

Thermoregulatory models

Recent research, current applications and future development

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WERNER J. Thermoregulatory models: recent research, current applications and future development. *Scand J Work Environ Health* 1989;15(suppl 1):34—46. This review traces the efforts of different fields of thermoregulatory modeling. The aims of the three diverging branches can be characterized by (i) insight into functional physiological mechanisms and prediction of physiological phenomena, (ii) prediction of human performance for the protection of industrial workers or military personnel, and (iii) prediction of the impact of accidents, diseases, and clinical treatments. Common current and future efforts may be recognized which improve the physiological quality of the models for purposes either of physiological research itself or of promotion of the field of application, namely, (i) to approach the models to real geometry and anatomy of the human body, (ii) to simulate more adequately heat transport processes induced by the circulating blood, (iii) to implement more sophisticated regulatory concepts, (iv) to take into account interaction with other regulatory systems. "Environmental Ergonomics" should be an adequate forum for linking these diversified fields together.

Key terms: circulatory heat transport, geometry of the body, interaction of physiological systems, mathematical simulation, regulatory concepts, temperature regulation.

General development in thermoregulatory modeling

The flourishing early era for the physiological modeling of the human thermal system has been clearly outlined in the famous review by Hardy in 1972 (1), which turned out to be a kind of epilogue to modeling in fundamental thermal physiology itself during the following decade. Milestones of these earlier physiological developments have been the Stolwijk model (figure 1 A) (2, 6), which is still the basis of many other modifications and applications, mainly in areas other than physiology, and the Wissler model (figure 1 B) (3, 7), which has been refined and enlarged in a very efficient way and is still under further development (8). Whereas the pioneers of physiological modeling had to cope with the prejudiced opinions that simplification and inaccurate models were an inadequate tool in view of the exact and complex biological reality, the further development of refined models in physiology has been impeded by the argument that the results emerge with an arithmetic precision which is unjustified in light of the inaccuracies of physiological measurements and data. Nevertheless many new and stimulating developments have taken place in diverse areas during the last decade, and these developments are often characterized by the fact that neither the modelers nor the physiologists take any notice of each other. This situation is, of course, very dangerous and unfruitful and should

be corrected by a linking together of the efforts and results which already exist. Experimental research in thermal physiology is in full progress [see, eg, *Thermal Physiology* (9), *Heat Stress* (10), both edited by Hales] and should be given more attention and credit by some modelers. On the other hand, some physiologists still have to recognize simulation as a valuable complementary tool to experimental research. A possible basis for renewed common efforts was established by the Yale Debating Symposium on Thermal Physiology (11), which, in conclusion, confirmed the research value of thermoregulatory models.

The present report is intended to serve the purpose of combining experiences, results, and efforts in diverse areas by reviewing the development in physiology, mechanical and chemical engineering, ergonomics, biomedical engineering, medical physics, and clinical areas such as radiotherapy and the treatment of hypo- and hyperthermia. However, the whole spectrum is too broad for complete coverage of the literature. Therefore I have concentrated on a personal selection of contributions from many scientific fields during the last decade. The more or less detailed descriptions come from my own experience and do not reflect the grade of relevance of single contributions, nor does the omission of modeling contributions imply lack of significance.

Recent and future developments in thermoregulatory modeling

Three diverging branches may be recognized from the last decade. They are characterized by three different

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aims and purposes, namely, (i) insight into functional physiological mechanisms and the prediction of physiological phenomena, (ii) the prediction of human performance for the protection of industrial workers and military personnel, and (iii) the prediction of the impact of accidents, diseases, and clinical treatments.

Clearly, prediction is the common feature, but the main objectives in the first branch, ie, the physiological branch, are to understand the regulatory concepts and the interaction with other systems of the body, to extrapolate to variables not experimentally attainable, and to simulate unperformable experiments. The sec-

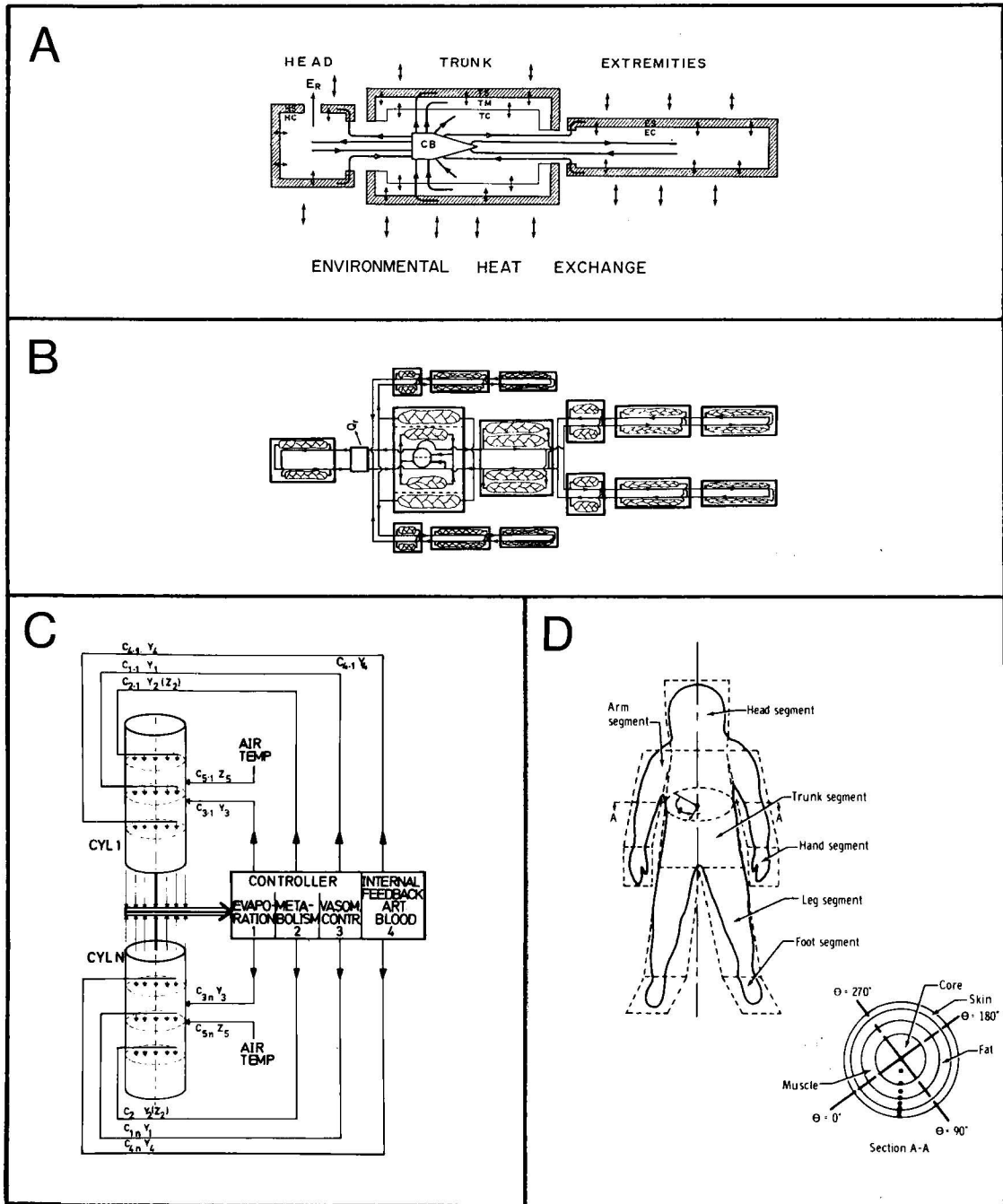


Figure 1. Examples of the classical versions of "cylindrical" thermal models. Part A shows the first version of the Stolwijk model (2) (reprinted with permission), a lumped parameter model, closed-loop; part B shows the second version of the Wissler model (3) (reprinted with permission), radial dependencies, open-loop; part C shows the first version of the Werner model (4), radial dependencies, closed-loop; and part D shows the first version of the Kuznetsov model (5) (reprinted with permission), radial and angular dependencies, closed-loop. (CYL = cylinder, TEMP = temperature, VASOM = vasomotor, ART = arterial)

ond branch is producing models primarily to learn the limits of performance and to calculate the effects of harsh natural environments such as the desert, the arctic, the atmosphere, or the ocean. Special emphasis is placed on workers in technically evoked environments, eg, workers in mines, steel works and glass factories, air crew members, and astronauts. The objective is, on one hand, a higher utilization of manpower and, on the other, the prevention of diseases and accidents. The third branch is concerned with the consequences of diseases and accidents, because they either are currently inevitable or occur because of insufficient precautions. Important aspects are the treatment of accidental hypo- or hyperthermia and also diathermy and radiotherapy. Although these developments take place independently of one another, common current and future efforts may be recognized which improve the physiological quality of the models for purposes of either physiological research itself or promotion in the field of application, namely, (i) to make the models approach the real geometry and anatomy of the human body, (ii) to simulate more adequately the heat transport processes induced by circulating blood, (iii) to devise more sophisticated regulatory concepts, (iv) to take into account interaction with other regulatory systems, and (v) to account for individual differences.

Recent developments towards the real geometry and anatomy of the body

The complexity of existing models depends primarily on the purpose of the models. The early Stolwijk model (2) was confined to three cylindrical body compartments with two or three concentric layers plus a central blood compartment allowing one to assign the same number of different values to different parameters and to compute the temperatures of these elements plus the global effector responses. The model is a reduction of complex reality and has turned out to be very useful in various applications, especially in the prediction of performance in hot environments. It has been modified and adapted by the originator himself (6) and by many others. Montgomery (12) and recently Tikuisis et al (13) used a special version with additional temperatures in each element for calculations of the effect of cold immersion. Konz et al (14) improved many details and showed good experimental validation. Special reference was given to clothing in the adaptation of Smith & Twizell (15). A considerable increase in the number of elements was introduced by Gordon et al (16) with the effect of better validation with respect to responses to cold exposure. A recent version of the early Wissler model computes 225 temperatures in 15 elements plus many other variables. [See Wissler (8) and the following discussion.]

All these models, although very successfully used in special applications, fail to account for temperature distribution in any spatial direction other than radially outward from the body centerline.

In 1975 and 1977 I introduced the principle of spatially distributed parameters into thermoregulatory modeling (figure 1 C) (4, 17), but the version presented in 1975 was confined to the dynamics of radial temperature profiles. Kuznetz (5) developed a two-dimensional transient model (figure 1 D), which, however, like all its predecessors, adhered to the approximation of the human body by various cylindrical elements and to the simplification that the only thermal transfer between body compartments is via circulating blood. However, as analyzed by Buse & Werner (18), the geometry and inhomogeneity of the body is the most important feature if one aims at a computation of temperature profiles close to reality. Simulations are far more sensitive to alterations of these features than to changes of other physical or physiological parameters.

In 1977 a data base of the macroscopic anatomy of the human body was developed by photogrammetric treatment of three-dimensional anatomic models (Somso Company, types: AS 23, NS 9—15) and the further analysis of the thereby obtained sectional maps; the procedure has been described in detail by Kelterbaum et al (19).

The global data of the available anatomic model are height 1.76 m, weight 67 kg, mean density $107 \text{ kg} \cdot \text{dm}^{-3}$, surface 1.8 m^2 , and volume 62.7 dm^3 . For computer treatment the anatomic model was projected on a three-dimensional grid, for which 0.55 cm was chosen for the head and the extremities and 1.1 cm was chosen for the trunk.

This procedure makes possible a representation of vessels with a diameter of ≥ 1.1 and ≥ 0.55 cm and of all essential organs of heat production. With the additional aid of anatomic atlases and data on the distribution and density of tissue a satisfactory digital representation of the body has been obtained. A higher resolution would have been desirable at many sites, eg, in the hands and feet or in other parts of the body for a more precise modeling of the circulatory system. Although computer tomography would make possible such a data base now, such a simulation would go beyond the capacity of currently available computers. Figure 2 shows examples of the head, leg, and trunk sections from the digital atlas. Different symbols represent different body components, which in this treatment of the body add up to 54 different types. The structures to which different values of parameters may be attributed are 16 skin areas, 10 muscle areas, 6 types of vessels, 4 areas of the central nervous system, the heart, the liver, the lungs, the kidney, the stomach, the gut, the fat, the connective tissue, the bladder, the thyroid gland, the spleen, the esophagus, the trachea, the eyes, the skeleton, the skull, air, and blood. The parameters attributed to these 54 types of body components are heat conductivity, specific heat capacity, density, basal specific metabolic heat production, and specific blood flow.

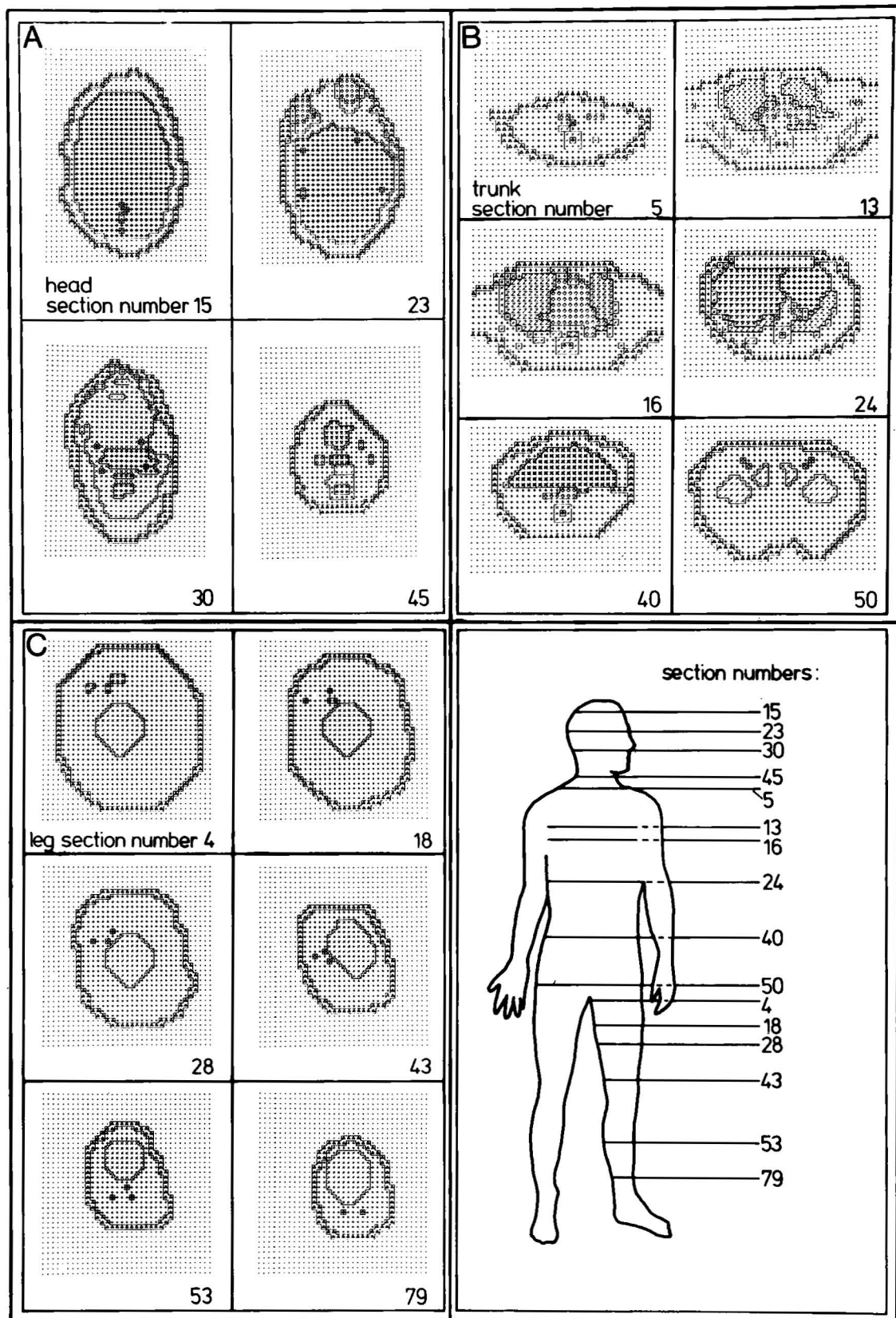


Figure 2. Examples of transverse sections from the digital atlas for the three-dimensional (nonscylinder) model of Werner & Buse (20).

The passive system is essentially described by a three-dimensional diffusion equation with coefficients as functions of the local coordinates x, y, z . Such equations are usually solved by the finite difference methods, and especially by a modification of the alternating direction implicit method. For the following two reasons this method seems to be advantageous: (i) it is an implicit method, the difference equation involved being stable for all quantities of $\Delta x, \Delta y, \Delta z, \Delta t$, and (ii) by partitioning one equation with three implicit directions into three equations with one implicit direction each, an algebraic reformulation results in three tridiagonal systems which can easily be solved by Gaussian algorithm.

The simulation first delivered a realistic picture of the topography of temperatures under neutral conditions (20, 21). The compatibility of reality and simu-

lation was tested by experiments and through a comparison with values given in the literature. It was achieved solely on the basis of physical considerations and physiological data. An adjustment of parameters of the passive system is not necessary, and the computation should be equally suited to delivering temperature profiles which cannot be obtained experimentally.

The first temperature profiles of transverse sections of the body in the indifferent status ($T_a = 30^\circ\text{C}$) have been computed (figure 3). For the head, temperature is extremely constant. A decrease in skin temperature starts only at the skull. This phenomenon is due to the high metabolic and blood flow rate of the brain. The profiles of the extremities are, due to the lower metabolic and blood flow rate, more convex, but equally rather homogeneous and smooth. For the trunk, es-

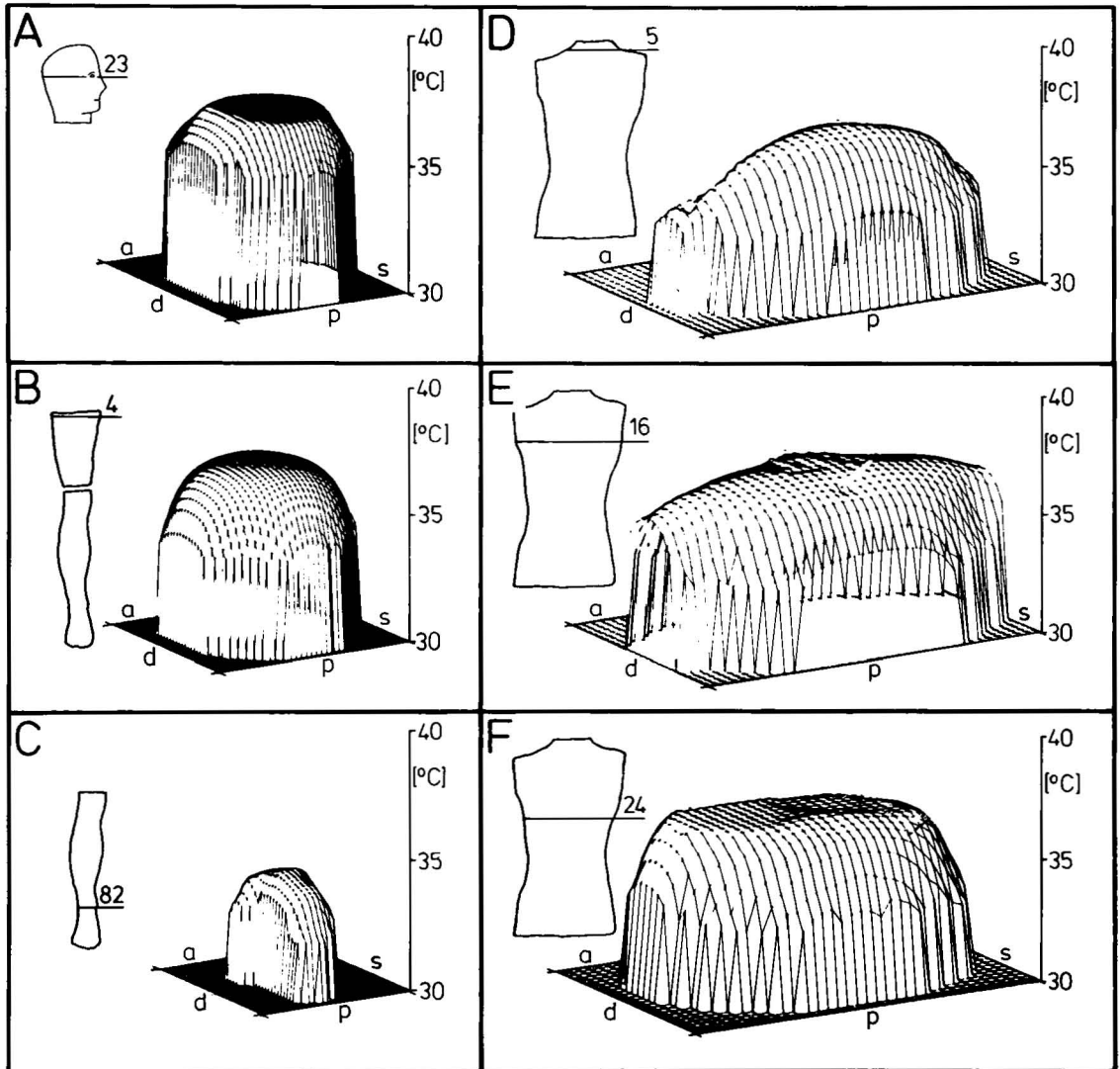


Figure 3. Temperature profiles of transverse sections in a neutral environment computed by the three-dimensional model (p = posterior, a = anterior, d = right, s = left. The sections are seen from caudal to cranial sites (see insets).

pecially the transverse profiles depend on the longitudinal coordinate. With the availability of more computer core capacity, it has become possible to compute the dynamics of every temperature profile within the body. For an example see figure 4.

A new two-dimensional version of the Wissler model will certainly fill a gap between the one-dimensional models and the three-dimensional model, which for many applications may be too complex.

Other approaches are primarily concerned with modeling the true anatomy of organs or parts of the body. An interesting new model presenting isotherms of the human thigh is under development (8). It uses an elliptical coordinate system and will, when provided with a finer grid near the surface, allow a more representative description of the subcutaneous fat distribution.

The thermal response of human thigh exposed to diathermy treatments has been described by Emery & Sekins (22), using the method of finite elements with a densely constructed grid in the vicinity of the diathermically heated zone and a relatively sparse grid elsewhere with the exception of the surface. The simulation can be used to predict the response of living tissue to a variety of treatment protocols, and it is particularly used for the definition of the correct diathermy dose for tumor treatment. A comparison of experimental and numerically determined transient responses shows good agreement, particularly in the region of the heated muscle.

The method of finite elements has also been used by Iskander & Khosdel-Milani (23) for calculating temperature distributions in cross-sections of the human thorax, also with respect to hyperthermia treatments. Whereas these are two-dimensional treatments, Olsen et al (24) presented a finite element representation of the monkey head by rotating one section about the heavy base line. This procedure is, of course, completely inappropriate for the lower head, but it seems to be acceptable for the brain. It was used to predict the effects of arterial blood cooling by cardiopulmonary bypass.

The effects of inhomogeneities and finite boundaries on temperature distributions with respect to application to tumors were analyzed by Jain (25) by modeling three spherical zones, ie, a heating core of a probe, the periphery of the probe, and a perfused medium. This contribution is interesting both with respect to radiotherapy and to thermal physiology because the model of a perfused porous medium has been used to circumvent a mathematical description of the complexities of the microcirculation of a tissue. (See the following discussion.)

A detailed discussion of the mathematical modeling of heat transfer with respect to cancer therapy has also been given by Jain (26), and a special survey of the simulation of hyperthermia in tumor treatments has been written by Strohbehn & Roemer (27). A two-dimensional, axi-symmetric, inhomogeneous patient

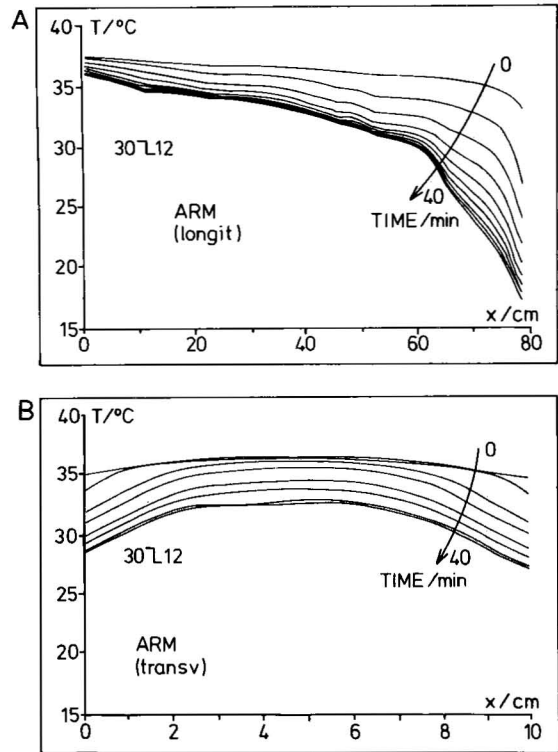


Figure 4. Example of the dynamics of the central longitudinal (longit) (A) and radial (transverse, transv) (B) temperature profiles of the human arm in response to a stepwise change of air temperature from 30 to 12°C (humidity 30 % and air speed $0.1 \text{ m} \cdot \text{s}^{-1}$).

model has been used by Paulsen et al (28) for computing temperature profiles for concentric coil induction heating devices. The finite element grid and an example of isotherms are shown in figure 5.

Another contribution should be mentioned in this context, although it uses a lumped parameter model (65 elements), because it is designed to evaluate the effects of thermal compensation (evaporative spray cooling) in hyperthermia treatments (29). However, it needs further experimental validation.

Recent developments towards a better representation of circulatory heat transfer

Convective heat transfer plays an essential role in temperature regulation. It is determined by the vessel geometry and the flow conditions within the vessels. The parameters of heat transport are the heat transfer coefficient vessel/tissue, viscosity, density, the heat capacity of blood and flow velocity, diameter, and the length of the vessel.

Whereas the aforementioned models assumed that the thermally significant heat transfer takes place in the capillaries, it was shown by Chen & Holmes (30) that thermal equilibrium is already reached in vessels of medium diameter. This phenomenon has been con-

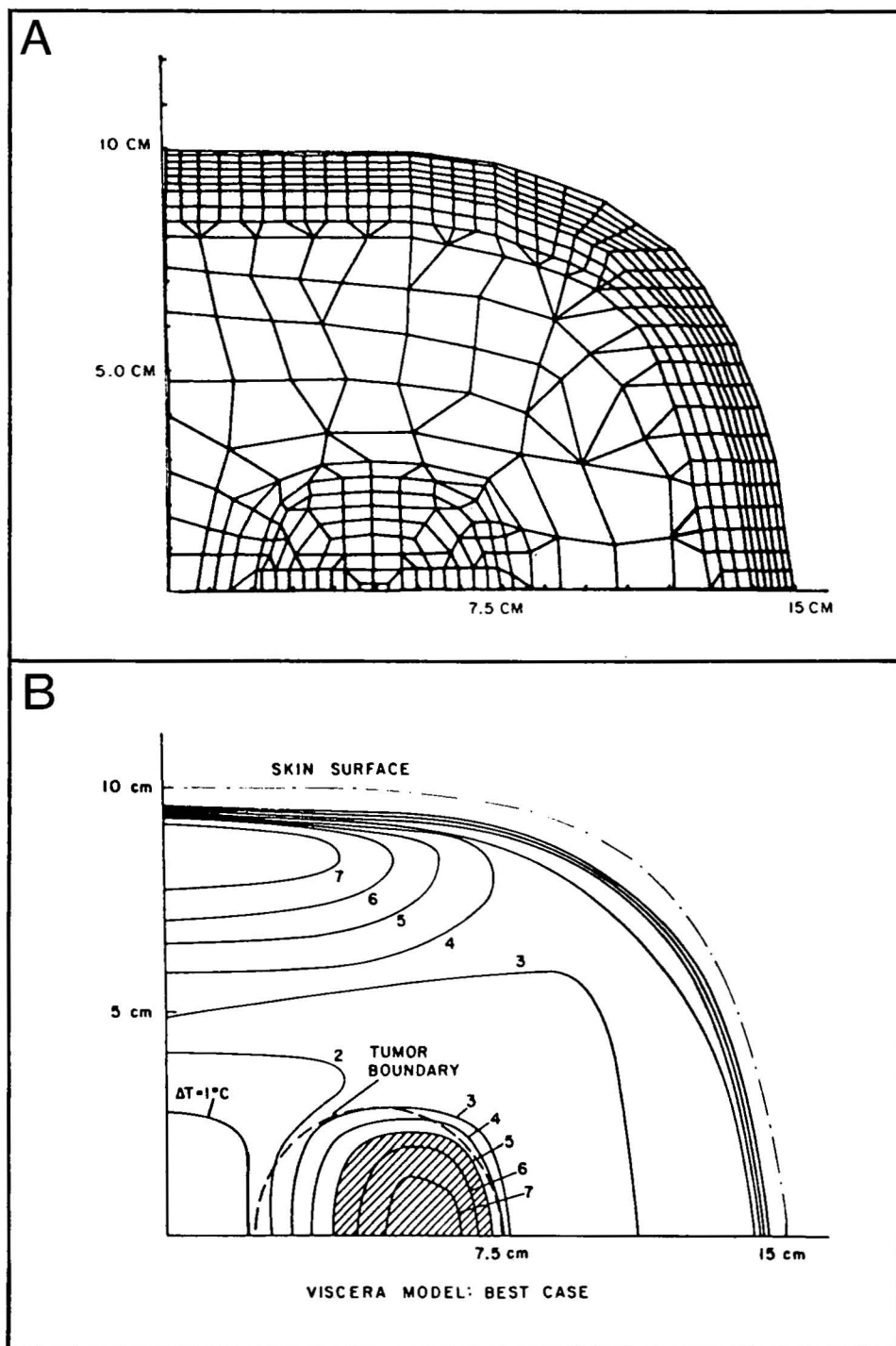


Figure 5. Example of modeling hyperthermia treatments (from Paulsen et al (28) and Strohbehn & Roemer (27), with permission). [A = the finite element grid used for calculating the isotherms for concentric coil heating; B = example of isotherms for concentric coil heating (viscera model: skin held at 20°C , blood flow in tumor = 0, in viscera $27\text{ ml} \cdot 100\text{ g}^{-1} \cdot \text{min}^{-1}$, in muscle/fat $18\text{ ml} \cdot 100\text{ g}^{-1} \cdot \text{min}^{-1}$)].

firmed both by further theoretical (31) and experimental studies (32). The lower limit for thermal nonequilibrium seems to be 50 to 100 μm for the arteries

and 400 μm for the veins. In this respect smaller vessels are thermally insignificant. These findings contrast with the view of former modelers that most heat trans-

fer occurs in the capillaries, and it suggests that vascular heat transfer analysis must take into account the vascular architecture of the 50- to 1000- μm vessels in which most heat transfer occurs. Therefore a three-layer representation of heat transfer in surface tissue has been developed both by anatomical and by theoretical investigations (31, 33). It takes into account the variation of the number, density, size, and flow velocity of the countercurrent arteriovenous vessels as a function of depth from the skin surface, the directionality of blood perfusion in the intermediate layer with transverse vessels, and the superficial shunting of blood to the cutaneous layer. The simplified three-layer model with the deep, intermediate, and cutaneous layer is shown in figure 6.

The body is thus able to conserve heat in a cold environment by providing a much thicker outer conduction layer than had previously been realized (34). On the other hand, the close proximity of these thermally insignificant vessels to the surface provides for a significant augmentation of the heat loss through the skin, and this augmentation is primarily controlled by cutaneous circulation. In general, the intermediate layer dissipates the small temperature perturbations due to the thermally significant vessels in both the deep tissue and the cutaneous layers. The circulation in the cutaneous layer is independent of the skeletal muscle circulation. It is provided by a few larger vessels which rise obliquely from the large arteries and veins, penetrate the skeletal muscle, and then connect directly with the larger vessels of the cutaneous plexus. The relatively large, thermally significant superficial vessels lie in the lower portion of the cutaneous layer. The critical pathways in the blood flow regulation of the cutaneous layer are the 20- to 40- μm arteriovenous anastomoses. While the vertical connecting vessels are themselves too small to transfer much heat into the more superficial regions of the skin layer, their vasodilation and vasoconstriction significantly controls the flow of blood into the more superficial plexus.

For a 5 to 10°C difference between the local arterial temperature in the major supply vessels and the skin temperature, a countercurrent arteriovenous temperature difference of only 0.1 to 0.2°C was found in the deep layer. The distribution of capillary perfusion does have a significant effect on this small arteriovenous temperature difference. Jiji et al (33) concluded that the principal mechanism by which the tissue and the microvasculature exchange energy is the slightly incomplete countercurrent exchange that occurs in the thermally significant vessels.

On the basis of these findings, Weinbaum & Jiji (35) developed a new simplified bioheat equation for the effect of blood flow on local average tissue temperature. The new theory claims that the vascularization of tissue causes it to behave as an anisotropic heat transfer medium. The Weinbaum-Jiji impact on the bioheat equation has recently evoked a continuing debate. Wissler (36, 37) has pointed out that the Wein-

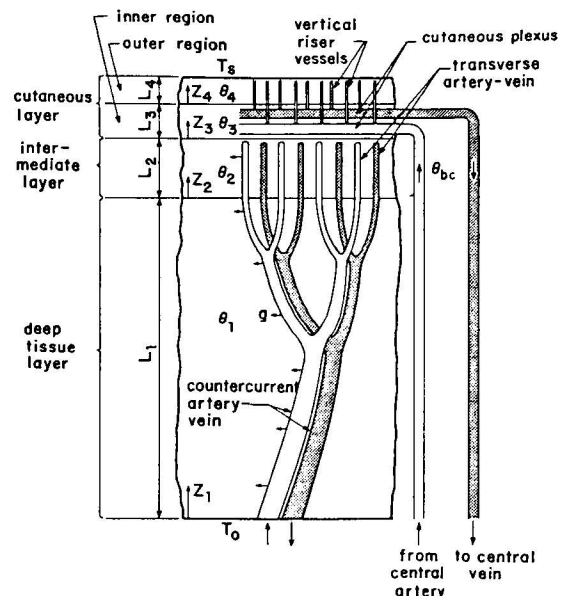


Figure 6. Simplified three-layer model showing basic vascular structure in deep, intermediate, and cutaneous layers (from Song et al (34), reprinted with permission). Only thermally significant counterpart vessels are shown in regions L_1 and L_2 . The capillary beds have been omitted throughout.

baum-Jiji formulation is probably appropriate for vessels that are smaller than 200 μm in diameter, but that its applicability is questionable for larger vessels, where blood flow is nearly perpendicular to the temperature gradient and where there is little enhancement of those elements of the thermal conductivity tensor that affect the radial temperature profile. It has been suggested that the bioheat equation should include elements of both the Weinbaum-Jiji formulations and the classic formulations treating the convective effects of the moving blood as a volumetric isotropic heat source and the assumption that the heat transfer is proportional to the blood flow rate and the temperature difference of blood and adjacent tissue.

Recent developments towards modeling the regulatory concept

Most of the published equations for the control of the thermoregulatory effector mechanisms are based on the concept that there are two integrated drives, one central signal and one peripheral signal. [For a review see Simon et al (38) and Werner (39).] Both additive and multiplicative processing of the two signals has been proposed. A comparison of the results of these models shows that, in spite of the apparent divergence, all the values are within the inter- and intraindividual variations measured by various authors. In view of this span of experimental data, it does not seem to be justified to favor a nonlinear approach. Moreover for moderate thermal load all models deliver comparable results as to the three global variables effector activi-

ty, core temperature, and mean skin temperature. There is general agreement that the weight of the peripheral signal has to be assessed at between 10 and 20 %.

With the use of more elaborate models of the passive thermal system, the question has to be asked of whether such simple controller concepts are able to account for the distributed temperature field in the cold. Especially the question of whether the inhomogeneous temperature field is primarily due to the inhomogeneous structure of the body or, in addition, to a distributed controller concept, ie, one must examine whether the spatial pattern of effector distribution is maintained after thermal load or whether there is active modification and control. In a comparison of both possibilities the generally used weighting of the thermal input signal was only slightly modified according to the results of Heising & Werner (40) and also other results which required that muscle temperature, at least, should be taken into account, the weighting of which should be near that of the skin temperature signal (10 % being assigned to both and 80 % to the core; the signal threshold being assumed to be 37°C). The increase in metabolic heat production is obtained by multiplication of the weighted thermal input signal by the controller gain. With the use of the three-dimensional model of the passive system that has al-

ready been described (20, 41), the optimal lumped parameter gain that delivers the best agreement with the global experimental variables was determined to be about $5000 \text{ W} \cdot \text{m}^{-3} \cdot ^\circ\text{C}^{-1}$, a value in agreement with that of other reports. However, when the spatial distribution pattern of temperature in the cold is examined, it becomes clear that maintaining the pattern of distribution of heat production yields amounts that are too high for the arms and legs, which do not contribute much to the stabilization of central trunk and head temperatures. This phenomenon is illustrated by figure 7. In this figure the simplest distributed parameter approach delivering a correct temperature distribution is given in the parts labeled B; they take into account at least three different regions, the gain factor varying from 5200 to $0 \text{ W} \cdot \text{m}^{-3} \cdot ^\circ\text{C}^{-1}$. There is therefore a concentration of heat production in the central areas and simultaneously a reduction of dry heat loss. In conclusion, for cold defense, a spatially distributed control of heat production is required.

A similar, but minor, relevance of the distributed control concept has been confirmed with regard to blood flow rate. However, the influence of the values of distributed minimal rates is more relevant than locally differing gains. On the other hand, the influence of distributed controller structures is not so obvious in the defense against heat with regard to evaporative

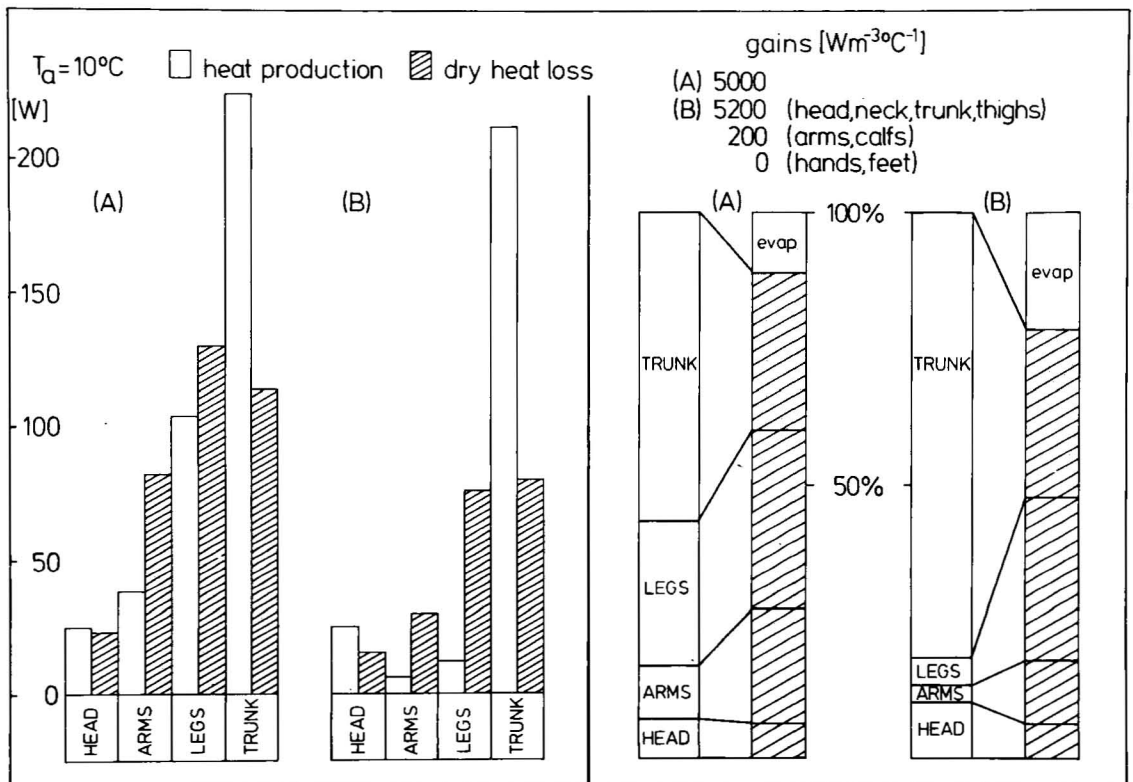


Figure 7. Distribution of heat loss and heat production according to the best case of lumped parameter control of skeletal muscles (A) and according to the simplest distributed parameter control (B) compatible with experimental results. Air temperature 10°C. Three dimensional model of Werner & Buse (20) used for the passive system.

heat loss. There are only very small temperature differences in the body after a stronger heat load. Therefore, for sweating rate, the question of whether there is distributed control or not can only be tested with the use of different thermal loads to different parts of the body.

Developments towards modeling interaction with other regulatory systems

Thermoregulation is highly interconnected with other regulatory systems of the body. There is a strong interaction with metabolism, circulation, respiration, osmoregulation, and other systems. Most of the models reduce their couplings to the minimum extent necessary to simulate thermal performance. However, with further insight into the physiological mechanisms, it becomes more and more necessary to take into account the multilateral influences and, in special situations, the competition between these subsystems. Although there is no model which can be called complete in this respect, the recent Wissler model (42) presents many interesting features. It contains mass balances for oxygen, carbon dioxide, and lactic acid in order to provide information required in the control equation for perfusion and ventilation. As for metabolism, the equations used in the model are based on a greatly simplified metabolic scheme, which does, nevertheless, include most of the essential features. It is assumed that energy is obtained from the oxidation of carbohydrate, which can be represented by glucose. The objective of the metabolic reactions involved in exercise is to form adenosine triphosphate from adenosine diphosphate and orthophosphate. Adenosine triphosphate is readily hydrolyzed in muscle cells and ultimately provides the energy needed to do mechanical work. The chemical reactions are incorporated into the model through material balances for each chemical species in tissue and blood. As for oxygen, it is assumed that equilibrium exists between oxygen in myoglobin and oxygen in hemoglobin. For carbon dioxide, equilibrium is assumed between the carbon dioxide stored in tissue and blood with a tissue concentration 50 % of that in blood. Lactate is supposed to be transferred from muscle to blood at a finite rate proportional to the difference in concentration. For the lungs, a special term is required to account for the exchange of gas between pulmonary capillaries and the alveolar space.

In evaluations of the exchange rate through the lungs, the periodic character of pulmonary ventilation is neglected. The model works with time-averaged values of such quantities as the ventilation rate and the temperature, humidity, and the partial pressure of oxygen and carbon dioxide in expired gas. The lungs are heated as a well-mixed region of constant volume through which gas passes at a constant rate.

Although this model still operates with an arterial and a venous pool, it contains some special circulatory features that take into account the fact, eg, that one

vein from each leg flows into the abdominal section of the trunk and that in the thoracic section all venous streams terminate and arterial streams originate. It is assumed that the temperature of the blood entering the pulmonary capillaries is equal to the mixing mean temperature of the venous streams entering the right ventricle.

The control equations are, on the whole, rather sophisticated. Wissler emphasizes that inferences concerning physiological mechanisms should not be drawn from the equations because they have been specifically designed to result in a system which responds to thermal stress and exercise in a manner similar to human subjects. This recommendation holds especially for the perfusion equations, which are elaborated well in the model but for which very few solid physiological data are available. The shivering equations, too, are given very detailed treatment consistent with various physiological findings. Because of the enormous amount of variability in experimental data, sweating is represented by a comparatively simple linear relationship. At present, this model is the most complete with respect to the interaction of systems. It is well validated in various applications, such as for exercise at increasing rates, head-out immersion in water, exposure to hyperbaric mixtures of helium and oxygen, and head-out immersion of lightly clothed subjects in cold water while resting and swimming, also followed by rapid rewarming in warm water. The model is, of course, still being developed. It will be worthwhile to extend it to a two-dimensional form.

The interaction or competition of systems is still a rare subject in modeling. Leigh (43) combined a special version of the thermoregulatory Stolwijk model with the Grodins model (44) of respiratory control. As respiratory heat loss can be important for miners, mine rescue workers, firemen, astronauts, and others, the model has potential practical value in addition to its role in the study of physiological control mechanisms.

Individual differences

For various applications it has been pointed out that there is need for taking into account individual variations. Some models principally allow for subject weight and body fat, especially mean skinfold thickness. However, most cold studies continue to be performed without determining subcutaneous fat thickness, and this lack could explain many variations between individual responses (8, 45). Although many models are very useful in the description of mean behavior, thermal and work performance, tolerance limits, etc, should also be predicted for the individual. This recommendation implies, however, that at present the most complex models are not suited for such tasks. In general, physiological models are still difficult to handle for individual evaluation, and such evaluation is still the domain of the practically useful empirical models such as that developed by Givoni & Goldman (46) and others.

Concluding remarks

The spectrum of current activity in thermoregulatory modeling is broader than it seems at first sight. However, the center of activities has shifted from physiological laboratories to diverse applied sciences. This is a positive development on one hand because most of the recent models are designed for definite applied purposes and demonstrate their usefulness by delivering practicable results. On the other hand, this is a dangerous development because modelers get used to working without contact with physiology, and this situation gradually leads to more phenomenological or heuristic models and to less functionally physiological models. In the long run this trend diminishes the amount of confidence in predictive results because validation is, if at all, primarily inferred from the compatibility of the system performance in simulation and in reality for certain selected situations and not necessarily from the congruence of the physical laws and mathematical operations used in simulation and reality. Furthermore, the impact of modeling on the design and the results of physiological experimental research is reduced to a minimum if the applied sciences and physiology operate independently of one another.

What are the main factors still impeding a more rapid progress in thermoregulatory modeling? Computer capacity, which formerly restricted thermoregulatory simulation to rather simple models, is principally no longer a factor. The spectrum of models now available covers all grades of complexity and all levels of computer types from the cheapest personal computer up to supercomputers, including array and vector processors. The main factor is still the lack of physiological knowledge about the structure and functional mechanisms of subsystems and their interaction within the organism. This situation is primarily due to the immense complexity of the real system. It is a hierarchical multilevel system, meaning, eg, that operating changes generated in higher centers may occur on the basic system level as spontaneous changes or as long-term adaptive changes. Furthermore, thermoregulation is part of an interacting multigoal system imbedded in various control loops of the body which influence one another or may even compete with one another. Thus experimental analysis has to cope with the enormous difficulties of isolating subsystems and analyzing their interactions. Moreover thermoregulation is a distributed parameter system, meaning that all variables and parameters are spatially distributed within the body, ie, are functions of time and the three-dimensional local coordinate. This phenomenon explains the difficulty of analyzing representative elements, variables, and parameter values. As for the active (controlling) subsystems, there is practically no adequate experimental method of analyzing afferent and efferent information processing. Evoked potentials are as inadequate as single unit recordings, not to mention the problems evoked by anesthesia.

Besides the lack of insight into functional mechanisms, the second factor is the lack of definite basic parameter values, which in the life sciences are not compiled in a systematic way, as is done in physics or the engineering sciences. Many studies are restricted to the principle effects. Routine quantitative parameter screening is not popular and probably not accepted by physiological journals. Generally there is no awareness that the determination of complete sets of data will be appreciated by all colleagues involved in biomedical simulation. On the other hand, it cannot be overlooked that, for some classes of parameters, there is no experimental approach or no measuring technique available. Finally intra- and interindividual differences impede the edition of complete parameter tables. [The pure compilation of the outer dimensions of the body comprises a three-volume data book (47)].

Third, there is apparently a lack of possibilities for validation. In addition to the obvious impossibility of testing all results experimentally, it is a fact that experimental research programs especially designed for validation are generally not supported, as they comprise types of experiments which were done formerly "in principle."

The question now arises of what can be and should be done besides waiting for further developments and new results in basic physiology. It is the interdisciplinary cooperation in biomedical modeling which has undergone much frustration during the past several decades and in many areas has degenerated to a pure declamation, but which has to be revived for the sake of more fruitful progress. More integrative research has to be encouraged and supported. Narrow-minded defense of special areas against invaders must be condemned. The multidisciplinary approach of carrying out comparable research with different methods independently of one another has to be transformed into a real interdisciplinary approach of experts with overlapping knowledge and experience. It is no use defining more thoroughly the borders of physiology, applied physiology, clinical physiology, occupational physiology, ergonomics, and bioengineering. On the contrary, it is necessary to recognize, and to convince those who would benefit, that these areas necessarily comprise various common sets, which can only be attacked by the community of the sciences involved. "Environmental ergonomics," if understood as the integrative and coordinated efforts of human physiology and human engineering to analyze performance in harsh environments and to protect those who are submitted to it, should be an adequate platform to improve the fruitful development of both the experimental and the modeling approach.

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