Equation 5 coincides with Equation 3 if $\mathbf{v}(\mathbf{r}, t)$ is replaced by the local average velocity $\langle \mathbf{v}(\mathbf{r}, t) \rangle$. The volume element to be averaged is of the same size as the thermo sensor.[6] The equation that accounts for a local dipole symmetry of the velocity field is:

$$\Delta T(\mathbf{r}, t) - \frac{\partial}{\partial t} T(\mathbf{r}, t) = q(\mathbf{r}, t). \tag{6}$$

Equation 6 is identical to Equation 1. The heat diffusivity, however, is replaced by the velocity-dependent effective heat diffusivity $\chi_{\text{eff}}$.[7] In this case the phenomenological model mentioned earlier is confirmed. This result is also confirmed by the investigation of Wodick,[8] who treated the diffusion–convection problem by means of the Monte Carlo method.

A mathematical derivation of the bio-heat transfer equation from the present theory has not yet been realized. Because of the fundamental importance of this equation, this derivation should be carried out in order to give the theory of heat transfer in biological tissue a solid foundation.

## References


1. Pennes, H. H. 1948. J. Appl. Physiol. **1:** 93–122.
2. Perl, W., 1962. J. Theoret. Biol. **2:** 201–235.
3. Shitzer, A. 1972. Israel J. Technol. **11:** 169–177.
4. Priebe, L. & E. Betz. 1969. Aerztl. Forsch. **23:** 18–30.
5. Klinger, H. G. 1974. Bull. Math. Biol. **36:** 403–415.
6. Klinger, H. G. 1978. Bull. Math. Biol. **40:** 183–199.
7. Klinger, H. G. & E. Gabriel. 1976. Arzneim. Forsch. **25:** 977/7.
8. Wodick, R. 1976. Möglichkeiten und Grenzen der Bestimmung der Blutversorgung mit Hilfe der lokalen Wasserstoff-clearance. Steiner Verlag. Wiesbaden.


# MICROVASCULAR CONTRIBUTIONS IN TISSUE HEAT TRANSFER


Michael M. Chen

*Department of Mechanical Engineering*
*and Bioengineering Faculty*
*University of Illinois*
*Urbana, Illinois 61801*

Kenneth R. Holmes

*Department of Veterinary Biosciences*
*and Bioengineering Faculty*
*University of Illinois*
*Urbana, Illinois 61801*


## Introduction

Many mathematical formulations of the heat transfer in living tissues[1-3] have been for the purposes of studying thermal regulation, comfort, or other phenomenon where significant localized (as opposed to whole-body or regional) variations in temperature and heat flux were of little interest. The advent of intensified interest in hyperthermia as a cancer therapy and the safety associated with ultrasound and microwave radiation, as well as attempts at a quantitative interpretation of thermographic measurements, however, have made it highly desirable to have formulations that are valid also for small-scale temperature variations.

Living tissues differ from nonbiological materials primarily because of the presence of the vasculature. The large number and the architectural and dimensional variety of blood vessels clearly make it impractical to account for their individual contribution to heat transfer processes in the tissue with the exception, of course, of the larger arteries and veins. In the fields of heat transfer and fluid flow, when one encounters problems with a large number of structures whose individual dimensions are small relative to the macroscopic phenomenon under study, a common practice is to adopt the so-called continuum description. In this description, only the collective behavior of the small structures is taken into consideration in a certain statistical manner. Usually the influence of the small structures are ultimately expressed in terms of continuum properties of the medium, in our case, the thermal conductivity, specific heat, and blood perfusion rate of the tissue. It is the purpose of this report to explore the theoretical basis for the relationship between these properties and the architecture and function of the vasculature.

It will be shown that because of the vasculature, and the large rate of blood perfusion, living biological tissues are fundamentally different from inert materials. Consequently, the familiar thermal properties can no longer be assumed to be independent of the parameters of the temperature field. In other words, these properties may vary, depending on the nature of the application. In view of the fact that existing formulations of the bio-heat transfer problem have been found to be more or less satisfactory for the description of heat transfer involving *large-scale* tempera-



0077-8923/80/0335-0137 $01.75/0 

ture variations (i.e., length scales of the temperature nonuniformity of the order of 100 mm or more), the attention here has been focused on small-scale (length scale of the order of 10 mm) temperature variations. In this light the contribution of the larger vessels should clearly be treated individually, rather than collectively. Therefore, although the theoretical approach presented here is essentially general, the results are most applicable to microvascular contributions.

While the present paper is concerned with the theoretical basis of the contribution of the heat transfer by the microvasculature, current data on the structural and functional parameters of the vasculature are inadequate to allow an evaluation of the thermal parameters involved. Thus the theory developed herein is intended to act as a guide to experimental evaluation of the actual thermal properties. Such experimental evaluation is currently in progress in our laboratory and will be described in a separate communication.

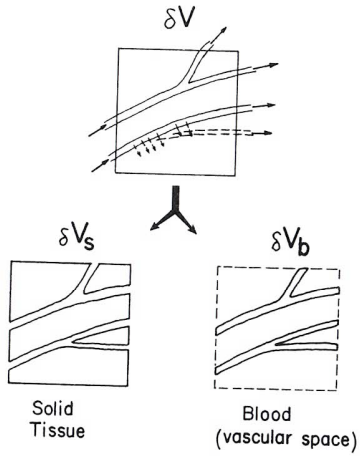


FIGURE 1. Two-dimensional schematic representation of the total tissue control volume $V$, as comprised of the solid tissue subvolume $V_s$ and the blood subvolume $V_b$.

## SYSTEM DESCRIPTION

Consider a differential control volume $\delta V$, shown schematically in a two-dimensional representation in FIGURE 1. To avoid certain confusion occasionally encountered in the literature, we shall distinguish the vascular space occupied by blood $\delta V_b$ and the space occupied by the solid tissue $\delta V_s$. Thus

$$\delta V = \delta V_s + \delta V_b. \tag{1}$$

It should be noted that mass is not conserved in either subvolume, since there is a small but finite fluid exchange between the vessel and the solid tissue as shown in FIGURE 1. To reconcile this with a minimum of theoretical complication, we shall



adopt the artifice of including enough (and only enough) of the lymph fluid volume in the vascular volume $\delta V_b$ to account for the fluid exchange between the vascular and lymph circulations. The remaining part of the lymph fluid shall be considered part of the solid tissue subvolume $\delta V_s$. This can be justified by the fact that lymph flow is usually quite slow, and that the lymph fluid can be expected to be fully equilibrated with the local solid tissue temperature.

It will be assumed that

$$\phi_b \equiv \frac{\delta V_b}{\delta V} \simeq \frac{\delta V_b}{\delta V_s} \ll 1, \tag{2}$$

and that the dimension of $\delta V$ (of the order of $\delta V^{1/3}$) is small relative to the scale of macroscopic temperature variations in the tissue, but large relative to the scale of the microscopic temperature variations due to the presence of the microvasculature. This permits us to define the "local mean temperatures" for solid tissue and blood. Respectively, they are

$$T_s \equiv \frac{1}{\delta V_s}\int_{\delta V_s} T\mathrm{d}V, \tag{3}$$

$$T_b \equiv \frac{1}{\delta V_b}\int_{\delta V_b} T\mathrm{d}V. \tag{4}$$

For simplicity of discussion it shall also be assumed that the solid medium in $\delta V_s$ has uniform thermal properties.

Conservation of energy for the solid tissue is expressed as

$$\delta V_s \rho_s c_s \frac{\partial T_s}{\partial t} = \delta Q_{ks} + \delta Q_{b-s} + \delta Q_m, \tag{5}$$

where $\rho_s$ and $C_s$ are the solid tissue density and specific heat, respectively. $\delta Q_{ks}$ is the conductive heat gain, $\delta Q_{b-s}$ is the heat gain from the blood subvolume, and $\delta Q_m$ is metabolic heating. A similar equation can be written for the blood subvolume:

$$\delta V_b \rho_b c_b \frac{\partial T_b}{\partial t} = \delta Q_{kb} - \delta Q_{b-t} \int_S \rho_b c_b T\mathbf{u} \cdot \mathrm{ds}, \tag{6}$$

where $\rho_b$ and $c_b$ are the blood density and specific heat, respectively; $\delta Q_{kb}$ is the conductive contribution; the integral over the surface area $S$ is the convective contribution due to blood (and lymph) flow; and $\mathbf{u}$ is the velocity (boldface denoting a vector quantity).

Addition of Equation 5 to Equation 6, and dividing by $\delta V$ results in

$$\rho c \frac{\partial T_t}{\partial t} = q'_k + q'_m + q'_p, \tag{7}$$

where $\rho$ and $c$ are

$$\rho = (1 - \phi_b)\rho_s + \phi_b \rho_b, \tag{8}$$

$$c = \frac{1}{\rho}[(1 - \phi_b)\rho_s c_s + \phi_b \rho_b c_b], \tag{9}$$

and $T_t$ is the local mean tissue temperature expressed as

$$T_t = \frac{1}{\rho c}[(1 - \phi_b)\rho_s c_s T_s + \phi_b \rho_b T_b]. \tag{10}$$

Clearly $T_t$ is approximately equal to $T_s$ for $\phi_b \ll 1$.

The quantity $q'_k$ denotes the conductive heat gain per unit volume. We shall assume the usual constitutive equation for heat conduction:

$$q'_k \equiv \frac{Q_{ks} + Q_{kb}}{\delta V} = \nabla \cdot k_k \nabla T_t, \tag{11}$$

where $k_k$ is the effective conductivity. The subscript $k$ indicates that this is the true thermal conductivity, associated with molecular transport processes, as distinguished from apparent conductivity, which will include perfusion contributions (to be discussed later). Because $\phi_b \ll 1$, it will be assumed that $k_k$ is independent of blood flow and essentially equal to the conductivity of the solid tissue.

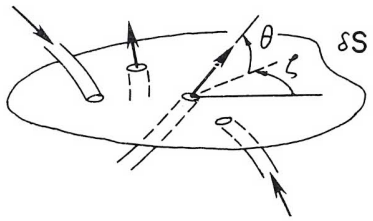


FIGURE 2. Schematic representation of blood vessels crossing an element of the control volume surface.

The quantity $q'_m$ denotes the metabolic heating per unit volume. This has been discussed by numerous investigators and will not be considered further within the scope of the present investigation.

For the term $q'_p$ we have

$$q'_p \equiv \frac{1}{\delta V}\int_S \rho_b c_b T\mathbf{u} \cdot \mathrm{ds}. \tag{12}$$

Close examination of Equation 12 will show that if $T$ were equal to $T_s$ and $\mathbf{u}$ were a continuous function of space, $q'_p$ would be in the usual convective transport form $\rho c\mathbf{u} \cdot \nabla T$. That this is not the case is, of course, the unique characteristic of living tissue heat transfer.

In a living tissue, contributions to the integral in Equation 12 are due mainly to blood flow in vessels crossing the surface $\delta S$, as shown in FIGURE 2. Accordingly, the convective heat flow through $\delta S$ can be written as a sum of the contribution of each vessel crossing the surface:



$$\int_{\delta S} \rho_b c_b T\mathbf{u} \cdot \mathrm{ds} = \rho_b c_b \sum_i T_{bi}{}^0 u_i A_i \sin\theta_i, \tag{13}$$

where $A_i$ is the flow area of the $i$th vessel and $\theta_i$ its inclination with respect to $\delta S$; $u_i$ and $T_{bi}{}^0$ are the mean velocity and mean blood temperature defined as

$$u_i = \frac{1}{A_i}\int_{A_i} u\mathrm{d}A, \tag{14}$$

$$T_{bi}{}^0 = \frac{1}{A_i u_i}\int_{A_i} Tu\mathrm{d}A. \tag{15}$$



Note that $T_{bi}{}^0$ is the flow-weighted average temperature of the $i$th vessel, often called the cup-mixing temperature in heat transfer literature. This is unrelated to the local mean blood temperature $T_b$ defined in Equation 4.

The evaluation of the integral in Equation 12, making use of Equation 13, is the primary objective of this report. This will be pursued below in the section on microvascular contributions, following an examination of the rate of blood temperature ($T_{bi}{}^0$) equilibriation with the solid tissue temperature.

## Equilibration of Blood Temperature with Tissue Temperature

We shall examine the manner by which the flowing blood equilibrates with the local solid tissue temperatures. Assuming that the time rate of change of $T_{bi}{}^0$ is small relative to $u_{bi}/L$, where $L$ is the characteristic length of axial variation of temperature (equal to $x_e$, to be derived later), the blood temperature is governed by the equation

$$A_i \rho_b c_b u_i \frac{\mathrm{d}T_{bi}}{\mathrm{d}x} = U_i P_i (T_s - T_{bi}), \tag{16}$$

where $U_i$ is the overall heat transfer coefficient and $P_i$ is the circumference of the blood vessel. The length $x$ is measured along the axis of the blood vessel, in the direction of flow. For purpose of analysis here, the origin of $x$ is of no consequence; $T_s$ shall be considered a known function of $x$.

Equation 16 can be written more compactly in the form

$$x_{ei} \frac{\mathrm{d}T_{bi}}{\mathrm{d}x} = T_s - T_{bi}, \tag{16a}$$

where $x_{ei}$ is the exponential equilibration length, signifying the length over which the temperature difference will be reduced by a factor $e$, and defined as

$$x_{ei} \equiv \frac{A_i \rho_b c_b u_i}{U_i P_i}. \tag{17}$$

In general, if $x_{ei}$ is small relative to the length scale of $T_s(x)$ variation, then the blood temperature will be essentially equal to $T_s$. If $x_{ei}$ is large, $T_b$ will essentially be independent of $T_s$.

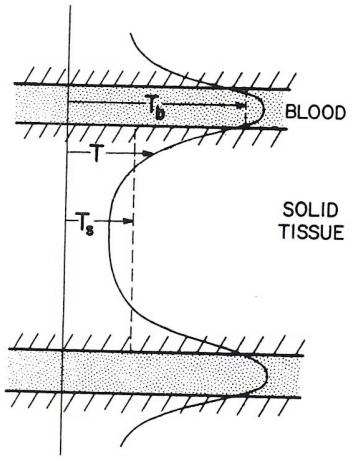


FIGURE 3. An illustration of the temperature variations in the blood and in the surrounding solid tissue.

A semi-quantitative estimate of $x_e$ for vessels of various sizes will now be made. The first step will be to estimate the overall heat transfer coefficient $U_i$. This can be done by referring to FIGURE 3, a schematic illustration of the temperature distribution in and near a blood vessel, caused by an elevated blood temperature. It is seen that there is substantial temperature drop in the solid tissue as well as in blood. Thus the total heat transfer resistance $1/U_i$ is the sum of the resistance in the solid tissue and in blood:

$$1/U_i = \mathrm{RES}_s + \mathrm{RES}_b. \tag{18}$$

Solutions of heat conduction problems in cylindrical geometry[4] suggest that the resistance is proportional to $r_i/k_s$ and the logarithm of $D_i/r_i$, where $D_i$ is the characteristic length representing the heat transfer path length, in the present case equal to about half the distance between vessels. Hence

$$\mathrm{RES}_s \simeq \frac{r_i \ln (D_i/r_i)}{k_s}. \tag{19}$$

On the other hand, $\mathrm{RES}_b$ can be expressed in terms of the Nusselt number (Nu):

$$\mathrm{RES}_b = \frac{1}{\mathrm{Nu}} \frac{r_i}{k_b}. \tag{20}$$

Studies in convective heat transfer[5] indicate that Nu based on tube radius is about 2 for fully developed laminar flows, and generally higher than 2 for entrance flows and turbulent flows. Since in typical vascular beds $D_i = 0(10r_i)$ and $k_b = 0(k_s)$, comparison



of Equations 19 and 20 suggests that as a rule, $\mathrm{RES}_s$ will dominate or at least be comparable to $\mathrm{RES}_b$. Thus it is convenient to express $U_i$ in terms of $k_s$ and $r_i$, as

$$U_i = \frac{1}{\Lambda} \frac{k_s}{r_i}, \tag{21}$$

where $\Lambda$ is a coefficient that can be determined by solutions of the detailed heat conduction equation and is dependent on $k_b$, $k_s$, $u_b$, and the geometrical configuration of the vascular bed. Because of the great variations of the latter, such a detailed analysis is not justified at this point. However, examinations of Equations 19 and 20 on the basis of typical values of $D_i/r_i$ and $k_b/k_s$ suggest that $\Lambda \simeq 3$, with an uncertainty of perhaps a factor of two. Substituting Equation 21 into Equation 17, and evaluating $A_i = \pi r_i^2$ and $P_i = 2\pi r_i$, one obtains

$$x_{ei} = \frac{\Lambda}{2} \frac{\rho_b c_b u_i r_i^2}{k_s}. \tag{22}$$

Although vessels have been assumed to be circular, this result should be applicable to veins of noncircular cross section as well, in the context of a semiquantitative estimate. Typical value estimates of $x_e$ for different generations of vessels based on tabulated vascular parameters[6,7] are shown in TABLE 1. Note that in general the blood velocity in vessels is roughly proportional to radius. Therefore Equation 22 indicates that the equilibration length $x_{ei}$ is very sensitive to vessel radius. This is evident in estimates of $x_{ei}$ (TABLE 1). It is seen that the equilibration length for the larger arteries and veins are in the range of meters, indicating that, in general, the blood in these large vessels is not equilibrated with the solid tissues. On the other hand, the equilibration lengths for precapillary arterioles, capillaries, and venules are generally of the order of micrometers, indicating that in these vessels the blood temperature is essentially equal to the solid tissue temperature.

TABLE 1

PROPERTIES OF VASCULAR COMPARTMENTS ($j$ = 1, 12)*

| $j$ | Vessel | % Vasc. Vol. | $r_j$ ($\mu$m) | $x_{ej}$ (m) | $l_j/x_{ej}$ | $k_{pj}/k_s$ $1/\beta \leq 10$ mm |
|---|---|---|---|---|---|---|
| 1 | Aorta | 3.30 | 5000 | 190 | 0.002 | 0.1 |
| 2 | Lg. art. | 6.59 | 1500 | 4 | 0.05 | 2 |
| 3 | Art. br. | 5.49 | 500 | 0.3 | 0.3 | 15 |
| 4 | Term. br. | 0.55 | 300 | 0.08 | 0.1 | 4 |
| 5 | * | 1.00 | 175 | 0.009 | 1 | 10 |
| 6 | Arteriole | 2.75 | 10 | 5 E−6 | 400 | 0.004 |
| 7 | Capillary | 6.59 | 4 | 2 E−7 | 6000 | 0.00008 |
| 8 | Venules | 12.09 | 15 | 2 E−6 | 800 | 0.002 |
| 9 | Term. veins | 3.30 | 750 | 0.1 | 0.1 | 4 |
| 10 | Venous br. | 29.67 | 1200 | 0.3 | 0.3 | 14 |
| 11 | Lg. veins | 24.18 | 3000 | 5 | 0.04 | 2 |
| 12 | Vena cava | 5.49 | 6250 | 190 | 0.002 | 0.09 |

*Compartment fraction of total vascular volume, % Vasc. Vol.; typical vessel radius, $r_j$ (micrometers); equilibration length, $x_{ej}$ (meters); ratio of typical vessel length to the equilibration length, $l_j/x_{ej}$; ratio of the estimated perfusion thermal conductivity to solid tissue thermal conductivity, $k_{pj}/k_s$, evaluated for temperature variation length scales of the order of 10 mm.

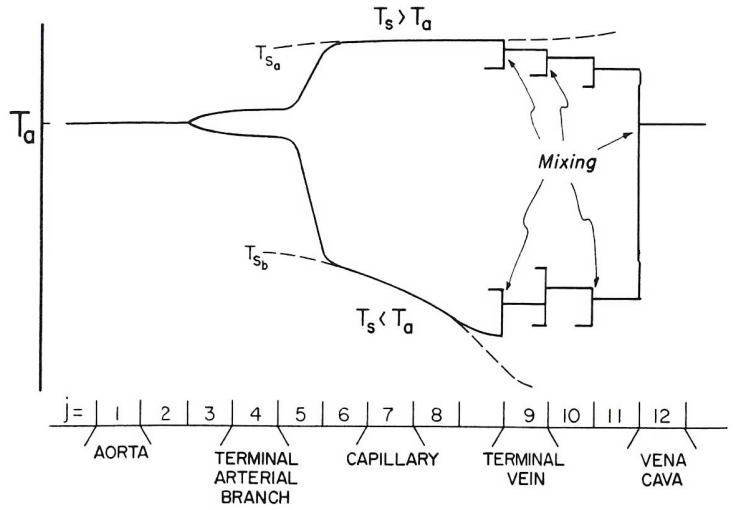


FIGURE 4. Schematic representation of the blood temperature as the blood traverses the systemic circulation ($j = 1, 12$). Blood at arterial temperature ($T_a$) is distributed to solid tissues that are warmer ($T_{sa}$) and cooler ($T_{sb}$) than $T_a$. Blood temperature rapidly equilibrates with $T_{sa}$ and $T_{sb}$ after leaving the terminal arterial branches, attaining the solid tissue temperature ($T_s$) prior to entering the arterioles ($j = 6$). Beyond the venules ($j = 8$), major changes in temperature are the result of mixing at venous confluences. Mixed vena cava ($j = 12$) blood will return to the heart at essentially the arterial temperature.

For a more precise comparison, it is perhaps more meaningful to examine the ratio of the vessel length and $x_e$ for different generations of the vessel divergence and confluence, as shown in TABLE 1. This ratio is a direct measure of the ability of blood to equilibrate its temperature with the solid tissue before it flows into a vessel of the next generation. Available data reporting vessel parameters show a large gap between the terminal arterial branches and the precapillary arterioles, where the vessel radius decreases by a factor of thirty between these vessel categories. A similarly large gap exists between venules and terminal veins. Unfortunately, our analysis shows that vessels with $l_j/x_{ej}$ equal to unity fall within these two gaps. To indicate the approximate size of such vessels, an entry was made in TABLE 1 ($j = 5$) between the terminal branch arteries and the arterioles. It is seen that a vessel with $l_j/x_{ej}$ equal to unity would have a diameter of perhaps 0.2–0.5 mm. A corresponding diameter on the venous side would be about 0.3–0.8 mm, although this vessel has not been shown in TABLE 1.

To further clarify the effect of these findings on the heat exchange between blood and solid tissue, it is useful to follow the blood temperature variations as the blood traverses the systemic vasculature, as shown schematically in FIGURE 4. As blood leaves the heart and travels in the large arteries, its temperature remains essentially constant at the major artery temperature ($T_a$) with little equilibration taking place. Some temperature equilibration will occur between blood and tissue as blood is



distributed to warmer ($T_s > T_a$) or cooler ($T_s < T_a$) structures via arterial and terminal arterial branches. However, most of the temperature equilibration occurs with passage through vessels whose diameter is between that of the terminal arterial branch and that of the arteriole. As blood reaches the latter, $T_b^0$ will essentially be at the solid tissue temperature ($T_{sa}$ or $T_{sb}$; FIGURE 4). Beyond this point, $T_b$ faithfully follows $T_s$ through its spatial and temporal variations until the blood reaches the terminal veins. At this point the blood ceases to equilibrate with the tissue, and remains virtually constant, except as it mixes with other blood of different temperature at venous confluences. Finally the cooler blood from peripheral structures and warmer blood from internal organs mix within the vena cavi and the heart, attaining the same temperature it had at the start of the loop.

Our suggestion that most of the heat exchange between blood and the solid tissue takes place after blood leaves the terminal arterial branches but before it enters the arterioles, is in sharp contrast to the common assumption that such heat exchange takes place in the capillary bed.[8,9] It is interesting to note, however, that when Pennes[10] first formulated the bioheat equation, he included an "equilibration constant," which accounted for the imperfect equilibration of the blood temperature as it traverses the capillary vessel. In light of the present results, it is clear that the coefficient should be unity, with a considerable margin of safety.

FIGURE 4 and TABLE 1 further show that the only parts of the vasculature that may have blood temperatures substantially different from the solid tissue temperatures are the major arteries. Typically these constitute less than 20% of the vascular space, which in turn is considerably less than the solid tissue volume. Accordingly, although the temperature difference between the blood in a given vessel and the surrounding solid tissue may play important roles in heat transfer, such a temperature difference would have negligible influence on the mean tissue temperature $T_t$. For all practical purposes $T_t$ can be considered equal to $T_s$, as long as $\phi_b \ll 1$. This would be especially true if the largest vessels were treated individually and not considered part of the total tissue volume.

## EVALUATING THE MICROVASCULAR CONTRIBUTIONS

We shall now proceed to evaluate the vascular contributions to tissue heat transfer by evaluating the integral in Equation 12, making use of Equation 13 and some of the insight gained in the previous section. For this, we shall adopt the coordinate system shown in FIGURE 5, where $x$ is measured along the axis of the vessel, following the blood through its course of bifurcations and confluences. All along the path, the temperature of the solid tissue $T_s(x)$ shall be considered known. So will the value $x_e$,

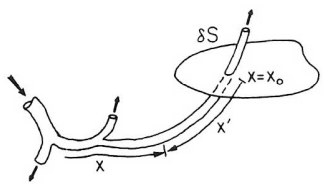


FIGURE 5. The coordinate system $x$ and $x'$.

which depends on vessel radius and blood velocity and hence is also a function of $x$. The differential equation and initial condition are

$$x_e(x)\frac{dT_b^0}{dx} = T_s(x) - T_b^0, \tag{23}$$

$$T_b^0(0) = T_a, \tag{24}$$

where $T_a$ is the temperature of blood in the major arteries, frequently called the arterial temperature or simply blood temperature in bio-heat literature.

It would be found convenient to use a Fourier integral representation for the unknown function $T_s(x)$:

$$T_s(x) = T_s(x_0) + \int_0^\infty B(\beta)\sin\beta x' d\beta, \tag{25}$$

where $x_0$ is the value of $x$ as it crosses the control surface $\delta S$. Note that $x_0$ serves as the origin of $x'$, which is measured backwards from $x_0$:

$$x' = x_0 - x. \tag{26}$$

The coefficient $B(\beta)$ can be determined from $T_s(x)$ using standard techniques. These will not be discussed here.

Because of the linearity of Equations 23 and 24, it is now possible to separate the problem into three linearly independent ones, with the following initial conditions:

(A)
$$x_e(x)\frac{dT_A}{dx} = -T_A, \tag{27a}$$

$$T_A(0) = T_a - T_s(x_0), \tag{27b}$$

(B)
$$T_B = T_s(x_0), \tag{28}$$

(C)
$$T_C = \int_0^\infty T_\beta d\beta, \tag{29a}$$

$$x_e\frac{dT_\beta}{dx'} = T_\beta - B\sin\beta x', \tag{29b}$$

$$T_\beta(x') = T_\beta(x' + 2\pi/\beta). \tag{29c}$$

The general solution is then

$$T_b^0(x) = T_A + T_B + T_C. \tag{30}$$

Subproblems (A), (B), and (C) will be discussed separately below.

*Subproblem (A):* This problem corresponds to the equilibration of blood temperature, from an initial temperature $T_a$, with a uniform solid tissue temperature. The solution to Equations 27a and 27b is clearly

$$T_A = [T_a - T_s(x_0)]\exp\left(-\int_0^x \frac{1}{x_e(x)}dx\right). \tag{31}$$



The integration in Equation 31 is carried out through different generations of bifurcation, $j = 1, 2, 3$, etc. Referring to the estimates in TABLE 1, one sees that there is practically no contribution to the integral by the major arteries and only moderate contribution by the arterial branches and terminal arterial branches. After the latter, the integral's value will grow quickly, with $\tau_a$ rapidly approaching zero.

Turning to the evaluation of $q_p'$ from the integral in Equation 12, it is evident that for a meaningfully small differential control volume $\delta V$, larger arteries or veins are simply too few in number to require an evaluation of their contributions to $q_p'$, which represent a distributed heat source intensity. Therefore, for the first two or three generations of the arteries, their contribution to tissue heating should be treated individually rather than collectively. It will be assumed that this procedure is practical up to and including $j^*$th generation. The temperature reached by $T_b^0$ at this point shall be designated $T_a^*$.

Since all heat exchange that took place before blood reached $T_a^*$ has already been accounted for, the evaluation of $q_p'$ in Equation 12 should include only vessels of $(j^* + 1)$th generation or higher, to avoid double counting. Similarly, the initial blood temperature should be considered to be $T_a^*$, and not $T_a$. If $\delta V$ is sufficiently large so that essentially all further bifurcations from $j^* + 1$ to precapillary arterioles take place within it, then it can be assumed that blood would leave the control volume essentially at the solid tissue temperature. Hence

$$q_{pA}' = W_j^*\rho_b c_b(T_a^* - T_s), \tag{32}$$

where $W_j^*$ is the total perfusion rate per unit tissue volume, delivered through the $j^*$th generation of vessels.

This result is reminiscent of the widely used perfusion heating term, originated by Pennes.[10] However, there are two important differences. Firstly, the perfusion rate $W_j^*$ includes only the contribution of vessels beyond the $j^*$th generation. Secondly, the arterial temperature employed is in $T_a^*$ and not the major arterial temperatures. This distinction is necessary because otherwise the contribution of the major arteries may be doubly counted. Estimates of $l_j/x_{ej}$ shown in TABLE 1 suggest that $(T_a^* - T_s)$ may differ from $(T_a - T_s)$ by tens of percent depending on the location of the major arteries.

*Subproblem (B):* This corresponds to the situation where the blood temperature is equal to the solid tissue temperature everywhere. Accordingly, from Equations 13 and 28

$$\int_{\delta S}\rho_b c_b T\mathbf{u}\cdot d\mathbf{s} = \rho_b c_b T_s\sum_i u_i A_i\sin\theta_i. \tag{33}$$

It may be found convenient to define a mean perfusion velocity, $\mathbf{u}_p$, whose component in the direction of any unit vector $\mathbf{k}$ is

$$\mathbf{u}_p\cdot\mathbf{k} = \sum_i u_i\alpha_i\mathbf{i}\cdot\mathbf{k}, \tag{34}$$

where $\mathbf{i}$ is the unit vector in the direction of flow for the $i$th vessel, and $\alpha_i$ is the area fraction for the $i$th vessel:

$$\alpha_i = A_i/\delta S. \tag{35}$$

$\alpha_i$ is a vascular bed parameter and independent of $\delta S$. Clearly $\mathbf{u}_p$ is the mass flux of blood permeating through the tissue (in mass per unit area per unit time) divided by blood density. It follows that

$$\int_{\delta S} \rho_b c_b \mathbf{T}\mathbf{u} \cdot d\mathbf{s} = \rho_b c_b T_s \mathbf{u}_p \cdot \delta S. \tag{36}$$

After Equation 36 is substituted into Equation 12 and simplified with the use of the divergence theorem and conservation of mass, we get

$$q'_p = \rho_b c_b \mathbf{u}_p \cdot \nabla T_s. \tag{37}$$

Equation 37 is reminiscent of a typical convective transport term. Its potential importance in living tissue heat transfer has been previously pointed out by Wulff,[11] among others.

*Subproblem (C):* This problem is concerned with the equilibration of $T_b$ with the sinusoidally varying components of $T_s(x)$. The solution with the periodicity condition of Equation 29c yields

$$T_\beta(0) = -\beta x_e B/(\beta^2 x_e^2 + 1). \tag{38}$$

From definitions, it can be seen that $T_\beta(0)$ is the temperature difference between the blood and the solid tissue at $x = x_0$ as contributed by the spectral component with wavenumber $\beta$. Because of this temperature difference, there is a net contribution of heat flux to the integral of Equation 12. We shall next show that the amplitude coefficient $B$ is associated with the temperature gradient at $x = x_0$. Thus the contribution of $T_\beta(0)$ to $q'_p$ has the basic characteristic of heat conduction, and gives rise to a perfusion conductivity $k_p$.

Space does not permit a more general and detailed development of the theory, which will be set forth in another communication. For the following discussion it is assumed that (1) $\delta S$ is so chosen as to be perpendicular to the temperature gradient, and (2) the tissue is isotropic. Assumption (1) is for mathematical convenience and involves no loss of generality. Assumption (2) implies that the heat flux associated with $k_p$ is parallel to the temperature gradient and hence $k_p$ is a scalar quantity. Furthermore, it also implies that the perfusion velocity $\mathbf{u}_p$ vanishes. Note that one of the contributions of $\mathbf{u}_p$ has already been discussed in *Subproblem (B)* above. The removal of Assumption (2) would lead to nonscalar contributions to $k_p$ as well as a contribution to heat flux that is proportional to both $\mathbf{u}_p$ and $\nabla T_s$. These can be viewed as higher order effects to be explored after the lower order effects are clarified. It is clear from assumptions and from the definitions of $B$ and $\beta$ that

$$\int_0^\infty B\beta d\beta = (\nabla T) \sin\theta. \tag{39}$$

In other words for any value of $\beta$, $B\beta$ is proportional to $(\nabla T) \sin\theta$. For simplicity and without loss of generality we shall consider only the contribution of the $i$th vessel and, assuming there is only one single spectral component with wavenumber $\beta$, set

$$\bar{B}\beta = (\nabla T) \sin\theta, \tag{40}$$

where the coefficient $\bar{B}$ now has units of temperature. From Equation 13, the contribution of $T_\beta$ to the integral of Equation 12 in the surface element $\delta S$ is



$$\int_{\delta S} \rho_b c_b T_\beta(0)\mathbf{u} \cdot d\mathbf{s} = \rho_b c_b \frac{x_{e_i}\bar{B}\beta}{x_{e_i}^2\beta^2 + 1} u_i A_i \sin\theta_i \tag{41}$$

$$= -\rho_b c_b \frac{x_{e_i}}{x_{e_i}^2\beta^2 + 1} u_i \sin^2[\theta_i \alpha_i(\delta S)\nabla T].$$

Substituting Equation 41 into Equation 12 and simplifying, we can express the contribution of the $\beta$ wavenumber component for the $i$th vessel in the form:

$$q'_{p\beta i} = -\nabla \cdot k_{p\beta i} \nabla T, \tag{42}$$

where $k_{p\beta}$ is given by the expression

$$k_{p\beta i} = \frac{\Lambda^2}{4k_s} \rho_b^2 c_b^2 \frac{u_i^2 r_i^2}{x_{e_i}^2\beta^2 + 1} \sin^2(\theta_i \alpha_i), \tag{43}$$

In obtaining Equation 43, Equation 22 has been employed to evaluate $x_e$ in the numerator, in order to display the dependence of $k_p$ on the different paramaters; $x_e$ is retained in the denominator since, for small vessels, $x_e^2\beta^2$ is expected to be small.

Note that $k_{p\beta i}$ is proportional to $\sin^2\theta_i$. This indicates that a vessel's contribution to $k_p$ depends on the relative angle between the vessel and the direction of the temperature gradient, though it does not depend on the direction of flow in the vessel—a reverse flow would have the same contribution. In a tissue with an isotropic arrangement of microvasculature, the collective contribution of all vessels would lead to an isotropic conduction effect. Because of the principle of superposition, it is possible to superimpose the contribution of all vessels and wavenumbers, leading to a combined perfusion thermal conductivity $k_p$:

$$q'_p = -\nabla \cdot k_p \nabla T. \tag{44}$$

Current data, however, are insufficient to permit the direct evaluation of $k_p$ from structural and functional parameters of the microvasculature. In order to gain some insight into the order of magnitude of this effect, the total contribution of each generation of vessels is estimated on the basis of Equation 43, using available vascular data and some estimated values of $\alpha_j$; $\sin^2\theta_j$ is assumed to be unity and $\beta_j$'s are taken to the $1/l_j$. It is seen that potentially large contributions to $k_p$ are possible from vessels situated between the terminal arterial branches and the therminal veins. Even though similarly large contributions can also be expected from the arterial and venous branches, these vessels are probably best considered individually, since they are too few in number to be considered collectively in a continuum formulation. The values shown in TABLE 1, however, are meaningful for comparative purposes only, since precise data on many parameters are not currently available.

## SUMMARY

Major conclusions of this study are the following:

(1) The equilibration of blood temperature with solid tissue takes place between

the terminal arterial branches and the precapillary arterioles, not in the capillaries as has previously been assumed.

(2) The heat transfer from the larger vessels should be calculated individually, and not collectively in a continuum formulation. To avoid double counting, the perfusion heating term in the continuum formulation should be based on the flow rate and blood temperature leaving the last individually computed generation of arteries.

(3) In addition to the perfusion heating term, which is proportional to the blood flow per unit volume of tissue, the blood flow in the microvasculature may have at least two other contributions to heat transfer: a contribution proportional to local blood perfusion velocity and a contribution to the effective thermal conductivity. The bio-heat equation including all these terms is

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot k \nabla T_k + W_f^*(T_a^* - T) - \rho_b c_b \mathbf{u}_p \cdot \nabla T + \nabla \cdot k_p \nabla T + q'_m, \quad (45)$$

where the subscripts $t$ and $s$ for temperature have been neglected because $T_s \simeq T_t$, as discussed in the text.

It is hoped that these results will stimulate experimental studies to further clarify the heat transfer processes in living tissue. Such investigations are currently in progress in our laboratory.

## References


1. Shitzer, A. 1973. IEEE Trans. Biomed. Eng. BME-**20:** 65–66.
2. Hwang, C. & S. A. Konz. IEEE Trans. Biomed. Eng. BME-**24:** 309–325, 1977.
3. Bowman, F., E. G. Cravalho & M. Woods. 1975. Ann. Rev. Biophys. Bioeng. **4:** 43–80.
4. Carslaw, H. S. & J. C. Jaeger. 1959. Conduction of Heat in Solids. Clarendon Press, Oxford, England.
5. Kays, W. M. 1966. Convective Heat and Mass Transfer. McGraw-Hill Book Company, New York, N.Y.
6. Whitmore, R. L. 1968. Rheology of the Circulation. Pergamon Press, London, England.
7. Burton, A. C. 1972. Physiology and Biophysics of the Circulation. Year Book Medical Publishers, Chicago, Ill.
8. Keller, K. H. & L. Seiler, Jr. 1971. J. Appl. Physiol. **30:** 779–786.
9. Priebe, L. 1970. Heat transport and specific blood flow in homogeneously and isotropically perfused tissue. *In* Physiological and Behavioral Temperature Regulations. J. D. Hardy, A. P. Gagge & J. A. J. Stolwijk, Eds. Charles C Thomas, Publisher, Springfield, Ill.
10. Pennes, H. H. 1948. J. Appl. Physiol. **1:** 93–122.
11. Wulff, W. 1974. IEEE Trans. Biomed. Eng. BME-**21:** 494–495.


# DISCUSSION PAPER: ALTERNATIVES TO THE BIO-HEAT TRANSFER EQUATION


W. Wulff

*Brookhaven National Laboratory*
*Upton, New York 11973*


The Bio-Heat Transfer Equation,

$$\rho_s c_s \frac{\partial T_s}{\partial t} - \nabla \cdot (k_s \nabla T_s) - q_m - w_b c_b (T_a - T_s) = 0, \quad (1)$$

is widely used to predict detailed local temperature distributions and thermal energy transport in living tissue, a heterogeneous, deformable structure of solids, and of liquids passing through capillaries. The four terms in Equation 1 are intended to represent thermal energy storage, thermal energy diffusion, metabolic heat generation, and perfusion of solids by liquids, primarily by blood, in that order.

Alternative forms of the bio-heat transfer equation are needed to meet at least three requirements:

1. The derivation of the transport equations (for heat and fluids) must be consistent with the principles of rational mechanics and with the complete definition of the system model.
2. All the hypotheses implied in the model and in the derivation of the transport equations must be identified.
3. The new forms of the transport equations must be practical, must have a stable solution, and should accommodate future efforts on modeling of thermophysiological processes.

## Current Status

Equation 1 has been obtained by *inserting*[1-3] the scalar source term for blood perfusion, $w_b c_b (T_a - T_b)$, into the heat conduction equation, which is valid only for points in an open domain $\mathcal{D}$, lying entirely within a homogeneous solid. This heat conduction equation, i.e., Equation 1 without the fourth term for blood perfusion, is a *local, instantantaneous* energy balance for an infinitesimal control volume in $\mathcal{D}$, and is derived for the condition that the heat flux $\mathbf{q} = -k\nabla T$, the thermophysical properties $\rho_s$, $c_s$, and $k_s$, and the heat generation term $q_m$ have *continuous, first-order* spatial derivatives at *every* interior point of the domain $\mathcal{D}$. This condition clearly is not met if hetereogeneous tissue structures occupy the domain $\mathcal{D}$.

The fourth term in Equation 1, which represents the blood perfusion of tissue, implies that arterial blood reaches any two points within the domain of tissue, with one and the same arterial blood temperature $T_a$, regardless of the difference in distances which separate the two points from the arterial supply vessel. No physically realistic transport mechanism has been identified to accomplish this. Moreover, the blood



0077–8923/80/0335–0151 $01.75/0 