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Hammel H T. Regulation of internal body temperature.
Annu. Rev. Physiol. 30:641-710, 1968.
[John B. Pierce Foundation Laboratory, Yale University, New Haven, CT]

Homeothermy in the vertebrate body illustrates physiological regulation in which the nervous system is involved. Central and peripheral temperatures are transduced to neural activities, and these signals are combined with reference signals to activate responses that minimize (when possible) deviation of central temperature from its optimal value for each species. [The *SCI*® indicates that this paper has been cited in over 385 publications.]

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I was invited by the editorial board of the *Annual Review of Physiology* to review the literature on temperature regulation from 1961 to 1967. I suppose I was chosen because we had shown that cooling the pre-optic and anterior hypothalamic nuclei (POAH) of conscious dogs elicited shivering and that the POAH temperature threshold for shivering was inversely dependent upon the skin and extrahypothalamic core temperatures.[1] I had also suggested a network of hypothalamic neurons that could account for the fact that each autonomic thermoregulatory response was proportional to deviations of POAH temperature from a threshold temperature and that these threshold temperatures were shifted up by low skin and rectal temperatures and by fever or were shifted down by high skin and rectal temperatures and by sleep.[2,3]

Homeostasis is a major physiological process that is exemplified by homeothermy. For homeostasis, three features of the nervous system are essential: (1) intensive properties of the internal environment of an organism must be transduced to neural signals, (2) a neural signal corresponding to the reference (optimal) value of each intensive property must be generated, and (3) autonomic and behavioral responses must be activated and controlled because their action minimizes the difference between an intensive property and its reference.

Much has been learned about these features since Claude Bernard discussed the "constancy of the internal environment" in 1865 and Walter Cannon coined the term "homeostasis" in 1929. But much more still needs to be learned. For example, almost nothing is known about the transduction of intensive properties (temperature, pressure, hydrogen ion concentration, electrolyte concentration, nutrient concentrations, metabolite concentrations) into generator potentials. This is a biophysical problem of immense importance. Little is also known about the neural network by which the neural signal of an intensive property is compared with its reference signal and from which network a neural-humoral connection is made with the appropriate organ to activate a response at an appropriate rate. At present, these networks can only be approximated. The majority of our knowledge concerns the way in which organs function, but too little is known about the neural elements that control the rate of response.

I am deeply gratified that my article has been frequently cited, but I wish for more: only when our younger peers glimpse the opportunities for monumental research on the fundamentals of regulation biology can we rest with modest satisfaction. I expect that autofacilitation will, in the future, be recognized as an essential feature of the controller network for some, if not many, regulatory responses.[4]

1. **Hammel H T, Jackson D C, Stolwijk J A J, Hardy J D & Strømme S B.** Temperature regulation by hypothalamic proportional control with adjustable set temperature. *J. Appl. Physiol.* 18:1146-54, 1963. (Cited 230 times.)
2. **Hellstrøm B & Hammel H T.** Some characteristics of temperature regulation in the unanesthetized dog. *Amer. J. Physiol.* 213:547-56, 1967. (Cited 100 times.)
3. **Hammel H T.** The regulator of body temperature. *Brody Memorial Lecture VI.* Columbia, MO: University of Missouri, 1966. 34 p. Special Report 73.
4. ————. Neural control of salt gland excretion: enhanced and sustained by autofacilitation. (Hughes M R & Chadwick A C, eds.) *Progress in avian osmoregulation.* Leeds, UK: Leeds Philosophical and Literary Society, 1987. (In press.)

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