Characteristics of spatiotemporal fluctuations of temperature in living tissue

I. A. Lubashevskii[1] and A. G. Cadjan[1,2]
[1]*The Russian Academy of Technological Sciences, Moscow 117049, Russia*
[2]*Moscow Physical Technical Institute, Moscow 141700, Russia*
and Brigham Young University, Provo, Utah 84602
(Received 24 March 1992; revised manuscript received 5 April 1994)

In this paper we study the characteristics of temperature fluctuations in living tissue associated with the existence of a branched vascular network. In particular, we have shown that under certain conditions such fluctuations can be of the $1/f$ type.

PACS number(s): 87.22.Pg, 87.45.−k

I. INTRODUCTION

In living tissue blood flow in vessels of a vascular network forms branched paths of fast heat transport as well as fast transport of O_2, CO_2 and some other components [1]. Owing to this, heat and mass transfer in living tissue posseses specific properties, and blood flow rate, treated in terms of a continuous field $j(\mathbf{r},t)$, is one of the fundamental characteristics of these processes.

Typically, blood flow in a vessel of length l directly controls the mean blood flow rate in a tissue domain Q, whose size is about l, whereas smaller vessels are responsible for blood flow redistribution over different parts of this domain [1]. Therefore, fluctuations in vessel resistance to blood flow in it, caused, for example, by time variations in its radius, are bound to give rise to spatiotemporal fluctuations in the blood flow rate $j(\mathbf{r},t)$ in the tissue domain Q which are correlated on spatial scales of order l and on temporal scales determined by the vessel characteristics. These fluctuations in $j(\mathbf{r},t)$, in their turn, cause spatiotemporal fluctuations in the tissue temperature as well as in the concentration of O_2, CO_2, etc. Since the vascular network involves vessels of different lengths, both the tissue temperature and distribution of these components can exhibit fluctuations characterized by a wide range of spatial and temporal scales.

The purpose of the present work is to investigate the characteristics of these fluctuations and their dependence on the vascular network architectonics. For the sake of simplicity we consider fluctuations of the tissue temperature only because fluctuations in distribution of O_2, CO_2, etc., are expected to have the same properties.

II. MODEL

For the sake of simplicity we assume that the heat capacities as well as the thermal conductivities of the cellular tissue and blood are the same and independent of temperature. In this case, the final bioheat equation, obtained within the different approaches to description of heat transfer in living tissue (for a review see, e.g. Refs. [2–4]), can be reduced to the following equation:

$$\frac{\partial}{\partial t}T=D\nabla^2 T-j(T-T_a)+g \ . \tag{1}$$

Here D is the thermal diffusivity of the tissue, T_a is the temperature of arterial blood, regarded as a constant, g is the density of heat sources associated, for example, with metabolic processes, and j is the rate of blood flow per unit volume of the tissue. Besides, in the living tissue domain under consideration the mean values of the heat source density g_0, the blood flow rate j_0, and thereby the tissue temperature T_0 are assumed to be constants.

Keeping in mind aforementioned in Sec. I we account for temperature fluctuations δT caused only by inherent fluctuations in vessel resistances to blood flow. Therefore linearizing Eq. (1) with respect to δT near T_0 we get

$$\frac{\partial}{\partial t}T=D\nabla^2\delta T - \left[j_0+\frac{\partial j}{\partial T}\bigg|_{T=T_0}(T_0-T_a)-\frac{\partial g}{\partial T}\bigg|_{T=T_0}\right]\delta T - \delta j(T_0-T_a) \ , \tag{2}$$

where the derivatives $\partial j/\partial T$ and $\partial g/\partial T$ are associated with the temperature dependences of the blood flow rate and the methabolic processes and δj is the blood flow rate fluctuations inherent to living tissue. According to (2) the temperature dependence of g leads solely to the renormalization of the blood flow rate j_0, thus this term in our analysis will be ignored. In the general case the derivative $\partial j/\partial T$ is an operator. However, first, when the difference (T_0-T_a) is substantially less than the width of the survival temperature interval of living tissue, this term is likely to be small enough in comparison with j_0. Second, when the $j(T)$ dependence is a local function it also leads to the renormalization of j. Therefore the term $(\partial j/\partial T)(T_0-T_a)$ in (2) will be ignored too.

To analyze the characteristics of temperature fluctuations, first, we shall find the correlation function

$$G_{\mathbf{r},t}=\langle\langle \delta T_{\mathbf{r}'+\mathbf{r},t'+t}\delta T_{\mathbf{r}',t'}\rangle\rangle \ , \tag{3}$$

where symbol $\langle\langle\ \rangle\rangle$ denotes averaging over both the time t' and the tissue points $\mathbf{r}'$ under the conditions $t=$const and $|\mathbf{r}|=$const.

Let us introduce the correlation function of the blood flow rate fluctuations

$$\Omega_{\mathbf{r},t}=\langle\langle \delta j_{\mathbf{r}'+\mathbf{r},t'+t}\delta j_{\mathbf{r}',t'}\rangle\rangle \ . \tag{4}$$

Then taking into account the adopted assumptions from (2) we obtain the following relationship between the Fourier transforms of the above two correlation functions (3) and (4) with respect to both the time t and the coordinates $\mathbf{r}$:

$$G(\mathbf{k},\omega)=(T_0-T_a)^2\frac{\Omega(\mathbf{k},\omega)}{\omega^2+(Dk^2+j_0)^2} \ . \tag{5}$$

Here ω and $\mathbf{k}$ are the variables conjugate to t and $\mathbf{r}$, respectively. It should be pointed out that when averaging the product $(\delta j\delta j)$ in (4) over the time t' only we get the function

$$\Omega_{\mathbf{r}',\mathbf{r},t}=\langle \delta j_{\mathbf{r}',t'+t}\delta j_{\mathbf{r}',t}\rangle \ , \tag{6}$$

which depends on both the variables $\mathbf{r}',\mathbf{r}$. This nonuniformity will be discussed below.

In order to find correlation function (4) or (6) we should specify a vascular network in a tissue domain which has to be large enough so that in the analysis of heat transfer it could be considered individually. Since a microcirculatory bed is the main element of any peripherical vascular system [1], for our analysis we may choose a living tissue domain containing a single microcirculatory bed [5,6].

Generalizing geometric structures of real microcirculatory beds of such organs as kidney, liver, etc. [7], we present the vascular network in the following form. (A more detailed model for the vascular network will be described in our following paper [5].) We assume that the tissue domain Q_0 under consideration (Fig. 1) is a cube of the volume $[(2l_0)/\sqrt{3}]^3$, where $2l_0$ is the length of the cube diagonal. The host artery of length l_0 goes into the cube Q_0 through one of its corners and belong to the initial level of the vascular network. The host artery reaches the cube center O_0 where it branches out into eight arteries of the first level. Each first level artery reaches a center O_1 of one of the eight cubes $\{Q_1\}$ composing together the cube Q_0. At the centers $\{O_1\}$ each of the first level arteries, in turn, branches out into eight second level arteries. Then the artery branching is continued in a similar way up to level $N\gg 1$. In the following, the domains Q_N of the last level will be called elementary domains.

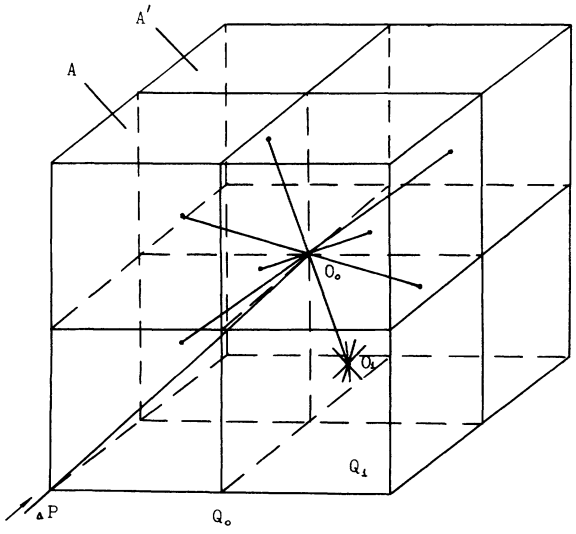

FIG. 1. Vascular network model (characteristic fragment).

We assume that the length l_N of an artery of the last level is well below $(D/j)^{1/2}$, i.e., $l_N\ll(D/j)^{1/2}$, because, first, for the typical magnitudes of $D\sim 1.7\times 10^{-3}$ cm^2/s and $j\sim 10^{-3}$ 1/s the value $(D/j)^{1/2}\sim 1.3$ cm is substantially larger than the mean length of a real venule or arteriole and, second, only in this case Eq. (1) is strictly justified [5]. Besides, the resistance to blood flow of a real arterial bed is substantially larger than the resistance of the corresponding venous one [1]. Therefore, in the analysis of the blood flow rate fluctuations we may take into account the arterial bed only. Implying the mean values we assume that arteries of the one level are the same and described by the length $l_n=l_0 2^{-n}$, the radius $a_n=a_0 2^{-\delta n}$ and the resistance $R(n)=R_0 2^{3n}\rho(n)$ to blood flow. Here n is the artery level number, $\rho(n)$ is a smooth function of n so that $\rho(0)=1$ and $\rho(n)\ll 1$, γ is a constant. When describing the properties of blood viscosity by the effective coefficient μ_{eff} of viscosity the resistance R of a given vessel can be represented in the form

$$R=\frac{8}{\pi}\mu_{\text{eff}}\frac{l}{a^4} \ . \tag{7}$$

Thus, when, for example, $\mu_{\text{eff}}(a)\sim a^{\alpha}$ [1] where α is a constant, the value of γ is assumed to be equal to $\gamma\approx 4/(4-\alpha)$ and, thus $\gamma\approx 1$ if the effective viscosity of blood is independent of the vessel radius. In addition, it should be noted that the smoothness of the function $\rho(n)$ follows from the requirement that the blood flow redistribution be directly controlled by a group of arteries of a wide length range [6]. This is a typical case for real microcirculatory beds [1]. For a given artery, for example artery i, fluctuations $\delta R_i(t)$ in its resistance are described by a single correlation time $1/\omega(n)$ which, however, can depend on the artery level number n. In other words, we represent the correlation function of these fluctuations in the form

$$\langle \delta R_i(t+t')\delta R_i(t')\rangle=R^2(n_i)\varepsilon\Delta(n_i)\exp[-\omega(n_i)|t|] \ , \tag{8}$$

where ε is a small constant ($\varepsilon\ll 1$), the function $\Delta(n)$ accounts for specific details of the correlation function dependence on n and $\Delta(0)=1$. In particular, $\Delta(n)$ is a smooth function of n providing that in the dependence $a_n=a_0 2^{-\gamma n}$ the value of γ is about $1(\gamma\sim 1)$, the resistance $R(n)$ is a power function of a and the ratio $\langle(\delta a_n)^2\rangle/a_n^2$ smoothly depends on n. Therefore in the following for the sake of simplicity we shall regard both $\Delta(n)$ and $\omega(n)$ as smooth functions of n. For different vessels fluctuation in their resistances are assumed to be uncorrelated.

The blood current pattern $\{J_i\}$ on the vascular network obeys the law of blood current conservation at its

branching points $\{B_i\}$, viz:

$$\sum_{B_i} J_{\text{out}} = J_{\text{in}} \tag{9}$$

where J_{in} and J_{out} are the blood currents in arteries going in and out of the branching point B_i, the sum runs over all the arteries going out of the given branching point. The rheological properties of blood flow in a vessel i are described by the following relationship between the blood current J_i in it and the pressure drop ΔP_i across the vessel:

$$J_i R_i = \Delta P_i \ . \tag{10}$$

Here the cofactor R_i called the vessel resistance to blood flow in the general case depends on the blood velocity v. However, this dependence has a significant effect on blood flow redistribution over vessels being small in comparison with the host artery or vein of microcirculatory beds [1]. Therefore, in the present paper the resistances R_i for all the vessels are assumed to be constants (v). The collection of Eqs. (9), (10) for different branching points $\{B_i\}$ and veins forms the system of Kirchhoff equations describing the blood current pattern on the venous bed.

The total pressure drop P across the arterial bed is assumed to be a given constant.

When fluctuations in the vessel resistances are negligible the solution of Eqs. (8), (9) is of the form

$$J_i = J_0(n_i) = 2^{-3n_i} J_0 \ , \tag{11}$$

where n_i is the level number of the artery i and J_0 is the blood current in the host artery of the microcirculatory bed.

Concluding this section we note that in this model the relationship between the blood current pattern $\{J_i\}$ and the blood flow rate $j(\mathbf{r})$ may be defined in terms of

$$j(\mathbf{r}) = \frac{1}{v_N} J_{i_{\mathbf{r}}} \ , \tag{12}$$

where $J_{i_{\mathbf{r}}}$ is the blood current in the last level vein $i_{\mathbf{r}}$ which belongs to the elementary domain $Q_{N\mathbf{r}}$ containing the point $\mathbf{r}$ and V_N is the volume of this domain.

III. CORRELATION FUNCTION

Due to $\varepsilon \ll 1$ to the first order in $\delta R_i(t)$ Eq. (10) can be replaced by the equation

$$J_i R(n_i) = \Delta P_i - J_0(n_i)\delta R_i(t) \ . \tag{13}$$

Equations (9) and (13) may be regarded as the system of the Kirchhoff equations describing blood flow distribution over a certain vascular network of the same architectonics where, however, the vessel resistances $R(n_i)$ are constant values and there are some additional effective pressure sources

$$\varepsilon_i = -J_0(n_i)\delta R_i(t) \tag{14}$$

associated with these vessels. Being pairwise independent and random quantities these effective pressure sources $\{\varepsilon_i\}$ cause fluctuations in the blood currents. As it is shown in [6] linearity of Eqs. (9), (13) with respect to the blood currents allows us to represent the solution of these equations in terms of

$$J_i = J_0(n_i) + \sum_{i'} \Lambda_{ii'}[\varepsilon_{i'} + P\delta_{n_{i'},0}] \ , \tag{15}$$

where the sum runs over all the arteries, $\delta_{n_{i'},0}$ is the Kronecker symbol, and the elements of the matrix $\|\Lambda_{ii'}\|$ are specified in the following way. Let us denote by $\{ii'\}_+$ such a pair of arteries i and i' which can be jointed by a path of constant direction on the vascular network. This path may be directed either from higher to lower levels or vice versa (Fig. 2). Then for an artery pair $\{ii'\}_+$

$$\Lambda_{ii'} = \begin{cases} \dfrac{1}{R_0 Z(n_i)} 2^{-3n_i'}, & n_i \le n_{i'} \ , \qquad \text{(16a)} \\ \dfrac{1}{R_0 Z(n_i')} 2^{-3n_i}, & n_i > n_{i'} \qquad \text{(16b)} \end{cases}$$

Here $Z(n)$ is the function defined by formula (17). The other pairs of arteries $\{ii'\}_-$ are characterized by paths with variable directions, i.e., for a pair $\{ii'\}_-$ the arteries ii' can be jointed by a path whose direction becomes opposite at a certain branching point $B_{ii'}$ (Fig. 2). Let us ascribe to a branching point B the level n of an artery, that goes out of it. Then

$$\Lambda_{ii'} = -\frac{\rho(n_{Bii'})}{7R_0 Z^2(n_{Bii'})} 2^{3(n_{Bii'} - n_i - n_{i'})} \ . \tag{16c}$$

In expressions (16a)–(16c) the function $Z(n)$ is defined as

$$Z(n) = \sum_{n'=n}^{N} \rho(n') \ . \tag{17}$$

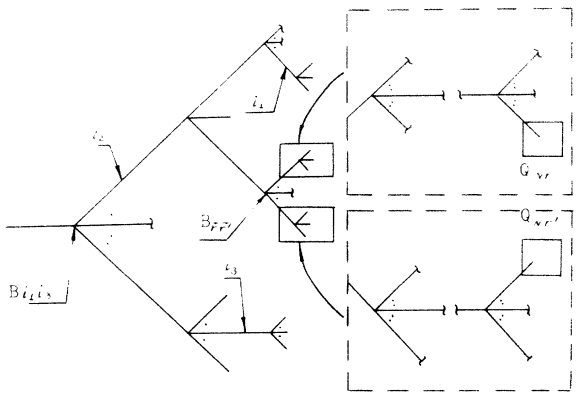

FIG. 2. Schematic representation of the arterial bed. Possible forms of connection between different arteries and tissue points throughout the vascular network are illustrated by the artery pair $\{i_1 i_2\}_+$, the pair $\{i_1 i_3\}_- \equiv \{i_1, i_3, B_{i_1 i_3}\}$ and the points $\mathbf{r}, \mathbf{r}'$. The cubes $Q_{N\mathbf{r}}$ and $Q_{N\mathbf{r}'}$ are elementary domains containing the points $\mathbf{r}$ and $\mathbf{r}'$, respectively.

It should be pointed out that because of $Z(n)$ being a smooth function the ratio $\rho(n)/Z(n)$ can be treated as a small parameter.

Relation (12) allows us to rewrite the correlation function $\Omega_{r,r',t}$ [see formula (6)] in terms of the correlation function of blood current fluctuations $\langle \delta J_{ir} \delta J_{ir'} \rangle$. Then substituting (14) and (15) into the obtained result and taking into account the properties of fluctuations in the vessel resistances [see formula (8)] we get

$$\Omega_{r,r',t} = \frac{\varepsilon}{V_N^2} \sum_i \Lambda_{i_r i} \Lambda_{i_{r'} i} J_0^2(n_i) \Delta(n_i) \times \exp\{-\omega(n_i)t\} R^2(n_i) . \quad (18)$$

At lower order in $\rho(n)/Z(n)$ expressions (11), (16a)–(16c), and the smoothness of the functions $\rho(n)$, $\Delta(n)$, and $\omega(n)$ enable us to represent the Fourier transform of (18) in the form

$$\Omega_{r,r'}(\omega) = 2\varepsilon j_0^2 \int_0^{n_{r,r'}} dn \left[\frac{\rho(n)}{Z(n)} \right]^2 \Delta(n) \frac{\omega(n)}{\omega^2(n)+\omega^2} , \quad (19)$$

where $n_{r,r'}$ is the level number of the branching point $B_{r,r'}$ corresponding to the pair of the arteries $\{i_r, i_{r'}\}$ (Fig. 2).

The mean distance r between the arteries $i'_r, i_{r'}$, of the pairs $\{ii'\}$ corresponding to the same branching point $B_{rr'}$ can be estimated as $r \sim l_{n_{rr'}} = l_0 2^{-n_{rr'}}$, thereby $n_{rr'} \sim \log_2(l_0/r)$. Due to the latter estimate and $\Omega_{rr'}(\omega)$ being a smooth function of $n_{rr'}$ on averaging (19) over the cube Q_0 for $r \ll l_0$ we may set

$$\Omega_r(\omega) \approx \Omega_{r',r}(\omega)|_{n_{rr'}} = \log_2(l_0/r) . \quad (20)$$

Let us consider in more detail the special case where $\Delta(n)=1$, $\omega(n)=\omega_0 \exp(n\nu_\omega)$ and $\rho(n)=\rho(0)\exp(-n\nu_\rho)$, when ν_ω and ν_ρ are small positive constants but $\nu_\omega N$, $\nu_\rho N \gg 1$. In this case as it follows from (19), (20) within the frequency interval $\omega(0) \ll \omega \ll \omega(N)$

$$\Omega_r(\omega) \approx 2\varepsilon j_0^2 \frac{\nu_\rho^2}{\nu_\omega} \frac{1}{\omega} \tan^{-1} \left[\frac{\omega_0}{\omega} \left[\frac{l_0}{r} \right]^{\nu_\omega/\ln 2} \right] . \quad (21)$$

In particular, if $\omega \ll \omega_r = \omega_0 (l_0/r)^{\nu_\omega/l_2}$

$$\Omega_r(\omega) \approx \pi\varepsilon j_0^2 \frac{\nu_\rho^2}{\nu_\omega} \frac{1}{\omega} \quad (22a)$$

and for $\omega \gg \omega_r$

$$\Omega_r(\omega) \approx 2\varepsilon j_0^2 \frac{\nu_\rho^2}{\nu_\omega} \frac{\omega}{\omega^2} \left[\frac{l_0}{r} \right]^{\nu_\omega/\ln 2} . \quad (22b)$$

According to (5) on spatial scales r where $Dr^{-2} \ll j_0$ or $Dr^{-2} \ll \omega$ the Fourier transform $G_r(\omega)$ of the correlation function $G_{r,t}$ is directly specified by the function $\Omega_r(\omega)$, viz.

$$G_{r'}(\omega) \simeq \frac{(T_0 - T_a)^2}{\omega^2 + j_0^2} \Omega_r(\omega) . \quad (23)$$

In particular, as it follows from (22a) and (23) if $\omega(0) \ll j_0$ then there is a frequency interval $\omega(0) \ll \omega \ll \omega_r, j_0$ where $G_r(\omega) \sim 1/\omega$, i.e., in this case fluctuations in the living tissue temperature can exhibit $1/f$ behavior.

Concluding the present work we would like to point out that there is a certain spatial nonuniformity of the correlation function caused by the vascular network architectonics. Indeed, as it can be seen from Fig. 1, in neighborhoods of the points A and A' being at a small distance from each other heat transfer can be controlled by different branches of the arterial bed. Owing to this in one direction fluctuations in the blood flow rate and, correspondently, in the tissue temperature could be correlated whereas in the opposite direction such correlations are practically absent. In addition we note, that because the typical values of the blood flow rate are about $j \sim 10^{-3}$–10^{-2} s^{-1} according to (23) the fluctuations of the tissue temperature can exhibit $1/f$ behavior for sufficiently low frequencies. However, fluctuations in the blood flow rate can exhibit $1/f$ behavior in substantially wider frequency interval [see formula (22a)] and can cause similar fluctuations in other physical quantities in living tissues.

[1] For a review of the vascular network characteristics see, e.g., G. I. Mchedlishvili, *Microcirculation of Blood,* General Principles of Control and Disturbances (Nauka, Leningrad, 1989). K. A. Shoshenko, A. G. Golub, and V. I. Brod, *Architectonics of Circulation Bed* (Nauka, Novosibirsk, 1982).

[2] M. M. Chen, in *Heat Transfer in Medicine and Biology, Analysis and Applications,* edited by A. Shitzer and R. C. Eberhart (Plenum, New York, 1985), Vol. 1, p. 153.

[3] H. F. Bowman, in *Physical Aspects of Hyperthermia,* edited by G. Nussbaum (American Institute of Physics, New York, AAPM Monograph, 1983), Vol. 8, p. 511.

[4] A. Shitzer and R. C. Eberhart, in *Heat Transfer in Medicine and Biology, Analysis and Applications,* edited by A. Shitzer and R. C. Eberhart (Plenum, New York, 1985), Vol. 1, p. 137.

[5] I. A. Lubashevskii and A. G. Cadjan (unpublished).

[6] I. A. Lubashevskii, A. G. Cadjan, and V. V. Gafiychuk, Physica A (to be published).

[7] M. Prives, N. Lusenkov, and V. Bushkovich, *Human Anatomy* (Mir, Moscow, 1985).