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A Feedback-Feedforward Mechanism Describing the Interaction of Central and Peripheral Signals in Human Thermoregulation

by
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Work in human thermoregulation in recent years has involved increased attention to the possibilities of developing mechanisms which embody the basic concepts of engineering control theory. Recent reviews of thermoregulation by Bligh (1966) and Hammel (1968) present comprehensive and critical assessments of the present status of the work in this field.

The control scheme presented in this paper appears to overcome a number of the limitations inherent in previously proposed mechanisms. Only one set point, that of the central hypothalamic temperature, is required; other so-called set points referred to by previous investigators may be viewed perhaps as activation thresholds of response mechanisms. Likewise, a proposed feedforward loop, activated by peripheral skin sensors, appears to serve a logical anticipatory function.

PRESENT STATUS OF KNOWLEDGE

Work reported by previous investigators has been considered from the viewpoint of discerning the most pertinent factors which would appear to affect the postulation of a plausible control mechanism in the form of an engineering signal-flow diagram. Some writers (Hammel, 1968; Stolwijk and Hardy, 1966) suggest that there are independent set points for both the central hypothalamic temperature and the skin temperature. Stolwijk and Hardy (1966) attempted to account for the effect of skin temperature by referring instantaneous values to that in a neutral environment; i.e., the error signal was represented as $(T_{s(neutral)} - T_s)$ with $T_{s(neutral)}$ serving the role of a pseudo-set-point.

Brown and Brengelmann (1970) obtained data from water-bath studies which indicate that dT_s/dt is an important input which interacts with T_s and T_{hy} to determine metabolic rate. They also concluded that both magnitude and direction (i.e., whether sign is + or -) of dT_s/dt appear important and that this dynamic factor may exceed the steady-state contribution of T_s. Data from these water-bath experiments show that a negative dT_s/dt caused an increase in metabolic rate and a positive dT_s/dt decreased the metabolic rate.

Banerjee, Elizondo and Bullard (1969) have presented considerable evidence suggesting the importance of both the absolute skin temperature, T_s, and rate of skin warming, dT_s/dt, in initiating sweating. Also, Wurster and McCook (1969) in a series of studies on 10 male subjects observed inhibition of sweating after transfer of subjects from hot to cool environments. This inhibition occurred while central core temperatures were rising and skin temperatures were falling.

The importance of the central temperature-sensitive structures in human thermoregulation is well recognized. A review of the work on the behavior of central

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sensors (Hammel, 1968) suggests that this action can be represented adequately by means of a feedback mechanism such as shown in our signal-flow diagram.

PROPOSED CONTROL MECHANISM

Consideration of control systems concepts along with existing physiologic information has led to the postulation of a mechanism for human thermoregulation, depicted in Fig. 1 in the form of an engineering signal-flow diagram. Three parallel control loops represent metabolic, vasomotor and sudomotor effects, which can be activated by means of central and peripheral signals, acting either alone or in combination.

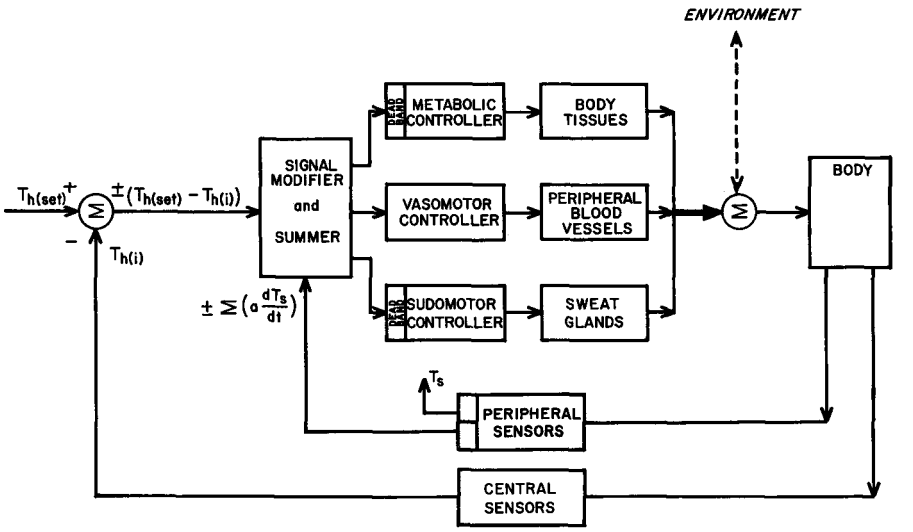

Fig. 1. Human thermoregulation: normal short-term control.

Since all parts of the body are in continuous thermal communication with one another, it is difficult to conceive of more than one independent set point. Once the set point for T_{hy}, the hypothalamic temperature, is established, all other temperatures are dependent. If the body simultaneously attempts to control T_{hy} to a given $T_{hy(set)}$ and also a T_s, the skin temperature, to a specified $T_{s(set)}$, the two control actions would be in conflict and an oscillatory, perhaps unstable, response would ensue.

Moreover, since the existence of a skin temperature set point has not been demonstrated experimentally, the signal-flow diagram is constructed around a single set point, the anterior hypothalamic temperature being the most probable in the light of available evidence. Although a controlled set point for the peripheral skin sensors appears unlikely, there appears to be an important role for the skin signals in connection with threshold adjustment as will be described later.

It is known that extremely precise control of internal temperature is achieved even in the face of major changes in environmental conditions. Furthermore, the thermoregulatory compensation occurs in an orderly, essentially non-oscillatory manner, e.g. an induced level of shivering may produce a little overshoot but

not enough to require subsequent sweating to correct for the minor overcompensation. Experience with engineering control systems suggests that such smooth and orderly compensation for drastic changes in environment could not be achieved solely by means of a feedback control mechanism, as an inherent weakness of feedback control is that the system must already have moved away from the desired state before any corrective response can be initiated; thus, the feedback system frequently over-responds in an attempt to catch up. In systems where there is an appreciable time lag between corrective action and response, improved precision of regulation has been attained by adding a feedforward component to the control strategy.

By analogy Fig. 1 assigns complementary roles to the central and peripheral sensors. The central sensors control the actions of the feedback loops, whereas the peripheral sensors, by virtue of their direct contact with the environment, serve an anticipatory ("early warning") function. Furthermore, it is logical for the amount of compensation initiated by the feedforward loop to be proportional to the rate at which environmental temperature is changing. Accordingly, the motivating potential for the feedforward loop has been postulated in terms of the magnitude of the time derivatives and the areas of skin exposed. Thus, the response initiated by feedforward elements alone can be stated in general terms as

$$\text{Feedforward response} = f\left\{\Sigma\left[\ (a)(dT_s/dt)\ \right]\right\} \qquad (1)$$

There is strong physiological evidence in support of this postulated motivating potential, i.e., dT_s/dt rather than T_s per se. Hensel (1963) distinguishes between "warm" sensors and "cold" sensors in terms of their response to rising or falling temperature. The level of response of each type of sensor is affected by not only temperature per se but also by the rate of change of temperature. Accordingly, warm sensors apparently are activated by $+(dT_s/dt)$ and cold sensors by $-(dT_s\ dt)$. There is also a reciprocal effect of inhibition as well as activation, i.e. a rising temperature inhibits the cold sensors as well as activates the warm sensors. Other studies in intact man as discussed above have also demonstrated the importance of rate of change of skin temperature. In contrast to skin temperature receptor response, there is no clear evidence suggesting that rate of change of hypothalamic temperature, dT_{hy}/dt, plays a role in human thermoregulation (Hammel, 1968).

Hammel (1968) and others have suggested a role for the skin temperature as that of adjusting the "set temperatures" at which vasomotor action, sweating and shivering are activated. In this connection the term "set temperature" is used in the sense of a threshold or activation point rather than as a control loop set point. However, in this discussion, "threshold" or "dead band" will be used to designate the signal level required for the activation of controllers. Although dT_s/dt appears to provide the actuating potential for the feedforward loop, there is no reason why T_s itself cannot influence the threshold conditions of individual controllers.

It appears appropriate that both the metabolic controller and sudomotor controller be provided with dead bands in order to prevent their activation by minor signals. In view of the available physiological information it appears that minor adjustments can be accomplished by means of vasomotor action, and there is no evidence of any threshold or dead band constraints on this response (Snell, 1954). It is only when the limited adjustment in body heat balance, provided by means of vasodilation or vasoconstriction, is insufficient that the major compensatory effects provided by shivering and sweating are called into action. Since these latter effects provide high levels of compensation, it would be inappropriate to activate them when only minor corrections are needed, to do so would probably set off over-compensation with perhaps ensuing undesirable oscillations. Thus, it would appear that both the metabolic and sudomotor controllers, whether activated by

means of feedback and/or feedforward signals, should be restrained by dead bands in order to prevent undesirable instabilities from arising, and this appears to be the case at least for the former (Downey, Miller and Darling, 1969).

The forcing signals generated by the feedback and feedforward elements are combined in some manner, as shown on the diagram, before being transmitted to the control elements. This could be a simple summation of signals or some type of nonlinear function. In this way the two loops work in tandem, reinforcing or attenuating each other as is appropriate. Moreover, it is possible for the output of this summing element to activate the hot side of the control system and inhibit the cold side simultaneously and vice versa.

Aside from the basic loop configurations and the nature of the motivating potentials, consideration must be given to the nature of the response action produced by each of the three controllers: metabolic, vasomotor and sudomotor. The nature of the controller functions for any of these actions has never been confirmed by observed data. Hammel (1968) represents the regulatory controllers in terms of the standard engineering three-mode control actions: proportional, integral and derivative. Since physiological control systems probably exhibit nonliner characteristics, it is likely that these linear control functions at best can only serve as approximations, but it appears appropriate to evaluate these functions carefully before proceeding to more complex representations. By analogy with engineering systems, it would be assumed that the action of each of the individual controllers is basically proportional but with possible modifying influences of integral and derivative actions.

EXPERIMENTAL CONFIRMATION

Studies designed specifically to provide data for testing our proposed feedforward-feedback mechanism for human thermoregulation are in progress. In a companion paper Downey, Huckaba and Darling (1971) have documented the individual metabolic responses which can be elicited by either central cooling or skin cooling separately. Additional data is currently being acquired to evaluate the dynamic properties of both metabolic and vasomotor actions with extension to include sudomotor response planned.

CONCLUSIONS

The proposed control mechanism for human thermoregulation as represented in Fig. 1 by the engineering signal-flow diagram appears to accommodate presently available physiological evidence. At the same time this combined feedforward-feedback configuration is in accordance with the established engineering methodology where precise control specifications must be met. The response data presented in our companion paper (Downey, Huckaba and Darling, 1971) provide a measure of corroboration of our postulated mechanism. These results, along with those recently reported by other investigators, supply mounting evidence of the importance of evaluating under dynamic conditions the separate responses which can be induced by central and peripheral sensors respectively.

Concurrent with this experimental program a mathematical model corresponding to the control configuration of Fig. 1 is being developed for use in making computer computations. The ultimate test of the adequacy of a mechanism for human thermoregulation will be in its ability to form the basis of predictive calculations of the thermal response of the body to the full range of physiologic and environmental conditions of interest.

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