Analysis of the optimality principles responsible for vascular network architectonics

I.A.Lubashevsky, V.V.Gafiychuk
Institute of General Physics Academy of Science of Russian Federation;
Moscow State University, Moscow
Institute of Applied Problems of Mechanics and Mathematics National Academy of Sciences of Ukraine, Lviv

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Abstract

The equivalence of two optimality principles leading to Murray’s law has been discussed. The first approach is based on minimization of biological work needed for maintaining the blood flow through the vessels at required level. The second one is the principle of minimal drag and lumen volume. Characteristic features of these principles are considered.

An alternative approach leading to Murray’s law has been proposed. For that we model the microcirculatory bed in terms of delivering vascular network with symmetrical bifurcation nodes, embedded uniformly into the cellular tissue. It was shown that Murray’s law can be regarded as a direct consequence of the organism capacity for controlling the blood flow redistribution over the microcirculatory beds.

1 Introduction

The great amount of natural systems have highly branching networks. As a evident example of such systems we may regard living tissue where blood supplies the cellular tissue with oxygen, nutritious products, etc. through branching vascular network and at the same time withdraws products resulting from living activities of the cellular tissue. A similar situation takes place in respiratory systems where oxygen reaches small vessels (capillaries) going through the hierarchical system of bronchial tubes. There is a question of what physical principles govern network organization living systems under consideration. In this paper we focus our attention on the analyzes of different known optimal principles of network formation for microcirculatory bed and developing new approach to this problem.
Table 1: Typical parameters of the vessel arrangement of a 13-kg dog, after [30].

| Vessel type       | Diameter, $2a, \mu m$ | Length, $l, \text{cm}$ | Tissue/Vessel radii, $d/a$ | Arrangement anisotropy$^*$ |
|-------------------|-----------------------|------------------------|---------------------------|-----------------------------|
| Primary arteries  | 300                   | 1.0                    | 30                        | 0.86                        |
| Small arteries    | 100                   | 0.5                    | 20                        | 0.50                        |
| Terminal vessels  | 50                    | 0.2                    | 10                        | 0.37                        |
| Arterioles        | 20                    | 0.1                    | 7                         | 0.25                        |

$^*$measured as $(\pi d^2 l)^{1/3}/l$

2 Analysis of the optimality principles

A microcirculatory bed can be reasonably regarded as a space-filling fractal being a natural structure for ensuring that all cells are serviced by capillaries [31]. The vessel network must branch so that every small group of cells, referred below to as “elementary tissue domain”, is supplied by at least one capillary. Since a typical length of capillaries is about 0.3 to 0.7 mm a vessel network generated by an artery of length of order of 1 to 5 cm should contain a sufficiently large number of hierarchy levels. At zeroth level we meet the host artery and the host vein, the mother and daughter vessels belong to $n$-th and $(n + 1)$-th levels, respectively, and the last level $N$ comprises capillaries. So at each level $n$ of the vascular network the tissue domain supplied by a given microcirculatory bed as a whole can be approximated by the union of the tissue subdomains whose mean size is about the typical length $l_n$ of the $n$-th level vessels. Thus, the individual volume of these subdomains is estimated as $V_n \sim l_n^3$ and their total number (as well as the total number of $n$-th level vessels) is about $M_n \sim V_0/l_n^3$, where $V_0$ is the total volume of the microcirculatory bed. The higher is the level, the more accurate become the independence of such estimates from the particular details of vessel arrangements. For internal organs they approximately hold also for large vessels of regional circulation. To justify the latter statement we present Table 1 relating the vessel lengths and radii to the radii of the corresponding tissue cylinders, i.e. the cylindrical neighborhood falling on one vessel of a fixed level.

This condition that the vascular network be volume-preserving from one generation to the next gives us immediately the local relation between the characteristic lengths of the vessels: $l_n^3 \approx gl_{n+1}^3$ (here $g = 2$ is the order of the vessel branching node). Whence it follows that $l_n \sim l_0 g^{-n/3}$, where $l_0$ is the characteristic size of the microcirculatory bed region or, what is practically the same, the length of the host artery.

The following analysis, however, will require a more detailed information about the vascular network architectonics. Namely, we need to know how the vessel radii change at the nodes and the relative arrangement of mother and daughter vessels. Actually here we meet the problem as to what fundamental
Figure 1: Characteristics of the vessel branching

regularities govern the vessel branching. These regularities manifest themselves in the relation between the radii $a_0$, $a_1$, $a_2$ of mother and daughter arteries, respectively, and the angles $\theta_1$, $\theta_2$, $\theta_{12} = \theta_1 + \theta_2$ which the daughter branches make with the direction of the mother artery and with each other (Fig. 1).

A detailed theoretical attempt of understanding this regularity was made first by Cecil D. Murray in 1926 [19, 20]. He proposed a model relating the artery radii at branching nodes (Fig. 1) by the expression

$$a_0^x = a_1^x + a_2^x$$

where $x$ is also called the bifurcation exponent. Murray’s approach was under development in a large number of works, see, for example, 1, 2, 22, 29 and a series of works by Zamir et al. 30, 37, 40, 41 and by Woldenberg et al. 33 (for a historical review see also 28, 40, 12). The idea of Murray’s model is reduced to the assumption that physiological vascular network, subject through evolution to natural selection, must have achieved an optimum arrangement corresponding to the least possible biological work needed for maintaining the blood flow through it at required level. This biological work $P$ involves two terms: (i) the cost of overcoming viscous drag during blood motion through the vessels obeying Poiseuille’s law, and (ii) the energy metabolically required to maintain the volume of blood and the vessel tissue. Dealing with an individual artery of length $l$ and radius $a$ with a blood flow rate $J$ in it we get:

$$P = \frac{8\eta J^2}{\pi a^4} + m\pi a^2 l,$$

where $\eta$ is the blood viscosity and $m$ is a metabolic coefficient. Minimizing function (4) with respect to $a$ we find the relation between the blood flow rate $J$ and the artery lumen radius $a$ corresponding to the given optimality principles:

$$J = ka^3,$$
Table 2: Integral characteristics of the vessel cross-section at different branching levels, after [12].

| Vessel type | Mean radius $a$, µm | $\sum a^2$ cm$^2$ | $\sum a^3 \cdot 10^4$ cm$^3$ | $\sum a^4 \cdot 10^{-3}$ cm$^4$ |
|-------------|----------------------|---------------------|------------------------|------------------------|
| **Homo sapiens** | | | | |
| Aorta | 12500 | 1.56 | 1.95 | 2.44 |
| Arteries | 2000 | 6.36 | 1.27 | 0.25 |
| Arterioles | 30 | 127.4 | 0.382 | $1.15 \times 10^{-3}$ |
| Capillaries | 6 | 1432 | 0.860 | $5.16 \times 10^{-4}$ |
| Venules | 20 | 1273 | 2.55 | $5.09 \times 10^{-3}$ |
| Veins | 2500 | 12.9 | 3.18 | 0.80 |
| Vena cava | 15000 | 2.25 | 3.38 | 5.06 |
| **Canis familiaris** | | | | |
| Aorta | 5000 | | 1.25 | |
| Large arteries | 1500 | | 1.35 | |
| Main arterial branches | 500 | | 0.75 | |
| Terminal branches | 300 | | 0.486 | |
| Arteriolas | 10 | | 0.400 | |
| Capillaries | 4 | | 0.768 | |
| Venules | 15 | | 2.70 | |
| Terminal veins | 750 | | 7.59 | |
| Main venous branches | 1200 | | 10.37 | |
| Large veins | 3000 | | 10.80 | |
| Vena cava | 6250 | | 1.53 | |
where the coefficient \( k = \sqrt{\frac{m\pi^2}{16\eta}} \) is a constant for the tissue under consideration. Due to the blood conservation at branching nodes we can write \( J_0 = J_1 + J_2 \) (Fig. 1) whence Murray’s law (3) immediately follows.

However, care must be taken in comparing measurements with prediction, particularly if averages over many successive levels are used. Already Mall himself noted that his data were approximate [17]. In particular, for large arteries of systemic circulation where blood flow can be turbulent the bifurcation exponent \( x \) should be equal to \( 7/3 \approx 2.33 \) as it follows from this optimality principle of minimum pumping power and lumen volume.

There is also another optimality principle leading to Murray’s law, the principle of minimum drag and lumen surface [36, 37]. The drag against the blood motion through vessels is caused by the blood viscosity and can be described in terms of the shear stress on the walls of vessels, \( 2\pi a \tau_t \), where

\[
\tau_t = \eta \nabla_n v = \frac{a}{2l} \delta P = \frac{4\eta}{\pi} \frac{J}{a^3},
\]

for the laminar flow and \( \delta P \) is the pressure drop along a vessel of length \( l \) and radius \( a \). Then the given optimality principle is reduced to the minimum condition for the function

\[
P' = \frac{8\eta l J}{a^2} + m'2\pi al,
\]

where \( m' \) is a certain weighting coefficient. Minimizing (5) with respect to \( a \) we get a relationship between \( J \) and \( a \) of the same form as (3), leading to Murray’s law again. There were a number works (see, e.g., [40, 33, 5, 7]) aimed at finding out what the specific optimality principle governs the artery branching by studying the angles of daughter vessels, \( \theta_1, \theta_2, \theta_{12} \), in relation to the asymmetry of the branching node, \( a_2/a_1 \) (Fig. 1). However, on one hand, all the optimality principles give numerically close relationships between the vessel angles and radii for the bifurcation exponent \( x \approx 3 \) [33]. On the other hand, it turned out that experimentally determined branching angles generally exhibit considerable scatter around the theoretical optimum. The matter is that small variations of the total “cost” of artery bifurcation about several percents causes the actual vessel angles to deviate significantly from the predicted optimum. This feature is illustrated in Fig. 2 showing the variations in the vessel angles governed by the minimality of functional (3) with imposed 10% perturbations. Namely, varying the coordinates of the branching node (Fig. 1) we get that the minimum of the function \( P_0' + P_1' + P_2' \) is attained when

\[
a_1 \cos \theta_1 + a_2 \cos \theta_2 = (1 + \epsilon)a_0, \quad (6)
\]

\[
a_1 \sin \theta_1 - a_2 \sin \theta_2 = \epsilon' a_0, \quad (7)
\]

where the additional terms \( \epsilon a_0 \) and \( \epsilon' a_0 \) with \( |\epsilon|, |\epsilon'| < 0.1 \) describes possible deviations from the optimality condition. The resulting values of \( \theta_1 \) and \( \theta_2 \) are depicted in Fig. 2. It should be noted that expressions (6), (7) correspond actually to the mechanical equilibrium of the node under the action of vessel
walls strained by the blood motion and the additional terms describe a possible effect of the cellular tissue.

Nevertheless, the optimality principles based on functional (2) seems to govern the artery bifurcations (3). Besides, this principles gives also adequate estimates of the integral characteristics of microcirculatory beds (10, 11).

The bifurcation exponent $x$, on the contrary, is well approximated by the Murray value, $x \approx 3$, at least starting from arteries of intermediate size (39). This value meets also the space-filling requirement for the vascular network fractal in geometry to fill precisely the space of a fixed relative volume at each hierarchy level (18). Indeed, assuming the volume of the tissue cylinders matching an artery of length $l$ and lumen radius $a$ to be about $l^3$ we get that the corresponding relative volume of blood is ($a/l)^2$. So it is fixed if $a = \text{constant} \cdot l$ and, thus, $a_0^3 = a_1^3 + a_2^3$ provided the tissue cylinder matching the mother artery is composed of the tissue cylinders of the daughter arteries.

In order to specify the microcirculatory bed structure we need also to classify vessels according to the symmetry of their branching (Fig. 3). The matter is that (11) arteries with predominantly asymmetric bifurcations give off comparatively little flow into its side branches along its way and, therefore, able to carry the mainstream flow across larger distances. Conversely, a more symmetric bifurcation pattern splits flow into numerous small branches, thereby delivering blood to its surrounding tissue. Such arteries have been attributed a “conveying” and “delivering” types of function, respectively. Since blood must be conveyed towards the sites at which to be delivered, both types of vessels occur in real arterial trees. Moreover, a larger conveying vessel may switch into
a bunch of small delivering branches.

Obviously, real arterial trees should contain a great variety of intermediate stages in between these extremes and as our field of view moves from the large systemic arteries to small arteries of regional circulation the vessel bifurcation should become more and more symmetrical. This has been also justified by numerically modelling the structure of arterial trees governed by the minimality condition of blood volume [24, 25, 26, 27]. According to the experimental data (see, e.g., the work [5] and Fig. 4 based on it) even sufficiently large regional arteries of diameter and length about 300 $\mu$m and 1 cm, respectively, (Table 1) branch symmetrically, at least at first approximation. Therefore microcirculatory beds as they have been specified above can be regarded as a vessel network with approximately symmetrical bifurcations.

In other words, we may think of the systemic arteries as vessels of the conveying type where the mean blood pressure is practically constant. Conversely, the arteries of microcirculatory beds should belong to the delivering type and mainly determine the total resistance of the vascular network to blood flow, with the blood pressure drop being uniformly distributed over many arteries of different length.

### 3 Physiological mechanisms governing the vessel arrangements

The universality of Murray’s law for distributed transport systems in many different live organisms raises questions as to: What cues are available to organisms to use in generating such systems? What physiological mechanisms enable them to adapt to altering conditions? Do in fact live organisms follow certain global optimality principles?

For Murray’s law (3) the shear stress $\tau_1$ is constant (see formula (4)) throughout a given artery system. Rodbard [21] proposed that the shear stress detected by the vessel endothelium leads to the vessel growth or contraction, and Zamir [38] suggested that this leads to the development of Murray’s system as vessels
maintain a constant value of shear stress. Concerning the particular mechanism by which organisms can implement the shear stress sensitivity we can say the following. Now it is established that the adaptation of conduit arteries as well as resistance arteries to acute changes in flow is mediated by the potent endogenous nitrovasodilator endothelium-derived relaxing factor, whose release from endothelial cells is enhanced by flow through the physical stimulation of shear stress (see, e.g., \[7\] and references therein). The adaptation of arterial diameters to long-term changes in the flow rate also occurs through a mechanism which appears to involve the sensitivity to shear stress and the participation of endothelial cells, but remains not to be understood well \[7\] .

It should be noted that the shear stress equality through a vascular network does not lead directly to a certain optimality principle. Different principles, for instance, \(2\) and \(5\), can give the same condition imposed on the shear stress. Moreover, it is quite possible that the case of this equality is of another nature. In particular, for large conduit arteries in the human pulmonary tree the bifurcation exponent \(x\) is reported to be in the range 1–2, whereas Murray’s law holds well beginning from intermediate conveying arteries \([34, 13]\). The matter is that in large systemic arteries the blood pressure exhibits substantial oscillations because of the heart beating, giving rise to damped waves travelling through the systemic arteries. The value of the bifurcation exponent \(x = 2\) matching the area-preserving law at the branching nodes ensures that the energy-carrying waves are not reflected back up the vessels at the nodes. How-

Figure 4: Bifurcation symmetry vs. vessel diameter for the porcine coronary arterial tree (based on the data of \[5\]). The darkness intensity indicates the density of the experimental points.
ever, this requirement is also can be derived from a certain optimality principle.

Summarizing the aforesaid we will model the microcirculatory bed in terms of a delivering vascular network with symmetrical bifurcation nodes embedded uniformly into the cellular tissue. Besides, the Murray’s law will be assumed to hold. The latter is also essential from the standpoint of the tissue self-regulation, which will be discussed in detail in the next section. Here, nevertheless, we make several remarks concerning the given aspect too, because it could be treated as an alternative origin of Murray’s law (3). Let us consider a symmetrical dichotomous vessel tree shown, e.g., in Fig. 3b. In order to govern blood flow redistribution over the microcirculatory bed finely enough so to supply with, for example, increased amount of blood only those regions where it is necessary and not to disturb other regions the blood pressure should be uniformly distributed over the microcirculatory bed, at least, approximately.

The blood pressure drop $\delta P_n$ along an artery of level $n$ ($n = 0, 1, 2, \ldots$, Fig. 3) for laminar blood flow is

$$\delta P_n = \frac{8\eta J_n}{\pi a_n^4}. \quad (8)$$

For the space-filling vascular network this artery supplies with blood a tissue region of volume about $l_n^3$ and, so, under normal conditions the blood flow rate $J_n$ in it should be equal to $J_n \approx j l_n^3$, where $j$ is the blood perfusion rate (the volume of blood flowing through a tissue domain of unit volume per unit time) assumed to be the same at all the points of the given microcirculatory bed. Then formula (8) gives us the estimate

$$\delta P_n = \frac{8\eta j}{\pi} \left( \frac{l_n}{a_n} \right)^4$$

whence it follows that $\delta P_n$ will be approximately the same for all the levels, i.e. the blood pressure will be uniformly distributed over the arterial bed if the ratio $l_n/a_n$ takes a certain fixed value, $l_n \approx \text{constant}\cdot a_n$ and, thus, $J_n \approx \text{constant}'\cdot a_n^3$.

Due to the blood conservation at branching nodes we can write

$$J_0 = J_1 + J_2 \quad (9)$$

(see Fig. 3). The later gives us immediately Murray’s law (1). In other words, Murray’s law can be also regarded as a direct consequence of the organism capacity for controlling finely the blood flow redistribution over the microcirculatory beds.

It should be noted that in the previous papers [14, 15, 16] we considered in detail the mathematical model for the vascular network response to variations in the tissue temperature on the given network architectonics. We have found that the distribution of the blood temperature over the venous bed aggregating the information of the cellular tissue state allows the living tissue to function properly. We showed that this property is one of the general basic characteristics of various natural hierarchical systems. These systems differ from each other by the specific realization of such a synergetic mechanism only.
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