.4c, have still to be explained. One therefore asks the question: if the entrained system can be represented by a single van der Pol equation, then is it is not conceivable to represent the spontaneous activity by a family of van der Pol oscillators?

FIGURE 4.5

THE PHYSIOLOGICAL SYSTEM
'a'



THE VAN DER POL SYSTEM
'b'



Each of the frequency components in figure 3.4c could be thought to correspond to the output waveform from a van der Pol oscillator with the correct value of ϵ to define its frequency of oscillation. The amplitude of each of these components (γ_c), is defined by equation (4.2), where x is the output vector and a, a scalar quantity.

$$\gamma_c = ax \qquad (4.2.)$$

The entire spectrum of spontaneous activity can be described in this manner, so the net result is a family of van der Pol oscillators which are represented in matrix form as:

$$X = -\epsilon (X^2 - 1) \dot{X} - \ddot{X} \qquad (4.3.)$$

Similarly, for the whole family, equation (4.2.) becomes:

$$\gamma = AX \qquad (4.4.)$$

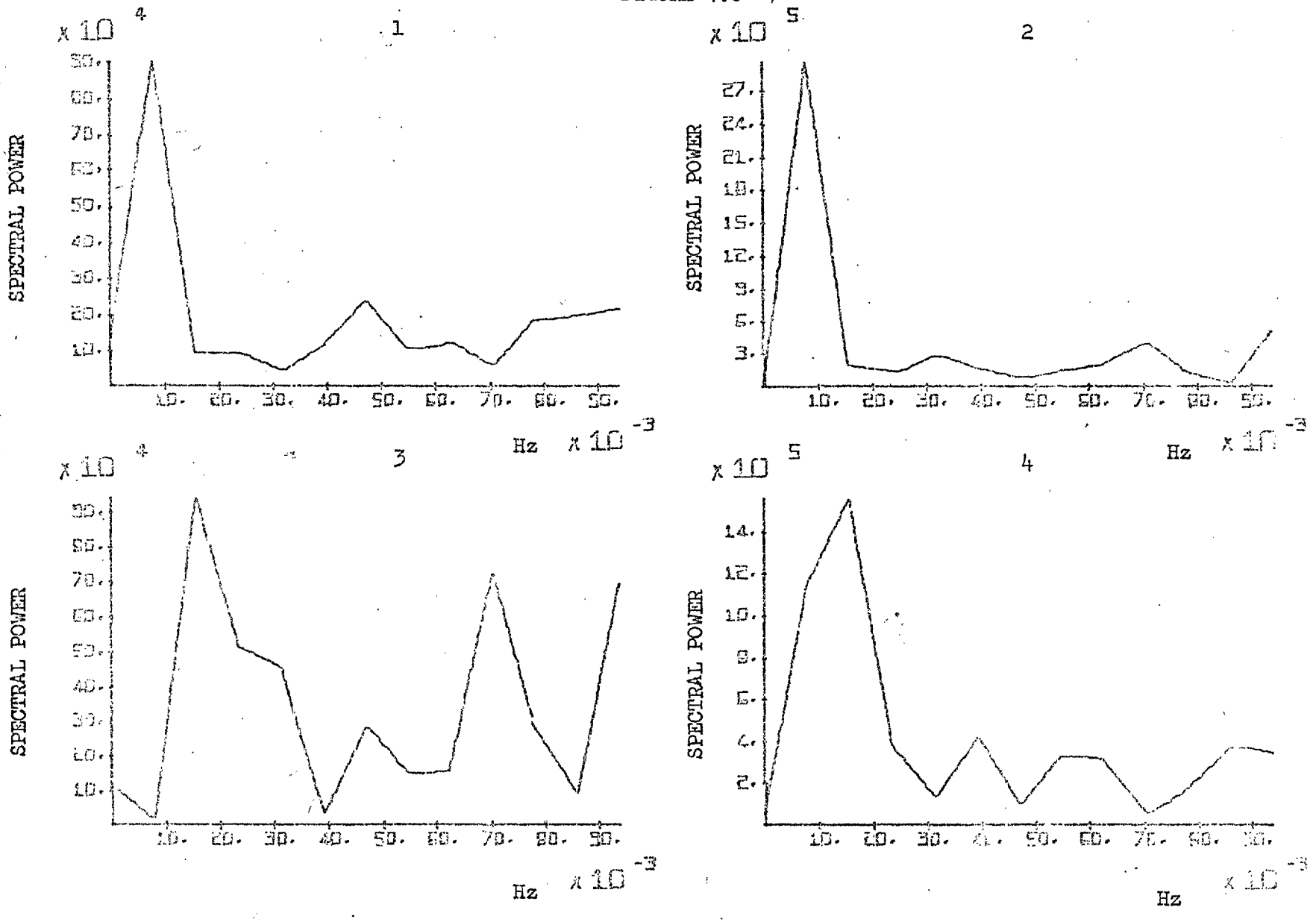
In this way, typical spontaneous activity would be represented by a family of van der Pol oscillators.

The analysis of a time series by using the fast Fourier transform (FFT), is based on the assumption that the process of transformation is performed on a stationary process. If this is not so, then the power spectrum of the complete record of data will contain components which may not be present during the entire record.

By treating the spontaneous data as a number of separate files, a running analysis of the data can be performed to determine the degree of stationarity. The running analysis is effected on files of data 256 words long. The power spectrum for the first 256 words is computed (1-256); the program then advances by 128 words, thus the second power spectrum is that of words 128-384. This procedure continues until the complete file of experimental data (1024 words), has been processed. Figures 4.6 and 4.7, illustrate the power spectra for the spontaneous data obtained from subjects RK and RC.

It is apparent from these plots that a high degree of non-stationarity exists. But, in view of the stability of the van der Pol system, non-stationarity in a set of such oscillators is unlikely. Hence, the possibility that the spontaneous activity results from a family of stable nonlinear oscillators is exceedingly unlikely. The evident alternative is a single van der Pol oscillatory system whose frequency of oscillation varies over finite time.

FIGURE 4.6


1
x 10^4
SPECTRAL POWER
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz x 10^-3
2
x 10^5
SPECTRAL POWER
3. 6. 9. 12. 15. 18. 21. 24. 27.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz x 10^-3
3
x 10^4
SPECTRAL POWER
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz x 10^-3
4
x 10^5
SPECTRAL POWER
2. 4. 6. 8. 10. 12. 14.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz x 10^-3

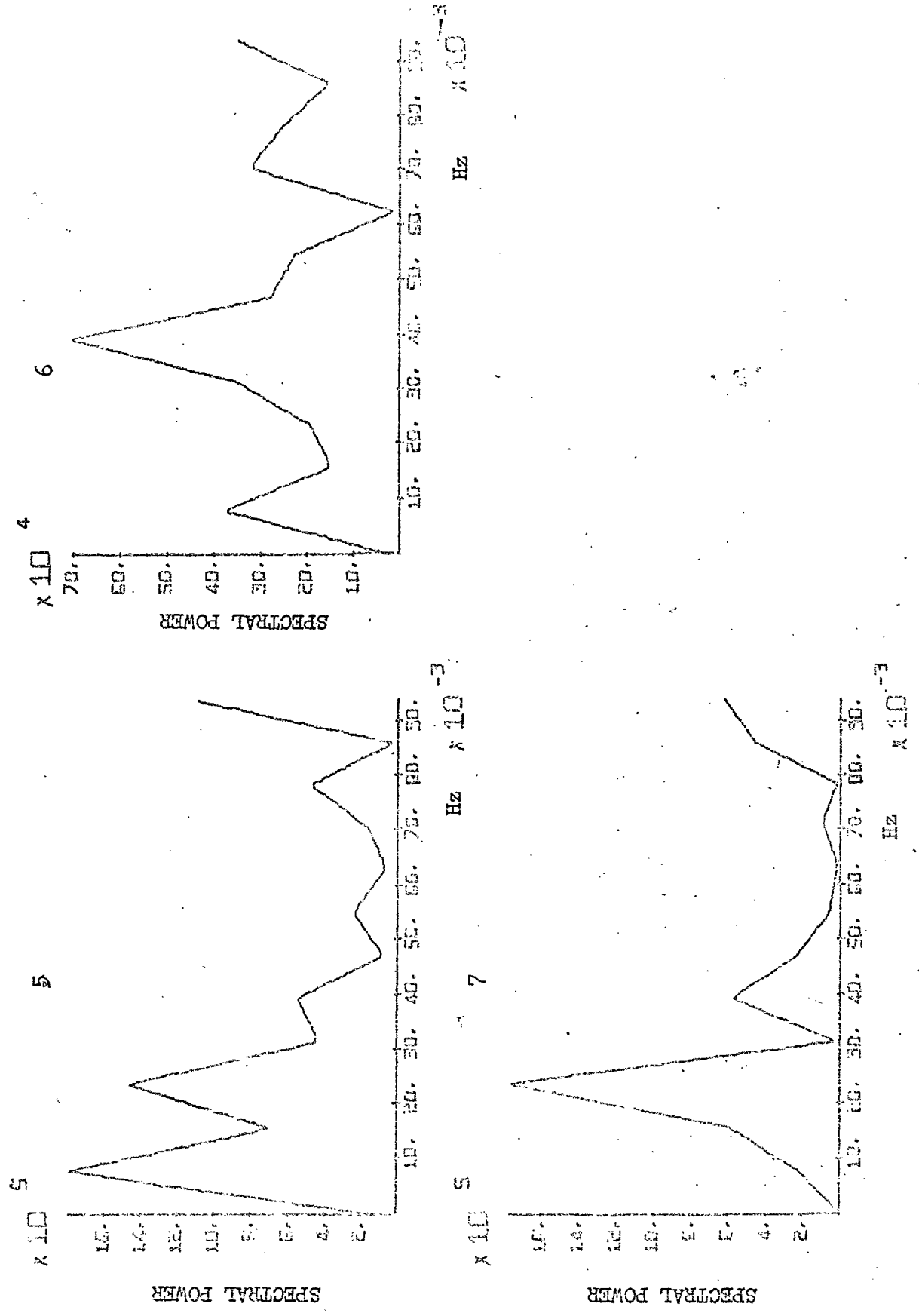
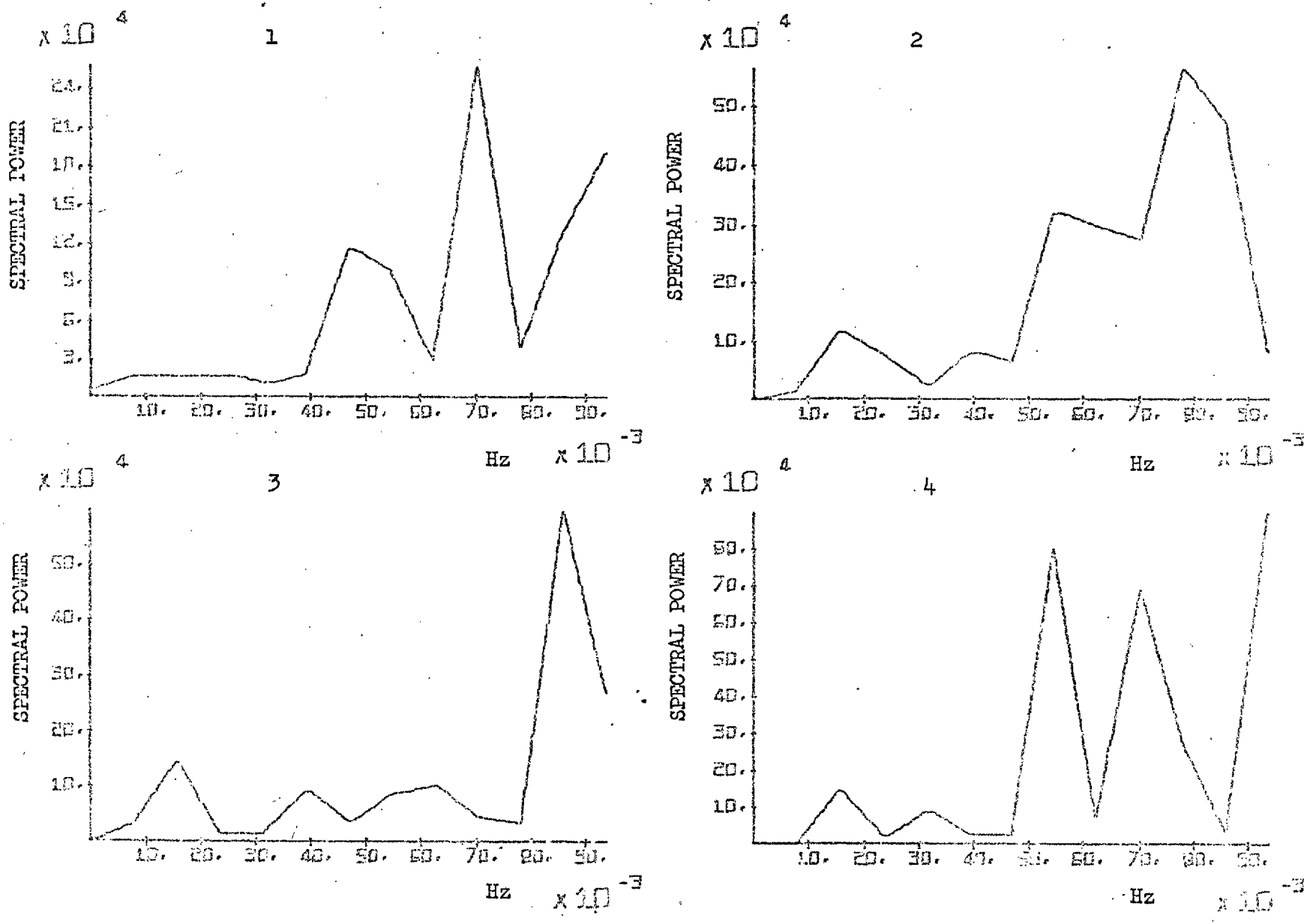
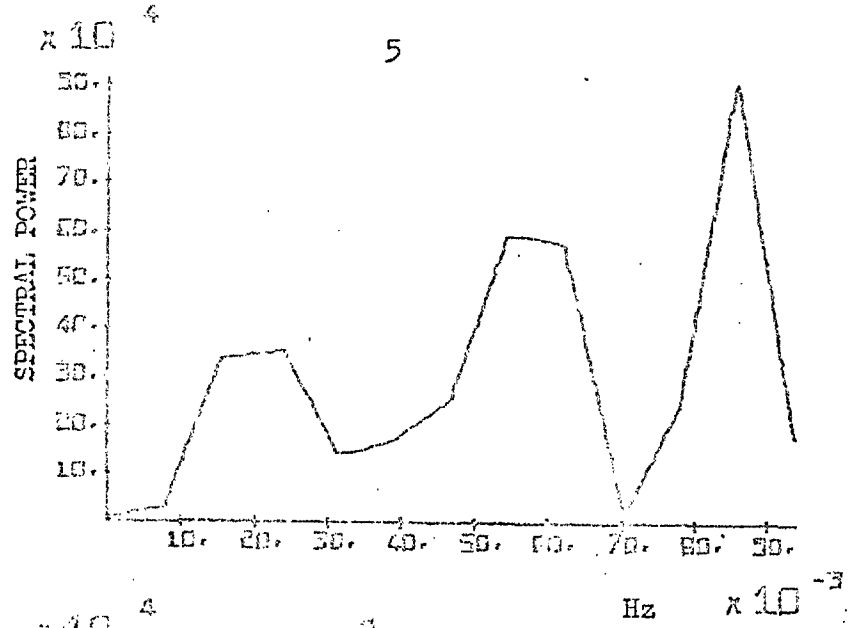
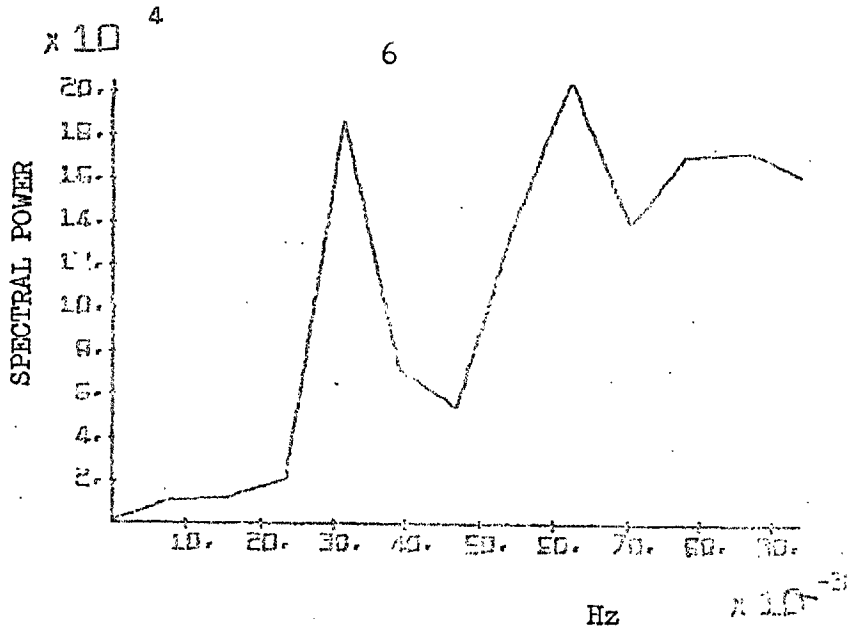
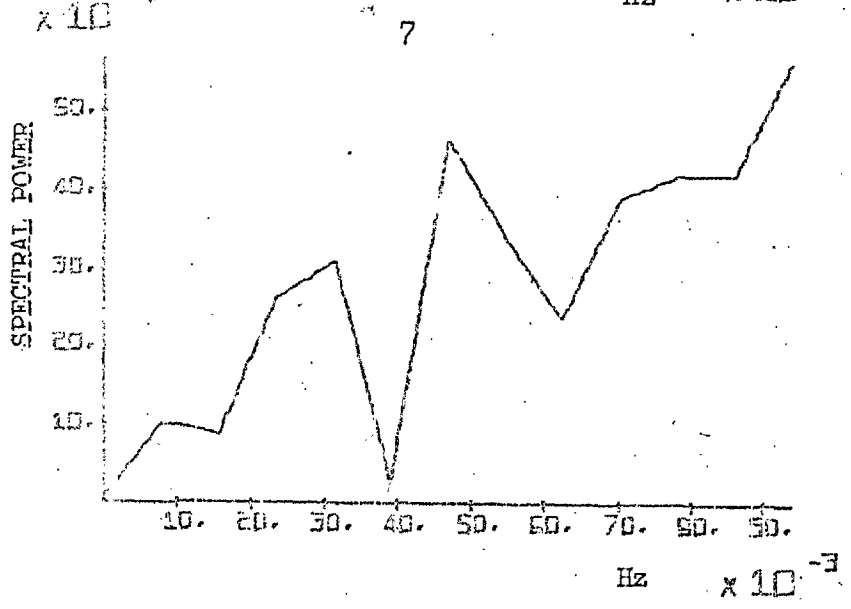

4
6
SPECTRAL POWER
Hz
5
SPECTRAL POWER
Hz
7
SPECTRAL POWER
Hz

FIGURE 4.7


x 10 4
1
SPECTRAL POWER
24.
21.
18.
15.
12.
9.
6.
3.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3
x 10 4
2
SPECTRAL POWER
50.
40.
30.
20.
10.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3
x 10 4
3
SPECTRAL POWER
50.
40.
30.
20.
10.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3
x 10 4
4
SPECTRAL POWER
90.
70.
60.
50.
40.
30.
20.
10.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3


x 10 4
5
SPECTRAL POWER
50.
60.
70.
80.
50.
40.
30.
20.
10.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3


x 10 4
6
SPECTRAL POWER
20.
18.
16.
14.
12.
10.
8.
6.
4.
2.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3


x 10 4
7
SPECTRAL POWER
50.
40.
30.
20.
10.
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3

4.4 THE STABILITY OF ONE VAN DER POL OSCILLATOR.

The spontaneous activity of the thermal control system would therefore seem to be due to the activity of a single van der Pol oscillator. However, one possibility remains, this being that the non-stationarity results from instability in the van der Pol oscillators.

This issue can be settled by using Liapunov's Second Method (Gibson 1963). A function V, analogous, though not exactly equal, to the stored energy of the system, is examined as a function of time. To prove the stability of the system it is, according to Gibson, sufficient to show that this V function approaches zero as time approaches infinity.

If $V(x_1,x_2)$ is the Liapunov function which describes the limit cycle of the system (in the phase plane), then for a stable solution the following conditions must be satisfied:

(a). $V(x_1,x_2) = 0$ only when $x_1 = x_2 = 0$.

(b). $\frac{d}{dt} V(x_1,x_2) < 0$ when x_1 and x_2 are not equal to zero.

For the system under consideration:

$$x_1 = x \text{ and } x_2 = \dot{x}$$

For the van der Pol equation, the relevant Liapunov function is:

$$V(x_1, x_2) = \tfrac{1}{2}\left[x_1^2 + x_2^2 \right]$$

Applying the stability criterion:

$$\frac{dv}{dt} = \frac{\partial V}{\partial x_1}\frac{\partial x_1}{\partial t} + \frac{\partial V}{\partial x_2}\frac{\partial x_2}{\partial t}$$

Therefore: $\frac{dv}{dt} = x_1 \dot{x}_1 + x_2 \dot{x}_2$ (4.5.)

But $\dot{x}_1 = x_2$ (4.6.) and $\dot{x}_2 = -\epsilon(x_1^2 - 1)x_2 - x_1$ (4.7.)

Substituting equations (4.6.) and (4.7.) in equation (4.5.) gives:

$$\frac{dv}{dt} = x_1 x_2 - x_2^2(x_1^2 - 1)\epsilon - x_2 x_1 = \epsilon x_2^2(1 - x_1^2)$$

Now $\frac{dv}{dt}$ is negative for all $|x_1| > 1$.

and $\frac{dv}{dt}$ is positive for all $|x_1| < 1$.

The system therefore has a stable limit cycle, which results in stable oscillations. Consequently, the observed non-stationarity in the spontaneous data must result from some other source as yet undefined.

4.5 THE LIMITS OF HARMONIC ENTRAINMENT.

Before this statement can be substantiated, it would seem necessary to gain a clearer understanding of the limits of harmonic entrainment for a single van der Pol oscillator.

When the system is oscillating spontaneously, the characteristic equation is:

$$\ddot{x} + \epsilon(x^2 - 1)\dot{x} + x = 0 \qquad (4.1.)$$

However, when the system is excited by a forcing function such that entrainment occurs, the characteristic equation of the system is re-defined as:

$$\ddot{x} + \epsilon(x^2 - 1)\dot{x} + x = B \cos wt + B_o \qquad (4.8.)$$

where the term $B \cos wt + B_o$ is the forcing function. Consideration of the Van der Pol equation with a forcing function leads to a quantitative analysis of the system dynamics related to digit blood flow.

A new variable v can be defined, where:

$$v = x - B_o \qquad (4.9.)$$

Thus giving an alternative form of equation (4.8.), namely:

$$\frac{d^2v}{dt^2} + E((v+ Bo)^2 - 1) \frac{dv}{dt} + (v + B_o) = B \cos wt + B_o \qquad (4.10.)$$

where $E=\epsilon$

Expanding the velocity term $\left\{\frac{dv}{dt}\right\}$

$$\frac{d^2v}{dt^2} - E(1- B_o^2) \left\{ 1- \frac{2B_o}{1 - B_o^2} v - \frac{v^2}{1- B_o^2} \right\} \frac{dv}{dt} + v= B \cos wt \quad (4.11$$

and letting $\mu = E(1- B_o^2)$, $\beta = \frac{2B_o}{1- B_o^2}$ and $\gamma = \frac{1}{1 - B_o^2}$

gives equation (4.1.) the form:

$$\frac{d^2v}{dt^2} - \mu (1- \beta v - \gamma v^2) \frac{dv}{dt} + v = B \cos wt \qquad (4.12.)$$

It can be seen from equation (4.12.) that if B=0, the system will oscillate at its natural frequency w_n. When B is sufficiently large and the driving frequency is in the neighbourhood of w_n, one would expect an entrained oscillation at the driving frequency w, that is, the occurrence of harmonic entrainment.

In his original paper, van der Pol assumes the solution of equation (4.12.) to be of the form:

$$v= b_1 \sin wt + b_2 \cos wt \qquad (4.13.)$$

Where w is the forcing function frequency.

This solution can be obtained by the method of harmonic balance. Substituting equation (4.13.) in equation (4.12.), and this allows an estimate of the value of B required to entrain the system.

Differentiating equation (4.13.):

$$\frac{dv}{dt} = b_1 w \cos wt - b_2 w \sin wt \qquad (4.14.)$$

and similarly:

$$\frac{d^2v}{dt^2} = - b_1 w^2 \sin wt + b_2 w^2 \cos wt \; = - w^2 v \qquad (4.15.)$$

Substituting equations (4.13.), (4.14.) and (4.15) in (4.12.) leads to the solution:

$$\sigma_1 x_1 + (1 - r_1^2) \, y_1 = 0 \qquad (4.16.)$$

and

$$(1 - r_1^2) \, x_1 - \sigma_1 y_1 + \frac{B}{\mu w \, a_o} = 0 \qquad (4.17.)$$

where

$$x_1 = \frac{b_1}{a_o} \quad y_1 = \frac{b_2}{a_o} \quad r_1^2 = x_1^2 + y_1^2$$

$$a_o = \sqrt{\frac{4}{\gamma}} \; ; \; \sigma_1 = \frac{1 - w^2}{\mu w} \qquad (4.18.)$$

One can now eliminate x_1 and y_1 from equations (4.16.) and (4.17.): also from (4.18.) $r_1^2 = x_1^2 + y_1^2$

$$\therefore \quad x_1 = \left[r_1^2 - y_1^2 \right]^{\frac{1}{2}}$$ substituting for x_1 in equation (4.16.)

$$x_1^2 = \frac{(1- r_1^2)^2 \, y_1^2}{\sigma_1^2} = r_1^2 - y_1^2$$

$$\therefore \quad y_1^2 = \frac{r_1^2 \, \sigma_1^2}{\sigma_1^2 + (1- r_1^2)^2} \qquad (4.19.)$$

v

Multiplying equation (4.16) by $(1- r_1^2)$ and (4.17.) by σ_1:

$$\sigma_1 (1- r_1^2) \, x_1 + (1- r_1^2) \, y_1 = 0 \qquad (4.20.)$$

$$\sigma_1 (1- r_1^2) \, x_1 - \sigma_1^2 \, y_1 = \frac{B \sigma_1}{\mu w a_o} \qquad (4.21.)$$

subtracting equation (4.21.) from (4.20.)

$$(1- r_1^2)^2 \, y_1 + \sigma_1^2 \, y_1 = \frac{B}{\mu w a_o} \qquad (4.22.)$$

and substituting for y_1 from (4.19.)

$$\left[\frac{r_1^2\,\sigma_1^2}{\sigma_1^2 + (1-r_1^2)^2}\right]^{\frac{1}{2}} \left[(1-r_1^2)^2 + \sigma_1^2\right] = \frac{\sigma_1 B}{\mu w a_o} \qquad (4.23.)$$

therefore:

$$\left[(1-r_1^2)^2 + \sigma_1^2\right] r_1^2 = \left[\frac{B}{\mu w a_o}\right]^2 \qquad (4.24.)$$

The response curves of the system are found from equation (4.24.), which specifies the value of B for an entrained system. This equation can be implemented on the computer to determine the response curves for the harmonic solution.

The Stability of the Harmonic Solution.

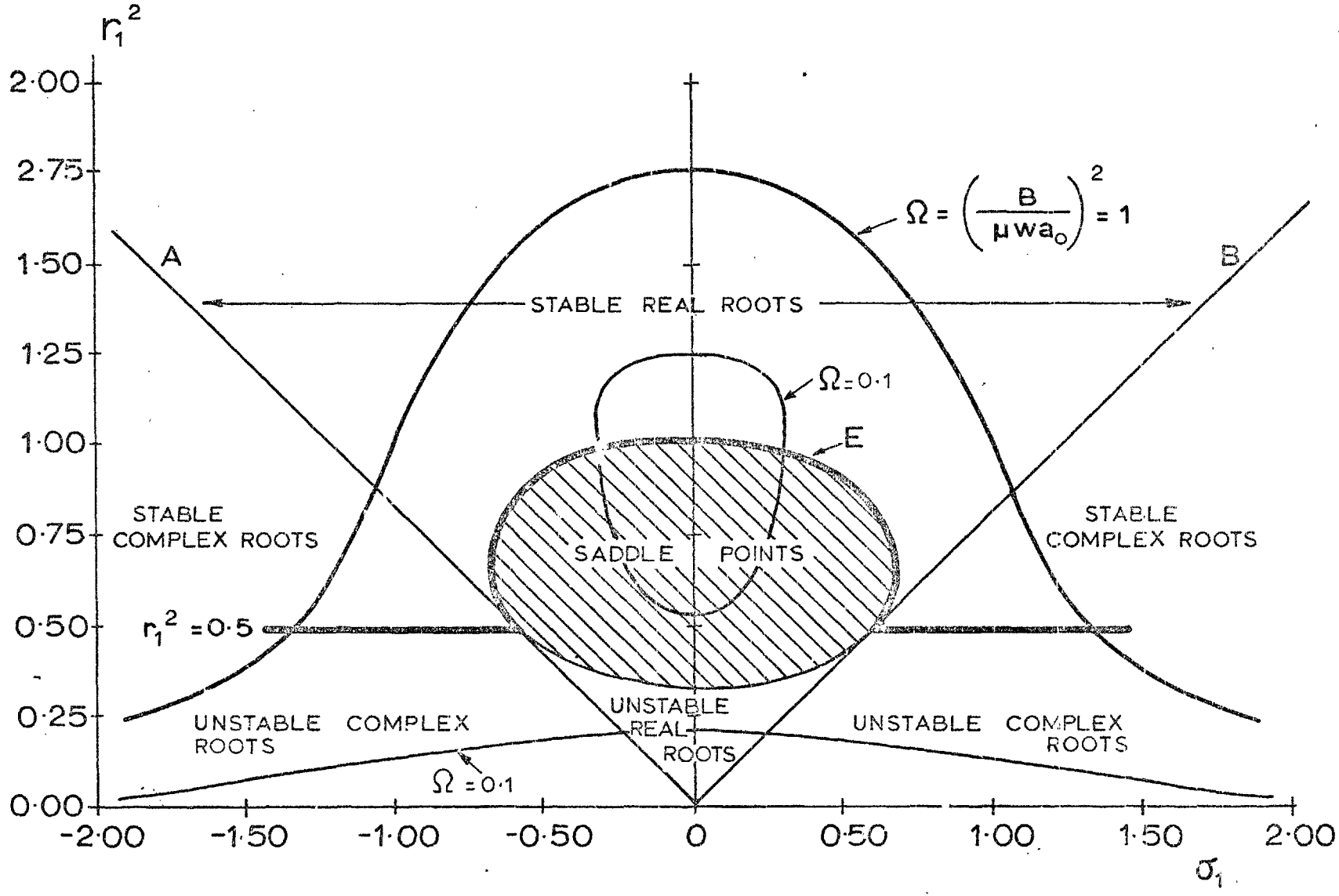
The stability of the harmonic solution was investigated by Andronov and Witt (1930). These authors replaced the x_1 and y_1 terms of equations (4.16.) and (4.17.) by $x_o + \xi$ and $y_o + \zeta$, where ξ and ζ are small variations. This procedure enabled them to obtain the variational equations for the system which lead to the following characteristic equation:

$$s^2 - 2(1-2r_1^2)s + (1-r_1^2)(1-3r_1^2) + \sigma_1^2 = 0 \qquad (4.26.)$$

where:

$$s = \sigma + jw$$

Fig.4·8


r_1^2
2·00
2·75
1·50
1·25
1·00
0·75
0·50
0·25
0·00
-2·00
-1·50
-1·00
-0·50
0
0·50
1·00
1·50
2·00
σ_1
$\Omega = \left(\frac{B}{\mu w a_o}\right)^2 = 1$
A
B
STABLE REAL ROOTS
$\Omega = 0·1$
E
SADDLE POINTS
STABLE COMPLEX ROOTS
STABLE COMPLEX ROOTS
$r_1^2 = 0·5$
UNSTABLE COMPLEX ROOTS
UNSTABLE REAL ROOTS
UNSTABLE COMPLEX ROOTS
$\Omega = 0·1$

The stability of the system can be discussed clearly, by referring to figure 4.8:
in the 's' plane (figure 3.1), the condition for stability is that σ , the real part of the roots of equation (4.26.), should always be negative. Therefore, rewriting equation (4.26.) in the form:

$$as^2 + bs + c = 0 \qquad (4.27.)$$

leads to the solution:

$$s = \frac{-b \pm \left[b^2 - 4ac\right]^{\frac{1}{2}}}{2a} \qquad (4.28.)$$

The condition for a negative real part of the root is:

$$b > \left[b^2 - 4ac\right]^{0.5}$$

This can be seen to be true if the alternative types of root are examined with reference to equation (4.28.).

1. If the root is complex, the real part will automatically be negative.
2. If $\left[b^2 - 4ac\right]^{0.5}$ is real, the negative solution of the square root will produce a negative real part; but for the positive solution of the square root:

$$b > \left[b^2 - 4ac\right]^{0.5} \qquad (4.29.)$$

is the condition for a stable root.

Therefore squaring both sides, equation (4.29.) becomes:

$$b^2 > b^2 - 4ac \text{ or } 4ac > 0 \qquad (4.30.)$$

which is the condition for a stable solution for the variational problem.

Applying this criterion to equation (4.26.):

$$(1-r_1^2)(1-3r_1^2) + \sigma_1^2 > 0 \qquad (4.31.) \text{ for stability}$$

$$(1-r_1^2)(1-3r_1^2) + \sigma_1^2 < 0 \qquad (4.32.) \text{for instability}$$

Hence, there is a region which is defined by the equation (4.33.), and is the boundary between stability and instability.

$$(1-r_1^2)(1-3r_1^2) + \sigma_1^2 = 0 \qquad (4.33.)$$

Equation (4.33.) is that of an ellipse(E), the interior of which consists of saddle points, i.e. not stable or unstable.

Returning to equation (4.28.), the term which determines whether the root will be real or complex is:

$$b^2 - 4ac$$

If $b^2 > 4ac$ there will be a real root; however, if $b^2 < 4ac$ there will be a complex root.

The boundary between real and complex roots occurs when $b^2 = 4ac$. For the system under investigation, this is when:

$$(1 - 2r_1^2)^2 = (1 - r_1^2)(1 - 3r_1^2) + \sigma_1^2$$

therefore: $r_1^4 - \sigma_1^2 = 0$ (4.34.)

or $(r_1^2 - \sigma_1)(r_1^2 + \sigma_1) = 0$

The real roots are separated from the complex ones by the straight lines:

$r_1^2 - \sigma_1 = 0$ (4.35.) and $r_1^2 + \sigma_1 = 0$ (4.36.)

which referring to figure 4.8, are the lines OA and OB. By co-ordinate geometry it is readily proved that these lines are tangential to the ellipse E when $r_1^2 = 0.5$.

The region of system stability between the lines OA and OB, and the σ_1 axis, requires definition. Over this region the roots of the characteristic equation are complex; hence, referring to equation (4.28.), to have a negative real part of the root, 'b' must be positive, that is:

$b < 0$ for the system to be stable.

and $b > 0$ for the system to be unstable.

The boundary between stability and in-stability is therefore when b=0. In terms of the system under investigation (from equation (4.26.).

$$1 - 2r_1^2 = 0 \qquad (4.37.)$$

The line therefore, which forms the boundary between stability and in-stability, in the zone of the complex roots of the characteristic equation, is the ordinate $r_1^2 = 0.5$.

Figure 4.8 provides a straightforward method of defining the system performance, for variations in the forcing function magnitude, and also detuning.

The parameter which represents the magnitude of the external stimulus, in figure 4.8, is Ω. The variable σ_1, defines the degree of detuning of the external stimulus from the natural frequency of

oscillation of the system. For small values of σ_1, and for a magnitude of the external stimulus of $\Omega = 0.1$ say, there is a region ($\sigma_1 = \pm 0.3$), where the solution of the characteristic equation gives a stable root, which ensures harmonic entrainment. However, as the degree of detuning increases to beyond $\sigma_1 = \pm 0.3$, for $\Omega = 0.1$, the solution of equation (4.26.) consists solely of unstable roots and hence entrainment is lost. For larger magnitudes of external stimuli, $\Omega = 1.0$ for example, the amount that the frequency of the external stimulus can differ from the natural frequency of the system is significantly greater than $\sigma_1 = 0.3$ before entrainment is lost. It is therefore apparent that a non-linear oscillatory system is entrained by an external stimulus, provided that the degree of detuning and the magnitude of the stimulus, are of suitable proportion to enable the solution of the characteristic equation to have at least one stable root.

4.6 THE PHYSIOLOGICAL REALIZATION OF THE PERIPHERAL THERMAL SYSTEM.

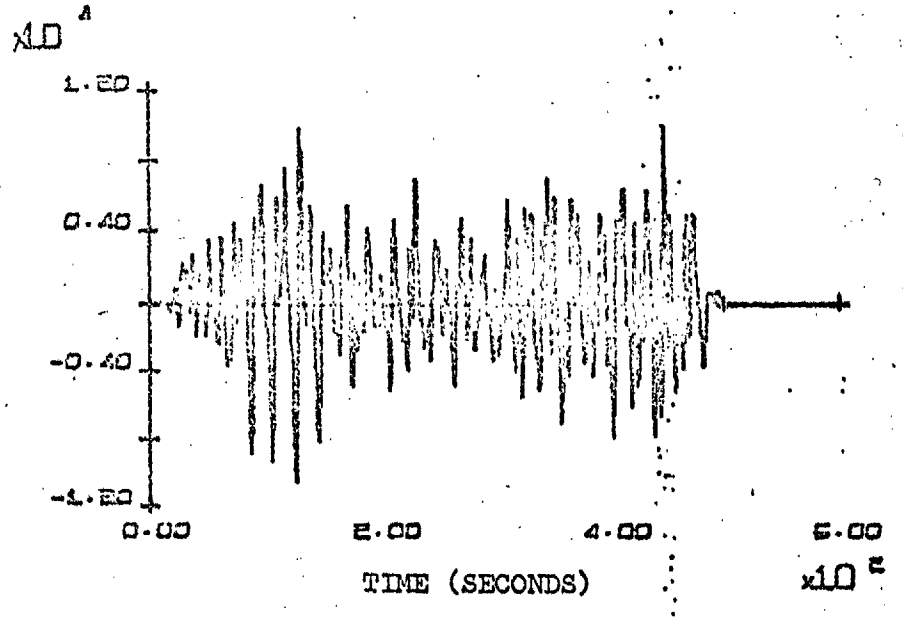
In the preceding sections, the peripheral thermo-regulatory system has been shown to be of the non-linear oscillatory type. Further, this nonlinear operation, termed a relaxation oscillation, could be defined by the generalized van der Pol equation (4.1.), with suitable parameter values, at least as far as the entrained case was concerned. There were also strong indications that the spontaneous activity of the physiological system, where the power spectrum showed a large number of frequency components (figure 3.4c), resulted from the activity of a single van der Pol system whose oscillatory behaviour was subjected to some kind of external perturbation which caused its frequencyof oscillation to vary. The most appropriate method of extending the analysis of human thermal control, therefore appeared to be to obtain a physiological realization of the system.

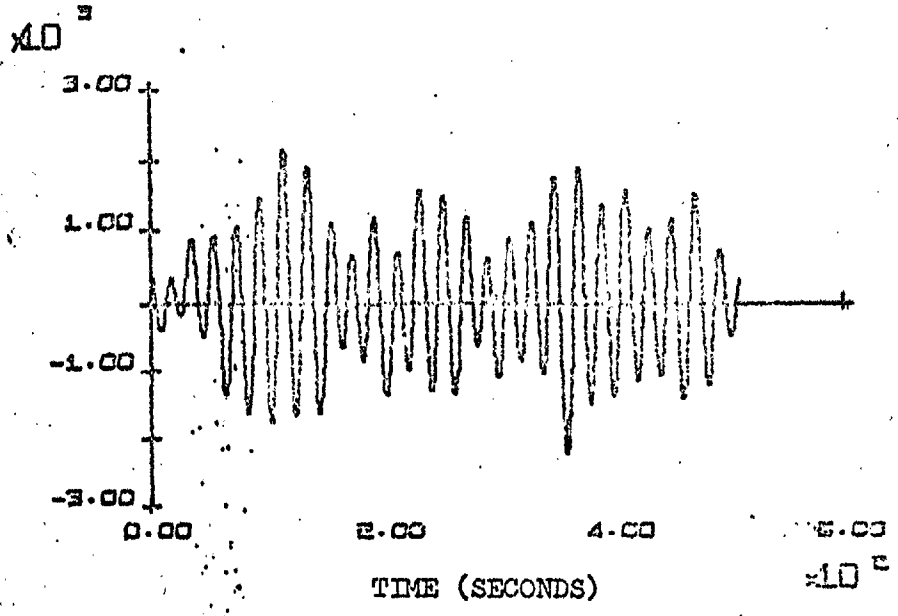
The following facts relating to the behaviour of the, so called, peripheral control system have been established: the afferent information seems to be obtained from the cutaneous receptors, while the efferent activity results in adjustments of the vasomotor tone applied to the vascular smooth muscle. In addition to these constituent elements the control system is also

thought to contain a discrete nonlinear element.

The dominant component in the experimental data during entrainment by a twenty second periodicity stimulus, is determined in the time domain by low pass filtering (corner frequency 0.055 Hz), the original waveform. Figure 4.9 illustrates these waveforms: plot a, shows the original waveform; plot b, the low pass filtered version, and plot c, the first 150 seconds of plot b. The dominant twenty second component is clearly present. A comparison of the filtered experimental waveform and the output from the van der Pol system with ϵ=10.5 (figure 4.10), reveals that although the waveforms have the same periodicity, their waveshapes are radically different. The question one therefore asks is: as the evidence already presented gives a clear indication that the activity of the peripheral system is closely matched by the appropriate van der Pol equation, then why are the two waveforms (figures 4.10a and 4.10b), so radically different?

The answer to this question would seem to be that in the experimental data the output from the thermoregulatory system reflected in the digit blood flow waveform, has been filtered by the characteristic of the vascular smooth muscle. Therefore, to reconstitute the vasomotor activity of the peripheral system at the





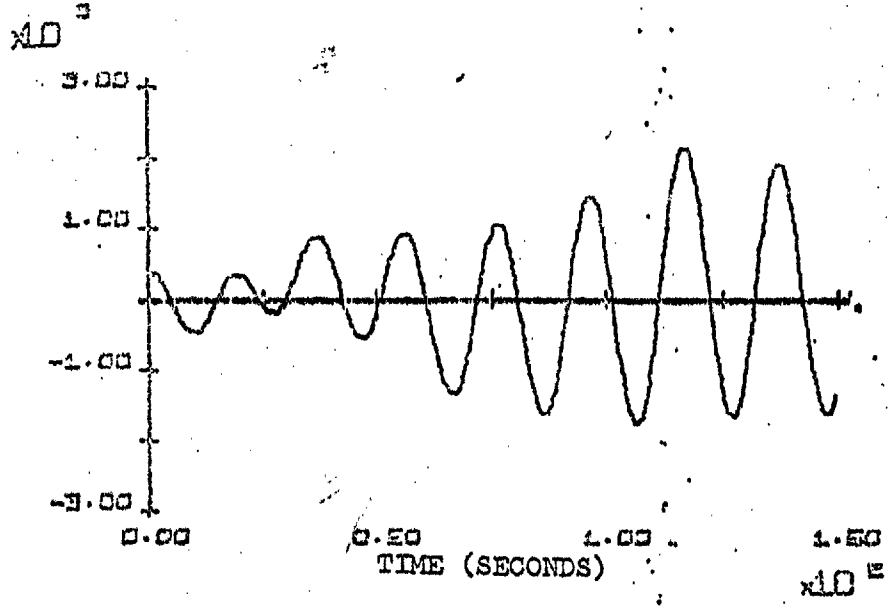
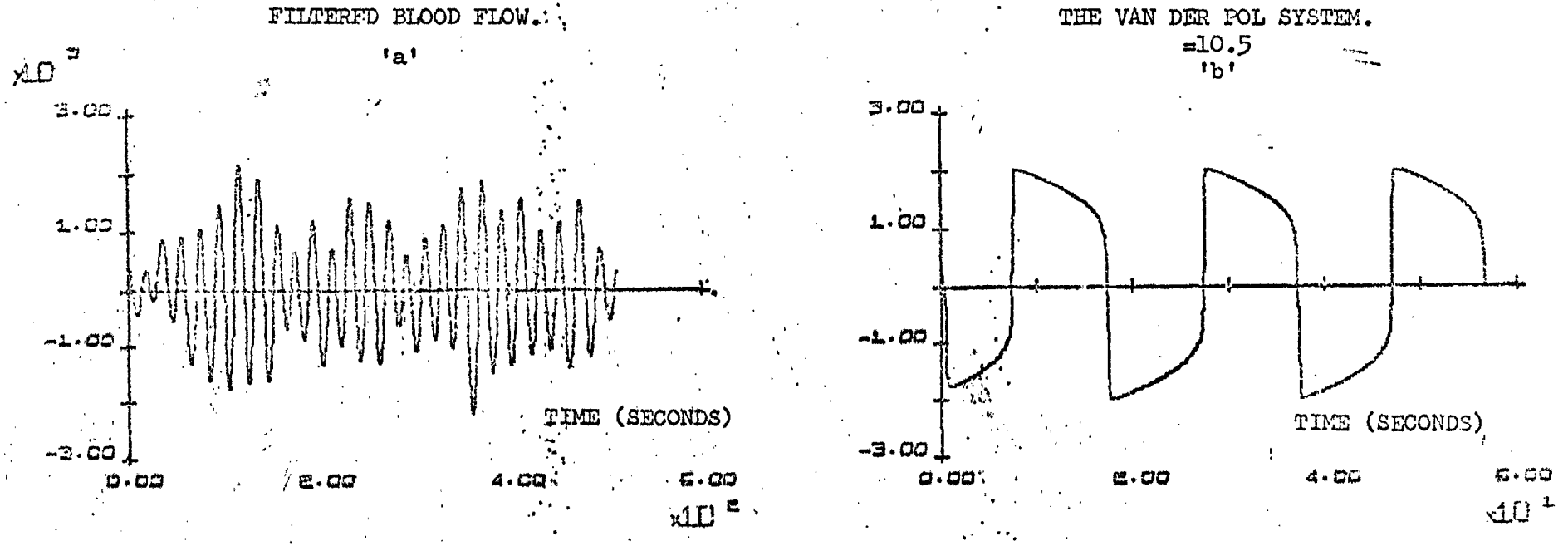


FIGURE 4.9

TIME DOMAIN PLOTS OF THE DIGIT BLOOD FLOW DURING ENTRAINMENT.

FIGURE 4.10


FILTERED BLOOD FLOW.
'a'
x10 -2
3.00
1.00
-1.00
-3.00
0.00
2.00
4.00
6.00
TIME (SECONDS)
x10 2
THE VAN DER POL SYSTEM.
=10.5
'b'
3.00
1.00
-1.00
-3.00
0.00
2.00
4.00
6.00
TIME (SECONDS)
x10 1

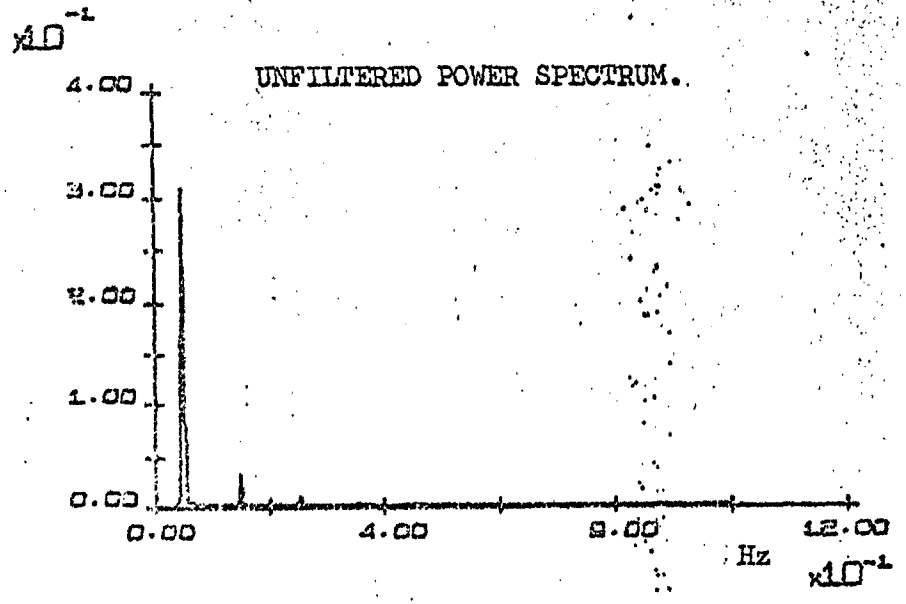
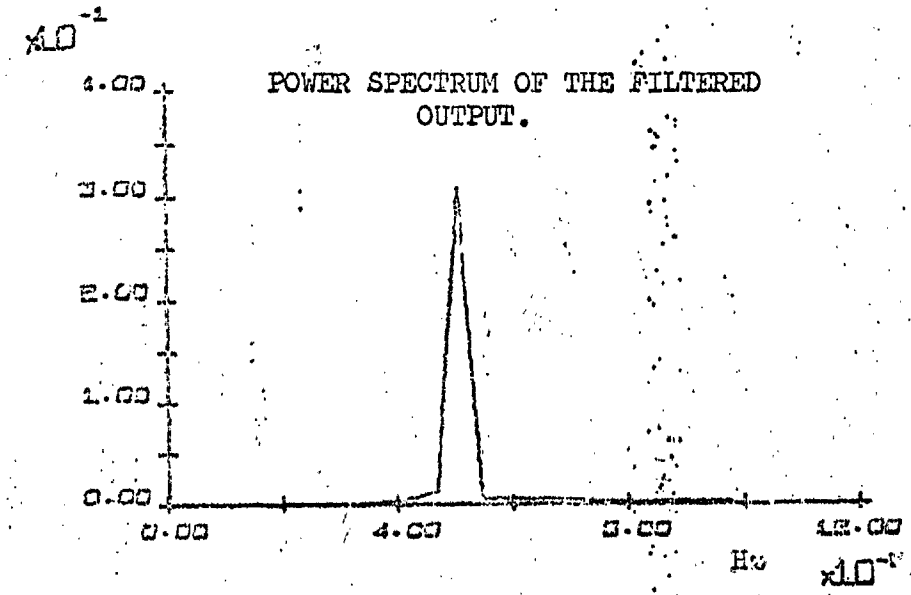
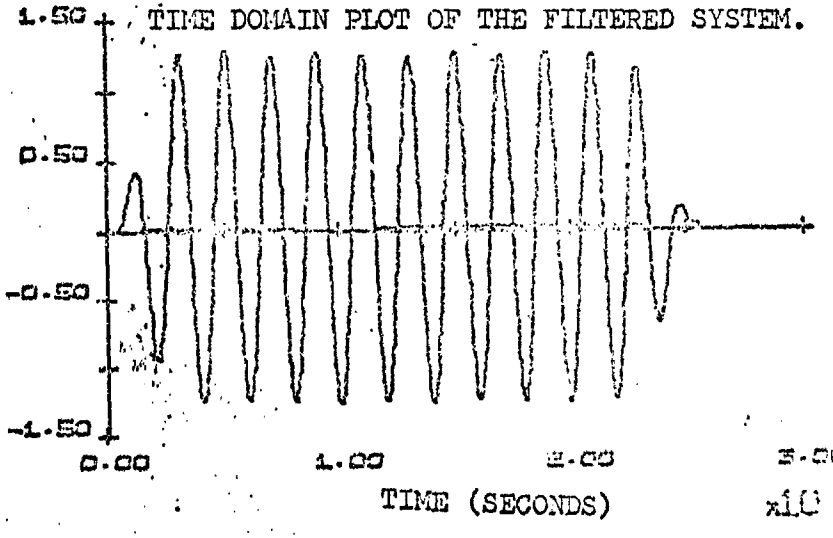


FIGURE 4.11

THE OUTPUT OF THE VAN DER POL SYSTEM.





smooth muscle, the high frequency components would have to be replaced. Unfortunately, the low pass filter action of the vascular smooth muscle results in irretrievable loss of the high frequency components, so that the pre-muscular waveform cannot be reconstructed. The alternative is to low pass filter the van der Pol data and re-compare the resultant waveform with that of figure 4.9b. The time domain representation of the filtered van der Pol system is illustrated in figure 4.11. Clearly, there is a high degree of similarity between this waveform and that of the experimental data. The van der Pol waveform would therefore seem suitable to describe the activity of the thermal system prior to the smooth muscle. As this waveform is highly nonlinear, one would expect the discrete nonlinear element in the physiological system to be situated between the comparator and the smooth muscle. Figure 4.12 illustrates the resultant basic block diagram of the peripheral thermal system. The question to be considered is, exactly what type of nonlinear element is present within the physiological system?

Siefert and Steeg (1960), together with Pipes (1958), discuss van der Pol systems of the relaxation type i.e. $\epsilon >> 1$, in some detail. These authors associate the nonlinearity in such systems with the class known as hard nonlinearities. A study of the shape of the van der Pol waveform, and consideration of work on other physiological systems e.g. Scher and Young (1963), and Hyndman et. al (1971),

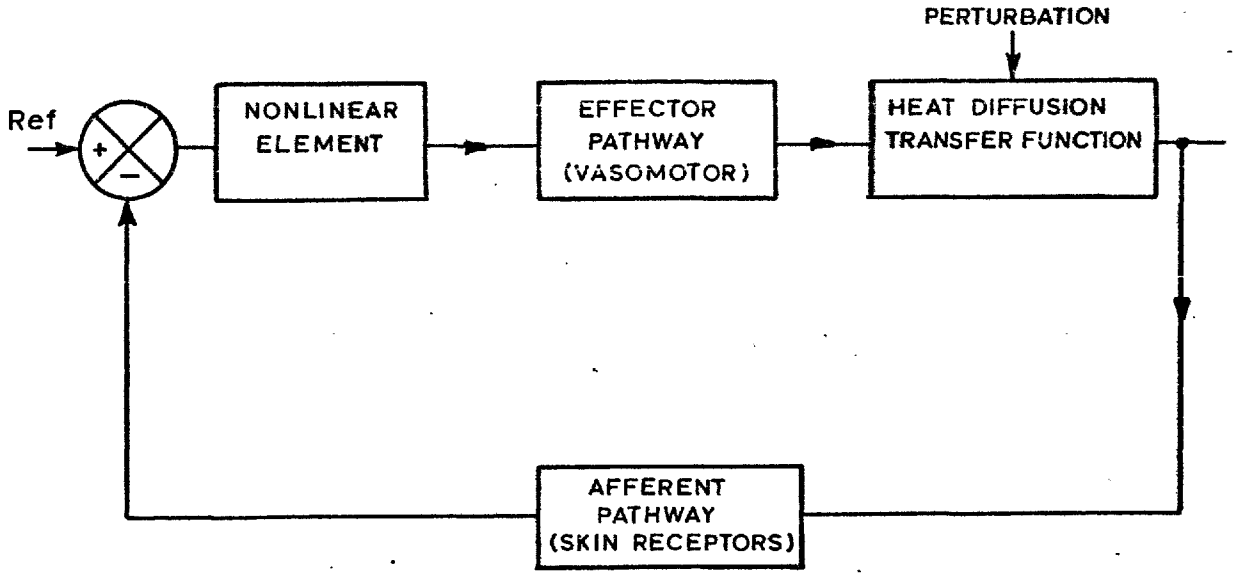


Fig. 4-12 The basic block diagram of the peripheral thermal control system.

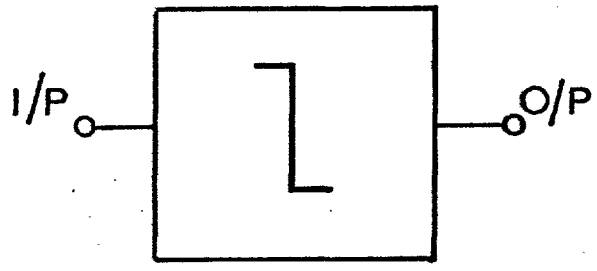


Fig. 4-13 The characteristic of the Bang-Bang nonlinear element.

led to the conclusion that the nonlinear element was of the bang-bang type (figure 4.13).

Considering first the van der Pol waveform, it is apparent from figure 4.1 that for the type of periodicities we are considering, this waveform closely resembles a squarewave; a bang-bang element would likewise result in a squarewave output.

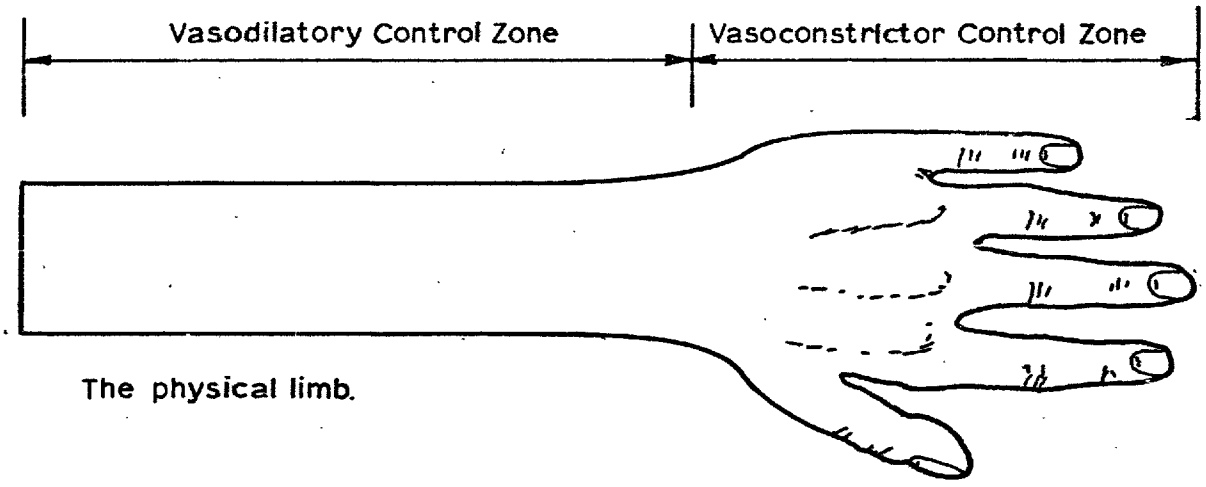
The suggestion that the nonlinearity is of the bang-bang type, is utilized in the modelling study reported below. Hyndman (1970), investigated the nature and origin of respiratory and spontaneous effects in both blood pressure and heart rate in man and the interaction between these effects. Consideration of published electroneurographic recordings led this author to the conclusion that the afferent-efferent interface in the brain stem associated with blood pressure control may be the physiological site of an on-off control element. Hyndman also suggests that the high degree of accuracy observed in other biological control systems might result from similar types of on-off control. This statement would seem to be confirmed by the present study.

CHAPTER 5

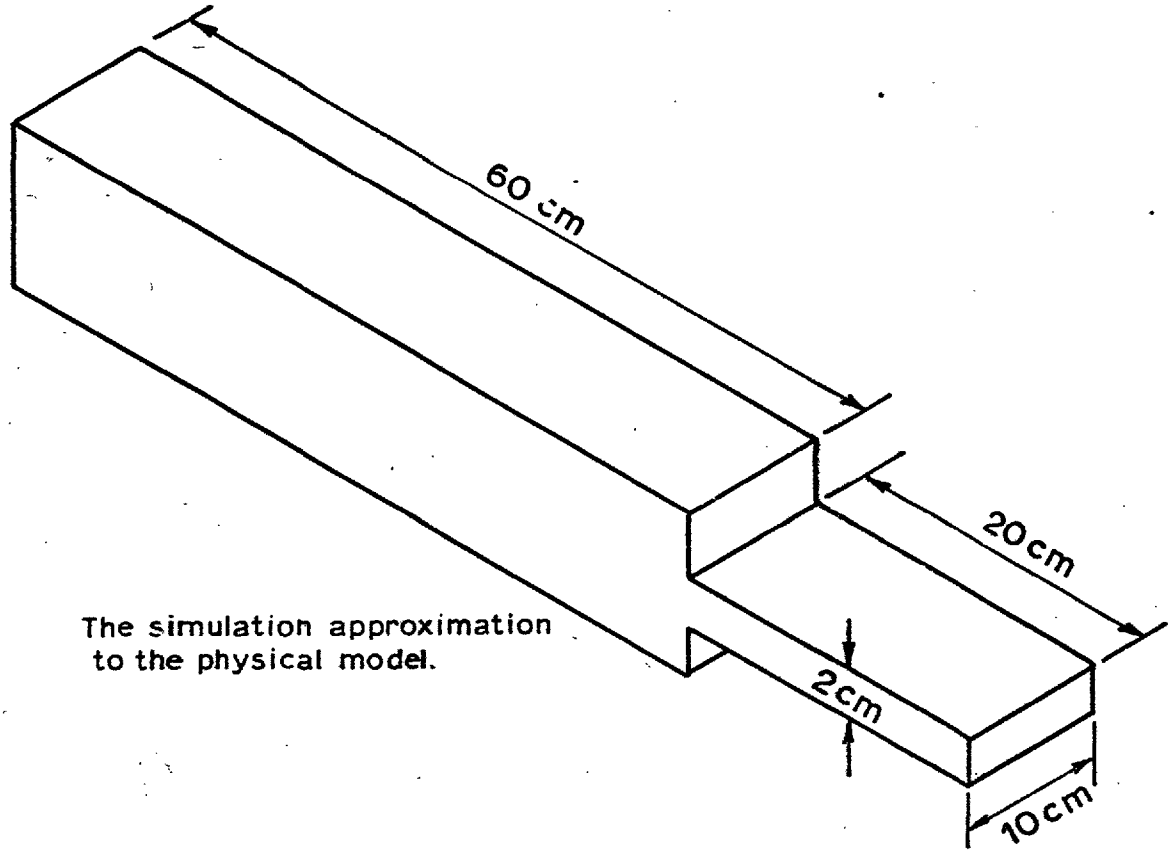
THE DIGITAL COMPUTER MODEL OF THE UNCONTROLLED PERIPHERAL THERMAL SYSTEM.

5.1 INTRODUCTION.

The theoretical analysis of the thermo-regulatory system can only be substantiated or disproved by implementing a computer model to describe the physical system. In recent years there have been a number of attempts to describe the human thermo-regulatory system in this way. The majority of these studies have been based on a model where the human body is represented by a single cylinder. This cylinder consists of a uniform mass of bone and tissue, which is covered by a layer of fat and skin. The basic elements of the method are described fully by Crosbie et. al (1963). Although satisfactory as a first approximation, this type of model is totally inadequate if one tries to simulate experiments where only one hand is stimulated. To overcome this difficulty, it is necessary to use a distributed model. For the purposes of the present investigation the computer simulation aims to describe the thermal state of the upper limb. Figure 5.1 shows the limb together with the simulation approximation.



The physical limb.



The simulation approximation to the physical model.

Fig. 5·1

Blood flow in the arm is essentially of two types: first, under conditions of high environmental temperature, the main blood flow in the arm is through the peripheral vessels which are situated at an almost cutaneous level. The volume of blood in the arm is a function of the size of the vessels. Flow in the deep blood vessels produces counter-current heat exchange because of the proximity of the arteries and veins. This mechanism was described as being effective in human subjects by Bazett in 1948.

5.2 A MATHEMATICAL DESCRIPTION OF THE THERMAL STATE OF THE ARM.

The study of heat flow in the arm is essentially a three dimensional problem. Referring to figure 5.2, the x and y components of heat flow are treated as due to conduction, while the z component is considered as a function of heat convection by blood flow.

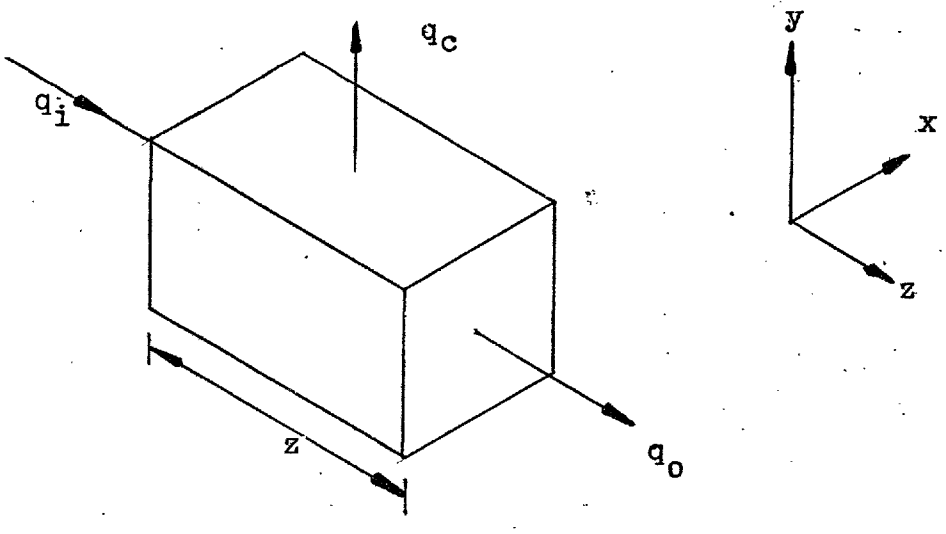


FIGURE 5.2

5.3 THE APPLICATION OF THE CONVECTION EQUATION.

Heat balance in a particular blood vessel can be determined by writing the heat flow equations for a small section (figure 5.2). Over a length Δz, the thermal balance equation can be written as:

$$\text{(heat input) } q_i = \text{(heat output) } q_o + \text{(peripheral heat loss) } q_c \qquad (5.1.)$$

Now from the input to the section:

$$q_i = G\ A\ C_p\ U_z \qquad (5.2.)$$

where:

G - the mass transfer coefficient

A - area

C_p - specific heat

U_z - blood temperature

and for the output:

$$q_o = G\ A\ C_p\ U_{z\ +\ \Delta z} \qquad (5.3.)$$

$U_{z\ +\ \Delta z}$ being the blood temperature at the output of the section.

For the peripheral heat loss:

$$q_c = (\ U_z - U_w\ )\ \alpha\ 2\ (\ x + y)\ \Delta z \qquad (5.4.)$$

where:

U_w - the temperature of the material surrounding the vessel.

α - the heat transfer coefficient.

x & y - the length of the sides of the vessel section.

Substituting equations (5.2.), (5.3.) and (5.4.) in equation (5.1.)

$$G\ A\ C_p\ U_z = G\ A\ C_p\ U_{z+\Delta z} + 2\ (\ U_z - U_w\ )(\ x + y\ )\ \Delta z$$

therefore:

$$\frac{G\ A\ C_p\ (\ U_{z+\Delta z} - U_z)}{\Delta z} = -\ 2\ (\ x + y\ )(\ U_z - U_w\ )$$

converting the equation to its differential form:

$$G\ A\ C_p\ \frac{dU}{dz} = -\ S_A\ (\ U - U_w) \qquad (5.5.)$$

where:

$$S_A = 2(\ x + y\ )$$

Equation (5.5.) describes the blood temperature along the z axis.

5.4 THE APPLICATION OF THE HEAT DIFFUSION EQUATION.

As we have observed, the heat flow in the x,y plane is by conduction. The conduction of heat in the plane is described by the two dimensional parabolic diffusion equation:

$$\frac{\rho C_p}{K}\frac{\partial U}{\partial t} = \frac{\partial^2 U}{\partial x^2} + \frac{\partial^2 U}{\partial y^2} \qquad (5.6.)$$

where: ρ - density of the medium

C_p - the specific heat

K - thermal conductivity

The solution of a partial differential equation of this type is by no means straightforward, it involves the use of highly specialized numerical methods.

The Numerical Solution of the Diffusion Equation.

The solution of equation (5.6.) involves the use of finite difference methods. In these methods a grid is layed over the area for which a solution is required (figure 5.3). Finite difference approximations to the derivatives of equation (5.6.) can be obtained from Taylors series. If the function u and its derivatives are single valued, finite and continuous functions of x, then the Taylor series for such functions can be defined as

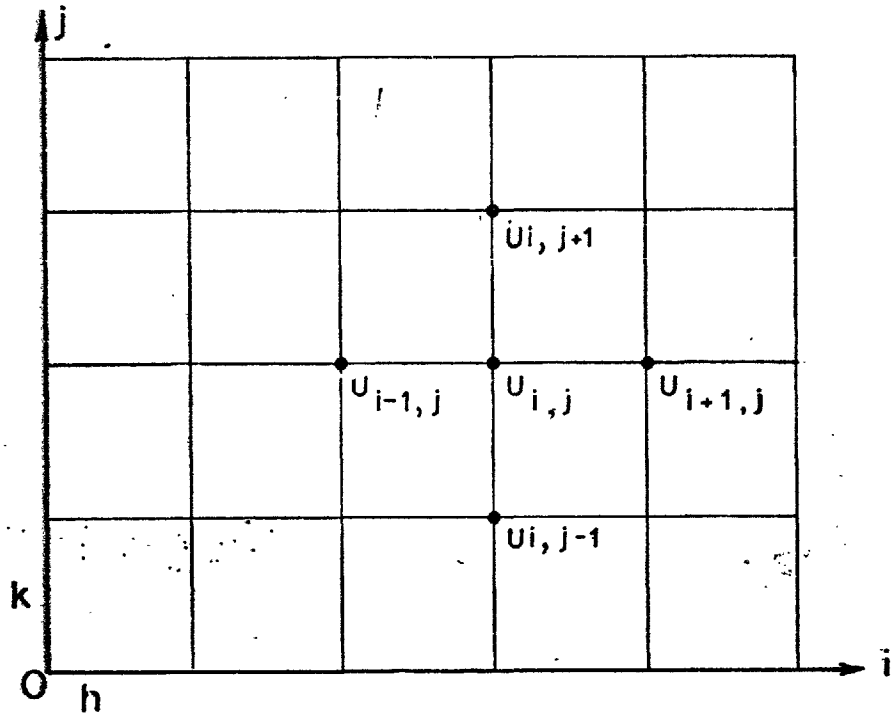


Fig. 5·3

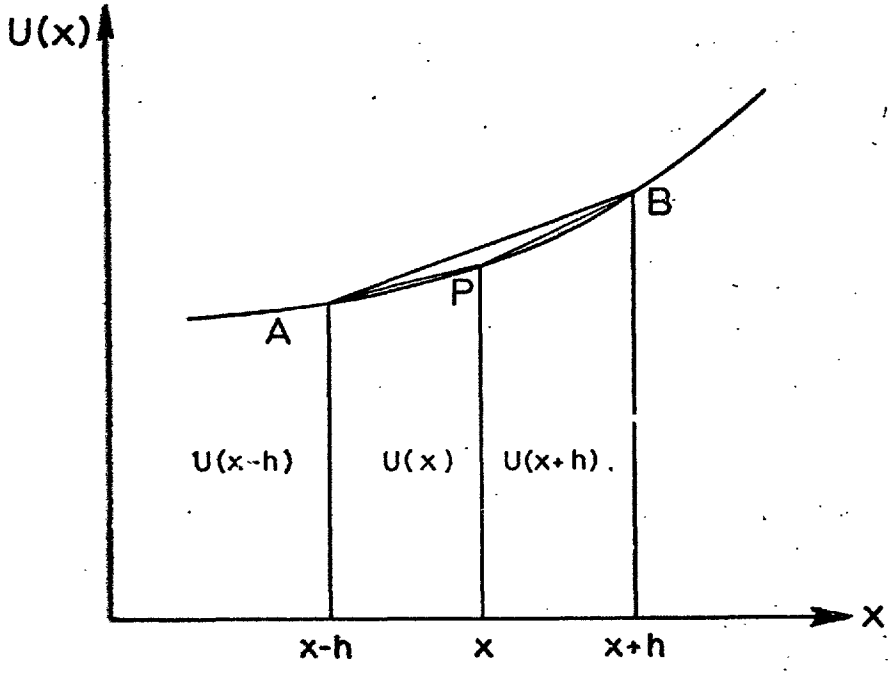


Fig.5·4

$$u(x+h) = u(x) + hu'(x) + \tfrac{1}{2} h^2 u''(x) \qquad (5.7.)$$

and

$$u(x-h) = u(x) - hu'(x) + \tfrac{1}{2} h^2 u''(x) \qquad (5.8.)$$

now adding equations (5.7.) & (5.8.)

$$u(x+h) + u(x-h) = 2u(x) + h^2 u''(x)$$

hence $$u''(x) = 1/h^2 \,(u(x+h) - 2u(x) + u(x-h)) \qquad (5.9.)$$

and subtracting equations (5.7.) & (5.8.)

$$u(x+h) - u(x-h) = 2hu'(x)$$

therefore

$$u'(x) = 1/2h \,(u(x+h) - u(x-h)) \qquad (5.10.)$$

Equation (5.10.) represents the slope of the chord AB and is known as the central difference approximation.

If we approximate the slope at P by the chord PB

$$u'(x) = 1/h \,(u(x+h) - u(x)) \qquad (5.11.)$$

and for the chord AP

$$u'(x) = 1/h \,(u(x) - u(x-h)) \qquad (5.12.)$$

Equations (5.11.) & (5.12.) are known as the forward and backward difference approximations.

If the partial derivative $\frac{\partial^2 u}{\partial x^2}$ has the cartesian co-ordinates (i,j);

then the function can be expressed numerically by equation (5.9.) namely:

$$\frac{\partial^2 u}{\partial x^2} = 1/h^2 (u_{i+1,j} - 2u_{i,j} + u_{i-1,j}) \qquad (5.13.)$$

Where u is the temperature of a point in the x,y plane.

The Crank-Nicolson Algorithm.

If the numerical approximation of equation (5.13.) were used to represent the terms of equation (5.6.) the computation would be exceedingly slow. To overcome this problem, a number of refined numerical methods have been developed. Crank and Nicolson (1947), developed a method for solving the diffusion equation in one space dimension; this has been extended to deal with the solution in two space dimensions. The method involves replacing the second order derivatives of equation (5.6.) by the mean of their finite difference representations on the N and N+1 time rows. Hence for the two dimensional equation

$$\frac{\rho C_p}{K}\frac{\partial U}{\partial t} = \frac{\partial^2 U}{\partial x^2} + \frac{\partial^2 U}{\partial y^2} \qquad (5.6.)$$

the Crank-Nicolson approximation is of the form:

$$A\left[\frac{u_{i,j,n+1} - u_{i,j,n}}{\delta T}\right] = \tfrac{1}{2}\left[\left[\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\right]_{i,j,n} + \left[\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\right]_{i,j,n+1}\right] \qquad (5.14)$$

where $A = \rho C_p / K$

Written in its difference form, equation (5.14.) becomes:

$$\frac{U(I,J,N+1)- U(I,J,N)}{\delta t} =$$

$$(U(I+1,J,N+1) -2U(I,J,N+1)+U(I-1,J,N+1) +U(I+1,J,N) -2U(I,J,N) +U(I-1,J,N))/2Ah^2 + (U(I,J+1,N+1) -2U(I,J,N+1) + U(I,J-1,N+1) + U(I,J+1,N) -2U(I,J,N) + U(I,J-1,N))/2Ak^2 \qquad (5.15.)$$

Here

h = step length in the x direction

k = step length in the y direction

δt = the time step.

Solution of the Finite Difference Equations by the Gauss-Seidel Iterative Method.

Unfortunately, unlike the one dimensional case, the difference equations for two dimensions have to be solved by means of an iterative method. The particular procedure employed here is the Gauss Seidel method. Letting the terms $\delta t/Ah^2$ and $\delta t/Ak^2$ in equation (5.15.), equal r, then equation (5.15.) becomes:

$$U(I,J,N+1) = U(I,J,N) + \tfrac{1}{2}r \left[U(I+1,J,N+1) -4U(I,J,N+1)+U(I-1,J,N+1) +U(I+1,J,N) -4U(I,J,N) + U(I-1,J,N) + U(I,J+1,N+1) + U(I,J-1,N+1) +U(I,J+1,N) +U(I,J-1,N) \right] \qquad (5.16.)$$

Now collecting all the terms of the N^{th} time row.

$$B= U(I,J,N) + \tfrac{1}{2}r\,(U(I+1,J,N) - 4U(I,J,N) + U(I-1,J,N) + U(I,J+1,N) + U(I,J-1,N)) \qquad (5.17.)$$

Therefore substituting equation (5.17.) in (5.16.)

$$U(I,J,N+1)= \tfrac{1}{2}r\,(U(I+1,J,N+1) - 4U(I,J,N+1) + U(I-1,J,N+1) + U(I,J+1,N+1) + U(I,J-1,N+1)) + B \qquad (5.18.)$$

The finite difference solution of the equation is obtained by using one core location for each point on the thermal grid. The solution converges by overwriting the value of U at each iteration, for each point on the grid. If the first approximation to $U(I,J,N+1)$ is denoted by $U(I,J,N+1)^1$, then the $m+1^{th}$ approximation is given by:

$$U(I,J,N+1)^{(m+1)} = \tfrac{1}{2}r(U(I+1,J,N+1)^{(m)} - 4U(I,J,N+1)^{(m+1)} + U(I-1,J,N+1)^{(} + U(I,J+1,N+1)^{(m)} + U(I,J-1,N+1)^{(m)}) + B$$

this gives

$$U(I,J,N+1)^{m+1} = \frac{r}{2(1+2r)}\,(U(I+1,J,N+1)^{(m)} + U(I-1,J,N+1)^{(m)} + U(I,J+1,N+1)^{(m)} + U(I,J-1,N+1)^{(m)} + \frac{B}{(1+2r)} \qquad (5.19$$

This iteration formula converges for all values of r. However, equation (5.19.) can still be improved by using the $(m+1)^{th}$ values where possible.

This gives:

$$U(I,J,N+1)^{(m+1)} = \frac{r}{2(1+2r)}\left(U(I+1,J,N+1)^{(m)} + U(I-1,J,N+1)^{(m+1)}\right.$$

$$\left. + U(I,J+1,N+1)^{(m)} + U(I,J-1,N+1)^{(m+1)}\right) + \frac{B}{(1+2r)} \qquad (5.20.)$$

Equation (5.20.) presents the Crank-Nicolson algorithm in the form best suited to computer solution.

5.5 INTRODUCTION TO THE COMPUTER PROGRAM.

The human upper limb, as far as temperature is concerned, has to be divided into two sections. The neural control of the hand results from vasoconstrictor tone, while the nervous control of the arm is of a vasodilatory nature. There is therefore, a division of the computer model into a number of sections. These sections comprise two main subroutines called Arm and Hand, together with a number of smaller subroutines and a main housekeeping program.

5.6 THE INITIALIZATION PROCEDURE FOR THE FIRST TIME STEP: SUBROUTINE INIT.

The computer model operates in terms of discrete time steps; therefore before calculation can begin, a number of program parameters have to be initialized. The primary step in subroutine Init is to define the temperature of all the tissue within the arm (model). The blood within the arteries and veins of the arm, has been found by physiological experimentation to be of a somewhat different temperature to the surrounding tissue. The temperature of this blood is consequently set to appropriate temperature values.

The latter part of the subroutine is only called once during a particular computer run of the model as any initialization procedures required during subsequent time steps are performed by other subroutines.

5.7 INTERFACING PROCEDURES AT THE AIR--SKIN INTERFACE: SUBROUTINE ENVIR.

The boundary conditions at the skin-air boundary are of cardinal concern when dealing with body heat loss. There are four channels by which heat can enter or leave the body, namely: conduction, convection, radiation and evaporation. Newtons Law of Cooling gives a good approximation to the total heat loss. While the law is useful as a first approximation, for the purposes of thermo-regulation simulation of the individual sources of heat loss have to be considered.

Lewis et. al(1969), have shown that under normal circumstances, the temperature of the skin in the comfort zone is about 33°C. Studies of the layer of air next to the skin, have revealed the presence of a micro-environment extending to a distance of about 2cm above the surface. The effect of this micro-environment is to produce an air temperature at the surface of the epidermis, which is significantly different from the environmental temperature. In the human body, the heat flow at the skin is normal to the surface. The rate at which heat is transferred to, or from, an external surface at temperature U, and the surrounding medium the temperature of which is V, is proportional to (U-V). Alternatively, the fundamental assumption of heat conduction theory is that the rate of heat flow across

any surface is equal to $- K \frac{dU}{dx}$. Hence the equation which describes the boundary condition is:

$$- K \frac{dU}{dx} = H (U-V) \qquad (5.21.)$$

where:

K - thermal conductivity of the medium.

H - the coefficient of surface heat transfer.

U - the average skin temperature.

and $A = {}^{H}/_{K}$

rewriting equation (5.21.):

$$\frac{dU}{dx} + AU = AV \qquad (5.22.)$$

The solution of this first order differential equation is:

$$U = V (1 - e^{- Ax}) \qquad (5.23.)$$

The Coefficient of Radiant Heat Transfer.

From the basic definition of radiation, it follows that the flow of heat by radiation does not depend on the presence of an intervening medium, and hence heat can pass from a hot body to a cooler one through a vacuum. Radiation in the general sense, refers to energy transfer of this type throughout the electro-magnetic spectrum. Planck's law of black body radiation defines the amount of energy radiated

at a given wavelength, and is written mathematically as:

$$H_R = \frac{C_1 \lambda^{-5}}{\exp\left\{C_2/\lambda U\right\} - 1} \qquad (5.24.)$$

For large wavelengths Planck's Law can be simplified by neglecting the minus unity in the denominator.

Therefore:

$$H_R = C_1 \lambda^{-5} \exp\left(-C_2/\lambda U\right) \qquad (5.25.)$$

This equation is Wien's Law.

The Stefan-Boltzmann Law defines the total radiation emitted from a black body as being proportional to the fourth power of the absolute temperature. The law can be written in terms of the heat transfer between a hot object and its surroundings as:

$$H_R = S_o E_1 E_2 \left(U^4 - U_o^4\right) A \qquad (5.26.)$$

where:

S_o - the Stefan-Boltzmann constant.

U and U_o - the absolute temperatures of the hot object and its surroundings.

E_1 and E_2 - the emissivity of the hot object and its environment respectively.

A - the effective radiating area of the hot object.

If it is assumed that the ratio of the surface area of the walls, to the surface area of the subject is large, and the emissivity of human skin is unity; then the rate of heat loss per unit area is given by:

$$Q = 1.356 \times 10^{-12} \left(U_s^4 - U_w^4 \right) \qquad (5.27.)$$

where:

U_s - the average skin temperature.

U_w - temperature of the surrounding wall.

The heat transfer coefficient is defined as:

$$H_R = Q / \left(U_s - U_w \right) \qquad (5.28.)$$

expanding equation (5.27.) :

$$Q = 1.356 \times 10^{-12} \left(U_s+U_w\right)\left(U_s-U_w\right)\left(U_s^2+U_w^2\right) \qquad (5.29.)$$

substituting equation (5.29.) in equation (5.28.)

$$H_R = 1.356 \times 10^{-12}\left(U_s^3 + U_s^2U_w + U_sU_w^2 + U_w^3\right) \qquad (5.30.)$$

The Coefficient of Heat Transfer By Convection.

Convection is a term which refers to the exchange of heat between hot and cold objects by the physical transfer of the liquid or gas, with which the objects are in contact. This type of heat transfer depends on the existence of a fluid medium between the warm and

cold objects, and upon the actual streaming movement of warm molecules from the warm object to the cooler one. Convection falls into two categories; namely, forced convection and natural convection.

(a) Natural Convection.

Under conditions of natural convection, a layer of still air exists next to the skin. It is thought that it is the low conduction of the heat through this layer that forms the major part of the heat barrier. The thickness of the film depends on the skin temperature, viscosity, velocity of the gas, and also the gas density. The amount of heat carried through the film, depends on the thermal conductivity of the gas, the thickness of the film and the temperature gradient. If we consider a hot surface at temperature U_S in contact with a gas at temperature U_A, then the layer of gas next to the surface should not move, and succeeding layers will partake in convective streaming in an approximately laminar fashion; that is, velocity increasing with distance from the wall until maximum velocity is reached. One can consider this thin film of gas as possessing a private climate. If we assume that the heat loss by convection is equal to the heat conducted through the surface gas layer, then the heat loss by convection is given by:

$$H_c = \frac{K\,A\,(U_s - U_A)}{\delta x} \qquad (5.31)$$

where:

H_c - the convection loss.

K - the thermal conductivity of air.

A - the effective surface area.

U_s - the average skin temperature.

U_A - the average air temperature.

δx - the thickness of the surface layer.

(b) Forced Convection.

Forced convection is all convection in excess of the natural minimum due to heat leaving a warm surface. Hence, body movement would come under the heading of forced convection. Normally however, forced convection results from air or liquid streams generated by external forces. The relative velocity of the air stream with respect to the warm skin is the additional variable which has to be introduced when considering forced convection related to human thermo-regulation. The greater the velocity of the air stream and the greater the difference in temperature between the gas and the warm surface, the greater will be the convection. For human limbs the following equation may be used to calculate H_c:

$$\frac{H_c\, D}{k_f} = 0.53 \left[\left[\frac{D^3\ \rho_f^2\ \beta\, g\, \Delta U}{\mu_f^2}\right]\left[\frac{C_p\ \mu_f}{k_f}\right]\right]^{0.25} \qquad (5.32.$$

where:

D – the characteristic dimension of the object.

g – the acceleration due to gravity.

C_p – the specific heat of the fluid.

ρ – the fluid density.

β – the volumetric coefficient of expansion of the fluid.

viscosity.

f – a subscript indicating that the fluid properties are to be evaluated at the mean film temperature, the mean of the surface, and undisturbed air temperatures.

Equation (5.32.) is for the limb in the horizontal plane, McAdams (1942), also developed an equation for the case of the vertical plane:

$$\frac{H_c L}{k_f} = 0.59 \left[\left[\frac{L^3\ \rho_f^2\ g\, \beta\, \Delta U}{\mu_f^2}\right]\left[\frac{C_p\ \mu_f}{k_f}\right]\right]^{0.25} \qquad (5.33.$$

where:

L is the height of the surface.

McAdams indicates that the equation is only true for laminar flow. If the value of the right hand side of equation (5.33.) exceeds 10^9, then the flow becomes turbulent. Under these conditions one uses the equation:

$$\frac{H_c L}{k} = 0.12 \left[\left[\frac{L^3 \ \rho_f^2 \beta g \Delta U}{\mu_f^2} \right] \left[\frac{C_p \ \mu_f}{k_f} \right] \right]^{0.33} \qquad (5.34.$$

Lewis (1969), has shown that when the air temperature is greater than the skin temperature the air flows downwards. Conversely, when the air temperature is less than the skin temperature, the air flow due to natural convection is upwards. When the human body is subjected to forced convection, the motion of the air tends to be turbulent; in this case the heat transfer coefficient is calculated from equation (5.34.)

Brebner et al (1958 a and b) and Clifford et. al (1959), developed a more approximate equation for the heat transfer coefficient of convection namely:

$$H_c = 0.23 \ V^{0.62} \qquad (5.35.)$$

where:

V - is the velocity of the air.

The Heat Transfer Coefficient for Evaporation.

In 1917 Du Bois and Soderstrom established that about 25% of the metabolic heat is carried from the body by the water evaporated from the skin and lungs. Evaporation occurs at the air-skin interface, the liquid sweat becoming vapour at skin temperature and passes to the environment where it cools and expands. The whole evaporation process involves the passage of sweat from water at skin temperature to vapour at skin temperature, and finally its cooling and expansion to equilibrate it with the atmospheric conditions. The entire process takes place within a few millimetres of the skin surface; hence, under still air conditions the skin provides the heat for the entire transition. Brebner et. al (1958 a and b) established a relationship between the rate of water loss, and the ambient water vapour pressure:

$$w = 0.8 \left(p_s - p_a \right) \qquad (5.36.)$$

where:

p_s - the saturated water vapour pressure at skin temperature.

p_a - the ambient water vapour pressure.

w - the rate of water loss.

5.8 THE PROGRAM STRATEGY FOR THE ARM: SUBROUTINE ARM.

At first sight it would seem worthwhile to solve the heat diffusion equations for the arm in terms of polar co-ordinates. However, when one is dealing with the human arm there are boundary conditions for each vessel which renders a polar solution to be exceedingly difficult. To overcome this problem, the blood vessels within the arm are represented by rectangular vessels which have the same surface area. The arm is considered to consist of two types of tissue; a homogeneous area of bone and tissue, and a covering of fat and skin. Because of their individual thermal properties these two areas are dealt with separately within the program. The vascular structure of the model comprises eight vessels; namely, one artery and seven veins. The topography of these vessels is illustrated in figures 5.5 & 5.6.

The initial stage of subroutine arm is the solution of the diffusion equation for section A (figure 5.5). The diffusion equation is solved for 1024 points within the section which is defined by the array U. The program solves the equation for discrete time steps, the duration of which are in turn defined by parameters which are also contained within the

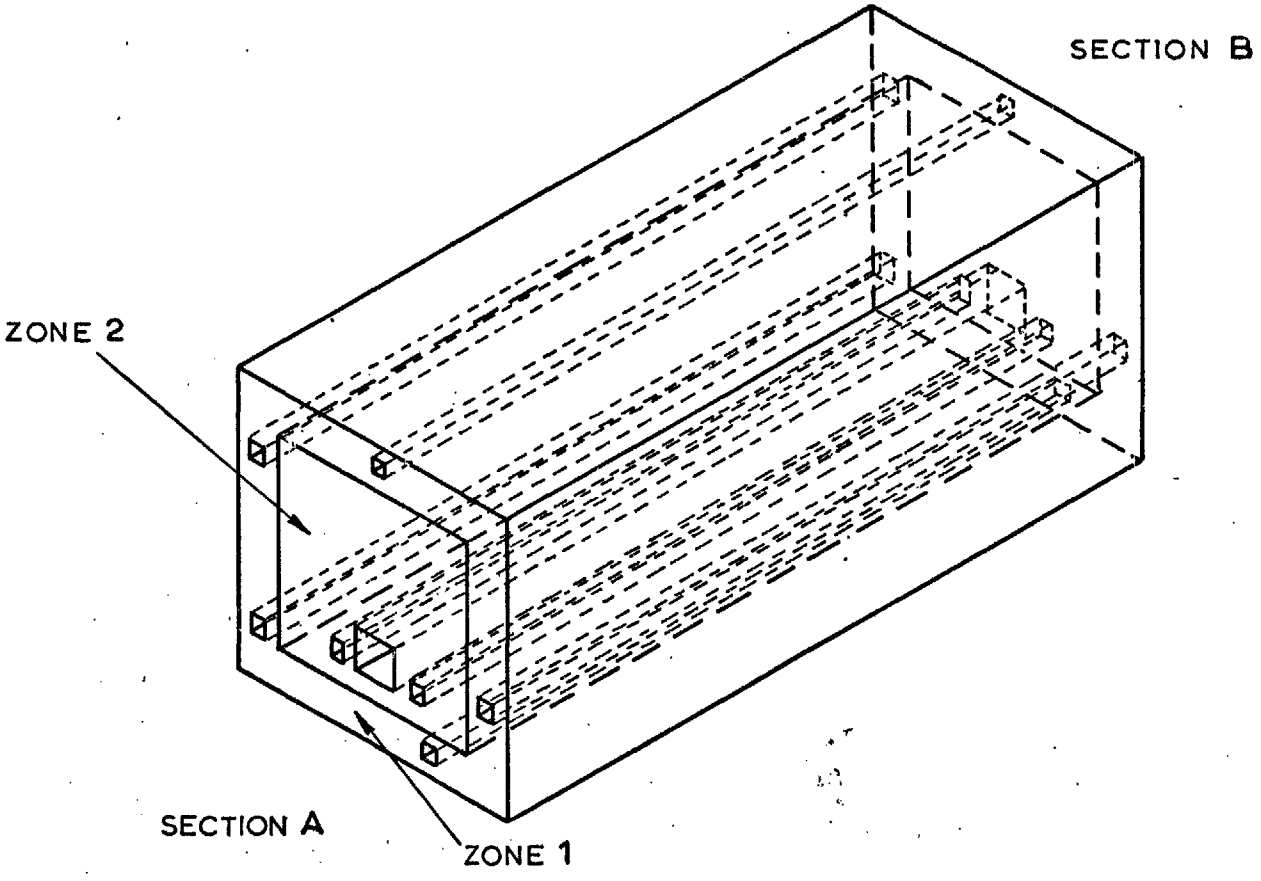


Figure 5-5

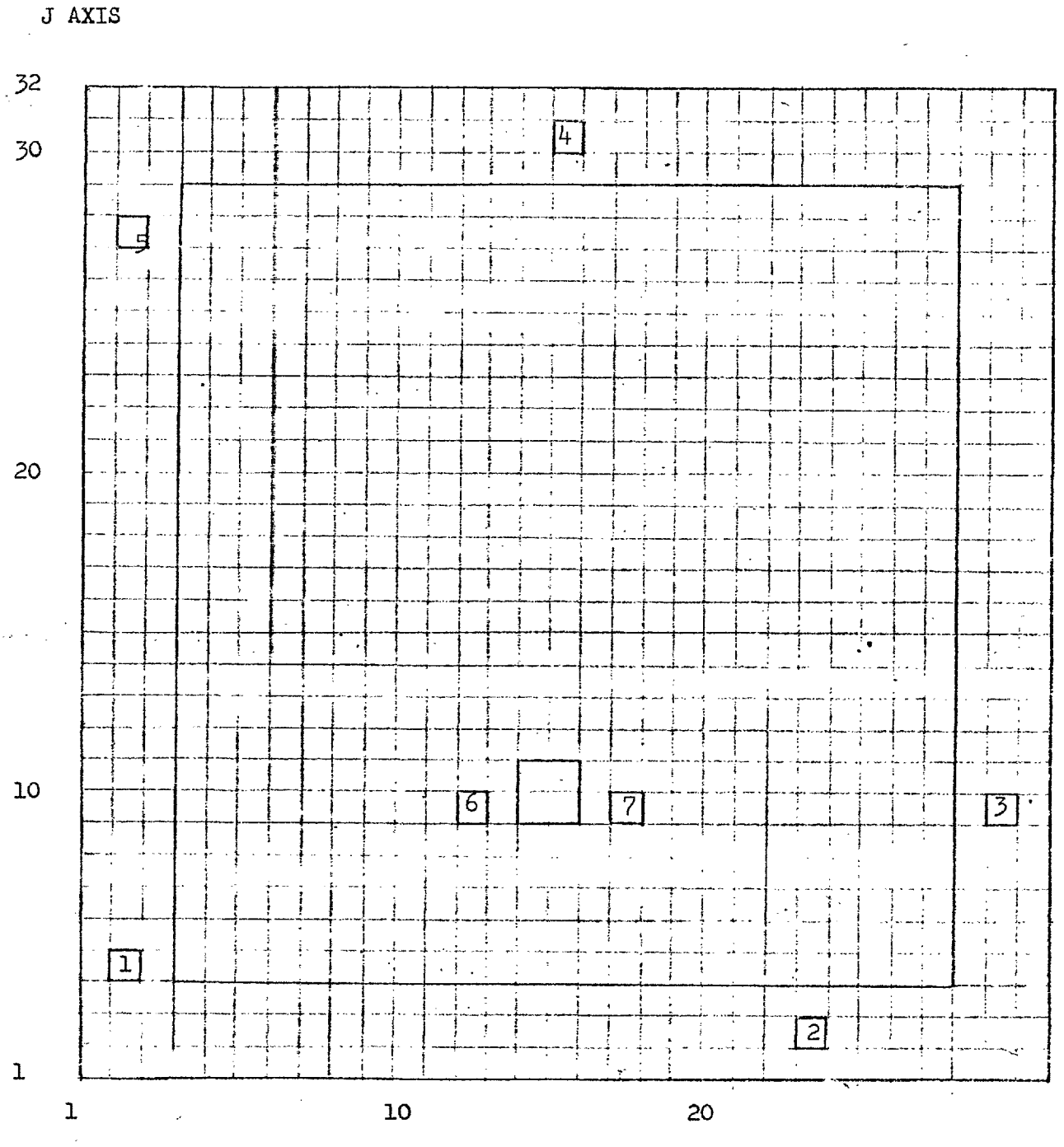


FIGURE 5.6

program. The temperature at each point in zones 1 and 2 of section A are computed by the Crank-Nicolson algorithm. As the temperature value of each point is calculated, it is compared to the temperature value for the same point obtained during the last iteration (for the present time step). The absolute value of this difference is called the residual. The maximum value of all the residuals is held in core until the iteration has been completed when it is compared to the maximum allowable error. If the value of the maximum residual is less than the error criterion, then the temperature values which are held in the array U are taken as correct for that time step. If this is not the case, the iteration continues until the error criterion is met.

The temperature of the tissue surrounding the artery is now known. The next step is to calculate the temperature of the blood within the artery at section B; this section of the arm is defined by the array UA. The temperature of the arterial blood at section B is found from the equation:

$$G\ A\ C_p\ \frac{dU}{dz} = -\ S_A\ (U - U_W) \qquad (5.5.)$$

The heat conduction in section B (figure 5.5), is calculated by the same iterative technique as the solution of the diffusion equation for section A. When the error criterion for the diffusion equation is met, Subroutine Arm returns to the main program. The next step is to call Subroutine Hand.

5.9 THE IMPLEMENTATION OF SUBROUTINE HAND.

When one is implementing the thermal situation within the human hand, as represented in the computer model, a number of factors have to be taken into account. First, the degree of blood flow within the human hand is a function of the vasomotor tone. Secondly, the tissue of the hand, like that of the arm, is divided for the purposes of the simulation into two types; namely an area of bone and tissue, which is covered by a layer of fat and skin. Figures 5.7 and 5.8 illustrate the simulation approximation of the hand. The co-ordinates of the vessels are listed in terms of L parameters (figure 5.8).

The technique allows one to simulate the vasomotor activity within a single digit, thus enabling a direct comparison to be made with data

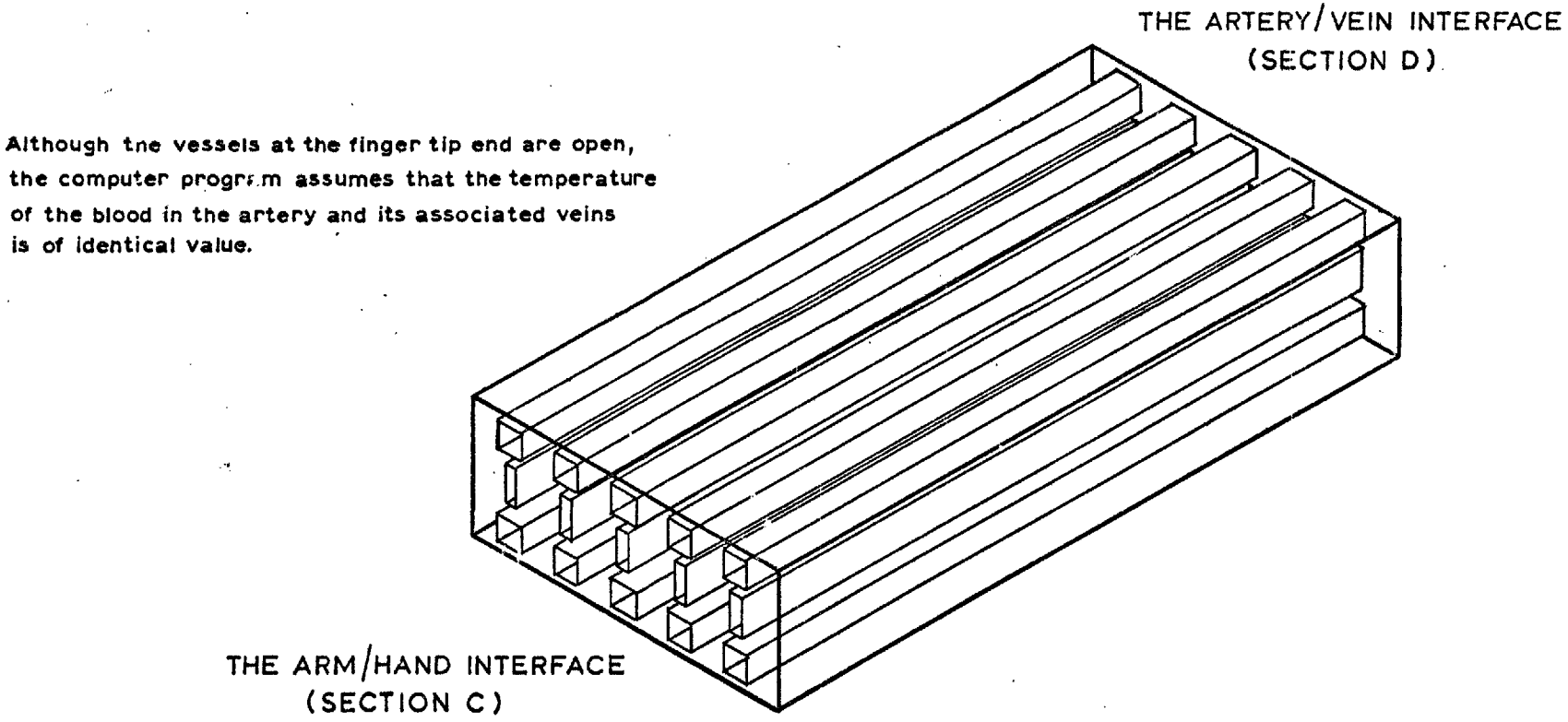


Fig. 5·7 An isometric projection showing the simulation approximation to the vascular structure of the hand.

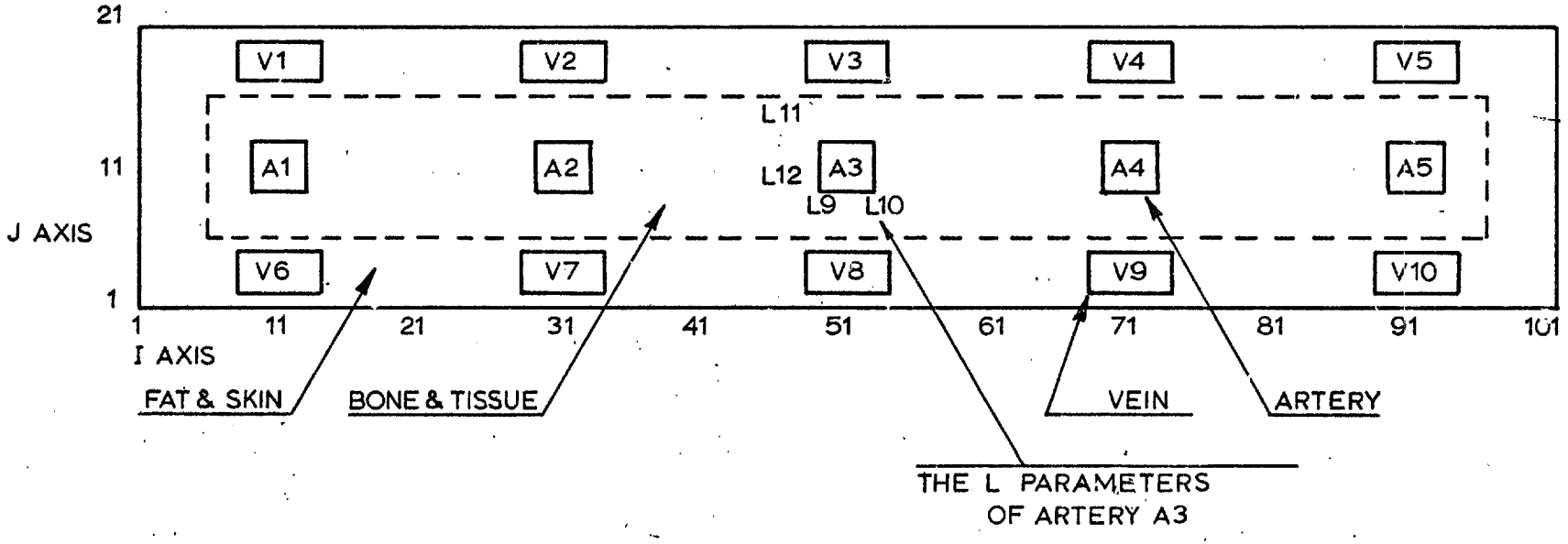


Fig. 5-8 Diagram showing the layout of the finite difference grid for the hand.

The blood vessels are shown under condi ions of maximum dilatation. (model)

resulting from experiments where only one hand is subjected to external thermal stimulation.

Adaptation on the Crank-Nicolson Algorithm to the Solution of the Heat Diffusion Equation Within a Rectangular Section.

The iterative methods which were developed to solve the heat diffusion equations pertaining to the arm operate within a square finite difference grid. Unfortunately the solution of the equivalent equations within the hand requires the use of a rectangular grid. It has already been noted that the structure of the hand includes two different types of tissue. Figure 5.9 shows the simulation approximation with these two types of tissue and their associated constants.

Zone 1 is the region of fat and skin. This is computed first during any time step. Zone 2 is the region of muscle and bone.

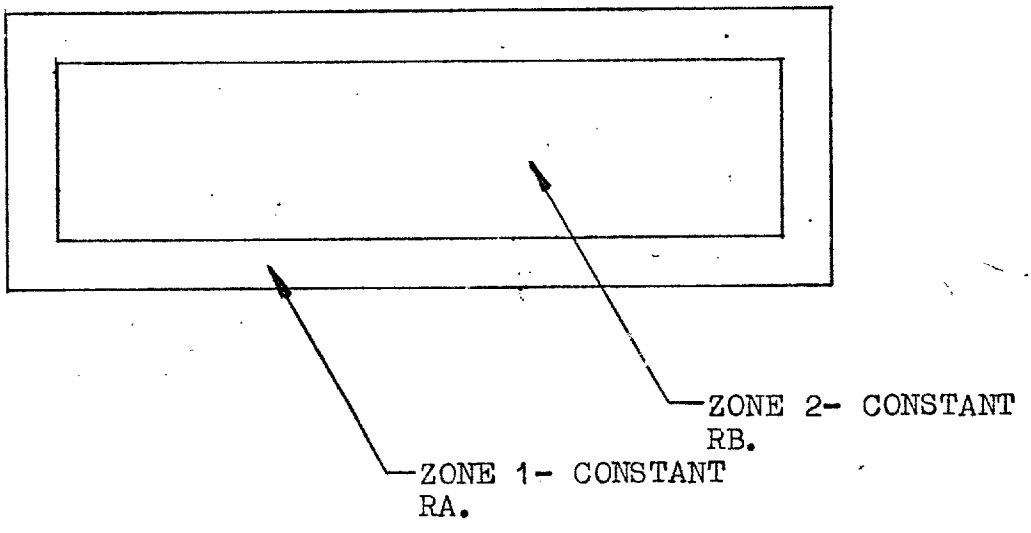


FIGURE 5.9

Assuming that any undefined constants are common to the section devoted to the Crank-Nicolson Algorithm for the hand, then referring to equation (5.15.)

$$RA=\frac{\delta t}{Ah^2} \qquad \text{and} \qquad RB=\frac{\delta t}{Ak^2}$$

therefore substituting RA and RB equation (5.15.) becomes:

$$U(I,J,N+1)=U(I,J,N)+0.5(RAU(I+1,J,N+1)-2RAU(I,J,N+1)+RAU(I-1,J,N+1$$
$$+RAU(I-1,J,N)-2RAU(I,J,N)+RAU(I-1,J,N)+RBU(I,J+1,N+1)$$
$$-2RBU(I,J,N+1)+RBU(I,J-1,N+1)+RBU(I,J+1,N)-2RBU(I,J,N)+RBU(I,J-1,N$$
(5.37.)

Now collecting terms of the N^{th} time row

$$B= U(I,J,N)+0.5RAU(I+1,J,N)-RAU(I,J,N)+0.5RAU(I-1,J,N)$$
$$+0.5RBU(I,J+1,N)-RBU(I,J,N) + 0.5RBU(I,J-1,N) \qquad (5.38.$$

Substituting the term B in equation (5.37.)

$$U(I,J,N+1)^{(m+1)} = 0.5RA(I+1,J,N+1)^{(m)} -2U(I,J,N+1)^{(m+1)}$$
$$+U(I-1,J,N+1)^{(m)}) +0.5RB(U(I,J+1,N+1)^{(m)}$$
$$-2U(I,J,N+1)^{(m+1)} + U(I,J-1,N+1)^{(m)}) +B \qquad (5.39.$$

The 'm' values denote which iterative value of U, for a given point, is being used in the $(m+1)^{th}$ solution of U(I,J,N+1). The updating of values during the iteration

results in a higher rate of convergence.

Collecting similar terms gives equation (5.39.) therefore:

$$U(I,J,N+1) = \frac{RA}{2(1+RA+RB)} \left(U(I+1,J,N+1) + U(I-1,J,N+1)\right)$$

$$+ \frac{RB}{2(1+RA+RB)} \left(U(I,J+1,N+1) + U(I,J-1,N+1)\right)$$

$$+ \frac{B}{1 + RA + RB} \qquad (5.40.)$$

5.10 THE PROGRAM STRATEGY FOR THE HAND.

The temperature of the blood in the arm artery was calculated during the execution of Subroutine Arm. The initial step in the execution of Subroutine Hand is the equation of the blood temperature in the arteries of the hand, at section C (figure 5.7), to that of the arterial blood in the arm at section B. The temperature of the tissue in section B is described by the array UB for 2121 points within the section. The diffusion equation is then solved for section B, enabling the establishment of the temperature of the tissue surrounding the blood vessels. These parameters are subsequently implemented in the convection equations for each artery. The solution of these equations establishes the blood temperature within the arteries at section C.

In the physical hand, blood is transferred at the finger tip from the arteries to the veins by way of the arterioles, capillaries and venules. In terms of the computer program such a transference of blood would involve an exceedingly complex procedure. To overcome this difficulty, within the program, the temperature of the blood in the veins at section D (figure 5.7), is equivalenced to that in the associated artery. The diffusion equation is then solved for section D. This solution provides the parameter values used in the convection equations which define the blood temperature along the length of each vein.

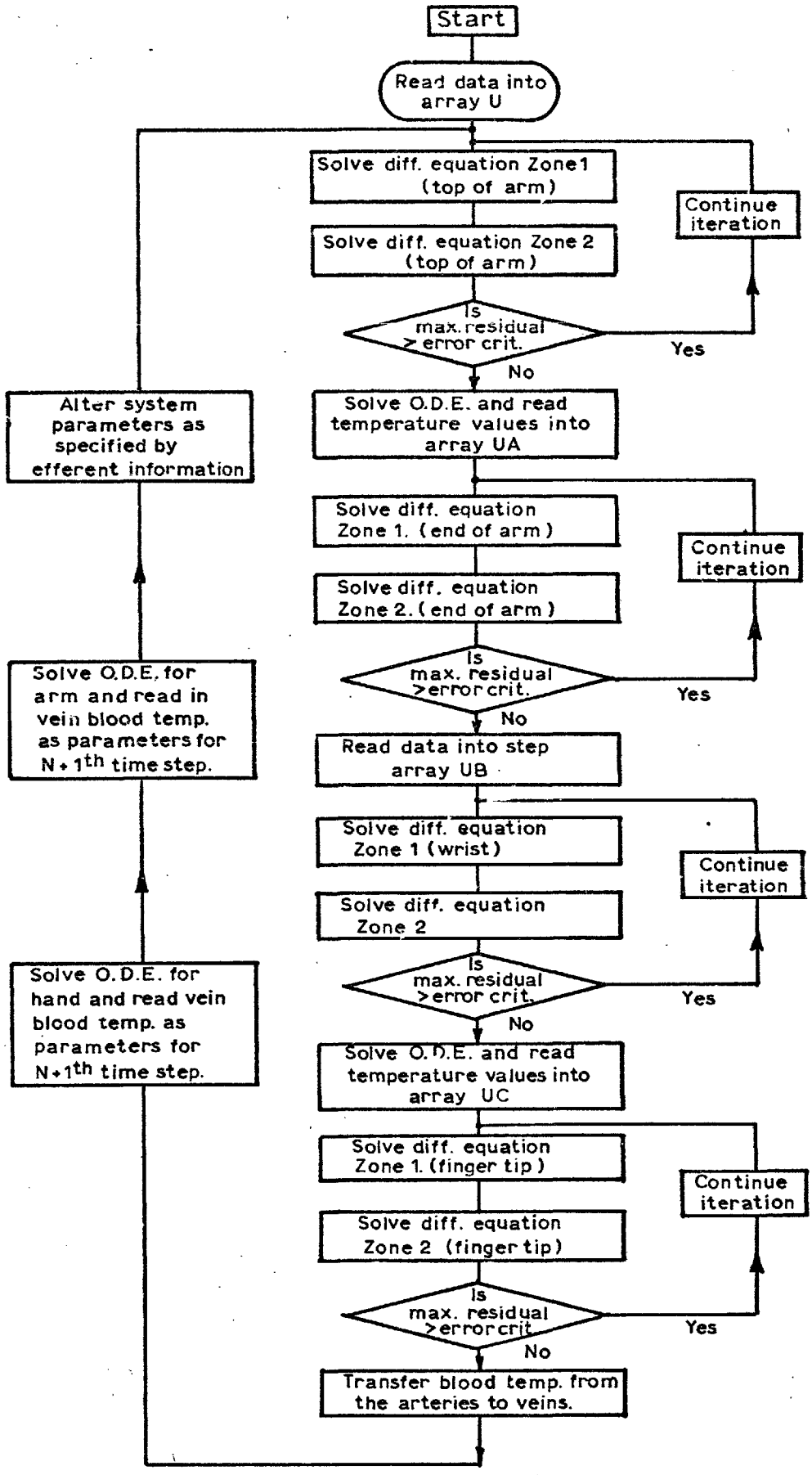


Fig. 5·10 The figure shows the computer flow diagram of the arm and hand.

5.11 THE MAIN PROGRAM INITIALIZATION PROCEDURE FOR THE $N+1^{th}$ TIME STEP: SUBROUTINE CONV.

The function of this subroutine is to initialize, during the N^{th} time step, any parameters which require alteration at the commencement of the $N+1^{th}$ iteration. The last section of Subroutine Hand which precedes this part of the model, solved the diffusion equation for section D of the hand. The temperature of the tissue surrounding the veins is calculated during this phase of the program and used to establish the temperature of the tissue at the vein wall, which forms a parameter of the convection equation. The solution of the convection equations for each vein determines the blood temperature within the vessel at section C. These values are used as boundary conditions in the solution of the diffusion equation for section C during the $N+1^{th}$ time step. A similar procedure initializes the blood temperature within the veins of the arm at section B, while the equivalent blood temperatures at section A, are established by solving the convection equation for each vein in the arm.

CHAPTER 6

THE CONTROL OF THE DIGITAL COMPUTER MODEL.

6.1 INTRODUCTION.

The analysis, of the relevant physiological data and the phenomenon of entrainment, led at the conclusion of chapter four to the postulation of a particular type of non-linear oscillatory system. To proceed with this type of analysis it was necessary to design a suitable mathematical computer model of the physical thermo-regulatory system. This present chapter deals with the control of the computer model.

6.2 THE ROLE OF THE AFFERENT PATHWAY IN THE CONTROLLED THERMAL SYSTEM.

The vasomotor control of cutaneous blood flow has been described on numerous occasions, in the following physiological terms: Newton's Law of Cooling indicates that a decrease in the thermal gradient, or difference between the temperature of the skin and of the surroundings, would decrease the heat loss from the body. The decrease of gradient is accomplished in two ways: by cutaneous vasoconstriction, and by shifts in limb blood flow. As a response to cold, the finger blood flow may

be decreased to less than 1% of that measured in heat. Under conditions of heat, the cutaneous blood flow is greatly increased.

It has been proposed that when the thermal control system is operating within the neutral region the, so called, first line of defence utilises the skin receptors as its primary source of afferent information. In addition to the physiological evidence already presented to substantiate this statement, Fusco (1963) concurs thus: "peripheral control depends upon afferent impulses arising in cutaneous thermo-receptors which are sensitive to changes in skin temperature."

To understand the manner in which the cutaneous receptors form part of the control system, it is necessary to note that such a system is required to accommodate the following physiological facts:

1. An increase in temperature at the skin surface produces a corresponding increase in cutaneous blood flow.

2. A decrease in temperature at the skin surface produces a decrease in cutaneous blood flow.

3. A hunting effect exists in the digit blood flow, as described by Burton, Taylor and others.

The basic block diagram of a control system which would seem to agree with the physiological facts is illustrated in figure 6.1.

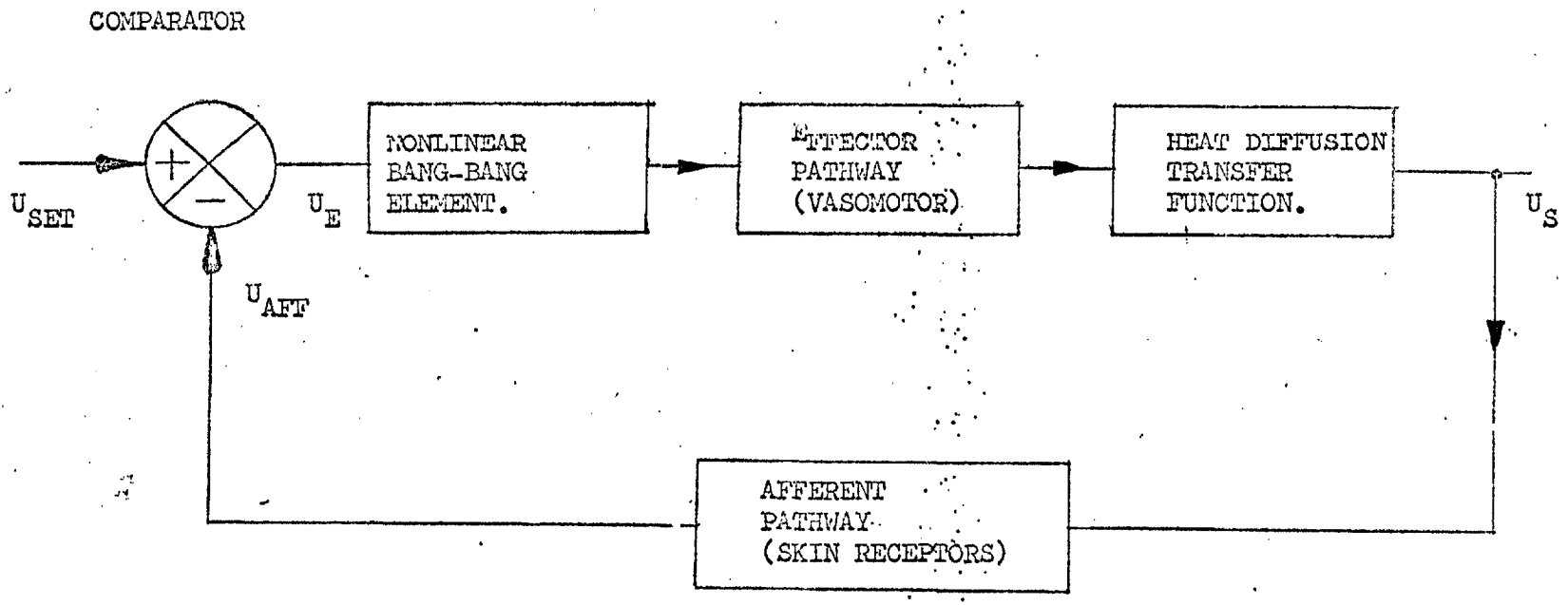


Figure 6.1

THE BASIC BLOCK DIAGRAM OF THE PERIPHERAL CONTROL SYSTEM.

The basic controlling equation is:

$$U_E = U_{SET} - U_{AFF} \qquad (6.1.)$$

The most common interpretation, Hensel (1963), of the activity of the thermal receptors, is to state that they respond to the temperature of the tissue immediately surrounding them. By applying the relevant physiological facts to equation (6.1.) it is possible to establish the manner in which the control system will respond to an increase in environmental temperature. A thermal gradient exists between the deep tissue and the air-skin interface. If for the sake of example, the temperature being sensed by the receptor in figure 6.2, is U_{AFF}, for an environmental temperature of 28°C, then an increase in the environmental temperature would be reflected in an increase in the receptor temperature that is:

$$U_{AFF} \longrightarrow U_{AFF} + \Delta_1 U_{AFF}$$

If it is assumed that for the sake of the argument, the 28°C environmental temperature produced a stable situation, then under these conditions $U_E = 0$. With the increased environmental temperature:

$$U_{AFF} + \Delta U_{AFF} \text{ is now greater than } U_{SET}$$

which results in U_E becoming negative. Under such conditions

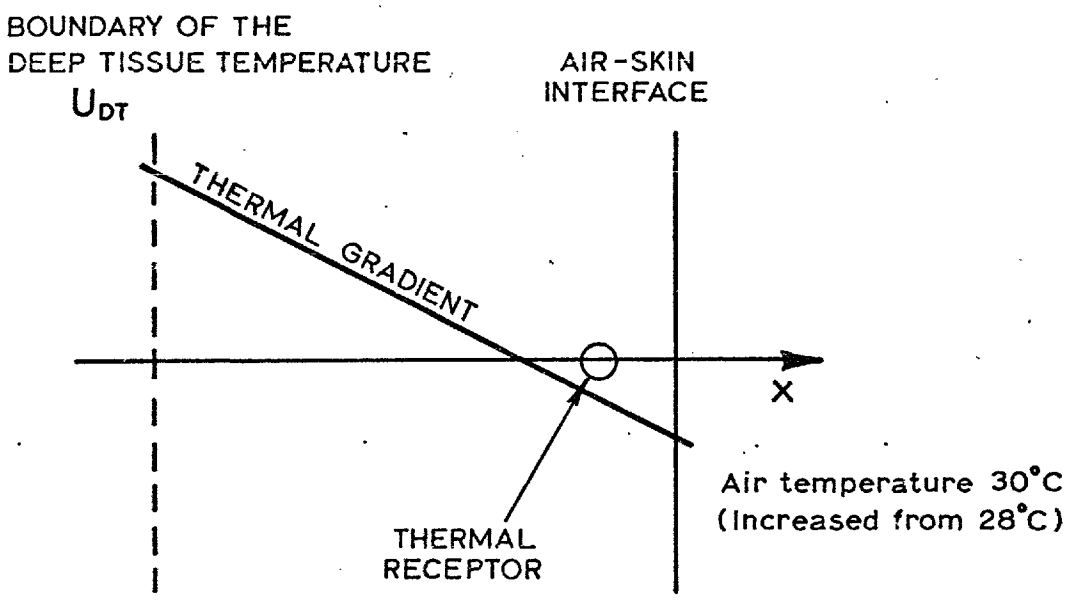

BOUNDARY OF THE
DEEP TISSUE TEMPERATURE
U_{DT}
AIR-SKIN
INTERFACE
THERMAL GRADIENT
X
Air temperature 30°C
(Increased from 28°C)
THERMAL
RECEPTOR

Fig. 6·2

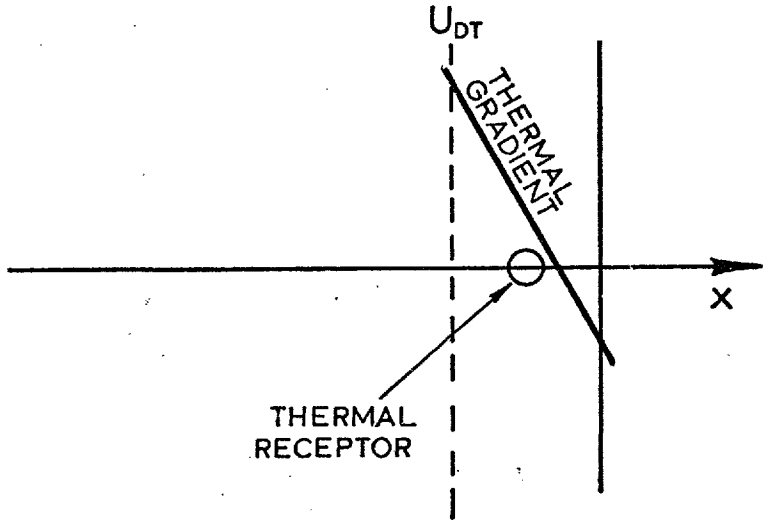

U_{DT}
THERMAL
GRADIENT
X
THERMAL
RECEPTOR

Fig. 6·3

the response of the thermo-regulatory system is to increase the cutaneous blood flow Hertzman (1959). The effect of such action is to move the area of tissue at U_{DT} nearer to the skin surface, which in turn results in an increase in the thermal gradient as illustrated by figure 6.3. The net effect at the temperature receptor is a further increase in temperature to a new value:

$$U_{AFF} + \Delta_2 U_{AFF}$$

such that:

$$U_{AFF} < U_{AFF} + \Delta_1 U_{AFF} < U_{AFF} + \Delta_2 U_{AFF}$$

As the thermal receptors respond to the temperature of the surrounding tissue, the effect of the temperature rise which results from increased cutaneous blood flow must, if it is to be consistent, result in a further increase in the supply of blood to the skin. It would therefore seem that any step like change in the environmental temperature causes an avalanche condition, which implies that U_{AFF} in figure 6.1 should be positive as an input to the comparator rather than negative. Such a system would continue to increase the cutaneous blood flow until saturation occurred. The work of Burton and Taylor (1940), together with our experiments, indicate that such an avalanche condition does not occur;

rather, there is definite control of the cutaneous blood flow. We are therefore forced to ask the question: what kind of negative feedback control system can control body temperature in a manner which results in increased cutaneous blood flow to compensate for a rise in environmental temperature?

To quote Burton and Edholm (1955), "The mechanisms involved in the regulation of body temperature include a control of the peripheral circulation. Heat loss from the surface of the body is modified by the rate of blood flow through the skin and superficial tissues". To understand the system modus operandi, it is necessary to restate Newton's Law of Cooling:

$$dQ = - K A \frac{dU}{dx} d\tau \qquad (6.2.)$$

where:

dQ - is the heat conducted in the direction dx (figure 6.4), during the time interval $d\tau$

U - temperature.

K - the thermal conductivity.

A - Area.

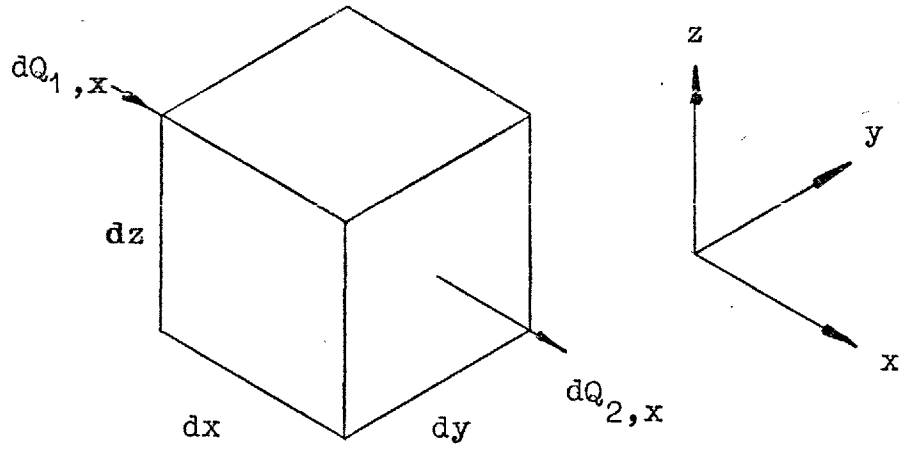
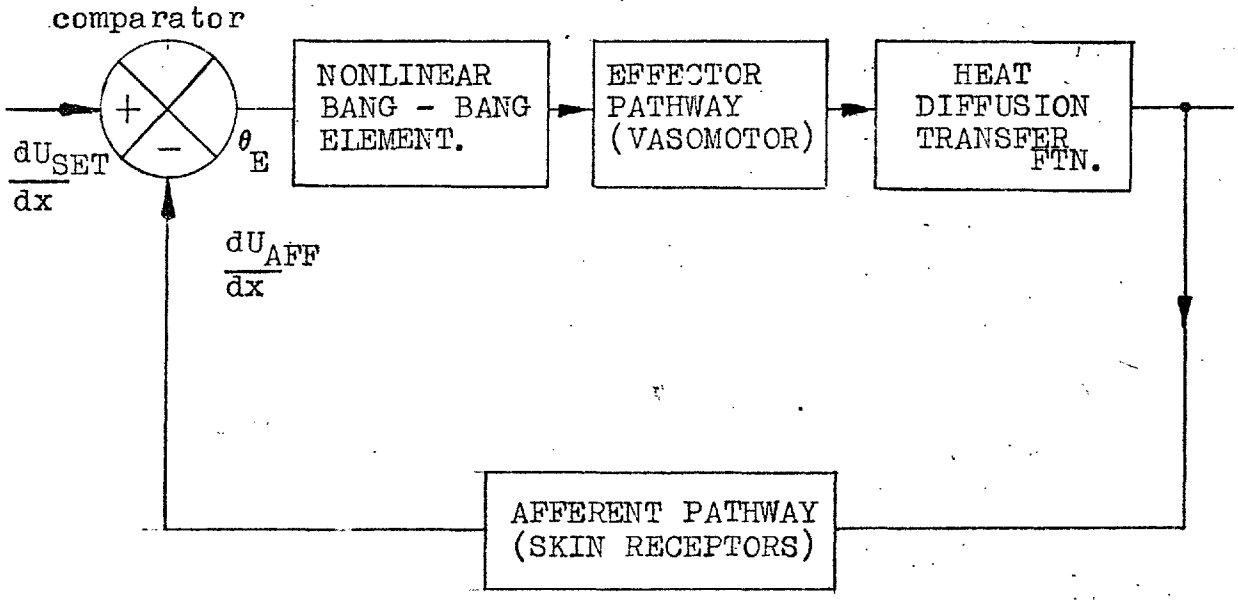


FIGURE 6.4

The minus sign follows from the second law of thermodynamics, according to which heat automatically flows from points of higher temperature to points of lower temperature. Thus if dx is taken positive in the direction of a positive heat flow, the temperature difference dU must be negative, and these conditions are consistent with each other only if a minus sign is used.

Applied to human temperature regulation Newton's law indicates that a decrease in the thermal gradient would decrease the heat loss from the body. It has been proposed earlier in this thesis, that the purpose of the peripheral system of thermo-regulation is to act as a first line of defence, that is to maintain the constancy

of the internal environmental conditions of the body. This constancy is a function of heat loss and not temperature. If the heat loss is kept constant in the face of external environmental temperature change, then it automatically follows that homeostasis will also be preserved. According to equation (6.2.) for a given length of time, the amount of heat loss dQ is proportional to the thermal gradient $\frac{dU}{dx}$. Therefore to preserve constant heat loss, $\frac{dU}{dx}$ must remain steady no matter what the environmental temperature may be. Stated slightly differently, the controlled variable, in figure 6.1 should be $\frac{dU}{dx}$, which means that the block diagram of the peripheral thermo-regulatory system would then be as is shown in figure 6.5.



θ_E - error signal.

FIGURE 6.5

Energy Balance at the Skin Surface.

The analysis of thermal balance, begins with the statement of the equation representing this balance:

$$M \pm R \pm C = E \qquad (6.3.)$$

where M - is the metabolic rate.

R - the rate of heat exchange with the environment via radiation.

C - the rate of heat exchange with the environment by convection.

E - the rate of heat exchange with the environment by evaporation.

The concept is that the physiological response is proportional to the thermal gradient from the body core to the thermal boundary with the air and the magnitude of the thermal stress is proportional to this gradient.

Heat flow from the interior of the body reaches the surface principally by forced convection, that is by way of blood flow to the skin. Hatch (1963) states that the adjustment of cutaneous blood flow, with proportional change in the rate of heat transport, is necessary to keep the core temperature U_c from rising when the temperature difference $(U_c - U_s)$ narrows as a result of increasing heat stress. The vasomotor regulation has considerable success in maintaining this thermal balance.

The problem of thermal gradients within the skin has, as Hatch (1963) mentions, been investigated in detail by Bazett (1941,1949,1951). Hatch (1963) also states that the results of his research, are in good agreement with the findings of Bazett which are well known. Bazett (1941) proposes that there exist both adequate data regarding the thermal gradients within the human forearm, and detailed knowledge of the arrangement of blood vessels in the same area. The thermal gradients, the arrangement of blood vessels, and the likely sites for the thermal receptors, of the forearm are shown in figure 6.6. In the forearm, the thermal gradient is undoubtedly modified by the arrangement of the blood vessels. The peak temperature occurs at the level of the arterial net, while the trough is at the deeper second venous net. These gradients were established experimentally by Bazett and McGlone (1927) and Mendelson (1936). The gradients demonstrate a peaked rise in temperature at a depth of about 0.8 mm, which according to Bazett (1949), can be ascribed to an arteriolar network existing at about this depth which has been described by Spalteholtz (1936).

On either side of this arteriolar network the temperatures fall abruptly due to the presence of venous plexi. The relations of these and other vessels

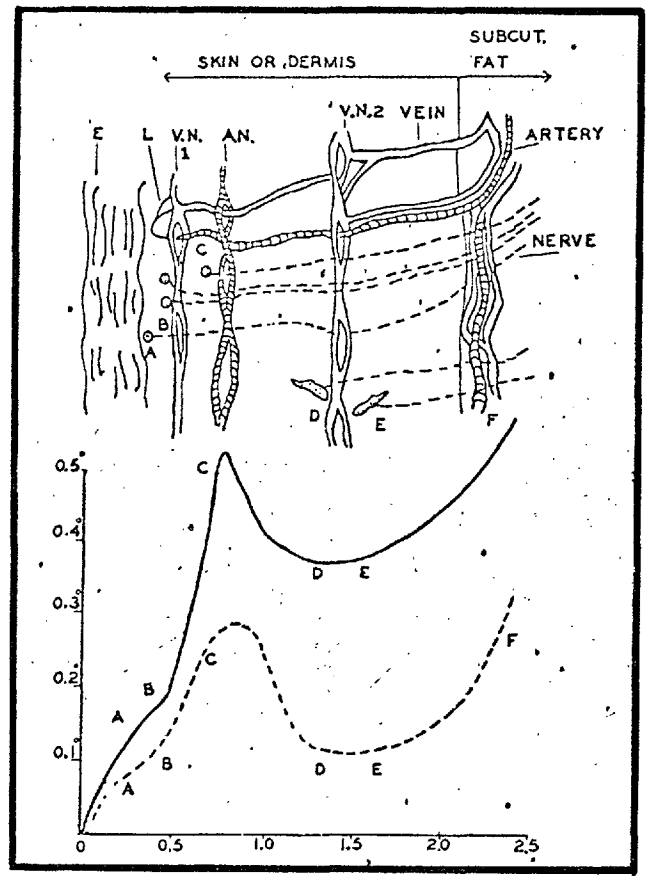


Figure 6.6. The diagram illustrates the sites of thermal receptors within the skin. A,B,C are the sites of the warm receptors, while D,E,F are the sites of the cold receptors. After Bazett 1941.

to the thermal gradients are shown in figure 6.6. Possible depths for the warm receptors are considered by Bazett (1941) to be D, E or F (figure 6.6), while the sites of the cold receptors are thought to be A, B or C. Although Bazett (1951) discusses the role of the cutaneous thermal gradients in the forearm, Burton (1963) and Pennes (1949) indicate that there exists a similar relation between the thermal receptors and thermal gradients in the hand.

According to Bazett (1951), the utilization of thermal gradients for sensory information as well as control, follows good principles of cybernetics. In the same paper he indicates that vasomotor changes in the dermis will modify heat transfer, resulting in alterations in the thermal gradient pattern which provides sensory information. Bazett (1951) suggests that while Pennes (1949) has found slightly different values of the cutaneous thermal gradients, this does not alter the discussion as to their use as a source of sensory information. Bazett continues by recounting, in the summary of his 1951 paper, the evidence and logic which led him to believe that reflex responses, in peripheral blood flow, are stimulated by temperature gradients.

Lele et. al (1954), have also investigated the relationship between heat transfer, skin temperature and cutaneous sensibility. Their hypothesis states that nerve impulses from the thermal receptors arise from a difference in temperature between different parts of the skin. These authors believe that it must therefore follow, that the nerve endings are arranged in the skin to behave like a thermopile rather than a thermometer. In other words, in relation to heat exchange the nerve terminals only give rise to propagated action potentials when conditions are such that the skin in which they lie is not isothermal. Hensel (1963) in a paper on the electro-physiology of thermo-sensitive nerve endings, refers to experiments which he has carried out in conjunction with Zotterman (1951), which tend to disprove the concept of spatial temperature gradients as an adequate stimulus for the cutaneous thermal receptors. Williams (1958) however, considered these experiments to be inconclusive because the experimental conditions used resulted in a cold receptors stationary discharge being virtually zero.

It has been established that thermal gradients exist in the skin, and that they are almost certainly intimately involved in the control of peripheral blood

flow. This statement is emphasised by the findings of Yamamoto et. al (1969), who show that the peripheral blood flow is closely linked to the environmental temperature (figure 6.7), within the control range of vasomotor tone. Whether the skin receptors detect thermal gradient or temperature directly is not the primary consideration; this is that the controlled variable in the peripheral thermal control system is temperature gradient. Even if the thermal receptors measure temperature, their spatial separation in a directional normal to the body surface could enable the central nervous system to continuously monitor the thermal gradients within the skin from the temperatures being sensed by individual receptors.

The question still to be decided is how the concept of temperature gradient as the controlled variable aligns itself with the physiological facts, and with the analysis of the system. Let us therefore consider the case of changing the temperature at the air-skin interface (U_{AS}), for example, from 28 to 30°C. (There is no special significance in the choice of these temperature values). A two degree increase of this type produces a decrease in $\frac{dU}{dx}$. Referring to figure 6.5, the effector action is defined in terms of the error signal as follows:

$\theta_E > 0$ Vasodilatation of the blood vessels.

$\theta_E < 0$ Vasoconstriction of the blood vessels.

$\theta_E = 0$ No change.

Hence a decrease in the thermal gradient should produce vasodilatation; physiological observations show that it does. As the cutaneous blood flow increases the boundary of the tissue at temperature U_{DT} (figure 6.2), moves nearer the skin surface. Figure 6.2 illustrates the thermal state just after the change in environmental temperature, while figure 6.3 shows that the effect of suitable vasodilatation is to increase the thermal gradient $\frac{dU}{dx}$ back to the set value defined by figure 6.5. Newton's law of cooling indicates that such action keeps the heat loss constant thus maintaining homeostasis. Similarly, a step reduction in U_{AS} results in an initial increase in the thermal gradient which causes vasoconstriction (according to the error signal criterion). Vasoconstriction produces a subsequent reduction in $\frac{dU}{dx}$ until the thermal gradient is again equal to $\frac{dU}{dx}_{SET}$. Such effector action will result in a hunting effect about the set value of thermal gradient.

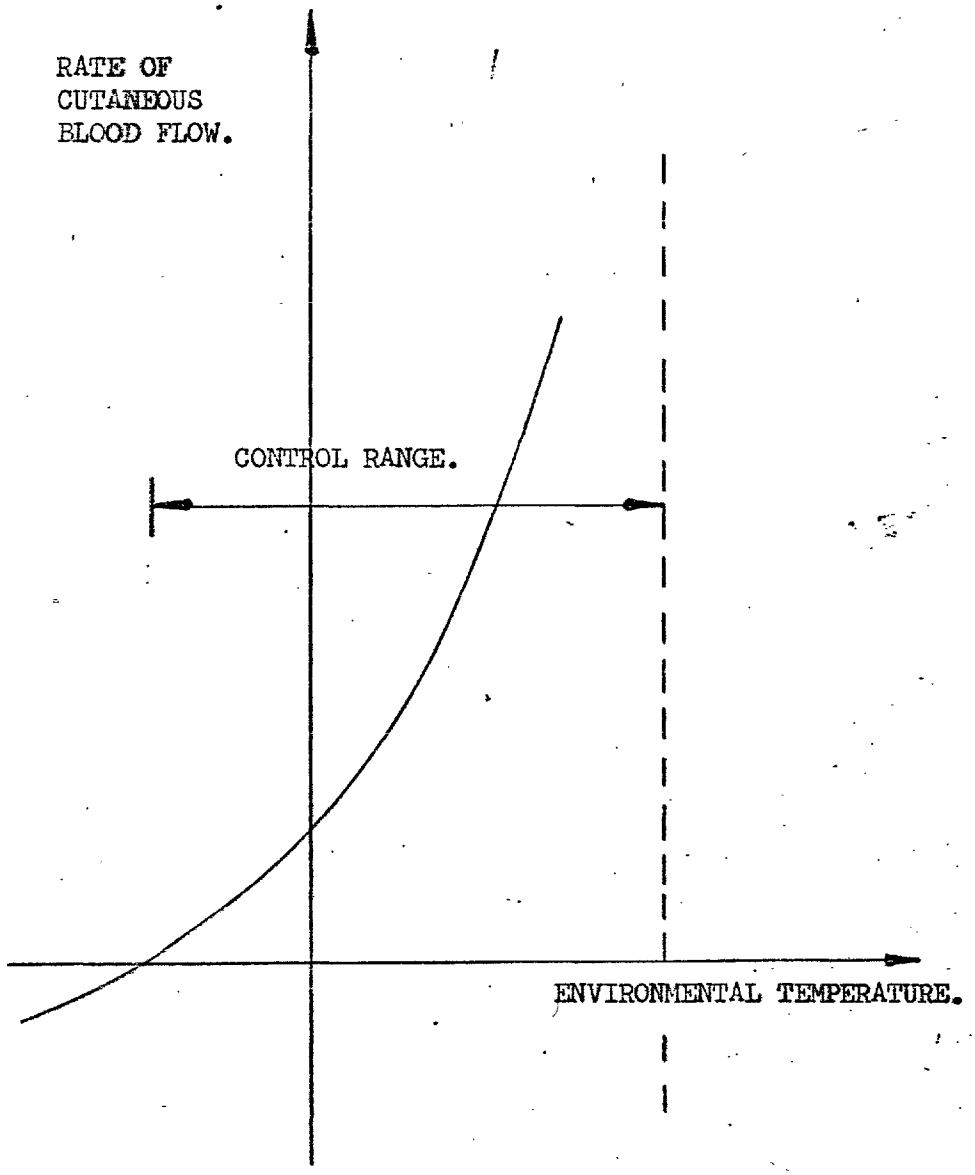


Figure 6.7 After Yamamoto et.al (1969).

6.3 THE INCLUSION OF THE CONTROLLING SYSTEM IN THE COMPUTER MODEL.

It has been proposed that the controlled variable in peripheral vasomotor control is temperature gradient. This statement raises the question of what set value of temperature gradient should be used in the computer model? Because the model is only an approximation to the physical situation, the value which is chosen will also be an approximation.

To define a value, it is necessary to re-examine the vasomotor activity. At one end of the control range, the vessels are in a state of maximum vasodilatation, while at the other extreme there is complete vasoconstriction. The maximum and minimum thermal gradients, in the skin, will therefore occur during the steady state conditions of maximum vasodilatation and vasoconstriction of the computer model. Hence to establish a suitable set value for temperature gradient ($\frac{dU}{dx}SET$), the model has to be solved under steady state conditions for maximum vasodilatation and vasoconstriction over a suitable range of skin temperatures.

The Steady State Solution of the Heat Diffusion Equation.

The heat flow in the upper limb due to conduction under dynamic conditions, as we have seen in chapter five, was found by solving the parabolic heat diffusion equation:

$$\frac{\rho C_p}{K} \frac{\partial U}{\partial t} = \frac{\partial^2 U}{\partial x^2} + \frac{\partial^2 U}{\partial y^2} \qquad (5.6.)$$

where

ρ = density.

C_p = specific heat.

K = thermal conductivity.

In the absence of any form of vasomotor control, the thermal state of the limb, at least as represented in the model, would eventually reach a condition of equilibrium. Brengelman and Brown (1966), state that the average skin temperature, in man, within the range of vasomotor control varies from approximately 31 to 34^{o}C depending on the vasomotor state. Hence to establish a suitable set value for temperature gradient, the model has to be solved over this range of skin temperature (under steady state conditions).

When a steady state has been attained, all the transient effects will have disappeared. Then $\frac{\partial U}{\partial t}=0$ and hence the diffusion equation (5.6.) becomes:

$$\frac{\partial^2 U}{\partial x^2} + \frac{\partial^2 U}{\partial y^2} = 0 \qquad (6.4.)$$

which is Laplaces equation. One consequence of removing the time dependent term is to transform the diffusion

equation from a parabolic partial differential equation into an elliptic equation. As in the case of the parabolic equation, the solution of the elliptic diffusion equation necessitates the use of specialized numerical methods which are, unfortunately, different from those used in the solution of equation (5.6.) in its dynamic form.

The Numerical Solution of Laplaces Equation.

The solution of Laplaces equation when related to the present study, is based upon the 101 x 21 grid which is illustrated in figure (5.11). Figure 6.8 is an illustration of part of that grid, or mesh as it is sometimes called.

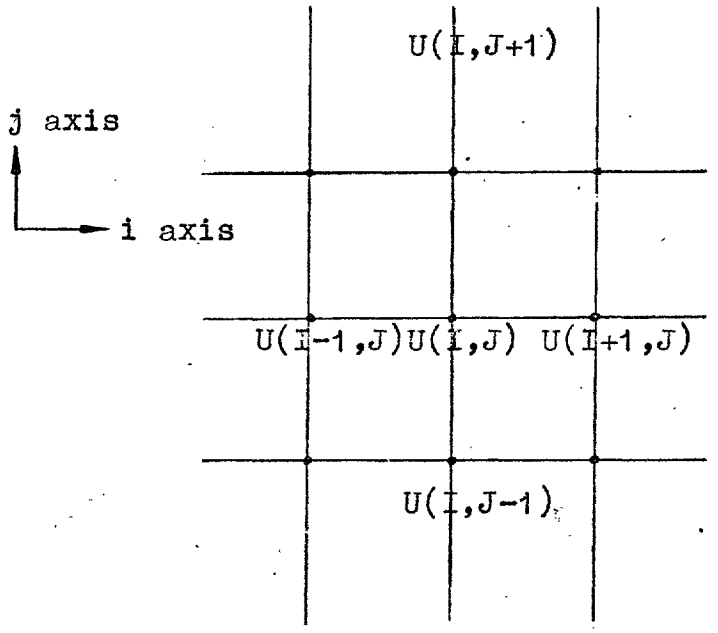


FIGURE 6.8.

The temperature distribution within the cross section is found by defining the temperature at the point (I,J) as being equal to the average temperature of the four points immediately adjacent. The temperature at the point (I,J) can therefore be expressed as a difference equation:

$$U(I,J) = \frac{1}{4}\left[U(I-1,J) + U(I+1,J) + U(I,J-1) + (I,J+1)\right] \qquad (6.5.)$$

The solution of equation (6.5.)on the computer, for the entire grid, requires the adoption of an iteration technique for two reasons: if the difference equation were solved in its raw form, the iterative solution would probably be numerically unstable. The second reason is that in its unmodified form, the difference equation, if not directly numerically unstable, would still require a large number of iterations to converge to a solution.

The iteration technique used here is known as the extrapolated Liebmann method or alternatively, successive over-relaxation. The algorithm which is used for this purpose is:

$$U(I,J) = w\,\alpha + (1-w)\,U(I,J) \qquad (6.6.)$$

where $\alpha = \frac{1}{4}\left[U(I-1,J) + U(I+1,J) + U(I,J-1) + U(I,J+1)\right]$

The parameter w is called the accelerating factor. An optimum choice of w results in the highest speed of convergence on to a solution. This fact has been illustrated by Carre (1961) who considered a problem where the best value for w was 1.9. This gave a rate of convergence forty times greater than that obtained using the Gauss-Seidal iterative technique (w=1). In general there is no simple method for finding the optimum value of w, but as a first approximation the value of the acceleration factor for the solution of Laplaces equation is said to lie in the range 1-2.

Program Strategy for the Numerical Solution of the Equation.

As we have seen, the steady state solution of the diffusion equation for the section of the hand shown in figure (5.11), is based upon a 101 by 21 mesh. The initial stages of the computer program are devoted to establishing the boundary conditions. These boundary conditions consist of the temperature at the air-skin interface together with the temperature of the blood within various vessels of the section.

Having established the boundary conditions, the second part of the program is devoted to the iterative solution of Laplaces equation. Using the algorithm of equation (6.6.), the temperature at each

point within the mesh is found from the temperatures of the adjacent points. Obviously, on the first iteration where the only known temperatures are those of the boundary conditions, the temperature values at most points within the mesh will be inaccurate. During the second iteration the temperature value for any point (I,J) is compared with the equivalent value found during the previous iteration. The difference between these two values is called the residual for that particular point. This process is repeated for each mesh point. The result is that at the end of each complete iteration, the residual value for each point is known. Selecting the largest residual automatically selects the maximum degree of error for that particular iteration. If one estimates that the maximum permissible error is say 0.01, then the iterative process continues until the maximum residual for a given iteration is less than 0.01.

The Estimation of the Set Value for Temperature Gradient.

As previously stated, Brengelman and Brown (1966) estimate that the range of skin temperature in the region of vasomotor control is 31-34^{o}C. The computer simulation was therefore used to solve the thermal topography of the hand under steady state

conditions, for this range of values.

Figures 6.9-6.12 are contour plots of a section of the slab model which represents the hand in the computer simulation. Figure a, in each case illustrates the situation for maximum vasodilatation of the model, while figure b, is the corresponding plot for the condition of maximum vasoconstriction, for a particular set of environmental conditions. The isothermals shown in these vary according to the thermal situation under investigation.

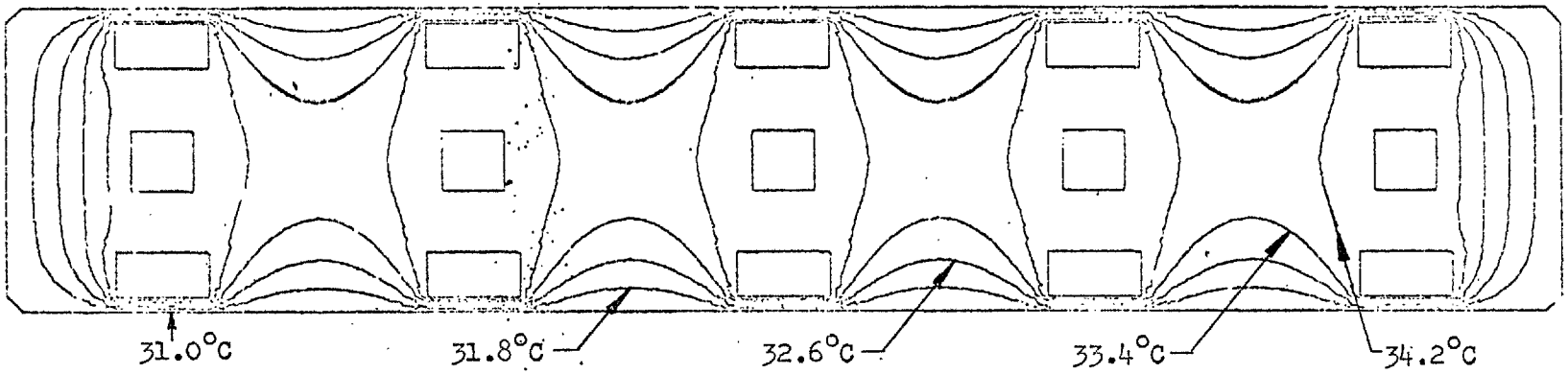
From a careful consideration of these contour plots it was estimated that a suitable value for temperature gradient over an appropriate spatial increment was $0.3^{o}C$. This value agrees with the data of Bazett (1941) and was subsequently used as the set value for thermal gradient within the computer model.

Subroutine Control.

The basic block diagram for the system which uses temperature gradient as its controlled variable is illustrated in figure 6.5. Referring to this figure, the error signal θ_E determines the efferent activity during the subsequent time step. If θ_E is positive, the appropriate efferent activity is vasodilatation, whereas, for a negative value of

FIGURE 6.9 SKIN TEMPERATURE 31°C

'a'



'b'

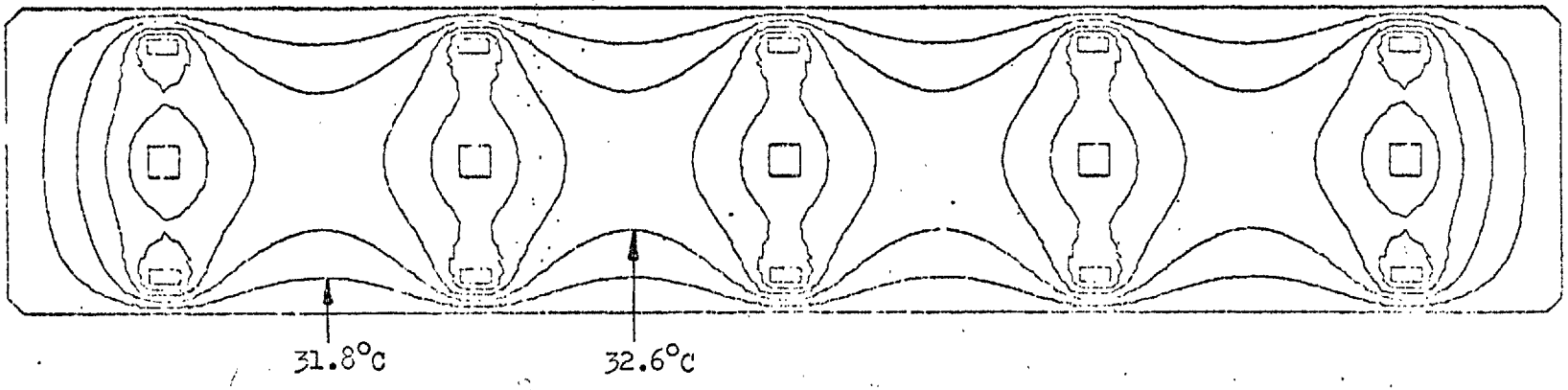
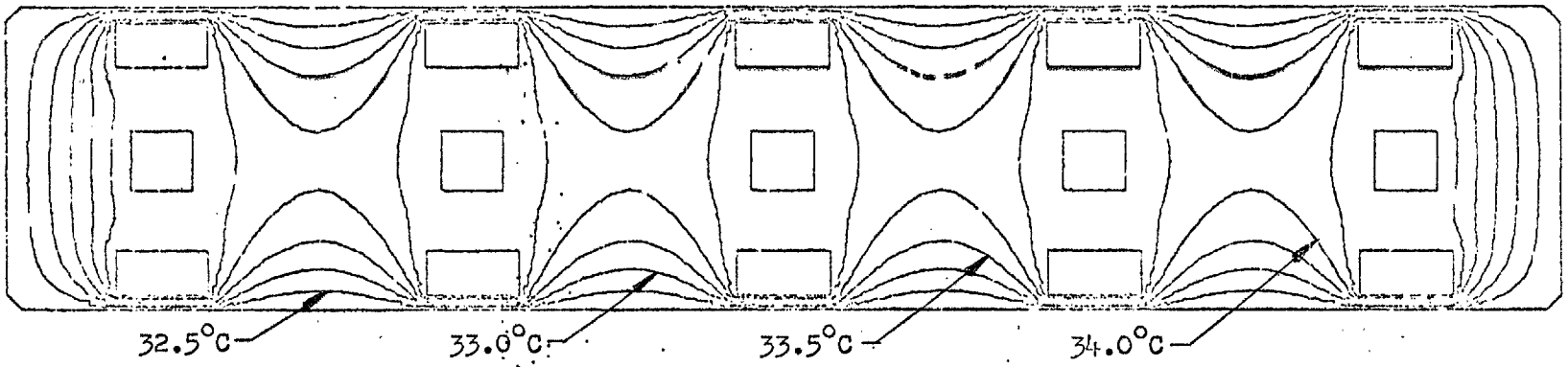


FIGURE 6.10 SKIN TEMPERATURE 32°C

'a'



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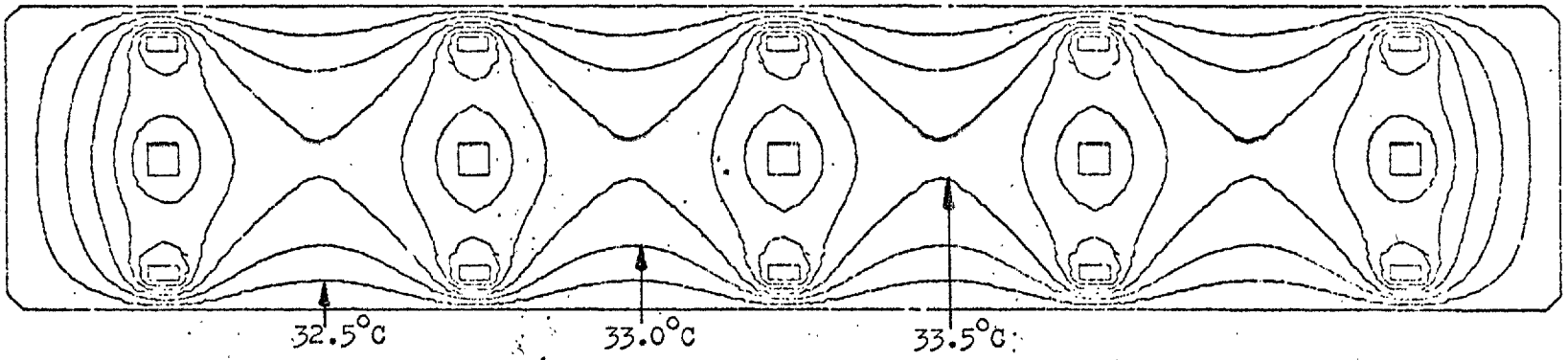
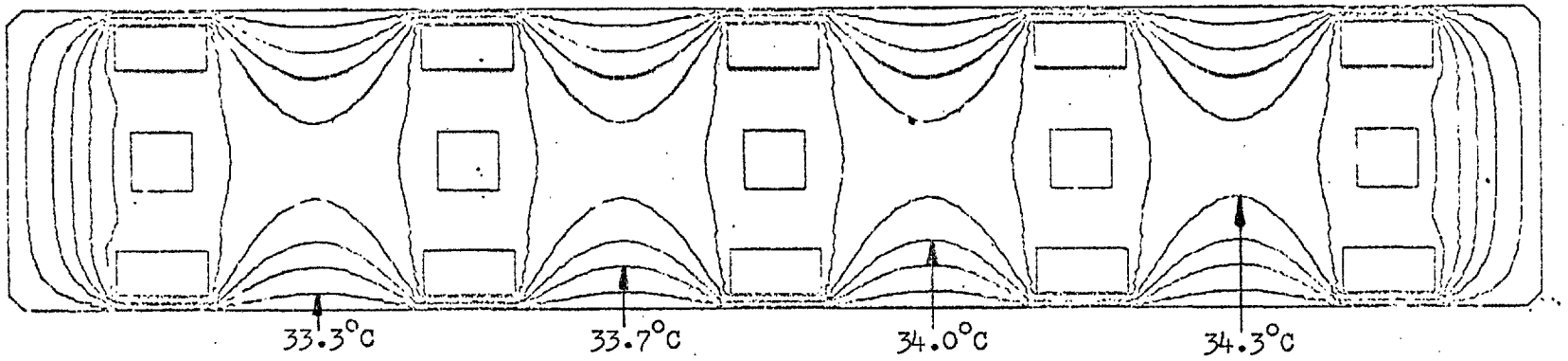


FIGURE 6.11 SKIN TEMPERATURE 33°C

'a'



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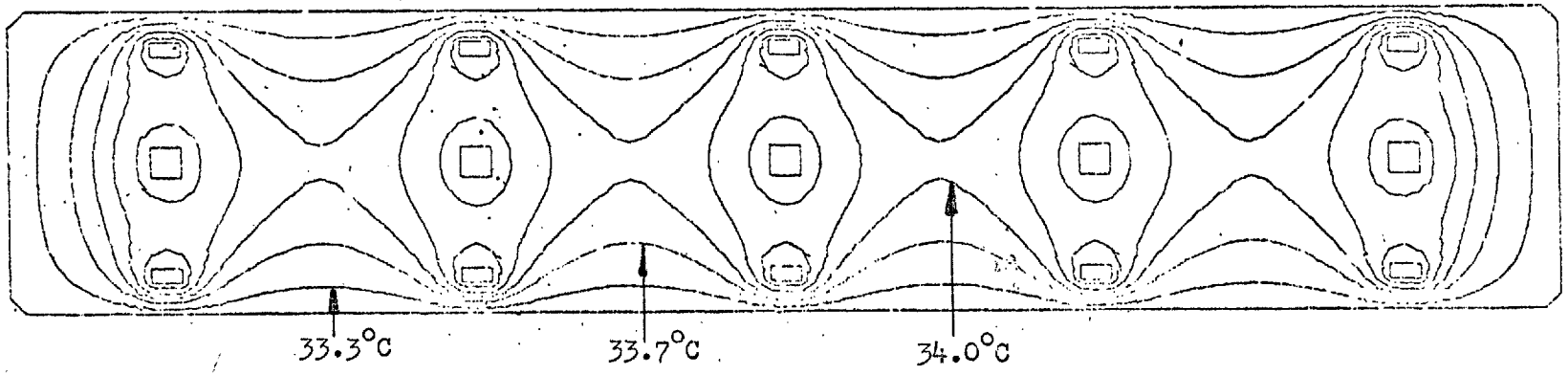
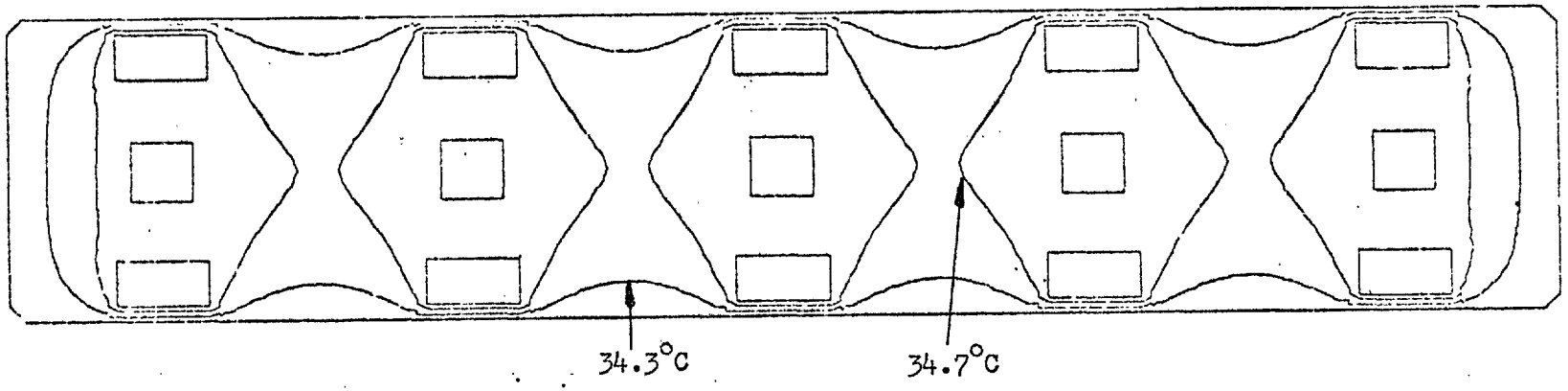


FIGURE 6.12 SKIN TEMPERATURE 34°C

'a'



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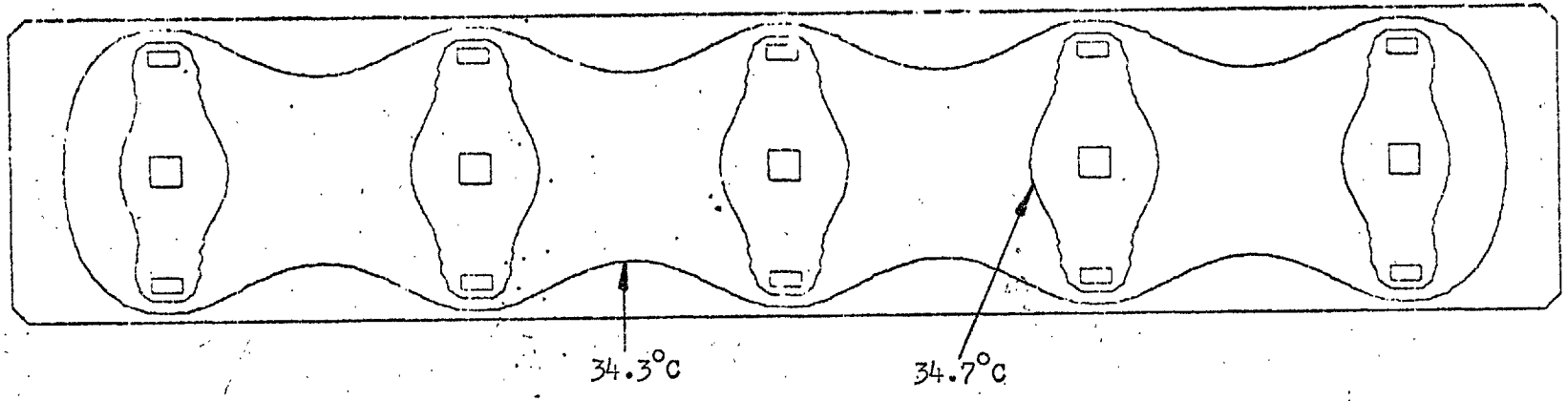


error signal the effector action results in vaso-constriction. Subroutine control is the section of the computer model which decides on the appropriate type of vascular adjustment.

The subroutine compares the thermal gradient established during the n^{th} time step, which results from the vascular adjustment during the $n-1^{th}$ time step, with the set point value. The next phase in the control procedure is to determine the vascular adjustments required to be consistent with the present time increments control philosophy.

6.4 THE ROLE OF THE EFFERENT PATHWAY IN THE CONTROLLED SYSTEM.

As we have seen, within the comfort zone, the control of body temperature depends largely upon vasomotor control of the peripheral circulation. Burton (1939), found that, both the frequency of waves of constriction, and the magnitude of the contractions of the blood vessels, are modified by the integrated sum of the afferent stimuli from temperature receptors.

It would now seem that the control system which influences peripheral blood flow in the neutral temperature zone, is of a non-linear type. Our experiments have investigated the entrainment of this peripheral blood flow, and the analysis of this phenomenon and the realization of the control system involved. One of the constituent parts of this control system, is a bang-bang element whose frequency of oscillation is dependent on the afferent activity of the system. An interesting factor which is involved in the efferent pathway is the characteristic of the vascular smooth muscle, and its effect on the output of the bang-bang element.

Both Grodins (1963), and Scher and Young (1963) have established that the arteriolar smooth muscle responds in approximately the same way as a first order

lag which has a time constant of about ten seconds. If a bang-bang nonlinear element is followed in the forward loop of a control system by a first order lag, the net result would be to low pass filter the output from the nonlinear element.

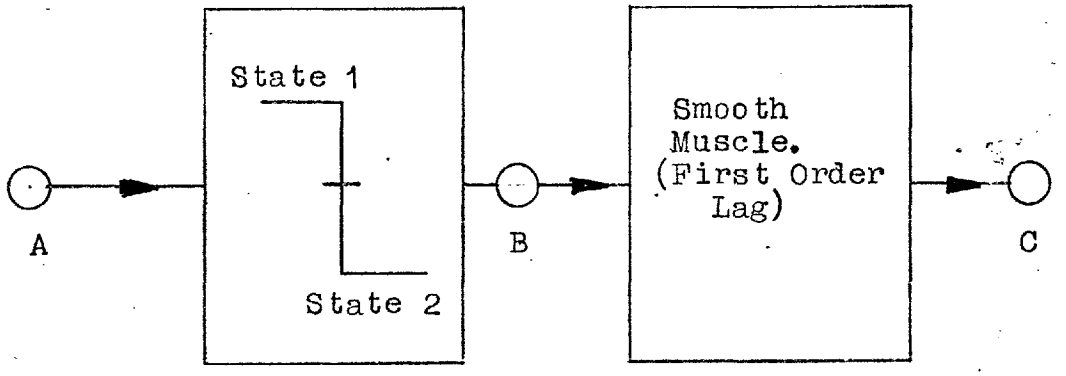


FIGURE 6.13 Node B is the location of the Efferent Signal Waveform.

The upper limit of the frequency of the output waveform at node C (figure 6.13), is dependent upon the time constant of the associated smooth muscle. The magnitude of the output waveform at node C is also limited at the ends of the range of adjustment by the maximum levels of vasoconstriction or vasodilatation in the arteriole. Within the range of vasomotor control, the degree of vasoconstriction is dependent upon the relative periods of time that the nonlinear element remains in either state.

It is interesting to reflect on a section of Burton's paper (1939), in the light of the present analysis, in which he states: "A crude analogy might be drawn with the operation of a temperature regulated water bath, where the constancy of the average temperature is accomplished by the adjustments of the durations of the 'on' and 'off' periods of the heater".

6.5 THE SIMULATION OF THE SPONTANEOUS ACTIVITY OF THE PERIPHERAL THERMAL SYSTEM BY THE COMPUTER MODEL.

The system of thermoregulation, via vasomotor activity, which has been defined, must be capable of explaining the spontaneous fluctuations in the magnitude of the muscular contractions of the cutaneous blood vessels, if it is to be consistent with the experimental findings. The system output was seen to oscillate spontaneously, when the thermal system was in the range of vasomotor control, even though no apparent thermal perturbation was present.

The most probable sources of thermal change are: variations which might occur at the skin surface due to changes in the environmental conditions, or variations in the metabolic rate which would cause the blood temperature in the hand to vary. Earlier in the manuscript, the peripheral thermoregulatory system was compared, in operation, to a van der Pol oscillatory system whose equation is:

$$\ddot{x} + \epsilon(x^2 - 1)\dot{x} + x = 0 \qquad (4.1.)$$

Dorodnicyn (1947), established that the frequency of oscillation of a van der Pol system is defined by the value of the parameter ϵ. The fact that spontaneous oscillations occur at all is a result of the system structure. As far as peripheral thermo-

regulation is concerned, the frequency of oscillation would appear to be determined by two factors: first, the largely invariant components of the system, for example the properties of bone and tissue; and secondly thermal variations. If therefore, the thermal inputs are kept constant, the system should, after the starting transients have subsided, oscillate at a relatively stable frequency.

The hypothesis that temperature is the controlled variable of the peripheral thermal system was found to be inconsistent with the basic theory of negative feedback control. If the alternative hypothesis that temperature gradient is the controlled variable is to be substantiated, then in addition to oscillations at a relatively stable frequency, the output data from the simulation must contain evidence that the system is exhibiting a controlling influence on the thermal situation.

Figure 6.14 illustrates the efferent signal waveform, referred to in figure 6.13, from the computer simulation, with the skin temperature held constant at 33°C. When the starting transients have subsided, the efferent signal comprises an oscillation with relatively stable frequency components. Figure 6.14(a) shows the actual efferent signal, while figure 6.14(b) is the

low pass filtered version. The system therefore oscillates spontaneously in the absence of a thermal perturbation. Figure 6.15(a) illustrates the monitored thermal gradient. Figure 6.15(b) is the low pass filtered version, and it is apparent that the thermal gradient is fluctuating about the set value. The system is therefore seeking to control the thermal situation.

If one looks at this efferent signal in the frequency domain (figure 6.16), it is apparent that under the conditions of spontaneous oscillation, with the skin temperature held at its neutral value of $33^{o}C$, there was one dominant component at about 0.038 Hz.

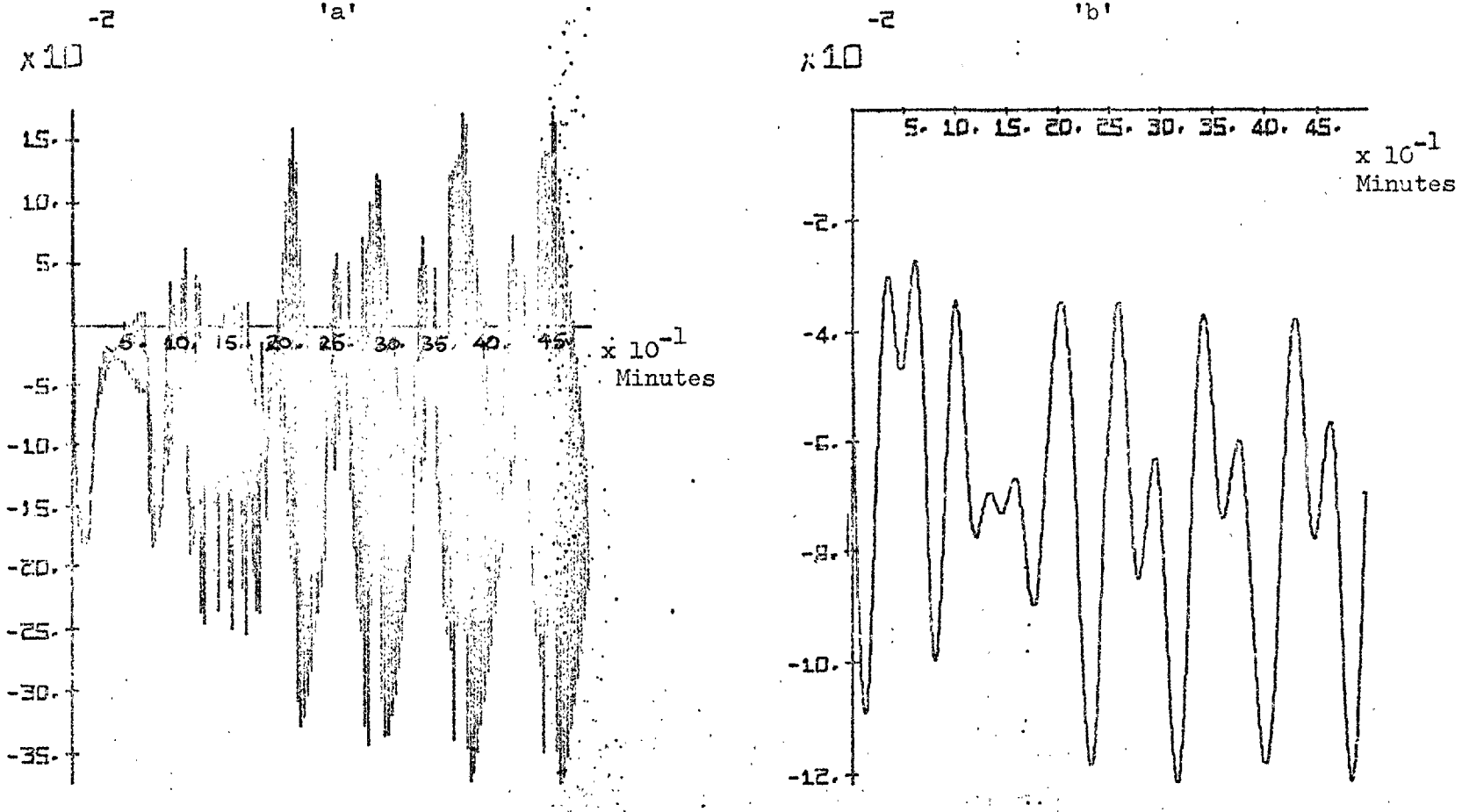
Even though there may be only slight variations in the temperature at the skin surface, it is extremely unlikely, because of the complex metabolic reactions within the human body, that the blood temperature within the vessels of the hand, remains constant for even a short period of time. If therefore, the blood temperature within these vessels is not held constant, but allowed to vary in a pre-determined manner, in this case $0.5^{o}C$ (six second periodicity), the waveforms of both the efferent signal, and the temperature gradient are seen to be

radically different from those of the steady state case. Figures 6.17 and 6.18, illustrate the efferent signal waveform and that of the thermal gradient; diagram b being the low pass filtered version in each case.

The response of the system in the frequency domain is illustrated in figures 6.19 and 6.20 (efferent signal and temperature gradient, respectively). These diagrams indicate that the single dominant component of figure 6.16 has been replaced by two large components at frequencies of 0.027 and 0.048 Hz. The component at a frequency of 0.0167 Hz is the thermal fluctuation in the blood temperature.

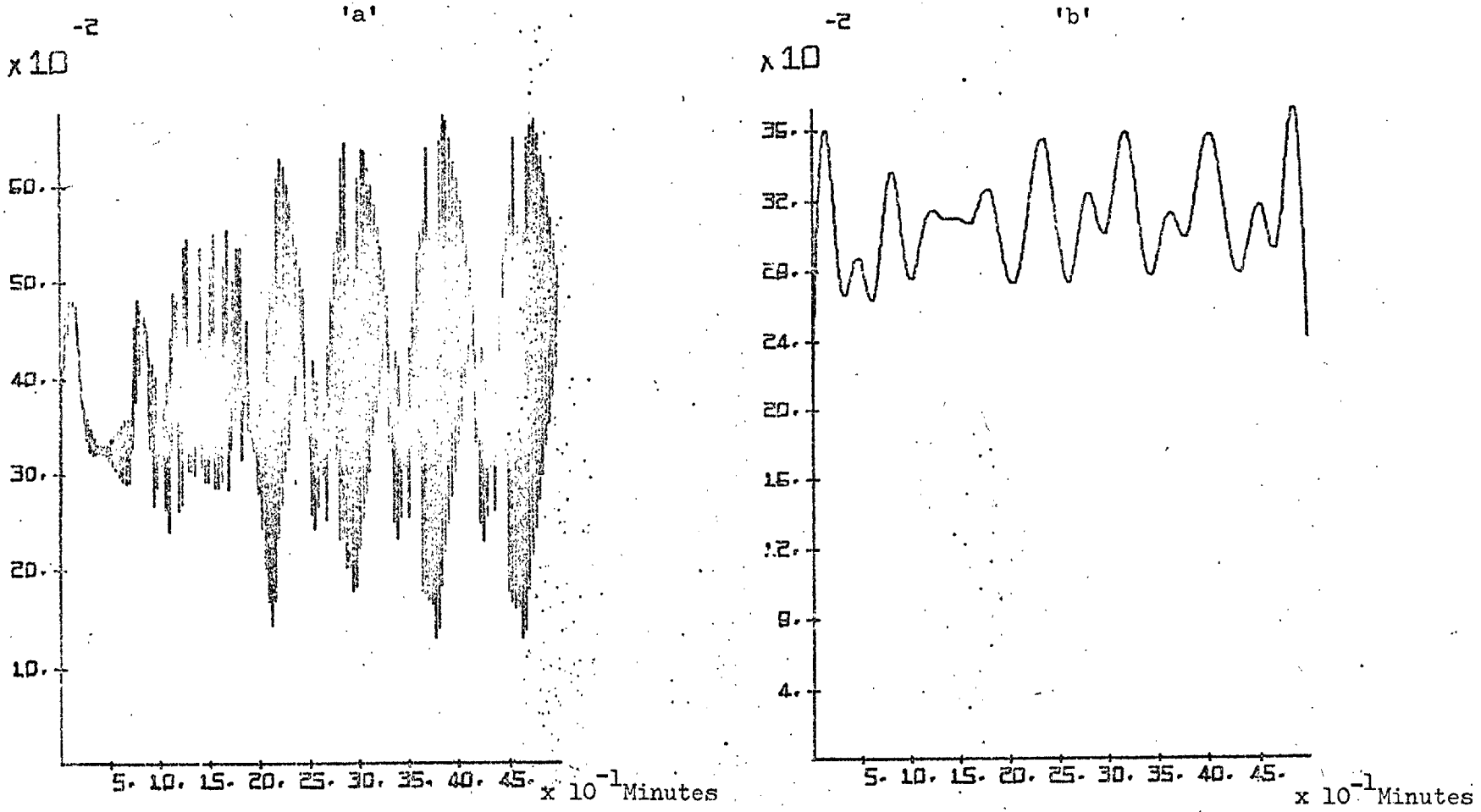
However, with the physical system in a quiescent state, fluctuations in blood temperature within the vessels of the hand would be far more likely to be of the order of $0.1^{o}C$. The power spectrum of efferent signal and temperature gradient under these conditions, illustrate that because of the reduced amplitude of the internal variations in temperature, the frequency component which represents the natural frequency of oscillation of the system, is no longer suppressed. If one compares figures 6.21 and 6.19, it is apparent that the two dominant frequency components at 0.027 and 0.048 Hz are present in both diagrams. The latter however, also exhibits the natural frequency component.

FIGURE 6.14



DIAGRAMS ILLUSTRATING EFFERENT SIGNAL PLOTTED AGAINST TIME.

FIGURE 6.15



DIAGRAMS ILLUSTRATING TEMPERATURE GRADIENT PLOTTED AGAINST TIME.

FIGURE 6.16- THE POWER SPECTRUM OF THE EFFERENT SIGNAL WITH A STEADY SKIN TEMPERATURE OF 33°C.

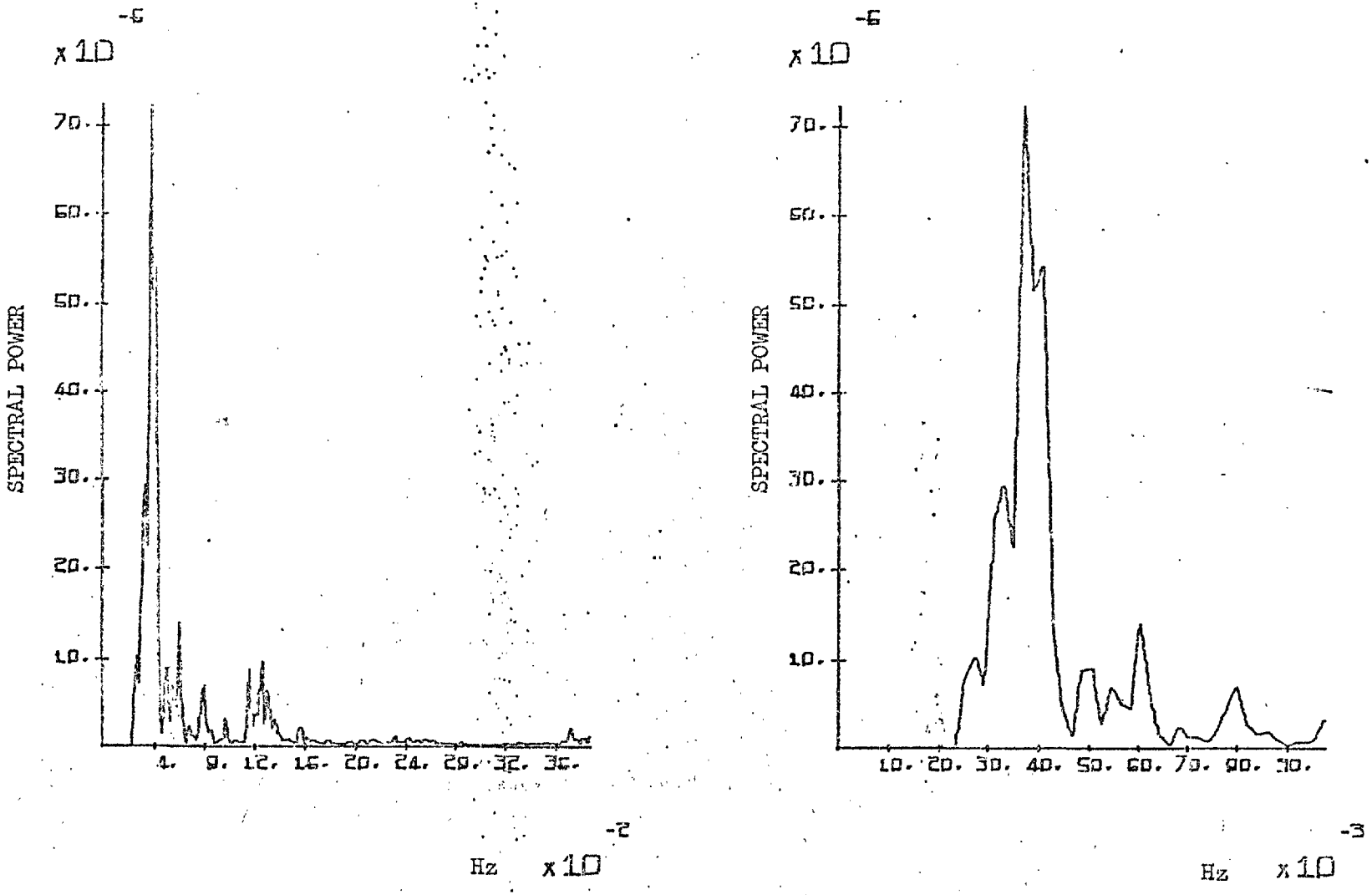
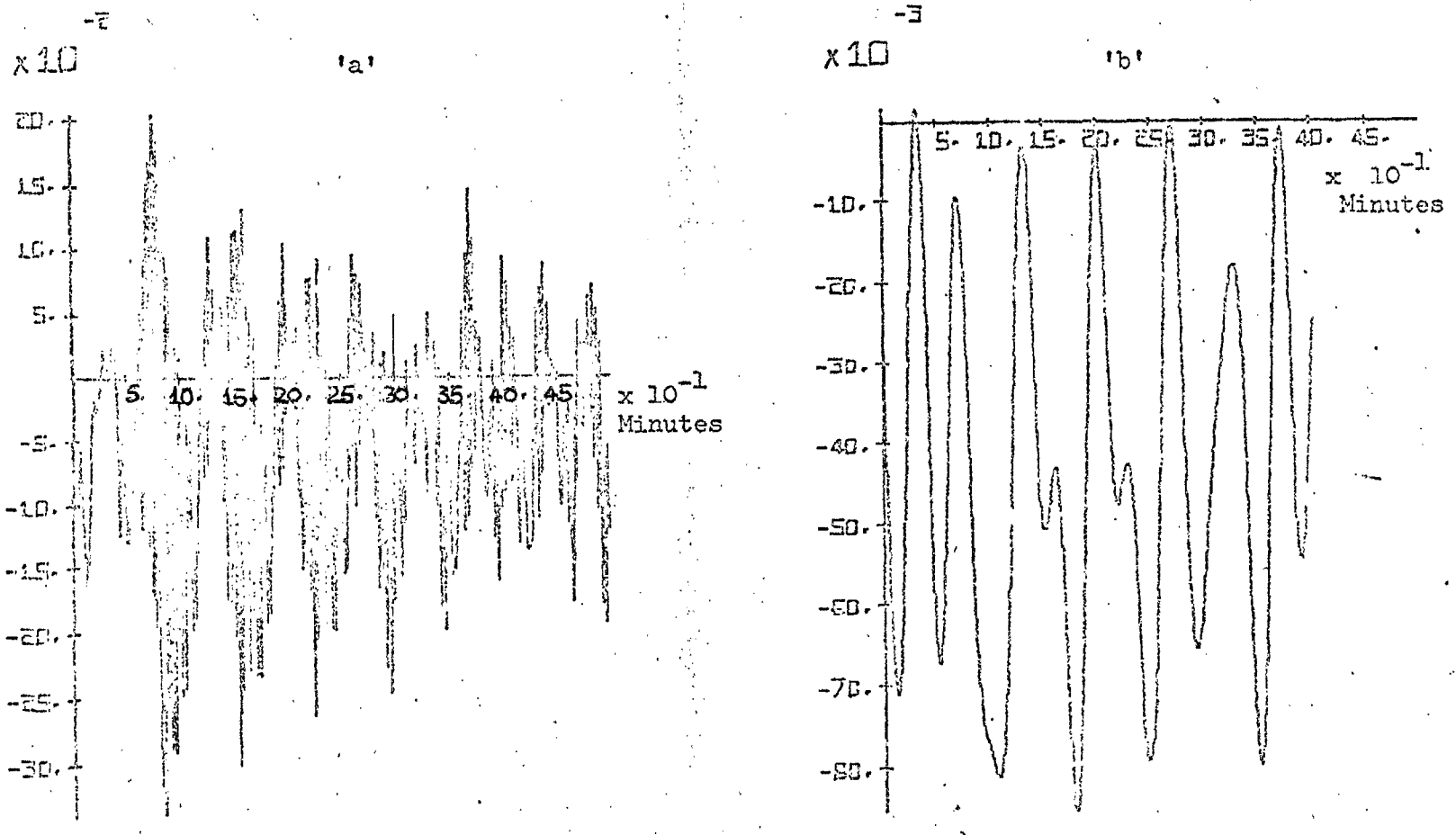
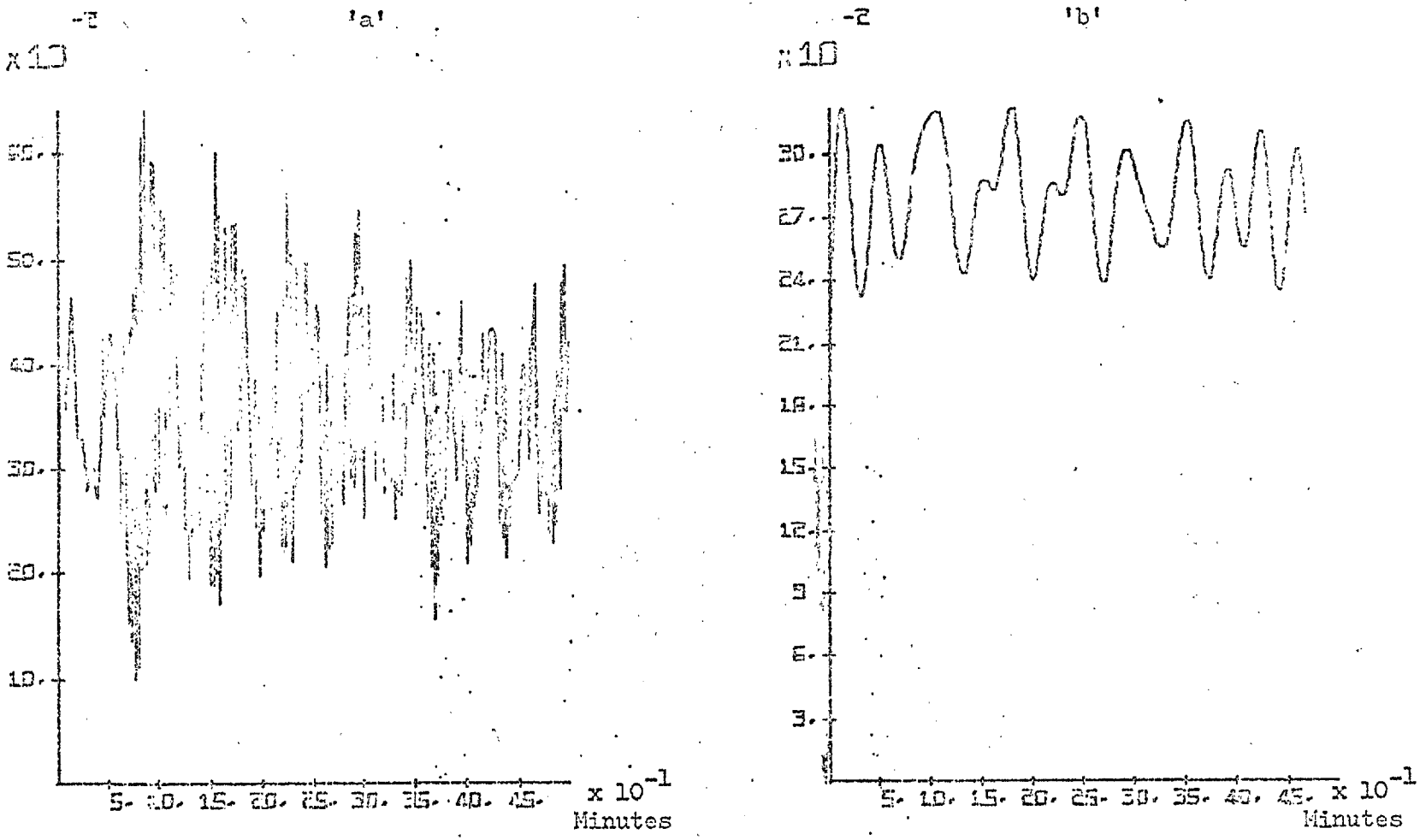


Figure 6.17



DIAGRAMS ILLUSTRATING EFFERENT SIGNAL PLOTTED AGAINST TIME WITH VARIATIONS IN BLOOD TEMPERATURE.

Figure 6.18



DIAGRAMS ILLUSTRATING TEMPERATURE GRADIENT PLOTTED AGAINST TIME WITH VARIATIONS IN BLOOD TEMPERATURE.

The response of the system to changes in vascular blood temperature was subsequently investigated by simulating the conditions within the hand for temperature changes of twelve, sixteen, and twenty seconds periodicity. Figures 6.23-6.27, illustrate the corresponding power spectra of efferent signal and temperature gradient. Under each set of conditions, the temperature of the blood varied between 34.9 and 35.0°C. Referring to figure b in each case, the power spectra comprise of a number of frequency components which vary in periodicity for different fluctuation frequencies of the vascular blood temperature. Figures 6.28 and 6.29, represent the efferent signal, and temperature gradient waveforms when the variation in blood temperature is 0.2°C (with a periodicity of twenty seconds).

The spontaneous activity of the system as simulated by the computer model, enables a greater understanding of the system dynamics.

Minorsky (1962), describes the effects of external perturbations on the output of non-linear oscillatory systems. To recapitulate: if the frequency of any stimulus, applied to the system, lies outside the range of entrainment, one observes a complicated spectral interaction, where the oscillation of the

FIGURE 6.19 - EFFERENT SIGNAL - BLOOD TEMPERATURE STIMULUS - 6 SECOND PERIODICITY - 34.5/35°C.

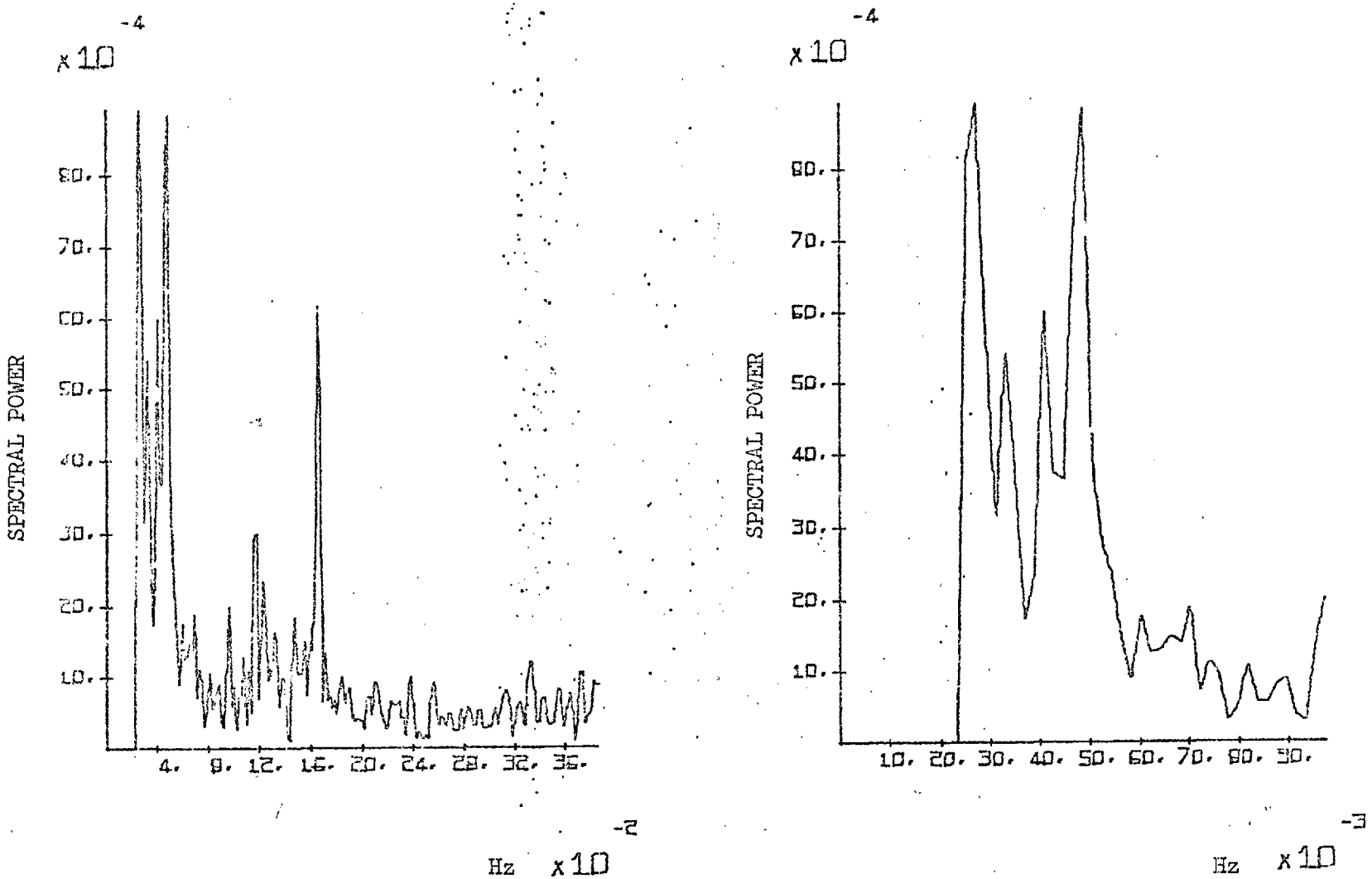
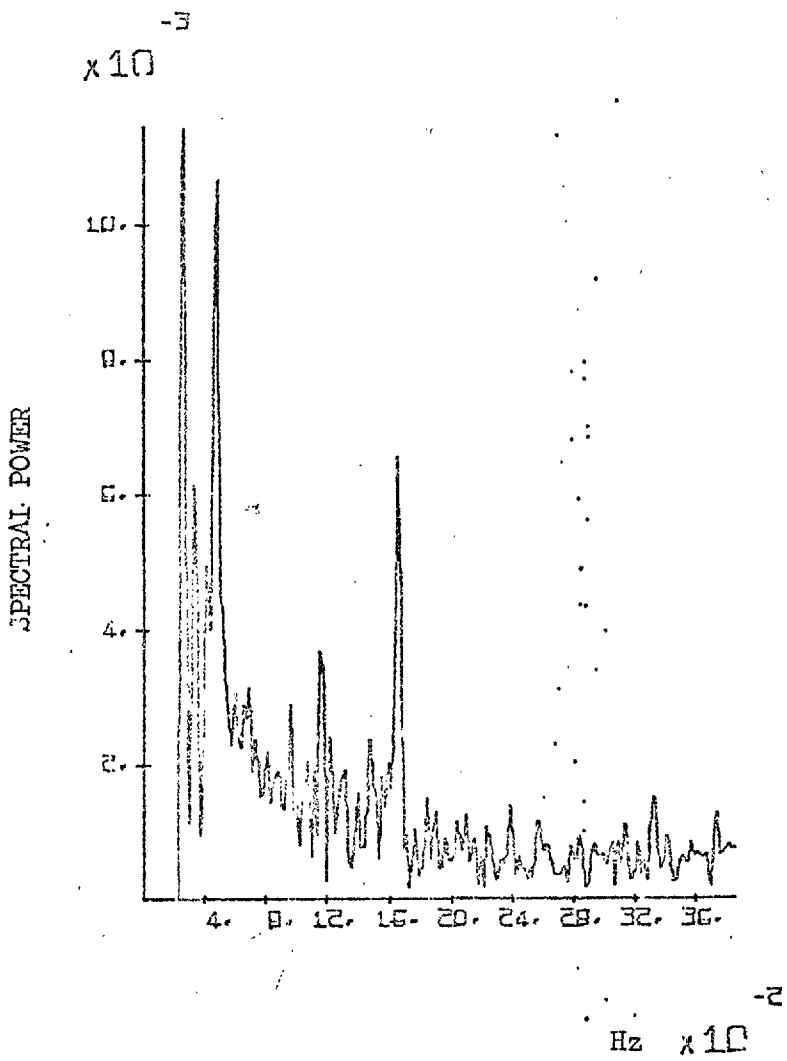


FIGURE 6.20 - TEMPERATURE GRADIENT - BLOOD TEMPERATURE STIMULUS - 6 SECOND PERIODICITY - 34.5/35°C.



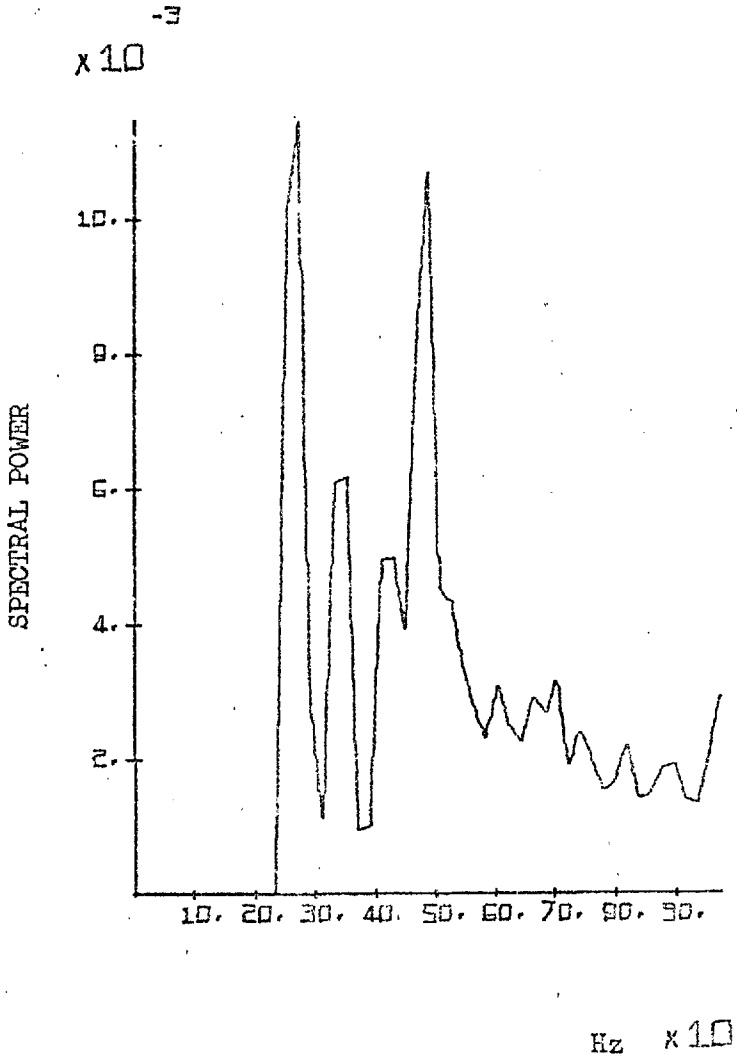


FIGURE 6.21 - EFFERENT SIGNAL - BLOOD TEMPERATURE STIMULUS - 6 SECOND PERIODICITY - 34.9/35.0°C.

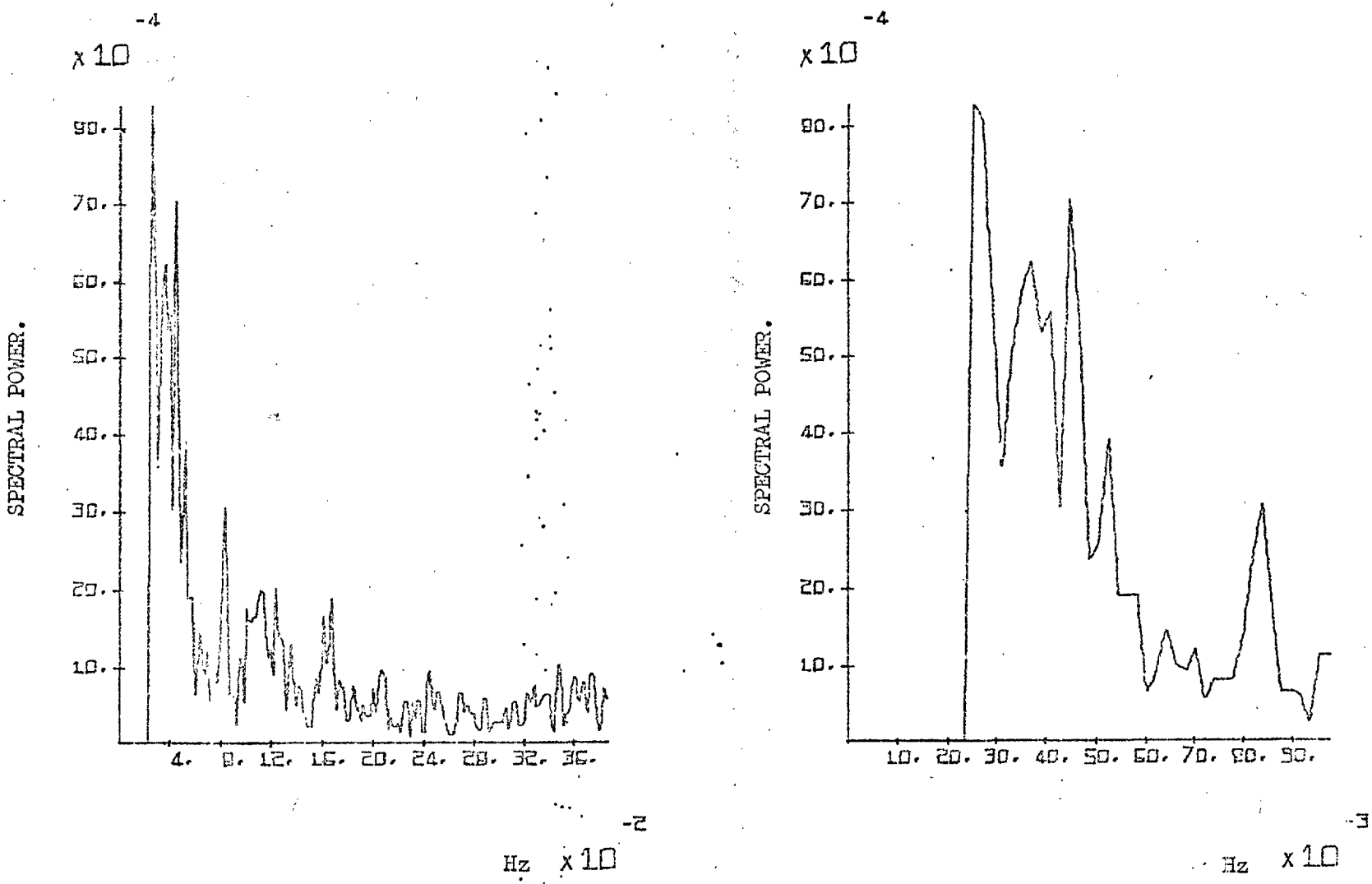
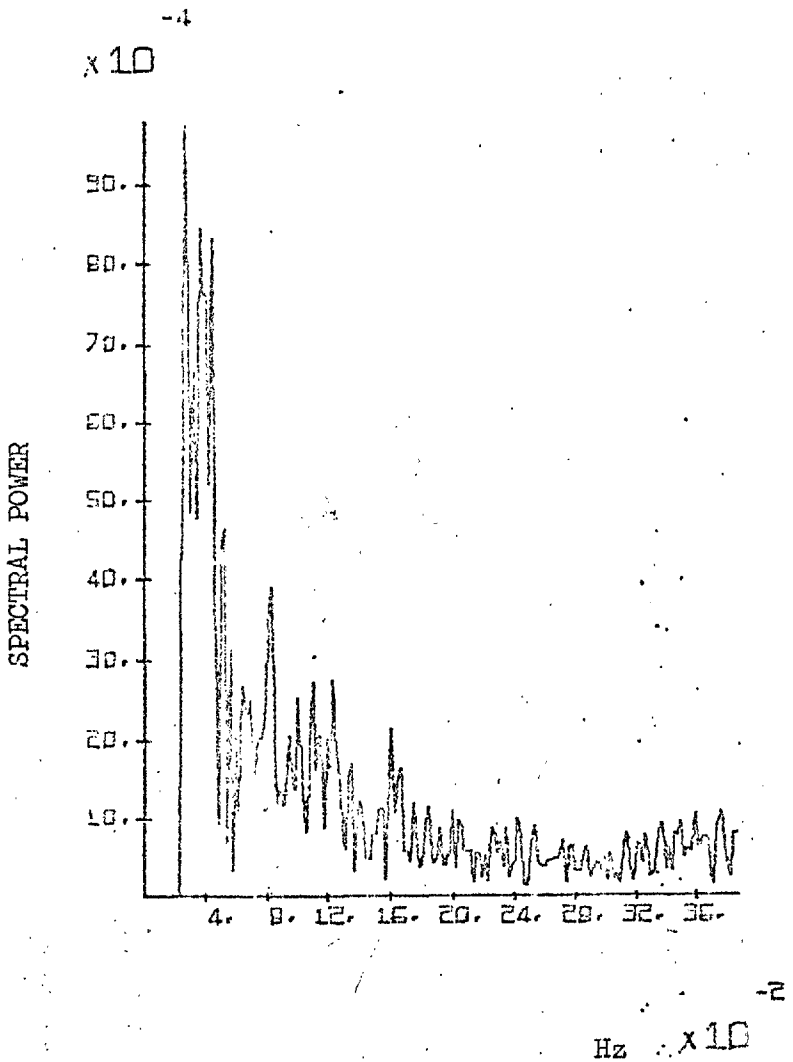


FIGURE 6.22 - TEMPERATURE GRADIENT - BLOOD TEMPERATURE STIMULUS - 6 SECOND PERIODICITY - 34.9/35.0°C.



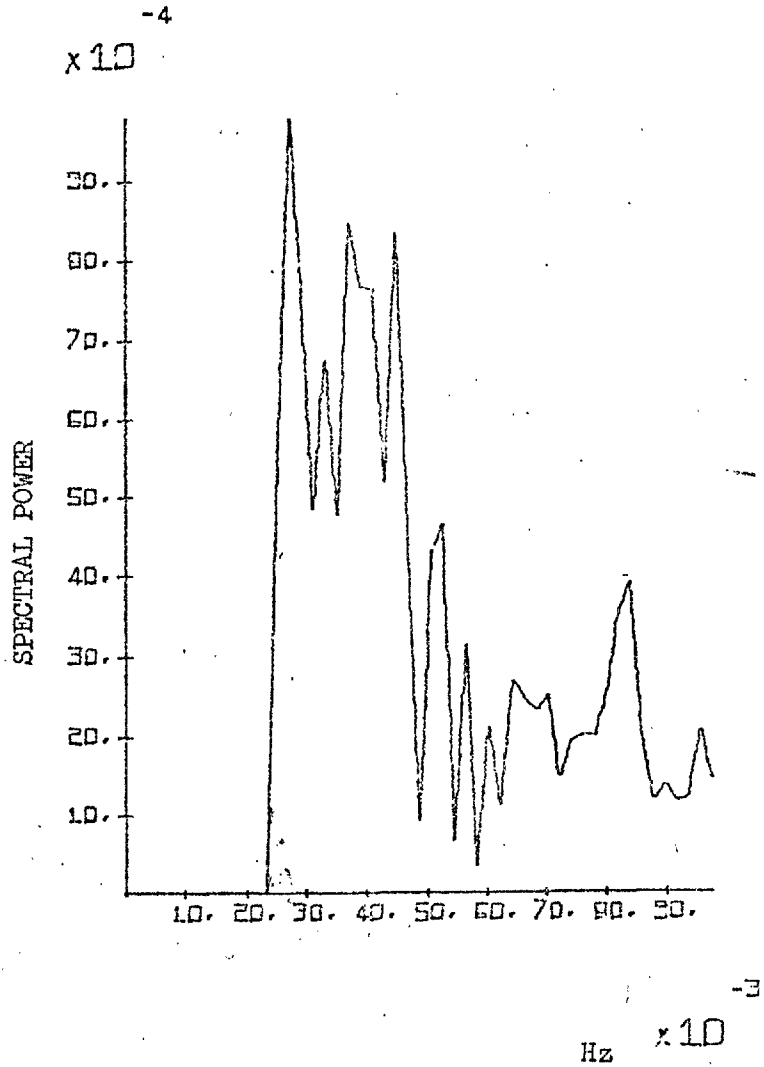


FIGURE 6.23 - EFFERENT SIGNAL - BLOOD TEMPERATURE STIMULUS - 12 SECOND PERIODICITY- 34.9/35.0°C

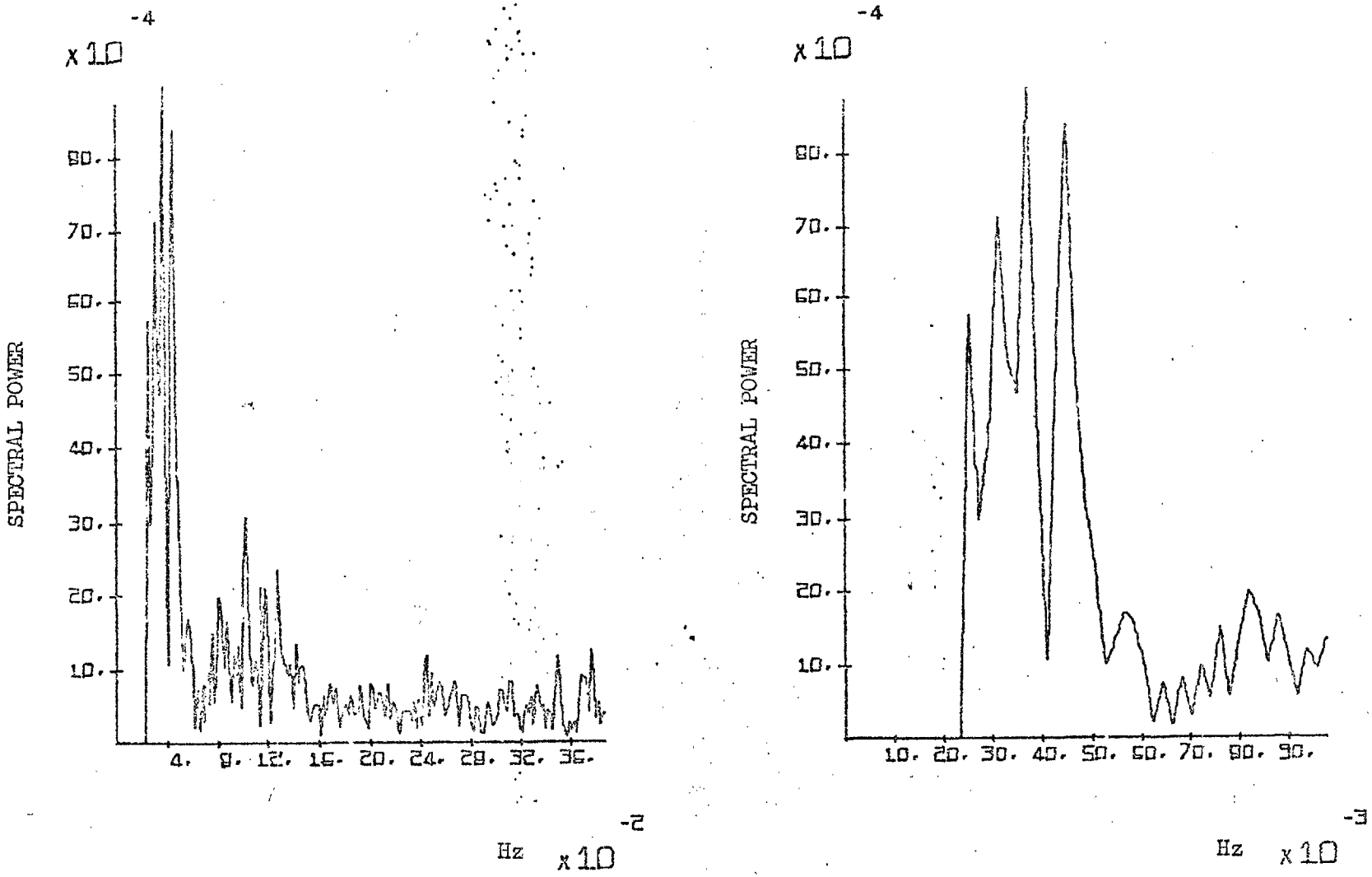


FIGURE 6.24 - TEMPERATURE GRADIENT - BLOOD TEMPERATURE STIMULUS - 12 SECOND PERIODICITY - 34.9/35°C.

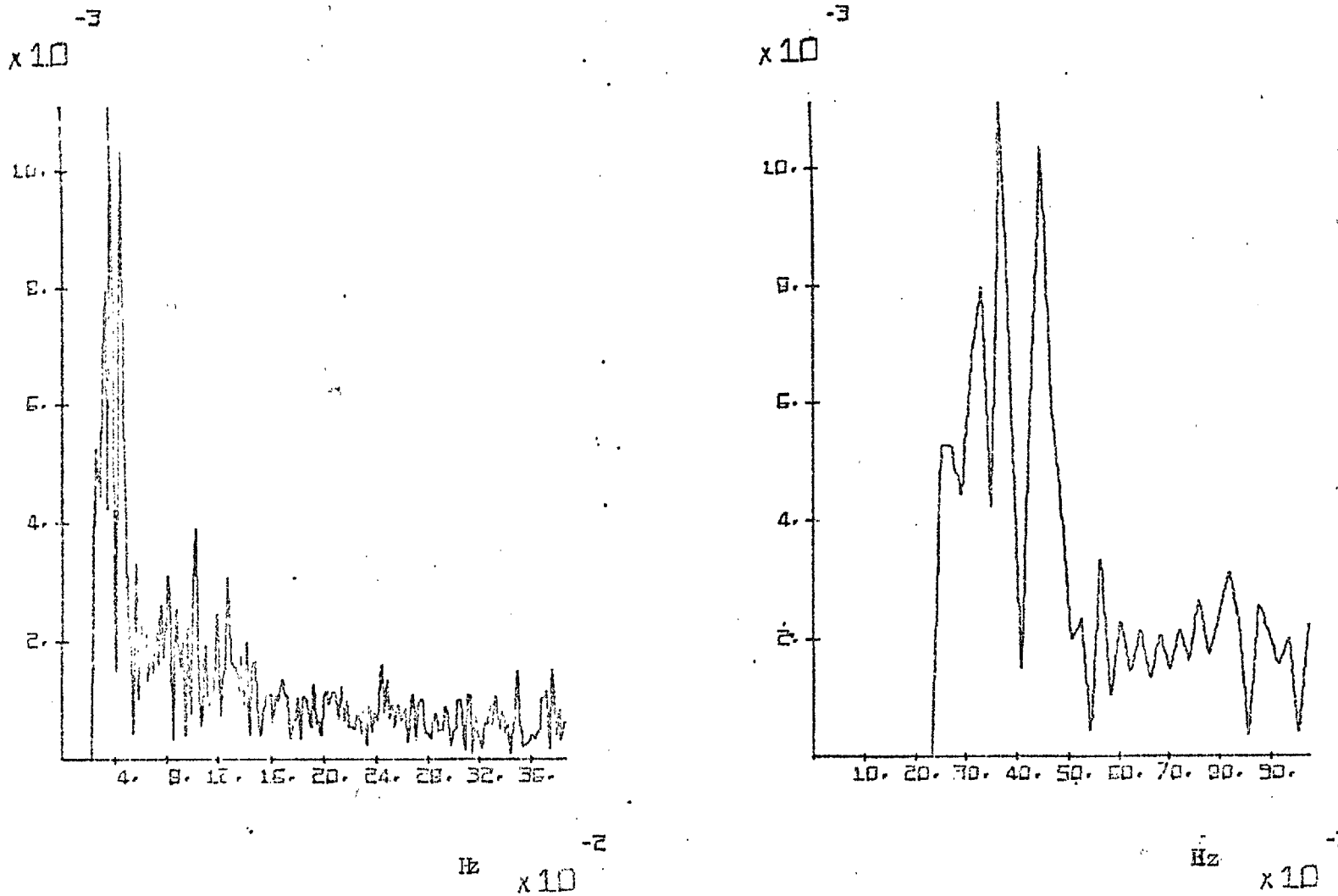


FIGURE 6.25 - EFFERENT SIGNAL - BLOOD TEMPERATURE STIMULUS - 16 SECOND PERIODICITY - 34.9/35.0°C.

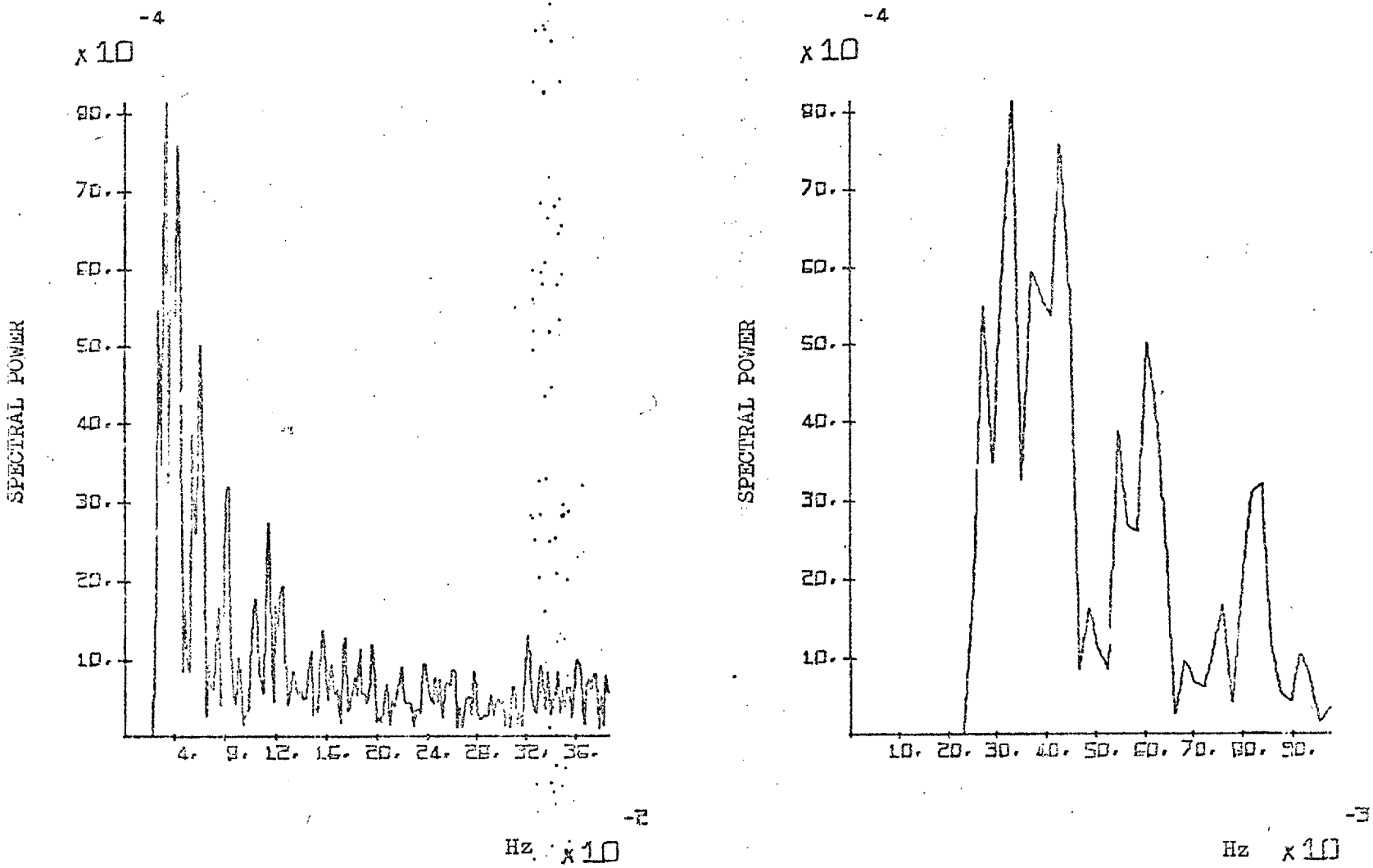


FIGURE 6.26 - TEMPERATURE GRADIENT.- BLOOD TEMPERATURE STIMULUS - 16 SECOND PERIODICITY - 34.9/35.0°C.

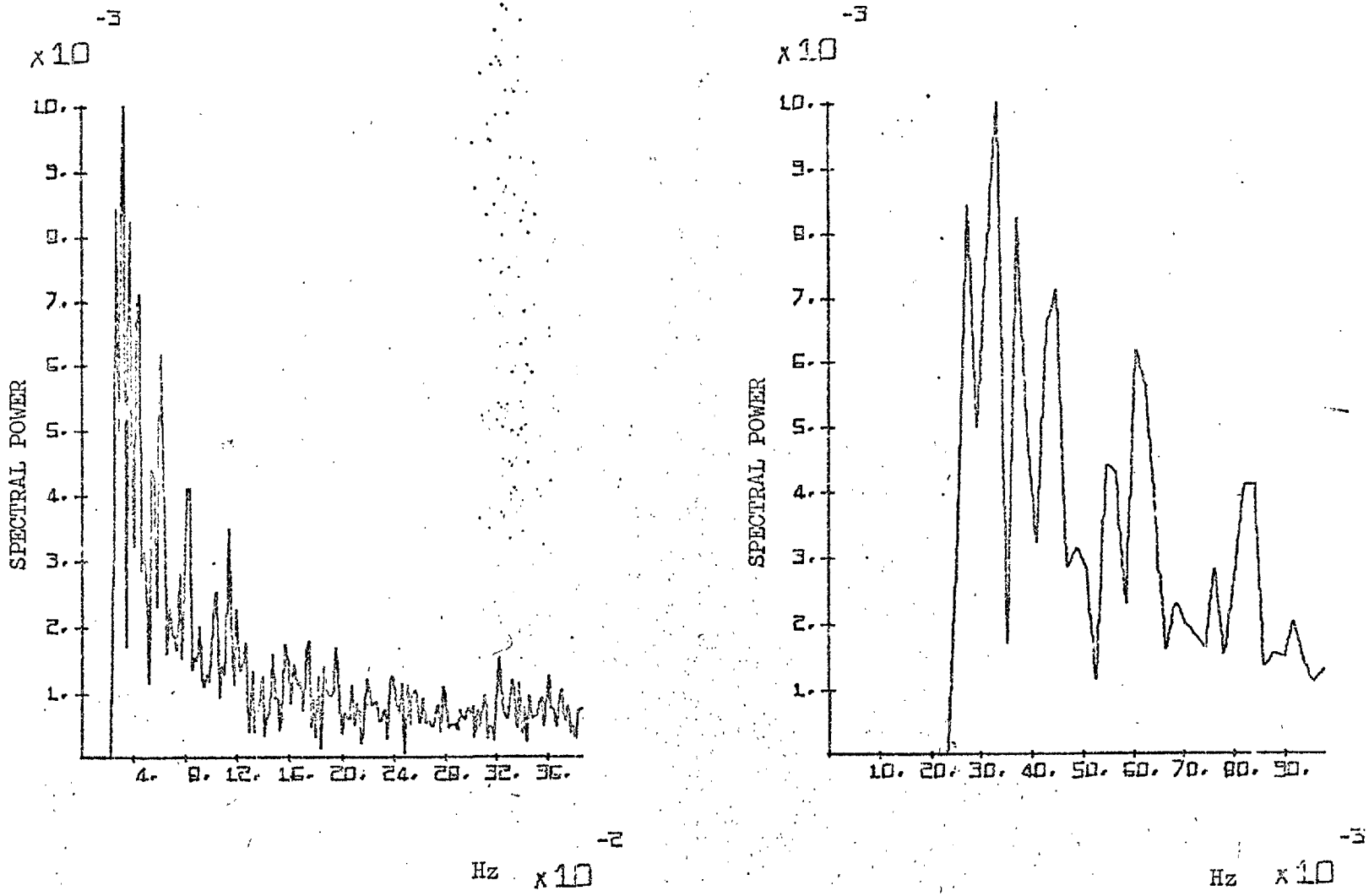
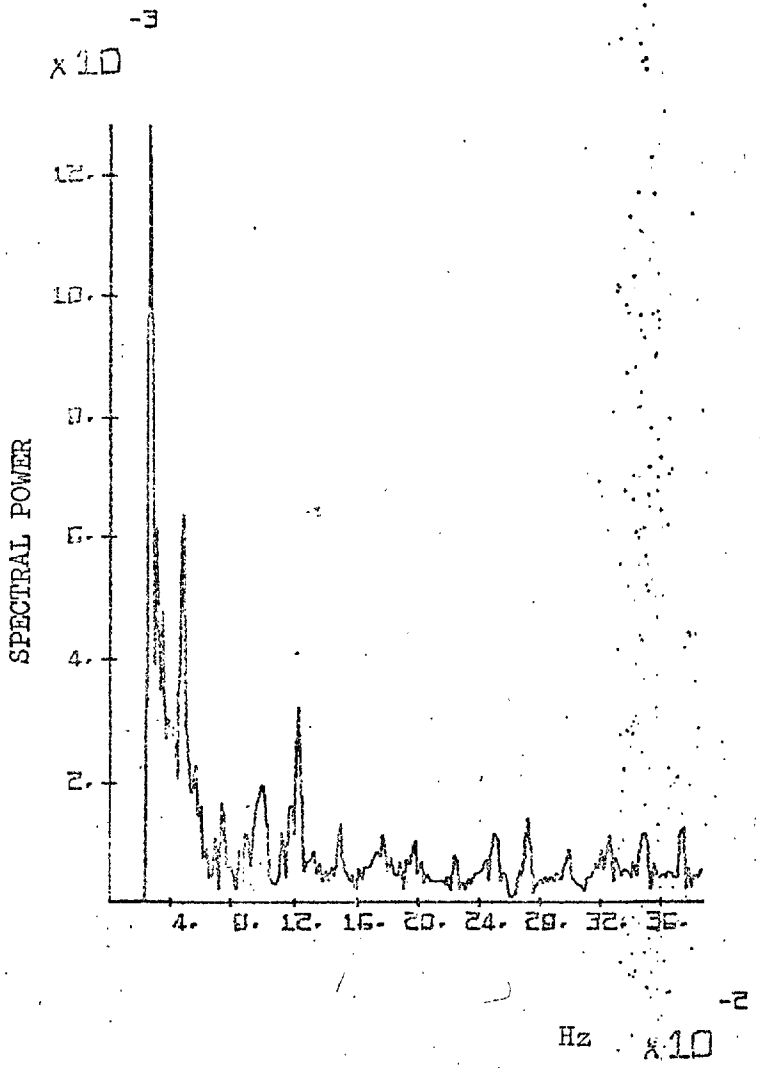


FIGURE 6.27 - EFFERENT SIGNAL - BLOOD TEMPERATURE STIMULUS - 20 SECOND PERIODICITY - 34.9/35.0°C.



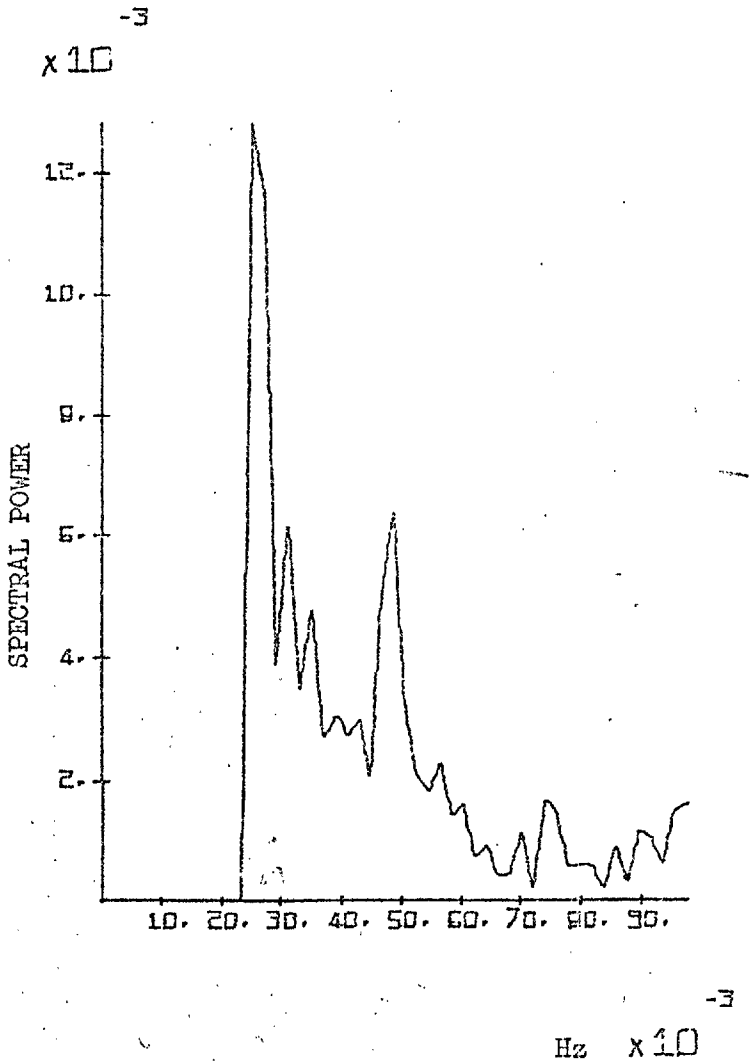
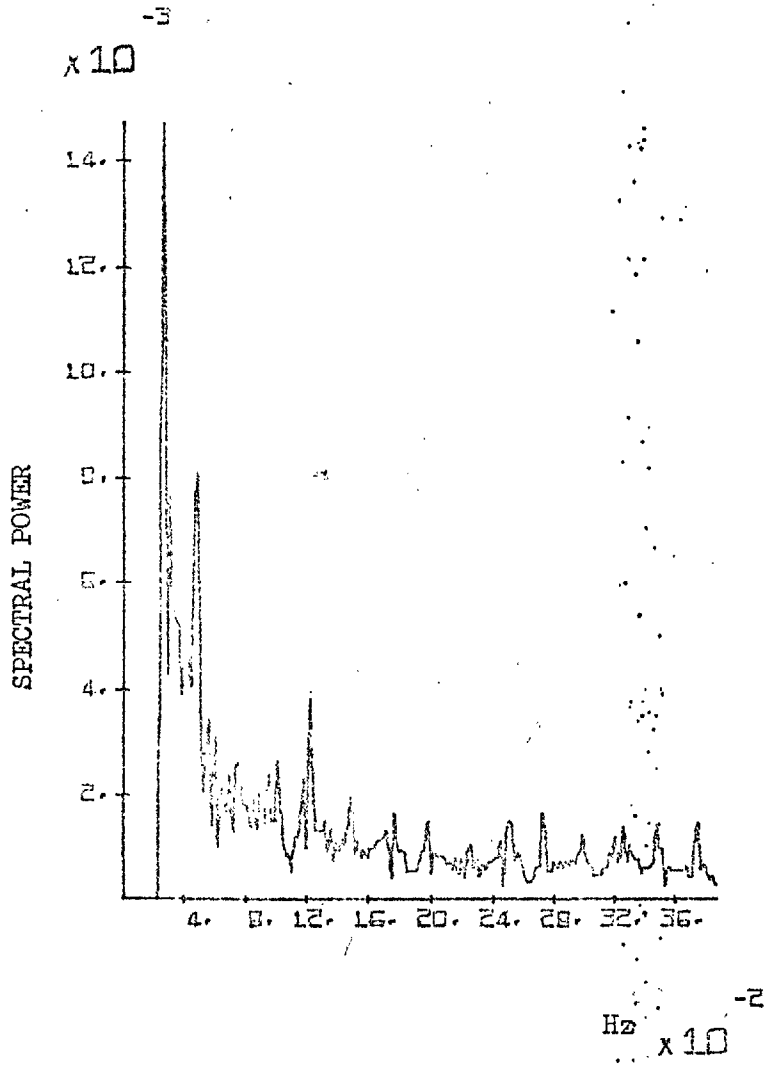


FIGURE 6.28 - TEMPERATURE GRADIENT - BLOOD TEMPERATURE STIMULUS - 20 SECOND PERIODICITY - 34.9/35.0°C.



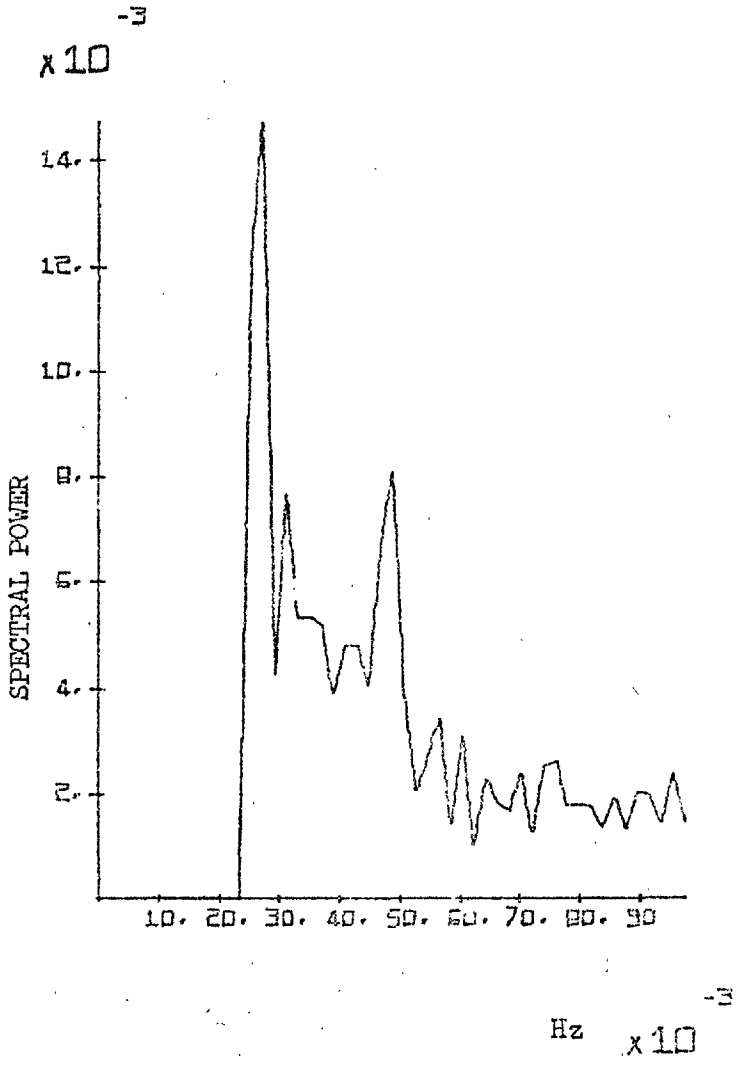


FIGURE 6.29 - EFFERENT SIGNAL - BLOOD TEMPERATURE STIMULUS - 20 SECOND PERIODICITY- 34.8/35.0°C.

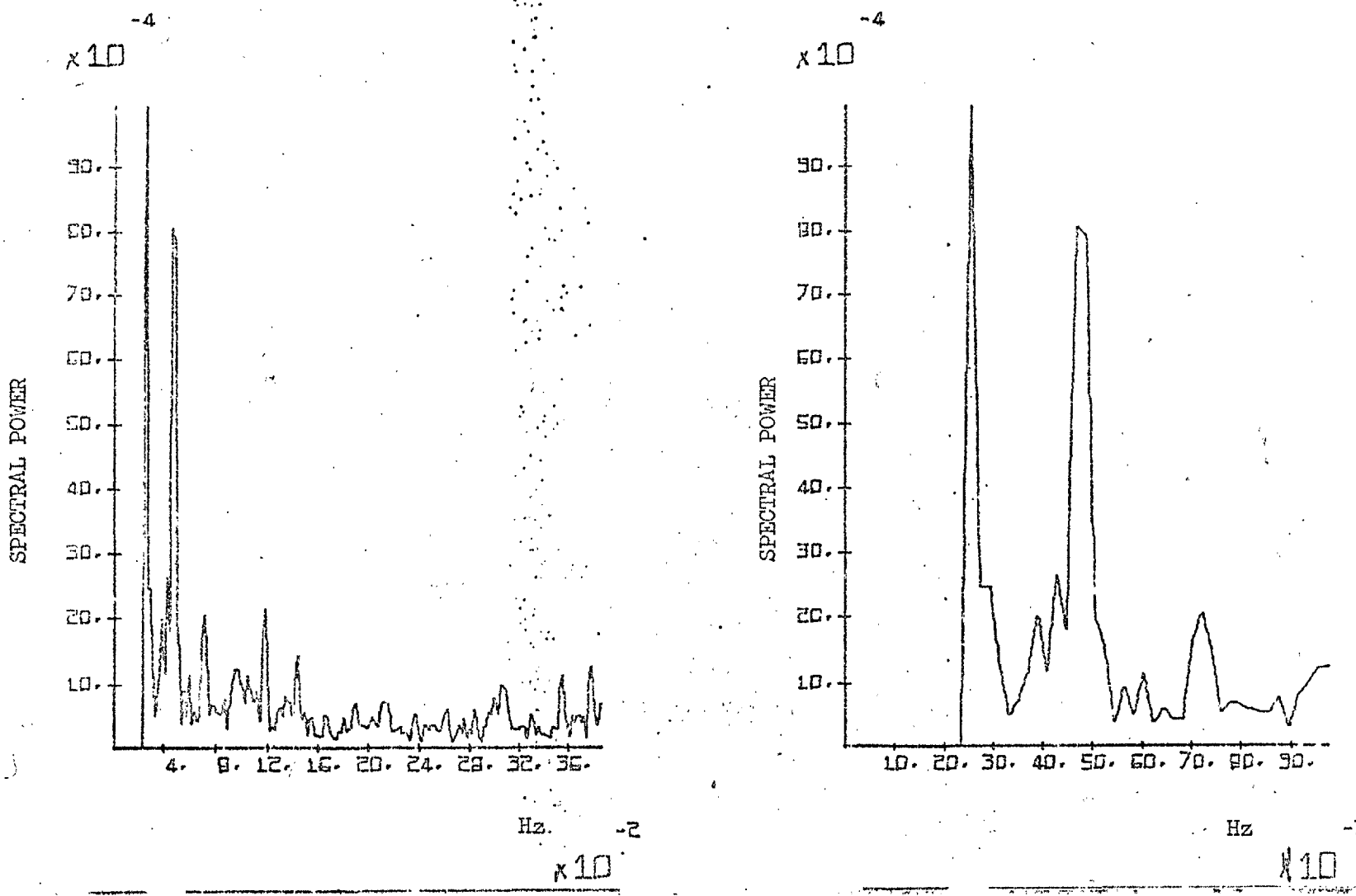
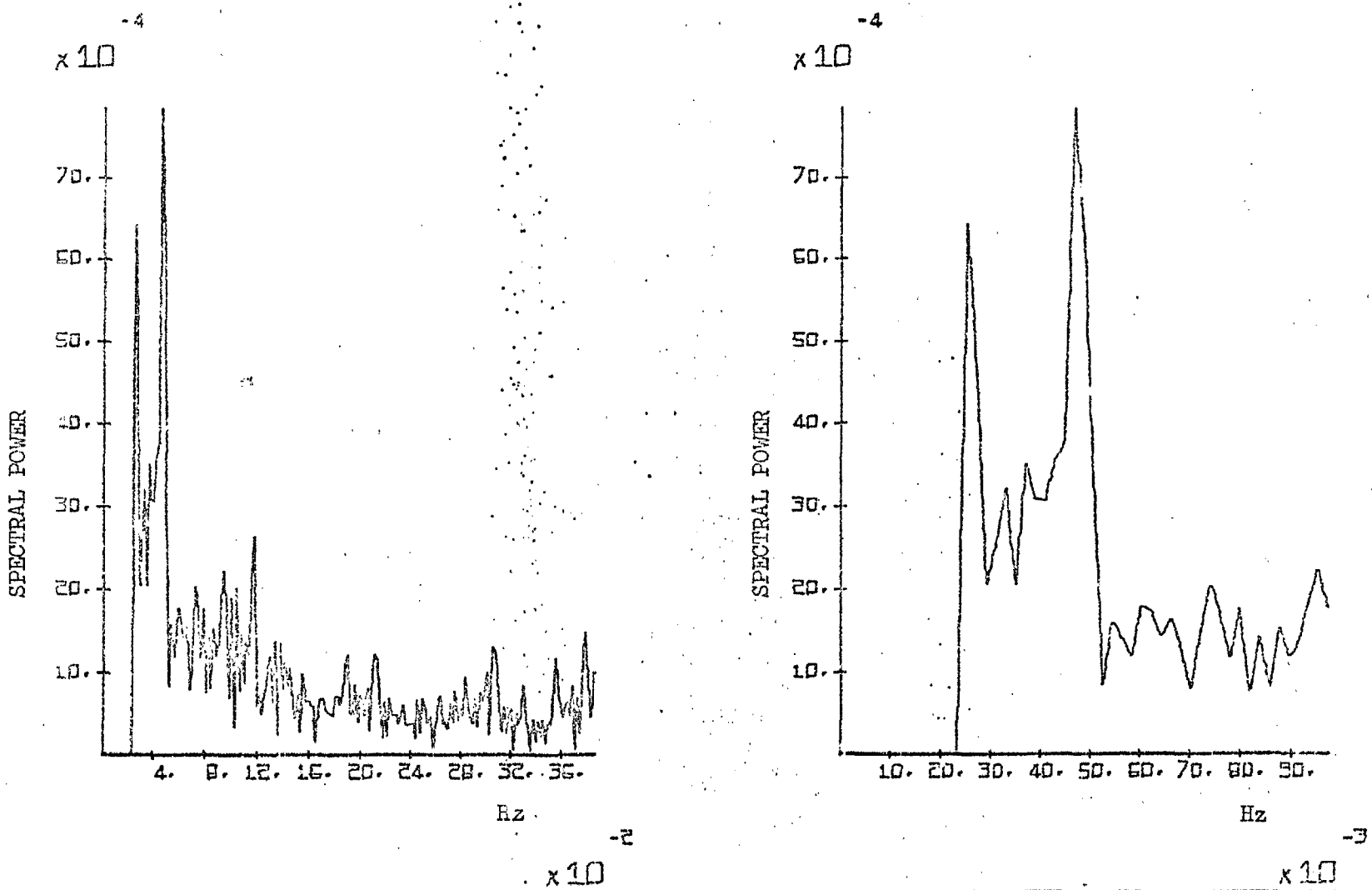


FIGURE 6.30 - TEMPERATURE GRADIENT - BLOOD TEMPERATURE STIMULUS - 20 SECOND PERIODICITY - 34.8/35.0°C.



system at its natural frequency and the stimulus interact. Referring to figure 4.6, it is apparent that frequency entrainment of the system is a function of both the stimulus, magnitude and frequency. In simple terms, as the stimulus magnitude increases, the frequency range of entrainment also increases.

When the vascular blood temperature is allowed to fluctuate, the effect is not frequency entrainment of the system, because the magnitude of these fluctuations is small. Their effect on the system is rather, one of producing a spectral interaction phenomenon. This explains why the natural frequency component of the system, illustrated in figure 6.16, is replaced by a number of components at different frequencies, depending upon the fluctuation frequency of the blood temperature within the vessels of the hand.

Under the conditions of the spontaneous blood flow experiment, the periodicity and magnitude of the variations in blood temperature within the hand tended to be of a more variable nature. Therefore, over the period of the experiment (ten minutes), the frequency components associated with temperature regulation (figures 3.4 and 3.5) would result from interactive effects produced by blood temperature fluctuations of

differing periodicity.

The Effect of an External Thermal Stimulus on the Spontaneous Activity.

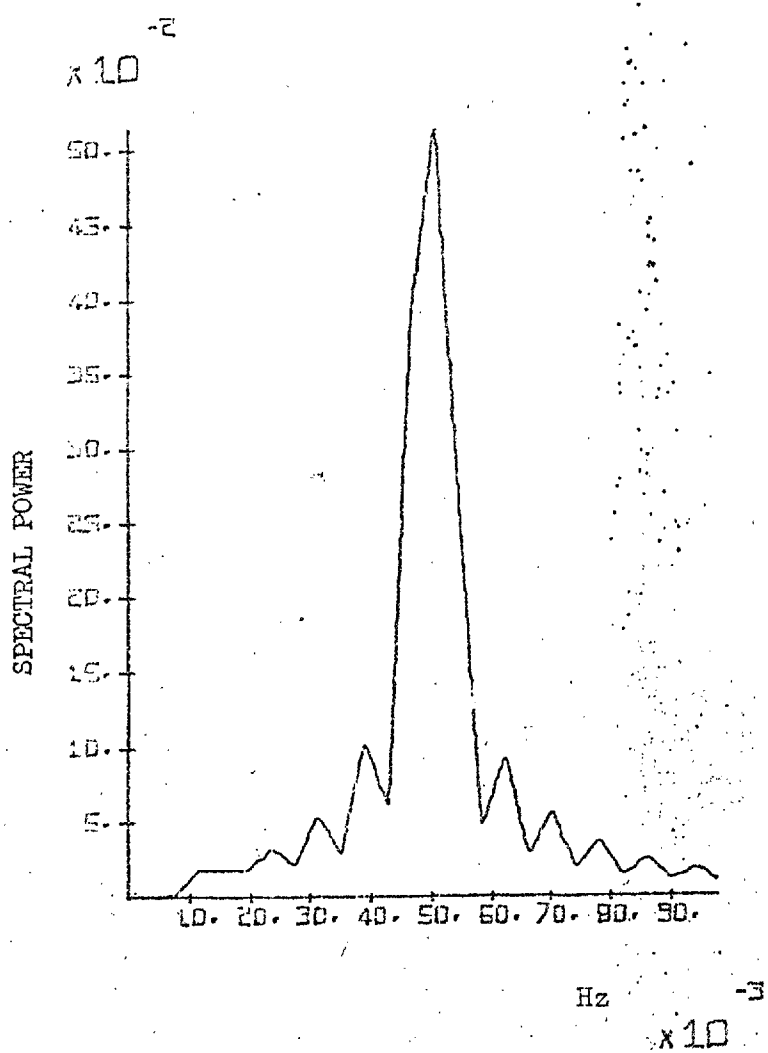
The nature of the spontaneous activity of the peripheral thermal system would seem to result from fluctuations in blood temperature within the vessels of the hand. The issue as yet unresolved is the effect, as far as the simulation is concerned, of applying a perturbation equivalent to that used in the first series of entrainment experiments.

Under the experimental conditions, the presumed fluctuations in the blood temperature are still present, but in addition an external thermal stimulus is applied. These conditions were incorporated in the computer model for the range of the spontaneous activity which had already been simulated. In each case the spontaneous activity was replaced by a single dominant component at a stimulus frequency (twenty seconds periodicity). The results indicate that the system can be entrained over the whole range of spontaneous activity by a suitable external stimulus. An example of the power spectra obtained from the model under these conditions is illustrated in figure 6.31.

The second series of entrainment experiments (reported in chapter three), were designed to determine

FIGURE 6.31

EFFERENT SIGNAL.



TEMPERATURE GRADIENT.

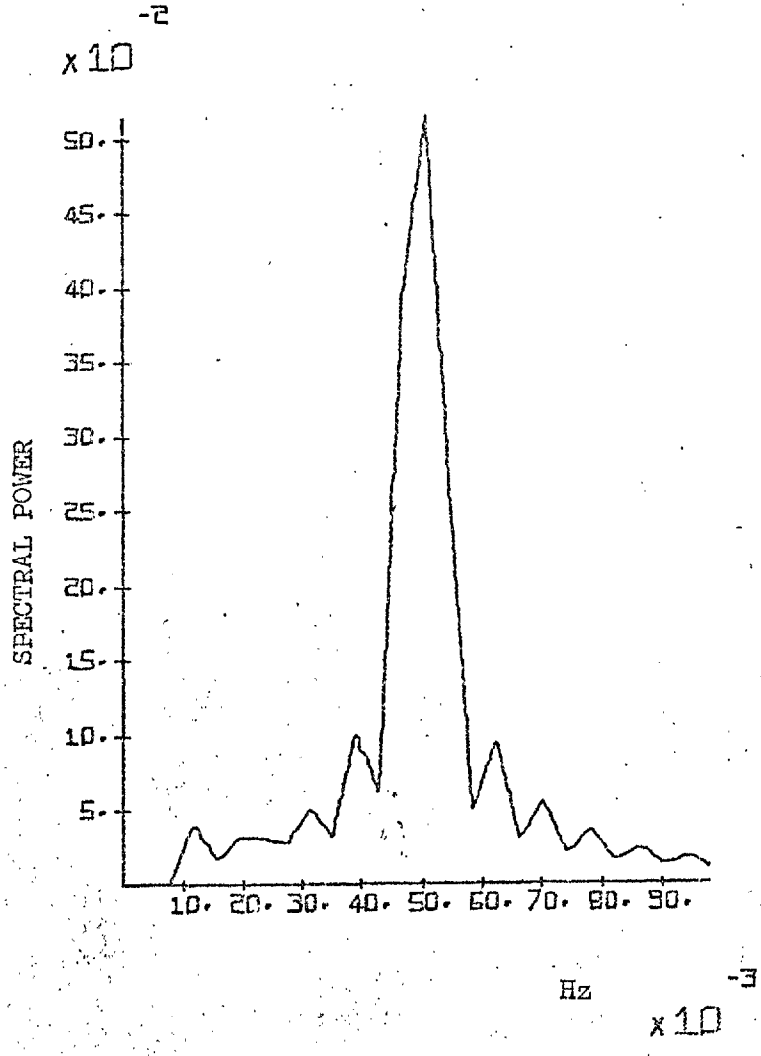


FIGURE 6.32 - EFFERENT SIGNAL (a) AND TEMPERATURE GRADIENT (b) - 40 SECOND PERIODICITY STIMULUS.

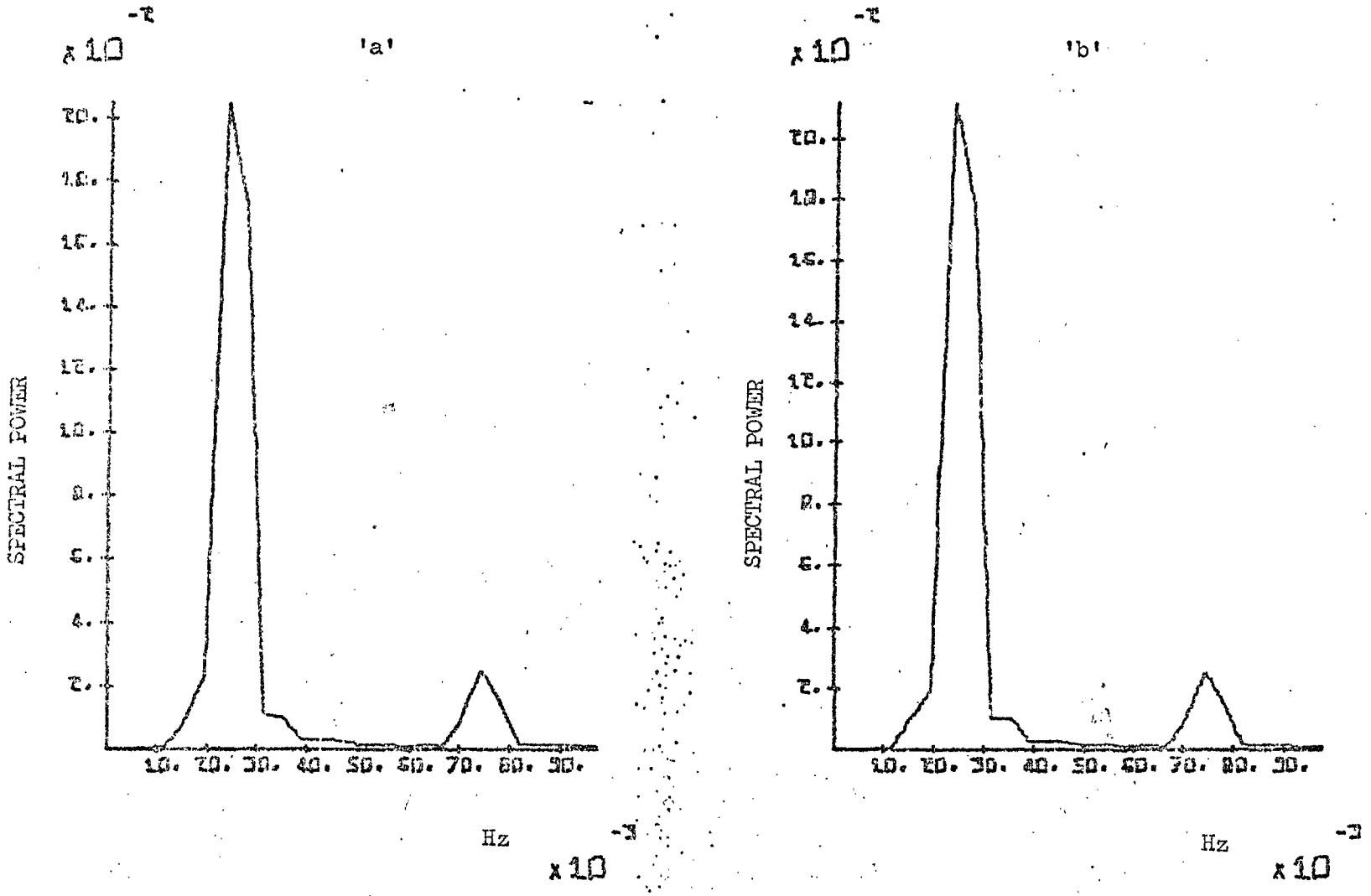


FIGURE 6.33 - EFFERENT SIGNAL (a) AND TEMPERATURE GRADIENT (b) - 60 SECOND PERIODICITY STIMULUS.

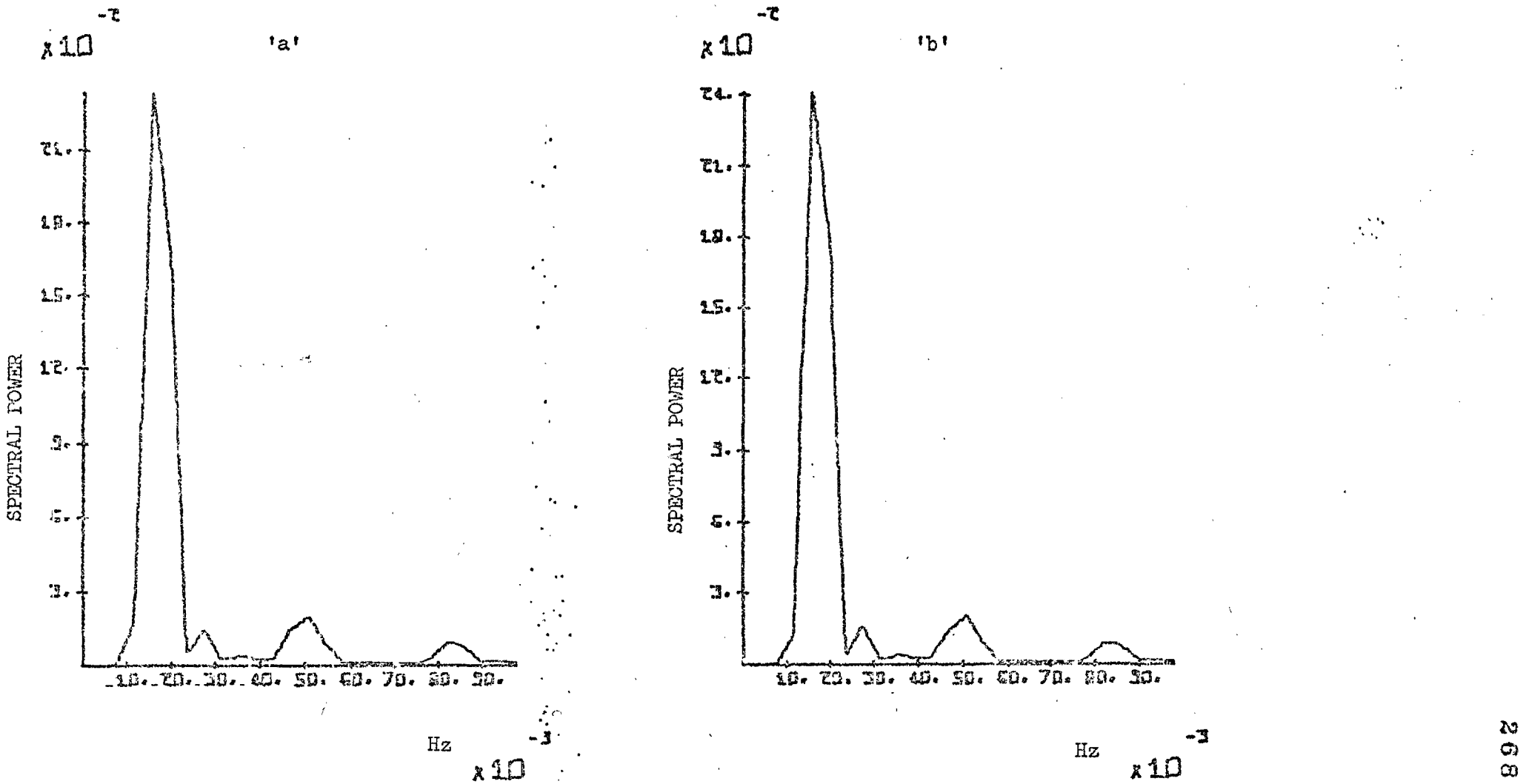


FIGURE 6.34 - EFFERENT SIGNAL (a) AND TEMPERATURE GRADIENT (b) - 80 SECOND PERIODICITY STIMULUS.

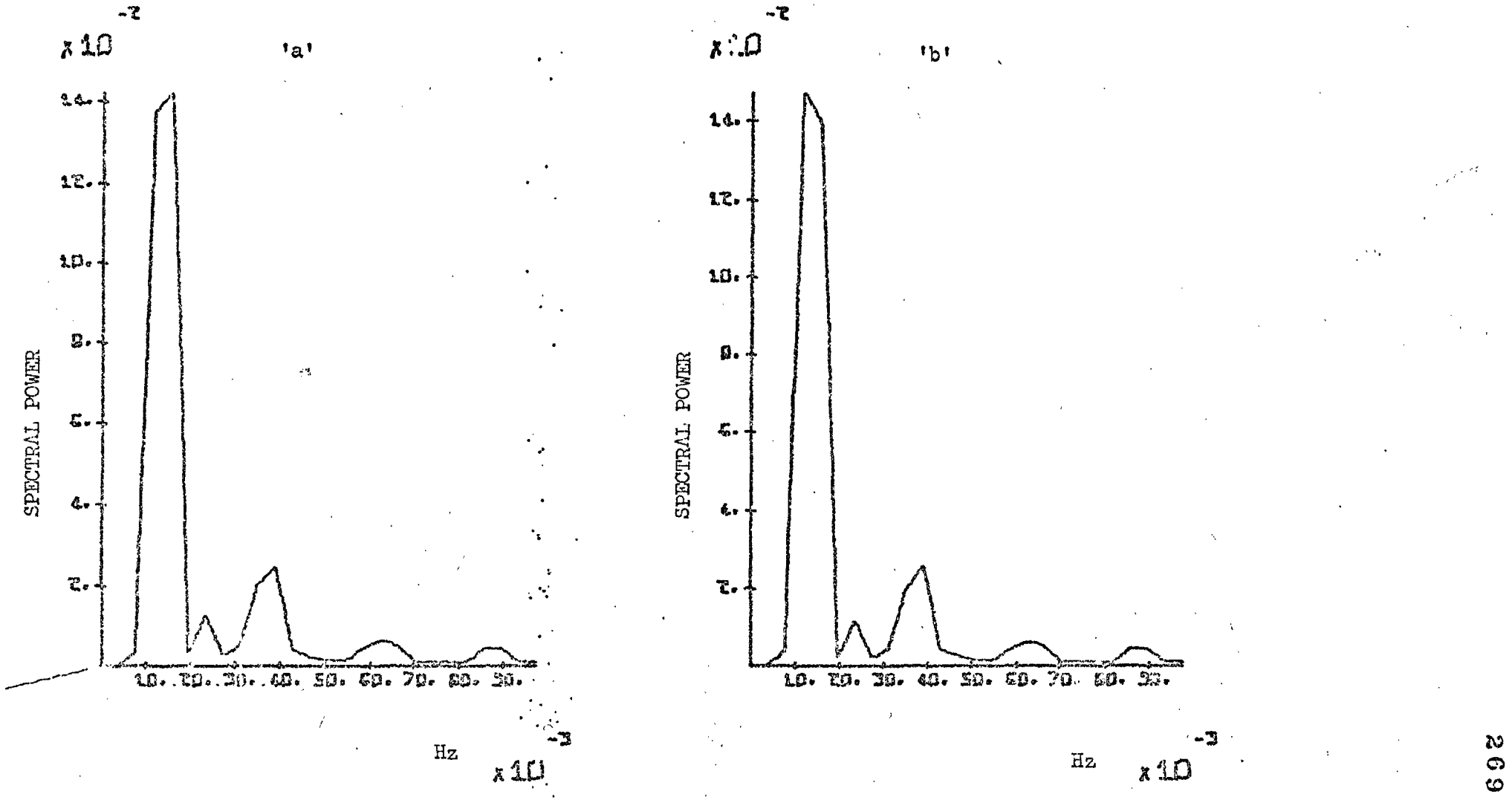


FIGURE 6.35 - EFFERENT SIGNAL (a) AND TEMPERATURE GRADIENT (b) - 120 SECOND PERIODICITY STIMULUS.

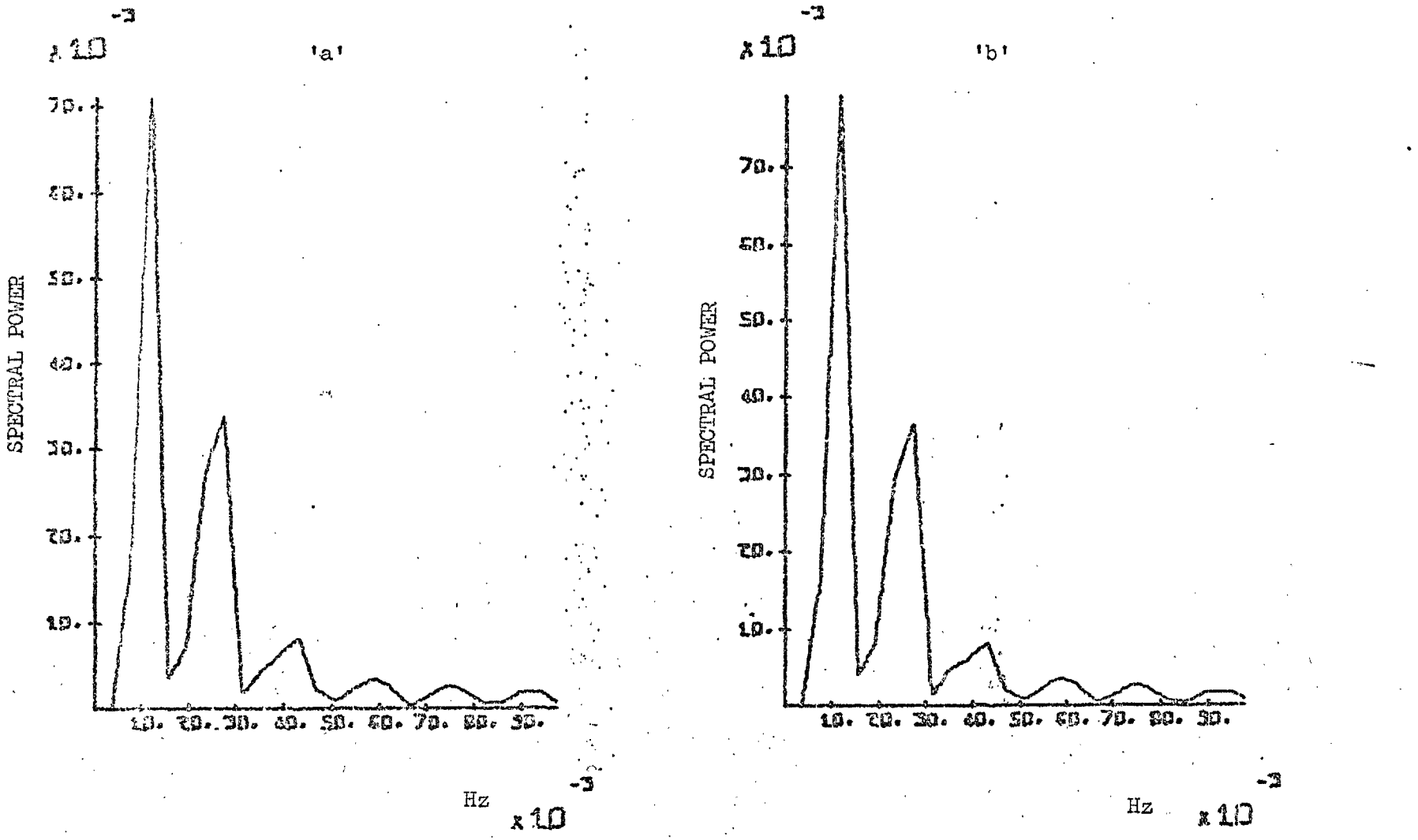
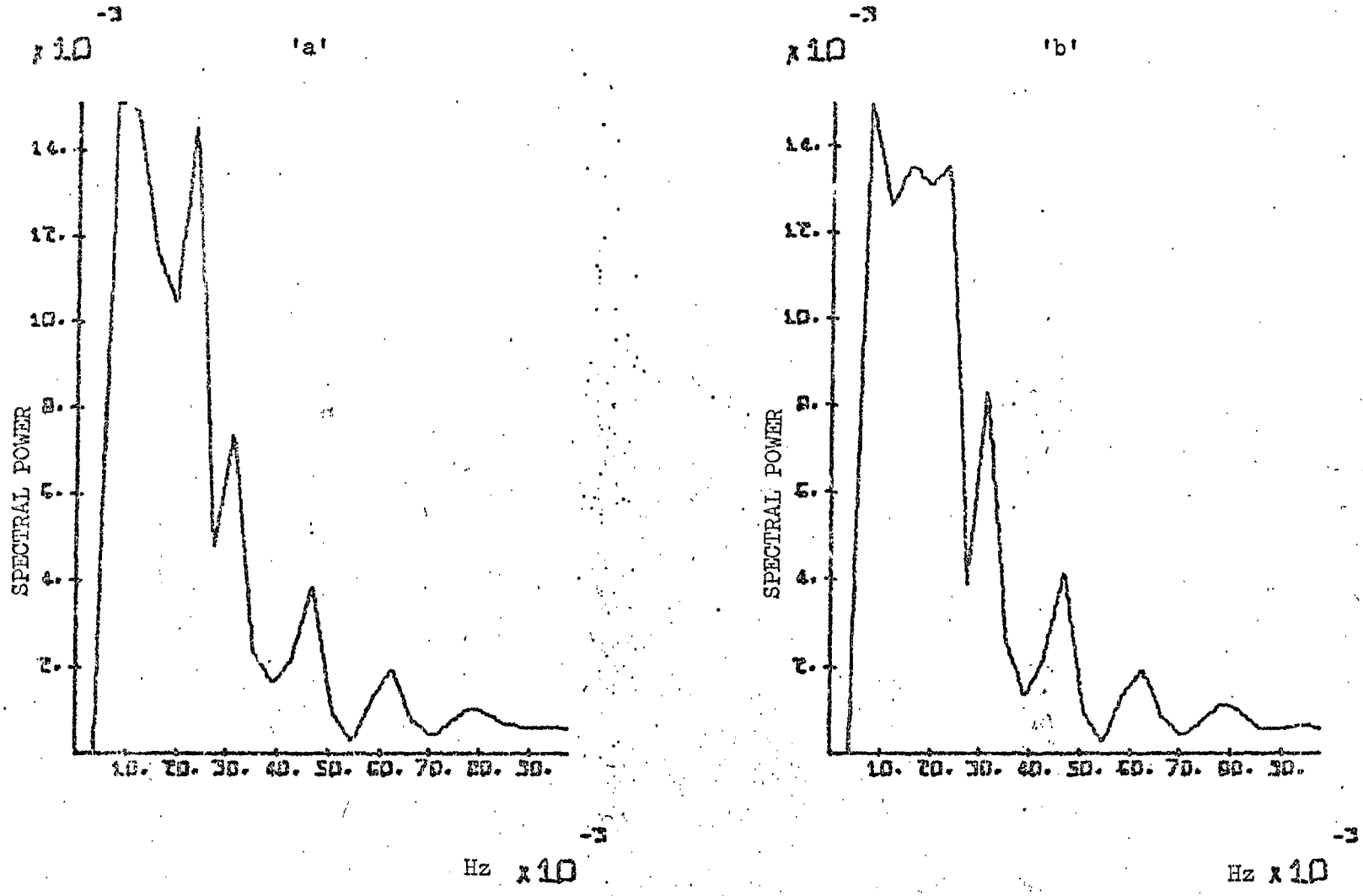


FIGURE 6.36 - EFFERENT SIGNAL (a) AND TEMPERATURE GRADIENT (b) - 160 SECOND PERIODICITY STIMULUS.



the range of driving frequencies which will cause the peripheral thermal system to be entrained. If the analysis of the thermal control system, discussed earlier, is correct, then the application of external thermal stimuli of differing frequencies in the computer model (with blood temperature variations present) should produce results similar to the equivalent experimental data. Figures 6.32-6.36 illustrate the efferent signal and temperature gradient waveforms obtained from the simulation, for thermal stimuli in the range 40-160 seconds periodicity.

It is apparent from these diagrams that the system is entrained by the forty, sixty, and eighty second stimuli; in each case the power spectrum comprises one dominant component at the stimulus frequency. The power spectrum of the efferent waveform with a one hundred and twenty second stimulus applied, has no component at the stimulus frequency, while the corresponding one hundred and sixty second stimulus spectrum exhibits definite spectral interaction effects. It is therefore apparent that the stimuli at the two lowest frequencies do not cause entrainment.

Considering these results, and those of the entrainment experiments described in chapter three, it is clear that the digital simulation successfully models the driving frequency dependence of the entrainment phenomenon in the physiological system.

CHAPTER 7

A SUMMARY AND DISCUSSION OF THE RESEARCH.

The subject of the research discussed in this thesis, is the analysis of the control system present in human thermo-regulation with the aim of clarifying the nature and structure of the system in more detail, and as far as possible determining its properties and interpreting its behaviour.

Chapter one reviewed the physiology associated with human temperature regulation. In 1958, Aschoff and Wever presented the, so called, core and shell hypothesis. According to these authors, the body, as far as temperature is concerned, can be divided into a central region (the core), where the temperature varies within narrow limits, and an outer shell, which consists of the more peripheral tissues, where there are considerable variations in temperature. Although the relative proportions of core and shell temperature are subject to difficulties in measurement, physiologists (Hardy and DuBois, 1937; Burton and Bazett, 1936), have estimated the mean body temperature for various environmental conditions. For normal conditions, the situation is represented by the equation:

$$U_{MB} = 0.3U_S + 0.7U_C$$

where U_S - the average skin temperature.

U_C - the core temperature.

For the condition of a cold environment, the skin temperature factor increases to about 0,4, while the core factor obviously decreases to 0.6. In warm environments the core expands, so that the resultant weighting factors become 0.2 and 0.8, for U_S and U_C respectively.

The initial conclusion indicated by a review of the physiolcgical investigations discussed in chapter one, is that the parameter used as a reference in the maintenance of homeostasis is core temperature. However, the rate of change of body heat content, $\frac{dQ}{dt}$, is determined by the difference between the rates of body heat production and heat loss. When the environmental thermal stress changes, heat production and heat loss are transiently imbalanced. The thermal control system then strives to reach a new state of thermal equilibrium. Because of the high heat capacity of the adult body, heat production and heat loss may be in a state of imbalance for several hours with only a slight variation in body temperature. This has two advantages. First, levels of motor responses related to heat production or

elimination need not be instantaneously in proportion to the severity of the existing thermal stress. Because of the large heat capacity of the body, exposure to considerable thermal stress for a relatively long period would be required (even in the absence of any compensation) before significant core temperature changes occurred. Secondly, the long latency provides time for the body to escape from highly stressful environments where physiological compensation is impossible.

The body responds in a number of ways to thermal change. The various types of response are not divided by sharp boundaries, but rather, are subject to a degree of overlap.

When the degree of thermal stress (hot or cold), during thermal change is insufficient to activate the sweat glands or cause shivering, the physical regulation of body temperature depends mainly upon the physiological control of peripheral circulation. Regulation of the average blood flow requirements, associated with temperature regulation, is achieved by sympathetic control of the tone of the peripheral blood vessels. On the other hand, when the degree of heat stress exceeds the range of vasomotor control, the coarser mechanisms of thermal control are activated and either shivering or sweating occurs.

In the introduction to chapter two it was pointed out that the fact of core temperature regulation (within a small amount) in the presence of wide variations of thermal stress, has been used to deduce the presence of a regulating system for internal body temperature; indeed, Hammel (1968) explicitly introduced the idea of a reference or set point of internal body temperature. Commenting on the success of the body in maintaining homeostasis, Hammel states: "This means that internal temperature is compared in some way with a reference, and when a difference occurs, an appropriate response is made tending to reduce the difference". Such comment emphasises that the homeostatic concept implies the existence of negative feedback control in the human thermal system. The important features of the control system implied by this viewpoint are illustrated in figure 2.1 and it can be seen from this diagram that the essential elements considered are: a comparator, efferent pathway (forward loop), and an efferent pathway (feedback loop).

Hammel (1968), Benzinger et. al. (1963), and Bullard et. al.(1971), are examples of papers which illustrate the widely accepted view that the controlling system originates within the hypothalamus. Hardy (1961), suggested that the thermal controller lay within the pre-optic region of the hypothalamus. Benzinger (1961) and

Fusco (1959), discuss the postulate that there are two central sites involved in thermo-regulation. The central site for the regulation of vasodilatation and sweating is thought, by these authors, to be in the anterior hypothalamus, while the corresponding site for the regulation of metabolism is thought to be in the posterior hypothalamus.

Having established the existence of a feedback control system regulating core temperature, and drawing on the work summarized above to define the basic elements of the system, the next phase of this work was to set up a more detailed description of the system and to analyse its behaviour. We start by considering the development of a basic block diagram, for example that of Stolwijk (1970), illustrated in figure 2.5. The effector section of the controlled system is represented in the model by three sectors, which were discussed earlier with relation to the basic physiology of thermo-regulation, namely: shivering, sweating, and vasomotor activity.

However, because of the complexity of the thermal control system in humans, a detailed study requires a much more comprehensive block diagram. As Hammel (1968) indicates, it is doubtful, because of the complexity of the system, whether any two modellers would produce the same block diagram of the controlling and controlled

system; such diagrams therefore outline a particular point of view. Figure 2.8 illustrates the block diagram which has been developed for this particular study, and the justification for the particular point of view on which this is based has been discussed in chapter two.

The analysis of the control system, and the development of the detailed block diagram, can only be achieved within the terms of reference of the appropriate system philosophy. Hardy (1953), states that it has become apparent from the physiological evidence that the brain temperature and skin temperature somehow combine to produce temperature regulation. Hardy suggested that the thermal response of the body was a function or the sum of the tissue temperatures above the set point, and the tissue temperatures below the set point. Other workers, notably Hammel et. al. (1963), have developed their own equations to describe the system philosophy.

Although the authors of such papers have made determined attempts to describe the system philosophy, they are always aware that such attempts are always simplifications of the true situation. It was therefore considered worthwhile in the present work to attempt to restate a system philosophy in the light of our own review of the physiological evidence and previous attempts at system modelling. It is useful to recapitulate here the

difference between the present view and that of previous workers.

Stolwijk (1970), and others, divide the efferent activity resulting from thermal control, into three regions: the low temperature region (shivering), the high temperature region (sweating), and the neutral temperature region (vasomotor activity). The afferent activity associated with thermo-regulation is thought to originate in two distinct sources: cutaneous thermo-receptors and hypothalamic thermo-receptors. As we have seen, the authors of current papers investigating the control philosophy of thermo-regulation feel that both sources of afferent information contribute to human thermal control. In the present model therefore, it was proposed that thermo-regulation in humans should be envisaged to emanate from two basic control systems which influence each other. These control systems have been called, in this thesis, the first and second lines of defence.

The first line of defence, refers to the body's initial response in the face of temperature change. The overriding algorithm of thermal control seems to be: always preserve heat in the core. Because of its role as a first line of defence, the efferent activity associated with this thermal control system is primarily vasomotor activity. Similarly, the prime source of

afferent information is obtained from the skin receptors. Thus when a change in the environmental conditions occurs, it is considered that the skin receptors will detect this change and the control system respond by producing vasoconstriction or vasodilatation, whichever is applicable. If these measures are effective, homeostasis will be maintained and the core temperature will remain in steady state. However, if such vasomotor adjustments prove to be inadequate, the thermal equilibrium of the core will be upset and the receptors in the hypothalamus will detect a change in temperature.

The Second Line of Defence.

When the receptors in the hypothalamus detect a change in temperature, the so called second line of defence is activated. By virtue of the fact that the thermal equilibrium of the hypothalamus has been upset at all, the degree of thermal stress must be significant. The resulting efferent activity would therefore be likely to produce gross control, which would constitute shivering or sweating in cases of severe disparity from the appropriate set value, and perhaps a more extreme vasomotor response when the degree of deviation from the set value is of a more minor nature.

The control system which has been described as the first line of defence, would seem to be primarily

involved in the minimization of the effects of environmental changes.

Chapter three begins with the assertion that for a considerable time it has been known that blood flow consists of a large number of spectral components which combine to produce a complex waveform. Burton (1939), and Burton and Taylor (1940), have investigated these waveforms in some detail and have managed to isolate certain spontaneous components which they attribute to thermo-regulation. In the light of the behaviour of the current model of the thermal control system, variations in vasomotor activity producing changes in peripheral blood flow form part of the first line of thermal defence and so changes in peripheral blood flow indicate the operation of this control system (because of its role as a first line of defence, the efferent activity associated with this peripheral control system is primarily vasomotor activity, while the skin receptors are the prime source of afferent information). Hence the variations in digit blood flow attributed by Burton and Taylor to thermo-regulation (within the terms of reference of the present system philosophy), must be associated with the first line of defence.

Having thus related peripheral blood flow fluctuations to the operation of at least one of the

relevant control systems, it was then feasible to investigate the nature of the spontaneous blood flow waveforms and to utilize this information to clarify in more detail the relevant feedback control system. In brief the question then was, what kind of control system would generate the spontaneous components in digit blood flow seen in practice (assuming that attention could be directed to components of specifically thermal origin). Consideration was given first to the question of system linearity.

For linear systems, oscillations of the type under consideration occur when the system is operating on the jw axis of the s plane (figure 3.1), but due to a number of factors (discussed in chapter three), this mode of operation can be ruled out. The alternative remaining is to assume that the relevant control system is nonlinear. Nonlinear control systems can be divided into two types: first, a system in which the nonlinearity is, in essence, purely due to the limitations of the dynamics of the physiological system; second, a system working within the limits of its response, but having within its structure discrete nonlinear elements. A test exists for the latter type of system; provided that the system exhibits spontaneous oscillations, as is the case here.

Minorsky (1962) discusses the second type of nonlinear oscillatory system in some detail, with particular reference to the entrainment of such a system by an external stimulus. If the natural frequency of the system is w_0, and the frequency of the external stimulus is w, then when the frequency of the stimulus (w), approaches w_0 a point is reached where the system output comprises a dominant component at the stimulus frequency. Under these conditions, the system is said to have been entrained by the stimulus. The region over which entrainment occurs is called, by Minorsky, the range of entrainment.

This principle can be extended to any oscillatory system which has discrete nonlinear components. It was therefore proposed to perform experiments to establish if the peripheral thermo-regulatory system could be entrained by an external stimulus; evidence of entrainment would confirm that the system was of the second nonlinear type. The entrainment experiments described in chapter three were divided into three sets. The first set of experiments involved obtaining a record of the spontaneous digit blood flow waveform for the small finger of the right hand under resting conditions. The power spectra for the two experimental subjects (figures 3.4c and 3.5c), illustrate the existence of a number of frequency components spread throughout the frequency

range thought to be associated with thermal activity: 0-0.1Hz. However, when a suitable thermal stimulus (twenty seconds periodicity), was applied to the left hand, the resulting power spectra (3.8c and 3.9c), exhibited one dominant component at the stimulus frequency. It was therefore established that entrainment could be induced in the peripheral system.

It is perhaps interesting to note that these experiments also provide evidence, of the existence of the peripheral control system, in general, and the role of the skin receptors in particular. Because the stimulus had a period of twenty seconds, it is apparent that the vasomotor activity in the contralateral hand resulted from afferent information supplied by the skin receptors because, apart from any other considerations, the response time of the central receptors to peripheral stimulation would be too large to be responsible for entrainment.

A second series of entrainment experiments was designed to investigate the entrainment phenomenon more thoroughly. In these experiments thermal stimuli of forty, sixty, and eighty seconds periodicity were used. These frequencies were chosen because a stimulus with a two minute period, used in the first series of experiments, was found to be unable to cause entrainment thus indicating that its frequency was outside the range of entrainment.

All the experimental data obtained for the three frequencies in the second series, showed evidence of entrainment, thus confirming the results of the first series and establishing that the system could be entrained by stimuli of differing frequencies. Thus the first and second series of entrainment experiments were designed to investigate the effect of an external thermal stimulus on the digit blood flow waveform under normal conditions and all of these experiments were performed therefore in conditions such that the core temperature remained within the comfort zone. The analysis of the system indicates, however, that human thermo-regulation results from two basic control systems which co-operate. It has been argued that the criterion of the system as a whole is to always preserve heat in the core. Hence, according to this proposition heating and cooling an upper limb, with an elevated core temperature, should not result in comparable vasomotor control; in other words, on the basis of the proposed system philosophy, the control resulting from the core system should override that of the peripheral system.

A third series of experiments was conducted to determine the influence of the core temperature (controlled by environmental temperature in a total body suit, Fox et. al 1967) on the behaviour of the thermal control system. In the first phase of the

experiment, with the core temperature at 37°C, scrutiny of the digit blood waveforms showed that a twenty second external stimulus was able to achieve entrainment of the spontaneous activity. On the other hand, the data from the second and third phases of the experiment (in each case with the core temperature elevated) showed no evidence of entrainment. An investigation into the body's thermal state during these phases of the experiment, by cross spectral analysis techniques, established that the skin temperature and core temperature were being driven by the air temperature within the suit.

Hence, the evidence presented in chapter three would therefore seem to confirm the existence of a peripheral thermo-regulatory system, as defined in the system philosophy. This system exhibits spontaneous fluctuations, which are observed in the digit blood flow waveform, and are attributed to the system structure, that is, an oscillatory system containing discrete non-linear elements. The problem unresolved at the beginning of chapter four, is the exact definition of the nonlinear element, or elements, within this system.

The relevant experimental results, and the work of Minorsky (1962), clearly indicate that the phenomenon of frequency entrainment occurs when a periodic stimulus is applied to a system whose free oscillation is of the

self excited type. Seifert and Steeg (1960), discuss systems of this type, stating that the oscillations arise from changes in the internal equilibrium of the system. Seifert and Steeg, together with Pipes (1958), describe this type of nonlinear oscillatory behaviour as relaxation oscillations. Pipes cites what he describes as a fundamental paper (published in 1926), in which van der Pol presents a generalized equation to describe the relaxation type of nonlinear oscillatory system, namely:

$$\ddot{x} + \epsilon(x^2-1)\dot{x} + x = 0 \qquad (4.1.)$$

By a suitable change in the ϵ parameter, the relaxation type of nonlinear oscillations for a particular system can be described by this equation. The parameter determines the shape of the output waveform, and also defines the frequency of oscillation (Dorodnicyn, 1947). It eventuates that the thermal control system, as it operates during entrainment, can be described as a van der Pol system and it appears that the type of van der Pol system which best describes the peripheral thermal activity requires ϵ to be large, that is typically about ten.

Although the entrained thermal system can be understood by matching to it a suitable van der Pol equation, one has yet to understand the factors which

produce the power spectrum of the spontaneous activity observed, as for example that illustrated in figure 3.4. The question is therefore asked: if the entrained case can be represented by a single van der Pol equation, then is it not feasible to represent the spontaneous activity of the system by a family of van der Pol oscillators?

It has been possible to conclude that the suggestion is unlikely, for the following reasons. A running analysis of the record (described fully in chapter four), of spontaneous data from subjects RC and RK revealed a high degree of non-stationarity in the signals. However, by invoking the theory of Liapunov (Gibson, 1963), it was possible to establish the stability of the van der Pol system, hence the observed non-stationarity must have arisen from a source other than system instability. As a consequence the possibility that the spontaneous activity results from a family of stable van der Pol oscillators becomes exceedingly unlikely. But there is another possibility. A single van der Pol oscillatory system whose frequency of oscillation varies over finite time, could also generate such non-stationarity, and it was suggested therefore that this probably might apply.

Before this possibility could be substantiated, it seemed necessary to achieve a clearer understanding

of the limits of harmonic entrainment. It was apparent from this analysis of the limits of harmonic entrainment, that a single van der Pol oscillator could be entrained by a suitable stimulus. The range of entrainment described by Minorsky (1962), and the results of the entrainment experiments, were seen to concur with the response of the entrained van der Pol system, and consequently to confirm that the particular van der Pol equation which had been chosen does describe the physiological situation adequately. Subsequently in chapter four, it was possible to establish that a single van der Pol oscillator seems to provide a satisfactory model for both the spontaneous and entrained behaviour of the system.

The situation at this stage of the work, to recapitulate, was that the peripheral thermo-regulatory system had been shown to be of the non-linear oscillatory type. Further, this non-linear operation, termed a relaxation oscillation, could be defined by the generalized van der Pol equation (4.1.), with suitable parameter values at least as far as the entrained case was concerned, and there seemed every reason to assume that this definition also applied to the condition of spontaneous oscillation. The issue as yet unresolved concerned the physiological realization of the system. Reconsidering the known physiological facts in the light of what was

known about the structure of the system, results in the block diagram of the peripheral thermal system which is illustrated in figure 4.10.

On the subject of the nonlinearity, it has been pointed out that Seifert and Steeg (1960), discussing van der Pol systems of the relaxation type ($\epsilon >> 1$), identify the nonlinearity in such systems with the type known as hard nonlinearities. The output waveform of a van der Pol oscillator entrained in the manner we have been discussing, and its consideration in the light of the basic physiological block diagram, led to the assumption that the hard nonlinear element within the peripheral thermal system was of the bang-bang type (figure 4.11). In addition, work of a similar nature on other physiological systems, Hyndman et. al (1971), tends to confirm that this kind of system is certainly possible.

At this stage it was decided that the analysis of the system could only be extended by a computer simulation of the physical system and its control. Certainly, there have been a number of attempts in recent years to simulate the human thermo-regulatory system. However, these models are not suited to the present analysis, or to the simulation of the conditions of entrainment we have been discussing. The simulation

which has been developed for this study is a description of the thermal situation within one upper limb, and the associated thermal control system. The simulation dealt with the upper limb in two sections, namely, the arm and hand. The thermal situation within these sections is described by the appropriate differential equations, which are in turn described by numerical techniques within the computer model. The vasomotor control of the vessels in the physical hand is simulated within the computer model in a manner closely resembling the real physiological control.

Chapter six deals with the inclusion of the regulator or control, of the thermal system represented in the computer model. The model provides that when the thermal control system is operating within the neutral region the so called first line of defence utilises the skin receptors as its primary source of afferent information. The basic block diagram of this control system is illustrated in figure 6.1. To understand the manner in which the cutaneous receptors form part of this control system, it is necessary to note that such a system is required to accommodate the following physiological facts:

1. An increase in temperature at the skin surface produces a corresponding increase in the cutaneous blood flow.

2. A decrease in temperature at the skin surface produces a decrease in cutaneous blood flow.

3. A hunting effect exists in the digit blood flow, as described by Burton, Taylor and others.

The basic controlling equation was first of all presumed to be: $U_E = U_{SET} - U_{AFF}$ (6.1.). The validity of equation (6.1.), has been tested by using the systems response to a change in the environmental temperature, the example chosen being a step increase in the environmental temperature at the skin surface from $28^{\circ}C$ to, say, $30^{\circ}C$ (there is no special significance in the choice of these temperatures). Such a step increase in the skin surface temperature would result in an increase in the temperature at the cutaneous receptors, which would subsequently produce a degree of vasodilatation. The evidence presented in chapter six indicates that such efferent action would cause the temperature at the cutaneous receptors to increase still further, which in turn would cause a greater degree of vasodilatation. The net result of such activity would therefore be an avalanche condition, which obviously would not provide the basic requirements of thermal control. There is no physiological evidence to suggest an avalanche condition of this type, but there is ample evidence to suggest the presence of thermal control. It therefore seemed that an alternative

hypothesis to equation (6.1.) was required.

Newton's Law of Cooling, leads to such an alternative. This law indicates that a decrease in the thermal gradient would decrease the heat loss from the body. Now it was proposed earlier in the text that the purpose of the peripheral system is to act as a first line of defence, that is to maintain the constancy of the internal thermal environment of the body; but this constancy is a function of heat loss and not temperature. If the heat loss is also kept constant, at constant heat input, in the face of external environmental temperature change, then it automatically follows that homeostasis will also be preserved. To maintain constant heat loss, according to Newton, the thermal gradient $(\frac{dU}{dx})$ must remain steady no matter what the environmental temperature may be. This means that the controlled variable should be thermal gradient rather than temperature. The physiological evidence in support of this statement is presented in detail in chapter six.

A necessary condition of the new hypothesis (that the controlled variable is thermal gradient), is to establish if the known effector activity in the physiological system provides control of the thermal situation. Returning to the case of a two degree step

increase in skin temperature, the initial effect (referring to figure 6.3), will be to reduce the thermal gradient. The known physiological response to a change in skin temperature of this type, would be increased vasodilatation. The effect of the increased blood flow is to increase the thermal gradient below the skin surface. Following this argument to its conclusion, the final result will be a return to the set value of thermal gradient. Hence a state of control exists with thermal gradient as the controlled variable.

The next stage was to establish a suitable set value of thermal gradient for the computer model. This was achieved by solving the model over a suitable range of skin temperatures (Brengelman and Brown, 1966), under steady state conditions. Having established the control of the computer simulation, one is now in a position to use the model to continue the investigation of the spontaneous activity of the peripheral system. The system which has been defined, must be capable of explaining the experimental findings; these are, that the system output was observed to fluctuate spontaneously (for example in frequency) when the system was in the comfort zone, even though no apparent thermal perturbation was present.

The most probable source of thermal change was considered to be variations in blood temperature within the vessels of the hand. Earlier in the text the system under consideration was compared, in operation, to a single van der Pol system. Dorodnicyn (1947), established that the frequency of oscillation of a van der Pol system is defined by the value of the ϵ parameter. As far as peripheral thermo-regulation is concerned, the frequency of oscillation would appear to be determined by two factors: firstly, the largely invariant components of the system, for example the properties of bone and tissue; and second thermal variations. It therefore seemed that if the thermal inputs to the model were kept constant in the model, the system should, after the starting transients had subsided, oscillate at a relatively stable frequency. With the skin temperature and blood temperature held constant, it was apparent that there was one dominant component in the system output; this occurs at a frequency of 0.038 Hz. It is however, extremely unlikely that in the physical system the blood temperature within the vessels of the hand will remain constant even for a short period of time. So that the spontaneous activity of the physical system almost certainly occurs in the presence of changes in the vascular blood temperature.

Minorsky (1962), describes the effects of external perturbations on the output of nonlinear oscillatory systems. To recapitulate: if the frequency of any stimulus, applied to the system, lies outside the range of entrainment, one observes a complicated spectral interaction, where the oscillation of the system at its natural frequency and the stimulus interact. When the vascular blood temperature is allowed to fluctuate, the effect is not frequency entrainment of the system, because the magnitude of these fluctuations is small; their effect on the system is rather, one of producing a spectral interaction phenomenon, which explains why the natural frequency component of the system, illustrated in figure 6.16, is replaced by a number of components at different frequencies in model experiments of different blood temperature fluctuations.

Under the conditions of the resting unstimulated blood flow experiment, the periodicity and magnitude of the variations in blood temperature must be presumed to be of a variable nature. As a result, over the period of the experiment (ten minutes), the frequency components associated with temperature result from interactive effects produced by blood temperature fluctuations of presumtively differing periodicity. This would be sufficient to explain the origin of the frequency

components in the power spectra of the spontaneous experimental data illustrated in figures 3.4 and 3.5.

With the computer model the application of an additional stimulus (equivalent to that used in the first series of entrainment experiments), causes the system to be entrained as previously described. But if this additional periodic stimulus was applied to the model while various simulated blood temperature fluctuations were allowed, it was found that in each case the spontaneous activity was replaced by a single dominant component at the stimulus frequency (twenty seconds periodicity). However the inclusion of a blood temperature fluctuation does not in any way modify the capability of the model to account for the entrainment phenomenon.

Concluding Remarks.

The analysis of available physiological data of experimental studies, theoretical analysis, and computer simulation described in this work has therefore led to a hypothesis about the behaviour of the thermo-regulatory control system. This system is envisaged as strongly nonlinear, and the activity of the peripheral thermo-regulatory system has been described as arising specifically from a nonlinear oscillatory system. The nonlinear element within this system is thought to be of the type known as a bang-bang controller. The system

as a whole oscillates spontaneously in a manner which produces a number of frequency components spread throughout the range 0-0.1 Hz. Conversely, when a suitable thermal stimulus is applied to the system, these spontaneous components disappear leaving a single dominant component at the stimulus frequency. Under these conditions the system is said to have been entrained by the external stimulus.

It has been shown that the elaborate spontaneous behaviour of the system could be fully accounted for by virtue of the interaction between the natural frequency of oscillation of the system (0.038 Hz), and variations in the temperature of the blood within the vessels of the hand. Computer simulation of these conditions supported this possibility.

The application of an additional thermal stimulus, equivalent to that used in the first series of experiments, was also incorporated into the simulation; the result was entrainment of the system. This procedure was extended to investigate the response of the computer simulation to stimuli with periodicities in the range 40-160 seconds. It is clear from these results, that the digital simulation successfully models the driving frequency dependence of the entrainment phenomenon that was illustrated in the second series of entrainment experiments discussed in chapter three.

It was therefore apparent that, on this basis, in the human thermal control system variations in blood temperature could cause spectral interaction with the natural frequency of oscillation of the system, although these variations would be too small to cause entrainment. If an additional stimulus of sufficient magnitude and appropriate frequency is superimposed on to this activity, the system will be entrained.

An on-off element has also been used in a study of the system involved in blood pressure control, indicating that nonlinear elements of this type may be common to a wide variety of physiological control systems.

APPENDIX 1: INITIAL TIME DOMAIN DATA PROCESSING PROCEDURES.

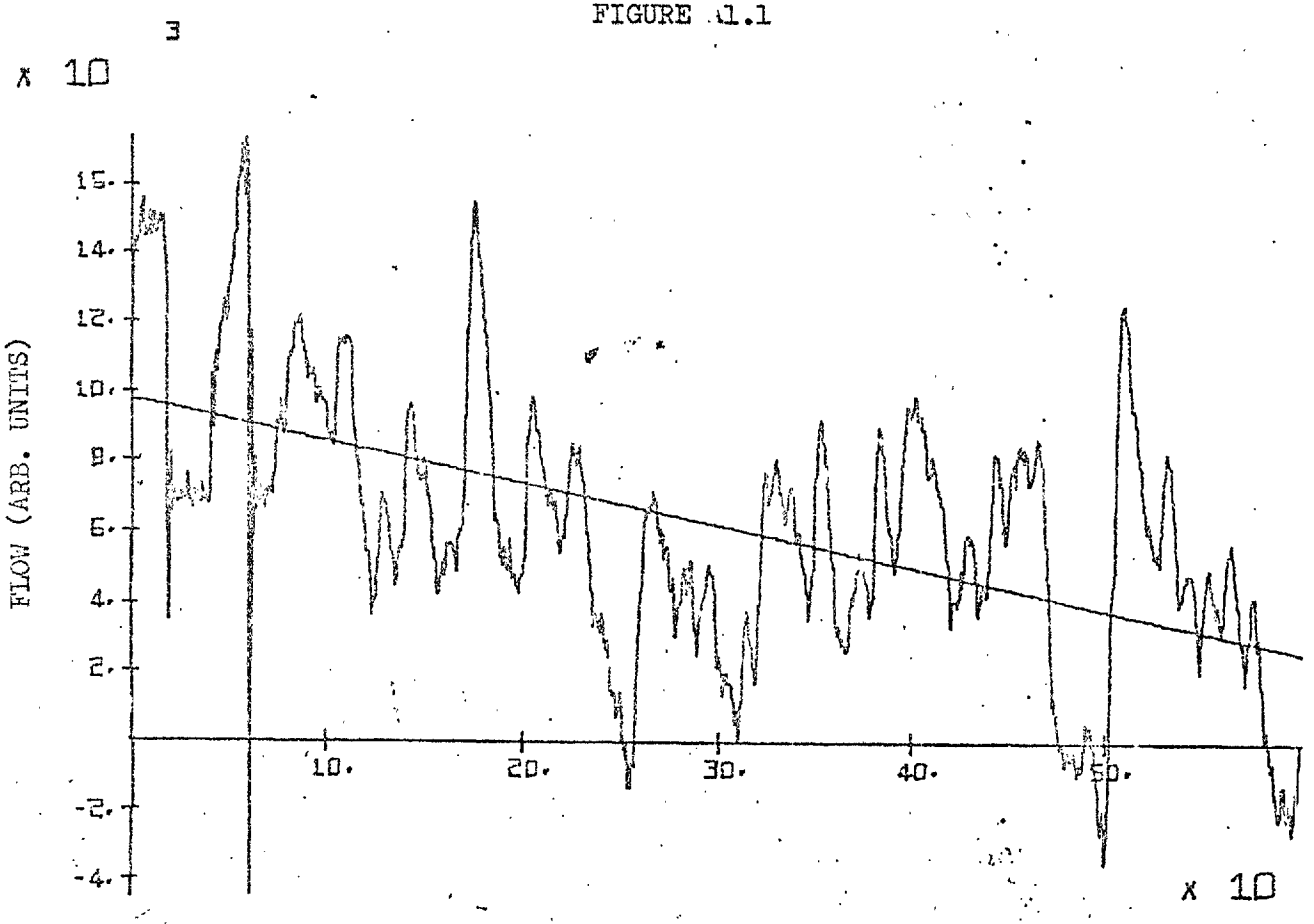
In order to establish significance in experimental data, it is often necessary to perform some initial processing. A particular case where such techniques proved necessary, was for the sixty second periodicity stimulus record of digit blood flow obtained from subject RK, during the second series of entrainment experiments. Hence, the relevant data processing methods will be considered for this record of data.

The Elimination of the Effects of Drift.

Figure A1.1, illustrates the record of the raw data under consideration. The line through the data represents the best straight line fit. Obviously, if no drift or dc offset were present in the data, this line would be superimposed on the horizontal axis. Drift can be considered as equivalent, in its effect, to a very low frequency sine wave component. Hence, any spectral power associated with drift will occur at the extreme low frequency end of the spectrum.

The best fitting line is found by the method of least squares. The least square line approximating the set of points $(X_1,Y_1),(X_2,Y_2)\ldots\ldots,(X_N,Y_N)$ has the equation: $Y = a_0 + a_1X$ (A1.1)

FIGURE A1.1


3
x 10
FLOW (ARB. UNITS)
16.
14.
12.
10.
8.
6.
4.
2.
-2.
-4.
10.
20.
30.
40.
50.
1
x 10
TIME (SECONDS)

where the constants a_0 and a_1 are determined by solving the simultaneous equations:

$$\sum Y = a_0 N + a_1 \sum X \qquad (A1.2)$$

$$\sum XY = a_0 \sum X + a_1 \sum X^2 \qquad (A1.3)$$

The constants a_0 and a_1 are found from the formuli:

$$a_0 = \frac{(\sum Y)(\sum X^2) - (\sum X)(\sum XY)}{N\sum X^2 - (\sum X)^2} \qquad (A1.4)$$

$$a_1 = \frac{N\sum XY - (\sum X)(\sum Y)}{N\sum X^2 - (\sum X)^2} \qquad (A1.5)$$

By substituting a_0 and a_1 in equation (A1.1), the best straight line fit to the data can be estimated.

The elimination of drift is achieved by subtracting the straight line from the data. The resultant waveform is illustrated in figure A1.2.

Cosine Bell Filtering.

This type of filter has a wide variety of uses. The particular application which will be considered here, is the removal of particular sections of data which are considered to be due to physiological systems extra to the one under consideration.

FIGURE A1.2

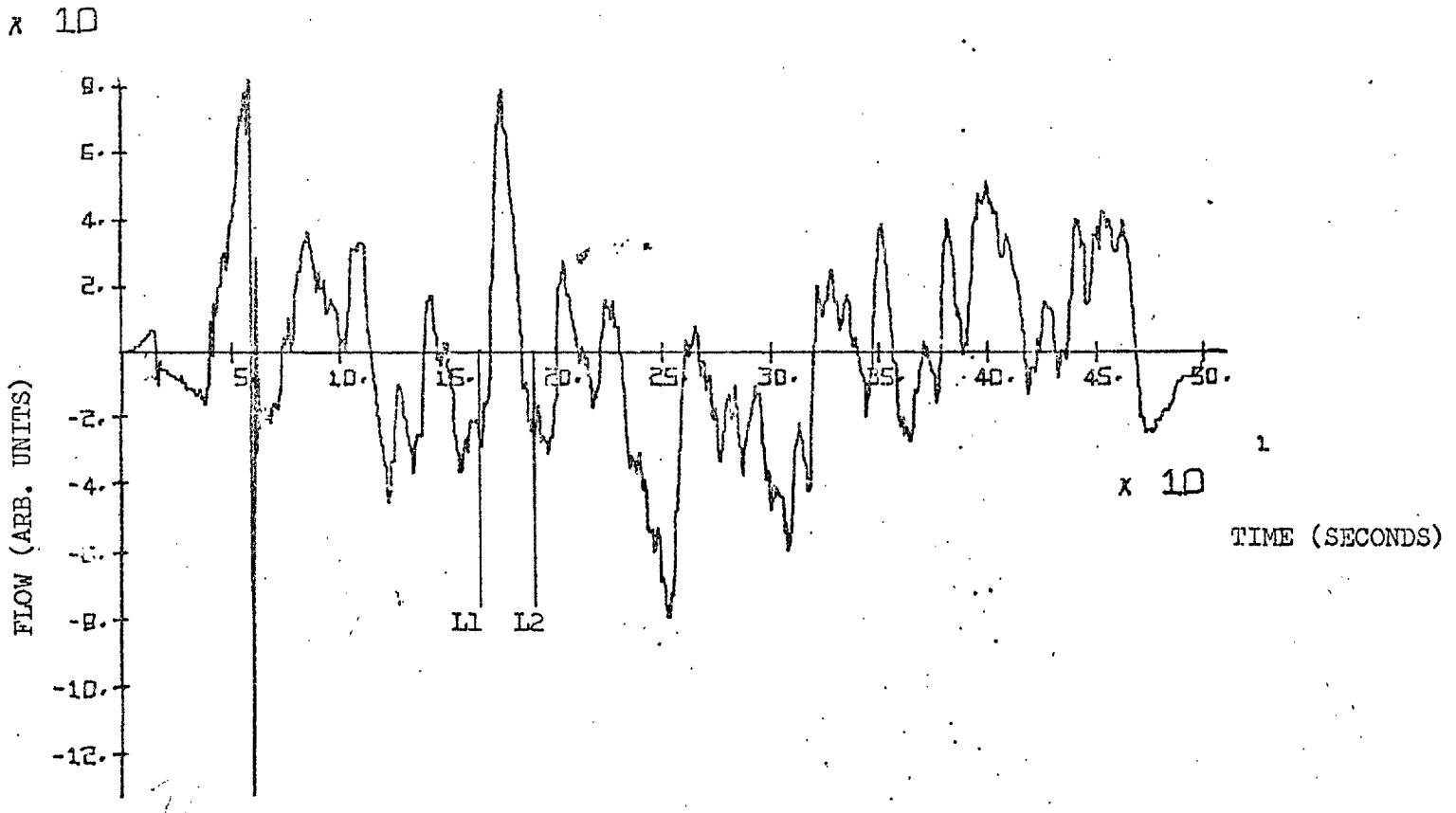
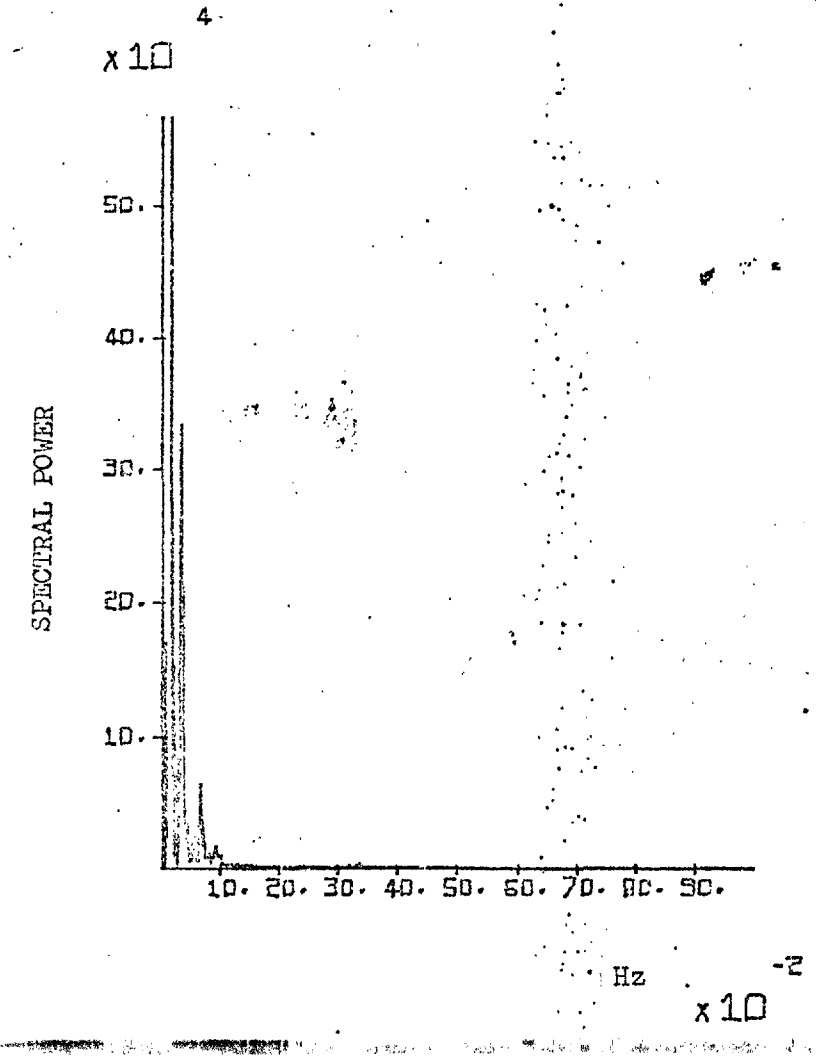

3
X 10
9.
6.
4.
2.
-2.
-4.
-8.
-10.
-12.
5.
10.
15.
20.
25.
30.
35.
40.
45.
50.
L1
L2
1
X 10
FLOW (ARB. UNITS)
TIME (SECONDS)

FIGURE A1.3


x 10 4
50.
40.
30.
20.
10.
SPECTRAL POWER
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -2

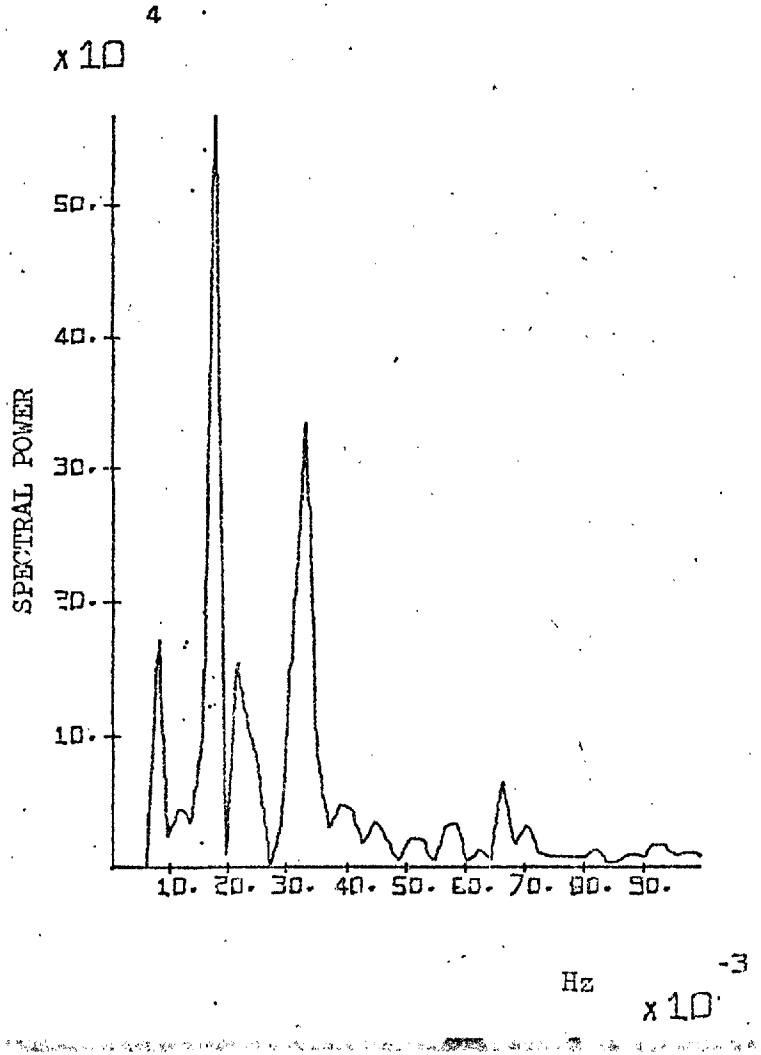

x 10 4
50.
40.
30.
20.
10.
SPECTRAL POWER
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
x 10 -3

FIGURE A1.4

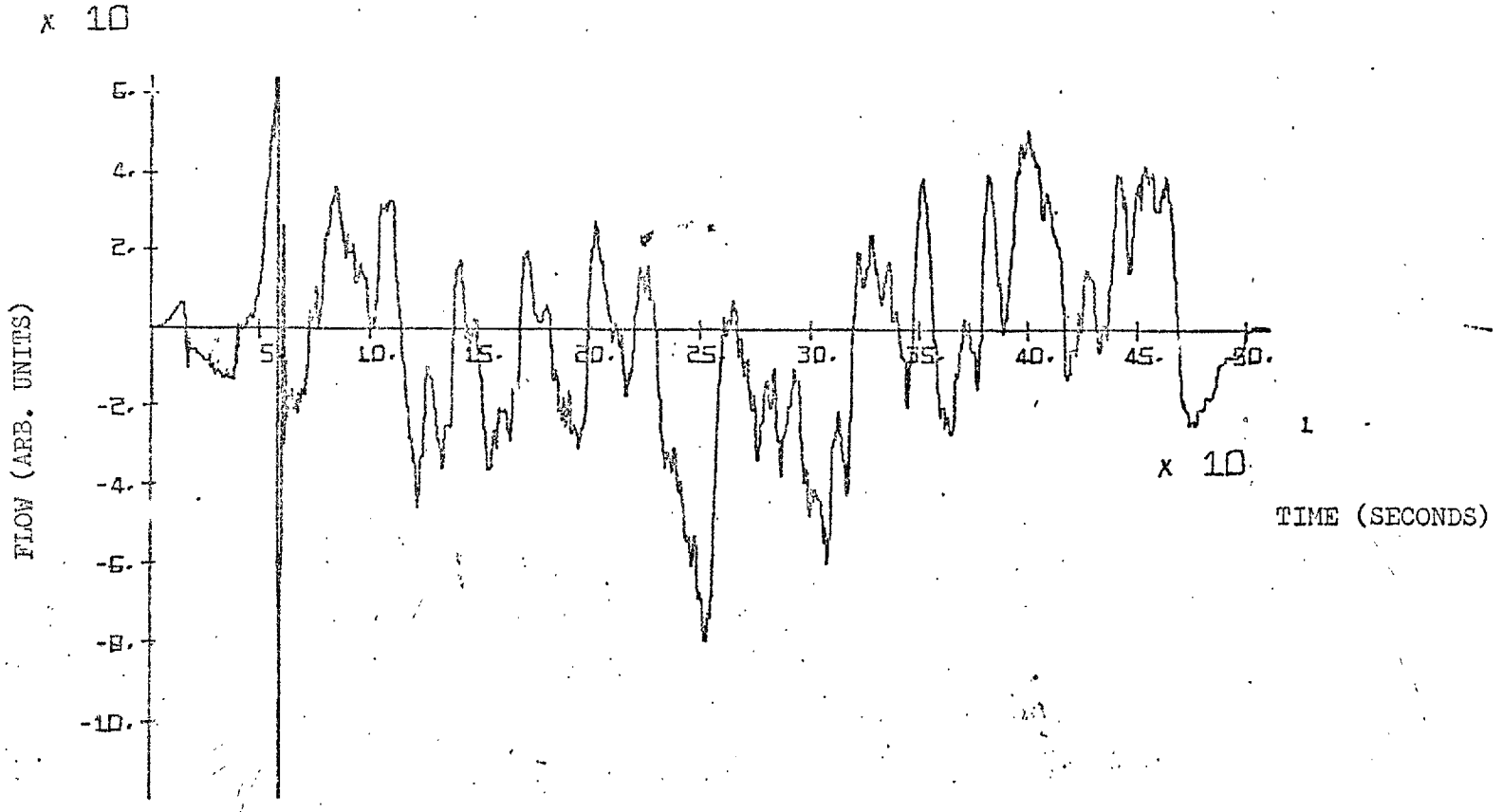
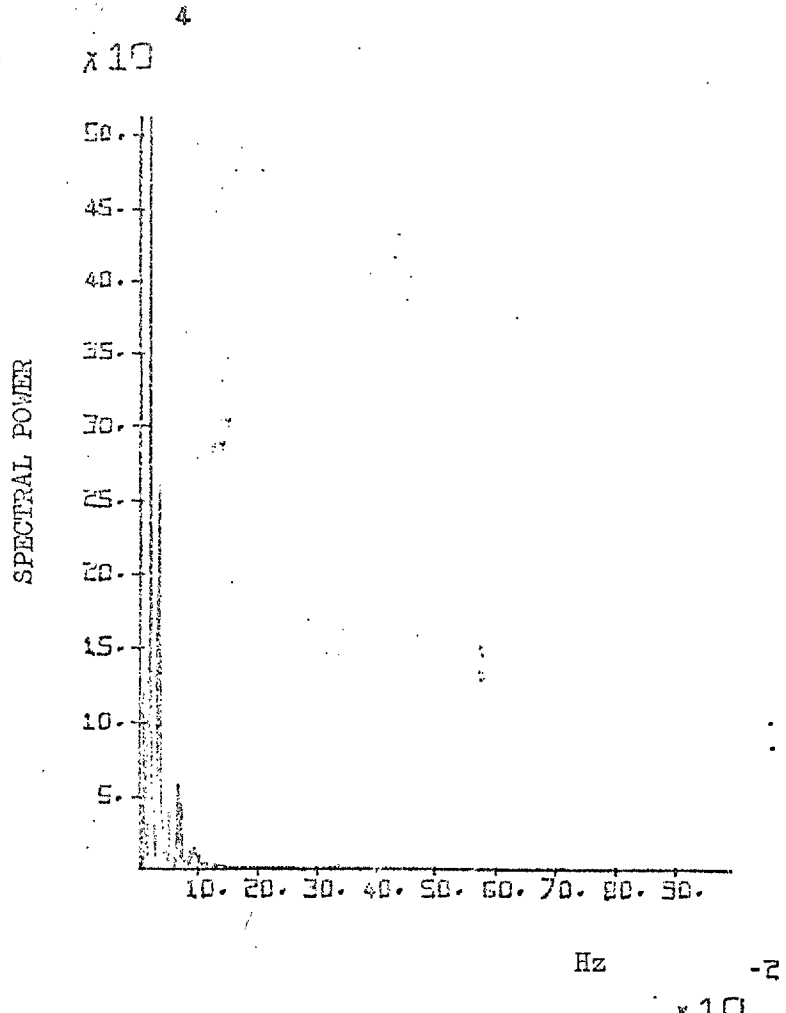
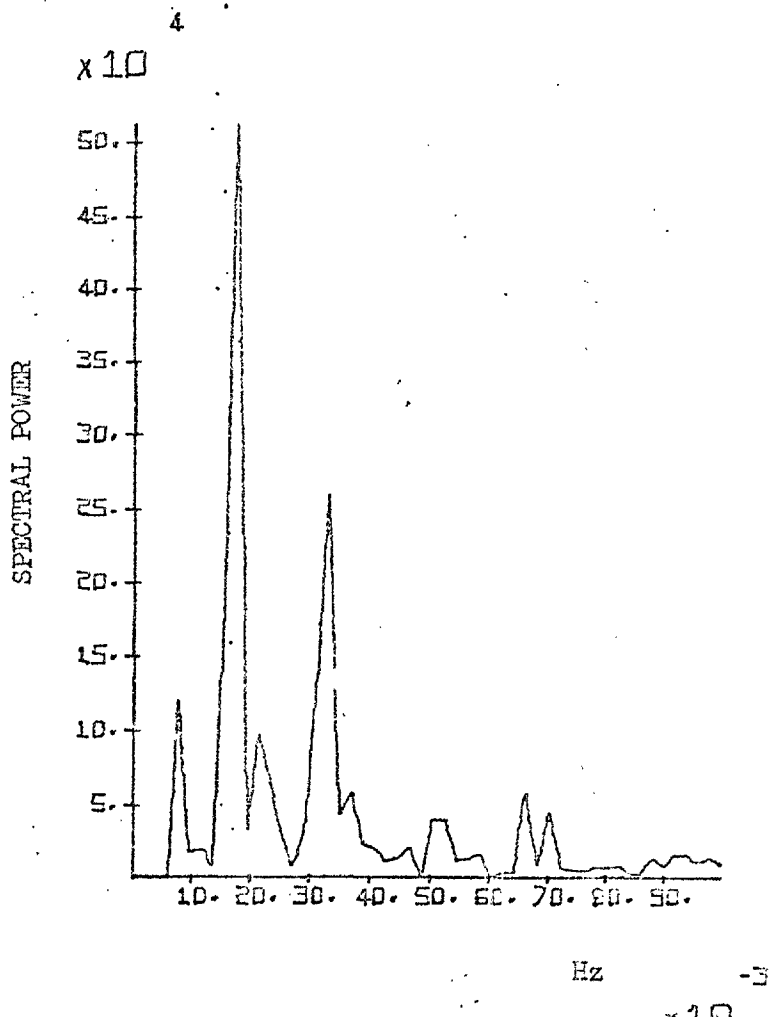

3
X 10
6.
4.
2.
-2.
-4.
-6.
-8.
-10.
5.
10.
15.
20.
25.
30.
35.
40.
45.
50.
1
X 10
FLOW (ARB. UNITS)
TIME (SECONDS)

FIGURE A1.5


4
x 10
50.
45.
40.
35.
30.
25.
20.
15.
10.
5.
SPECTRAL POWER
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
-2
x 10


4
x 10
50.
45.
40.
35.
30.
25.
20.
15.
10.
5.
SPECTRAL POWER
10. 20. 30. 40. 50. 60. 70. 80. 90.
Hz
-3
x 10

Referring to figure A1.2, the filter is applied over the range L1, L2. If the magnitude of a particular point L, is defined A(L), then the filtered value of the magnitude for this particular point is defined by the equation:

$$A(L)_{new} = \frac{(A(L)-A(L_1))}{1+k}\left[1 + k\cos\frac{2\Pi(L-L1)}{N}\right] + A(L1) \quad L=L_1, L_2$$

and $N=L_2 - L_1$ (A1.6)

Considering the case of the transient illustrated in figure A1.1, here: $L_1=332$ and $L_2=377$, therefore N=45.

When $L=L_1$, $A(L)_{new} = A(L_1)$

and when $L=L_2$, $\cos\frac{2\Pi(L-L_1)}{N}=1$

therefore, $A(L)_{new} = A(L2)-A(L_1)+A(L_1) = A(L_2)$

The maximum effect of the filter is at the point where $L-L_1 = 2N$. Then if k=0.5:

$$A(L)_{new} = \frac{(A(L)- A(L_1))}{3} + A(L_1)$$

Hence the maximum effect of the filter is to reduce the data to a third of its unfiltered magnitude. The power spectrum of the data of figure A1.2 is illustrated in figure A1.3; while the effect of applying the filter to the transient under consideration is shown in figure A1.4. The power spectrum which corresponds to the time domain data of figure A1.5. Comparing the pre and post, filtered power spectrum indicates the influence of the transient effect.

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(1944) (d) Pflugers Arch 248:178.

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(1944) (g) Pflugers Arch 248:436.

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