# Arterial Bifurcations in the Human Retina

M. ZAMIR, J. A. MEDEIROS, and T. K. CUNNINGHAM

From the Departments of Applied Mathematics, Biophysics, and Physics, University of Western Ontario, London, Ontario, Canada N6A 5B9

ABSTRACT The branching angles and relative diameters of blood vessels in 51 arterial bifurcations in the retina of a normal human eye were measured. In eight other bifurcations, only the total branching angles were measured. The results are compared with theoretical predictions in an attempt to understand the physiological principles governing arterial branching in the cardiovascular system.

## INTRODUCTION

The morphological structure of the cardiovascular tree has been the subject of sporadic study in the past few decades. The pioneering steps were made in two papers by C. D. Murray in 1926. Of particular interest are the branching angles and the relative diameters of the vessels involved in an arterial bifurcation. The subject is of mainly physiological interest, not anatomical, because these geometrical properties of the arterial tree form the basis of its physiological function. Indeed, attempts to explain these properties have so far been made in terms of mainly physiological principles. These principles were compiled recently and their results compared with one another and with what is qualitatively observed in the cardiovascular system (Zamir, 1976, 1978).

In general, these theoretical studies suffer from an almost total lack of quantitative data relating to branching angles and vessel diameters in the cardiovascular system. Data on the corresponding amount of blood flow in each vessel is also required. The measurement of these quantities is extremely difficult whether in vivo or *in situ*, and a sufficiently large amount of data is required for a meaningful comparison with theoretical results.

The present study explores the retina of the human eye as a means for providing some of the required data. In the retina a large number of arterial bifurcations can be studied in vivo. In fact, the retinal blood vessels have been studied a great deal in the past (see, for example, Wise et. al., 1971) but mainly qualitatively. Here we attempt to derive quantitative information on the branching angles and relative diameters of retinal arteries. The results reported here follow a number of earlier failures and a number of improvements in the measurement techniques. We have no doubt that other workers will produce further improvements in the future.

In the absence of other experimental data at present however we have only the theoretical results to compare with and to judge by. In so doing, it is not

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being suggested that the theoretical or experimental results have authoritative status at this time. The comparison is made rather because both the theoretical and experimental efforts in this field are still at an infant stage, and each requires the guidance of the other to make further progress.

## METHODS

The subject was a healthy 34-yr-old human male with 20-20 vision. The eyes had normal pigmentation and no visible pathologies. The left eye was used throughout the study.

Topically administered drops of Neo-Synephrine (Winthrop Laboratories, New York) in 10% solution were used to dilate the pupil. The fundus was then photographed using a Topcon retinal camera (Kogaku Kikai K. K., Tokyo) with Kodachrome 25 film (Eastman Kodak Co., Rochester, N.Y.) and a Xenon flash (Kogaku Kikai K. K.) to provide the lighting.

Six overlapping photographs were taken to cover an area of ~ 25% of the fundus. One of these is shown in Fig. 1. The area from which the measurements were derived was an even smaller part of the fundus, perhaps only 10%. For this reason, and because this area was viewed at right angles, the curvature of the retina was estimated to have a small effect compared with the variability found to prevail in the data.

### *Measurements*

Pictures of the fundus were projected onto a distant background to produce a magnification of about × 100. In the magnified pictures the retinal blood vessels were large and clear, with diameters of the order of a few millimeters. However, attempts to take measurements directly from these images were not successful. Attempts to take measurements from photographic prints of various sizes were also not successful. Instead, enlarged images of the blood vessels were carefully traced onto a white sheet, the projected picture was then switched off, and measurements were taken from the tracing.

The six photographs of the fundus were in this way pieced together to produce a single map of the retinal vessels as shown in Fig. 2. On this map all arterial bifurcations were labelled by following each major artery from its point of origin along each of its branches, then along the branches of each branch, etc. In this way each arterial bifurcation was identified by a particular label, and a table of these was produced with the measurements associated with each. The map was used mainly for locating individual bifurcations relative to one another. Some measurements were taken from it, but the majority were taken from enlargements and tracings of particular regions or, in some cases, of individual junctions. It was not necessary to maintain the same magnification in all regions because, as will be explained in the next section, only the relative diameters were required, i.e., the ratio of the diameter of a branch to the diameter of its parent vessel.

At each bifurcation the diameters of the parent artery and its two branches were measured, as well as the angle which each branch makes with the direction of the parent artery as illustrated in Fig. 3. Diameters were measured with the aid of either vernier calipers (MTI Corp., New York) or a comparator (MTI Corp.) with a magnifying lens. Branching angles were measured by drawing the center lines of the vessels near the junction and then using a simple protractor to read the angles between them.

Two types of uncertainties were encountered in the course of these measurements. First, the images of some vessels were faint and the definition of the vessel walls was rather weak. Second, because the diameter of a blood artery is not generally constant along its length, and because most arteries are not straight, the branching angles and vessel diameters were not always well defined. The errors associated with these uncertainities are discussed later. At this point we mention only that as a counteractive measure the measurements of some bifurcations were repeated two, three, or four times. These repetitions were performed either by a different person, or at a different time, or from a different image at a different magnification. In total 59 different bifurcations were surveyed, and of these, 23 were measured once, 22 were measured twice, and 14 were measured three or more times. In eight cases only the total bifurcation angle could be measured.

FIGURE 1. One of six photographs used for mapping out and measuring the retinal vessels. The subject was a healthy 34-yr-old caucasian human male with 20-20 vision. The eyes had normal pigmentation and no visible pathologies. ×20.

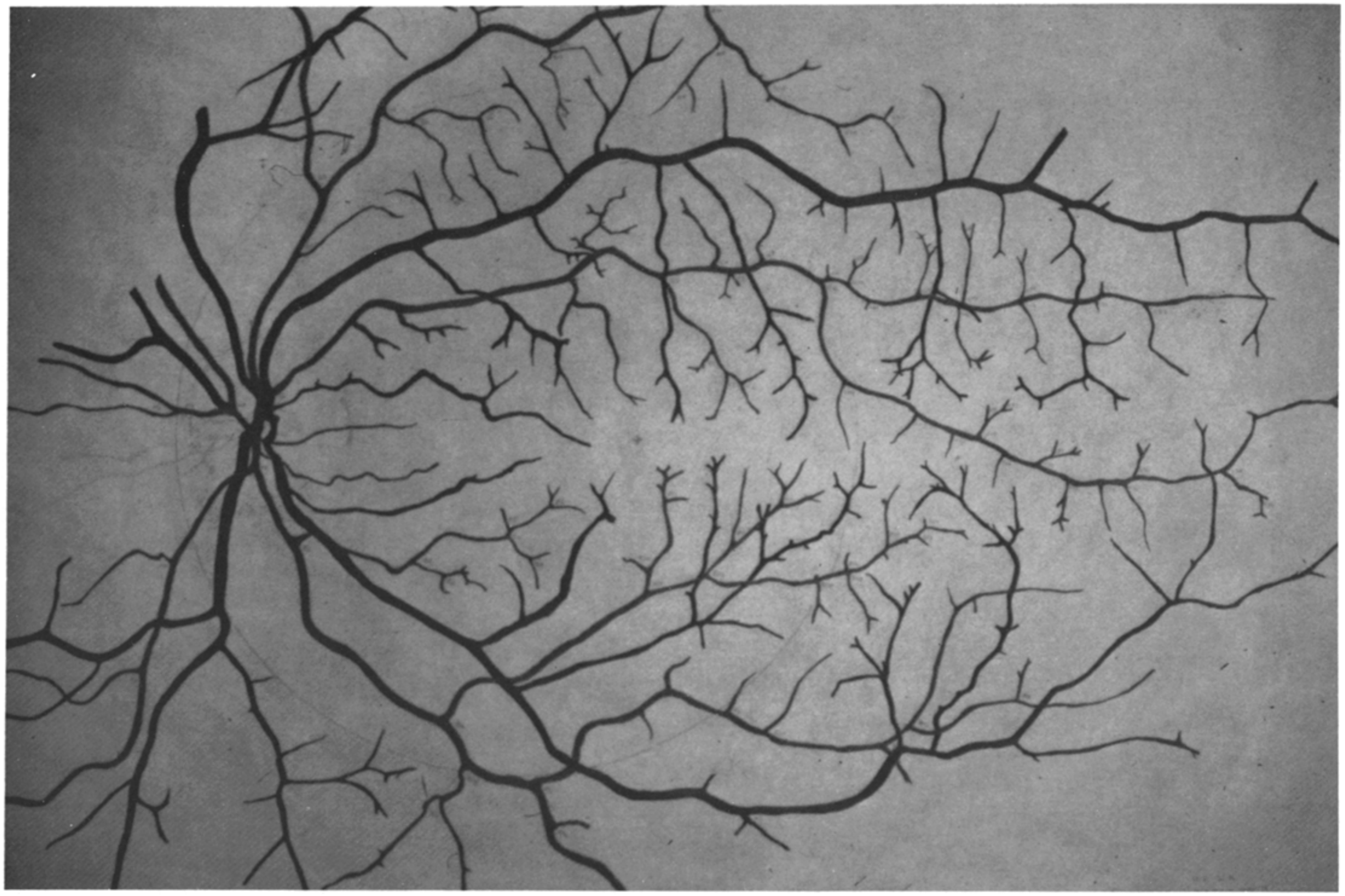

FIGURE 2. A map of the major retinal vessels produced by piecing together six overlapping photographs of the fundus. The photographs were first projected onto a distant background to produce a magnification of the vessels of ~ ×100, and the resulting images were then carefully traced with a pencil to produce this map. The actual size of the map was ~ 36 × 48 in.

## RESULTS

An arterial bifurcation is specified in terms of the diameters $d_0$, $d_1$, and $d_2$ of the parent vessel, the larger branch, and the smaller branch respectively; and the angles $\theta_1$ and $\theta_2$, which the larger and smaller branches make with the direction of the parent vessel as illustrated in Fig. 3. Subscripts 0, 1, and 2 will always be used to denote the parent vessel, the larger branch, and the smaller branch, respectively.

The use of actual diameters is associated with difficulties and errors, particularly if the measurements are taken from a magnified image of the vessels. These problems can be avoided by specifying a bifurcation in terms of relative rather than actual diameters. This is achieved by introducing two nondimensional parameters: the area ratio,

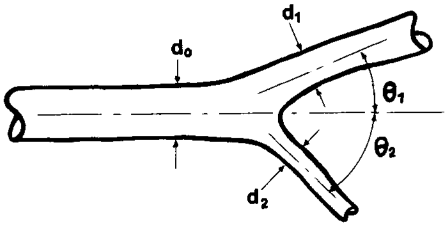

FIGURE 3. A schematic diagram of an arterial bifurcation to indicate the measurements made and the notation used. Subscripts 0, 1, and 2 were used throughout to denote the parent vessel, the larger branch, and the smaller branch, respectively.

$$\beta = (d_1^2 + d_2^2)/d_0^2; \tag{1}$$

and the asymmetry ratio,

$$\alpha = d_2^2/d_1^2. \tag{2}$$

The following results are therefore presented in terms of $\alpha$ and $\beta$ in place of actual diameters. Given $d_0$, $d_1$, and $d_2$ in terms of any length scale, a value for each of $\alpha$ and $\beta$ is obtained from Eqs. 1 and 2, and this pair of values then represents the particular bifurcation in hand.

Thus, all the bifurcations measured in this study can be put on a graph of $\alpha$ against $\beta$, as shown in Fig. 4. A point on this graph represents a set of measurements of $d_0$, $d_1$, and $d_2$. At this stage repeated measurements are represented by separate data points rather than averaged. The theoretical curve shown in the same figure is discussed in the next section and the scatter of the experimental data is discussed in the following section.

Measurements of total bifurcation angles ($\theta_1 + \theta_2$) are shown in Fig. 5 plotted against the asymmetry ratio $\alpha$. Measurements of the branching angles $\theta_1$ and $\theta_2$ are shown separately in Figs. 6 and 7. Again, the theoretical curves shown in these figures and the scatter of the data points will be discussed in the next two sections.

In eight cases not included in the above results, only the total bifurcation angles ($\theta_1 + \theta_2$) could be measured. It was not possible to measure the diameters. Thus, no values of $\alpha$ or $\beta$ are available for these bifurcations, and they cannot be included in the graphical presentation of the results. The angles measured in degrees were 120, 110, 80, 90, 85, 60, 90, and 70.

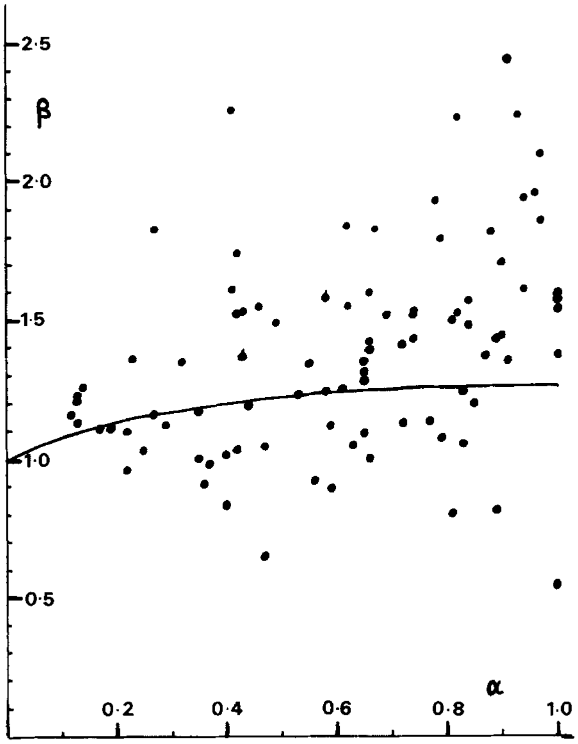

FIGURE 4. Measurements of the area ratio ($\beta$) and the asymmetry ratio ($\alpha$) of arterial bifurcations in the human retina. The solid curve is based on the theoretical result in Eq. 3. Both the theory and the data points are identical with those of Figs. 8 and 9. Comparison of these figures suggests immediately therefore that the extent of the vertical scatter is *magnified* here because the diameters are squared in the expression for $\beta$ (Eq. 1). In Figs. 8 and 9 the diameters are used directly. A flag on a data point indicates that there is another point in the same position.

### *Comparison with Theory*

On theoretical grounds it has been proposed by several authors that arterial branching is governed by certain optimality principles. Briefly stated, each of these principles proposes that the branching angles and relative diameters in

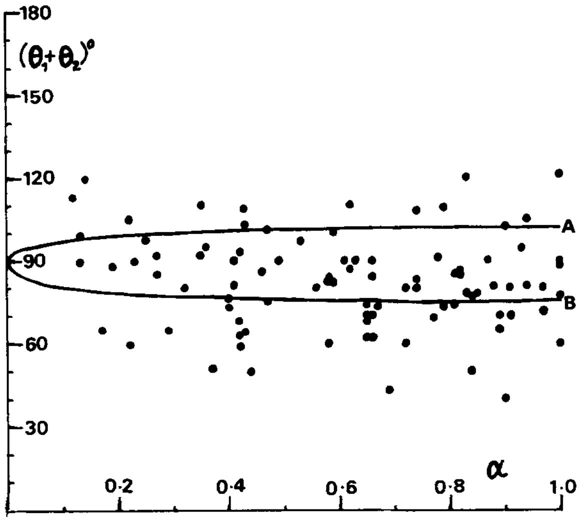

FIGURE 5. Measurements of the total bifurcation angle ($\theta_1 + \theta_2$) and the asymmetry ratio ($\alpha$) of arterial bifurcations in the human retina. The solid curves represent theoretical predictions based on conditions of minimum lumen surface and drag (A), and minimum lumen volume and pumping power (B).

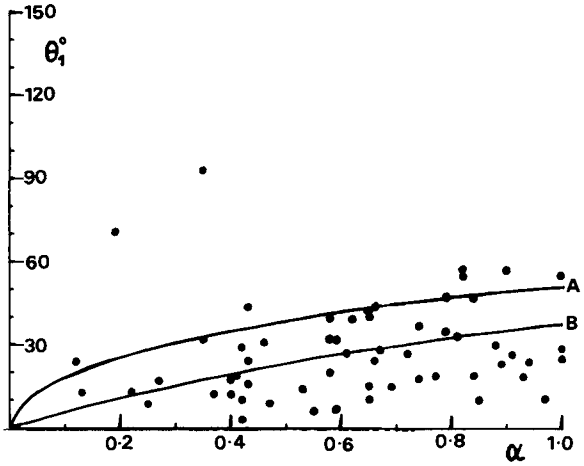

FIGURE 6. Measurements of the branching angle ($\theta_1$) made by the larger branch and of the asymmetry ratio ($\alpha$) in arterial bifurcations of the human retina. The solid curves represent theoretical predictions based on conditions of minimum lumen surface and drag (A), and minimum lumen volume and pumping power (B).

an arterial bifurcation are such that a certain property of that bifurcation is minimized to a functional advantage of the system. Lumen surface, lumen volume, pumping power, and endothelial drag are four such properties which have been considered so far. More details can be found in Zamir (1976).

Because the results of these studies rest almost entirely on theoretical grounds, they need not necessarily command agreement with the biological data. Nevertheless, the studies offer a useful framework in which to examine the data. We therefore compare the theoretical and experimental results with only this view in mind here, and in the next section we discuss the differences between them.

It was first suggested by Murray (1926 *a*) that the diameter of a blood vessel is proportional to the cube root of the flow which the vessel is designed to convey. More recently the suggestion was studied further by Rodbard (1975), Hooper (1977), and Zamir (1977). It then follows that in an arterial bifurcation the area ratio $\beta$ is related to the asymmetry ratio $\alpha$ by

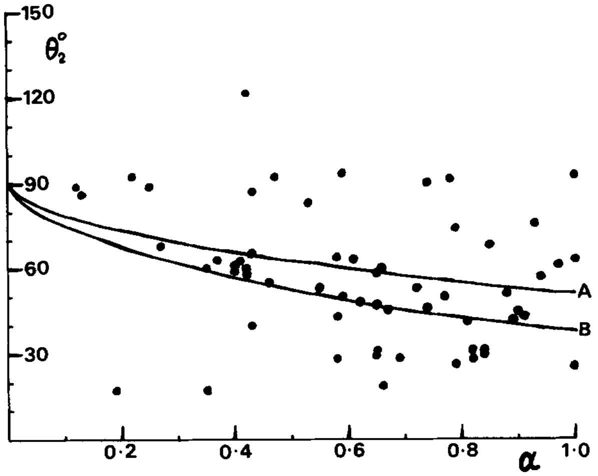

FIGURE 7. Measurements of the branching angle ($\theta_2$) made by the smaller branch and of the asymmetry ratio ($\alpha$) in arterial bifurcations of the human retina. The solid curves represent theoretical predictions based on conditions of minimum lumen surface and drag (A), and minimum lumen volume and pumping power (B).

$$\beta = (1 + \alpha)(1 + \alpha^{3/2})^{-2/3}. \tag{3}$$

The curve representing this relation is shown in Fig. 4. It also follows that the diameter of the larger branch is related to the asymmetry ratio by

$$d_1/d_0 = (1 + \alpha^{3/2})^{-1/3}, \tag{4}$$

and the diameter of the smaller branch is related by

$$d_2/d_0 = \alpha^{1/2}(1 + \alpha^{3/2})^{-1/3}. \tag{5}$$

The curves representing these relations are shown in Figs. 8 and 9.

The branching angles in an arterial bifurcation can be predicted theoretically on the basis of any one of four different optimality principles, coupled

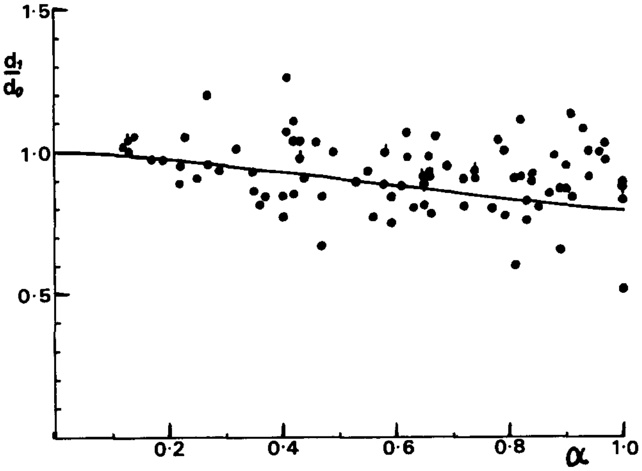

FIGURE 8. Measurements of the diameter ratio of the larger branch to parent vessel ($d_1/d_0$) and of the asymmetry ratio ($\alpha$) in arterial bifurcations of the human retina. The solid curve is based on the theoretical result in Eq. 4. A flag on a data point indicates that there is another point in the same position.

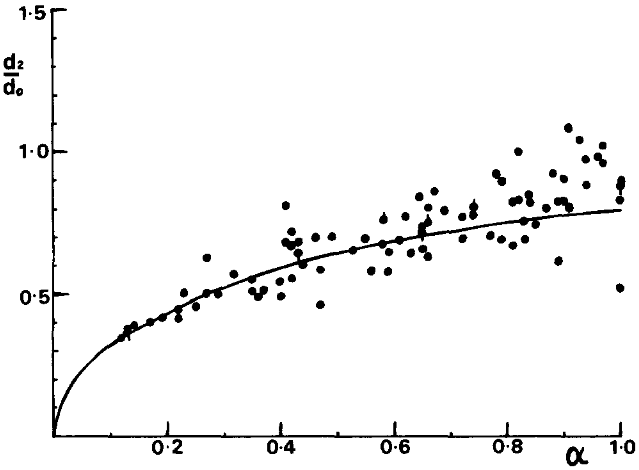

FIGURE 9. Measurements of the diameter ratio of the smaller branch to parent vessel ($d_2/d_0$) and of the asymmetry ratio ($\alpha$) in arterial bifurcations of the human retina. The solid curve is based on the theoretical result in Eq. 5. A flag on a data point indicates that there is another point in the same position.

with Murray's relation between the flow in and diameter of a blood artery. These predictions can be put in the form of relations between the branching angles $\theta_1$ and $\theta_2$ and the asymmetry ratio $\alpha$ (see Zamir, 1978). These relations are represented by the curves in Figs. 5–7. Given the asymmetry ratio of an arterial bifurcation, the optimum angles of the two branches are predicted to be determined by one or the other of the two curves depending on the principle used.

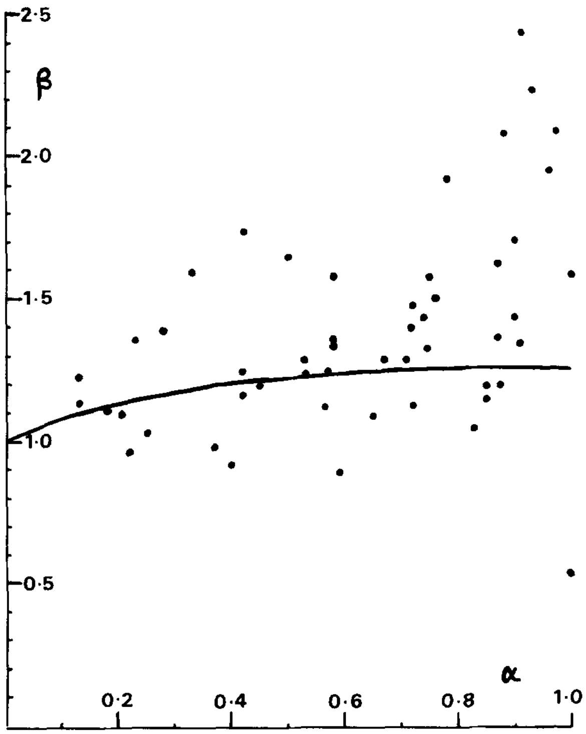

FIGURE 10. Measurements of the area ratio ($\beta$) and the asymmetry ratio ($\alpha$) as in Fig. 4. Here repeated measurements of the same bifurcation are averaged and the average is represented by a single data point.

## DISCUSSION AND CONCLUSIONS

The scatter of the data points in Figs. 4–10 can be attributed to three distinct factors:

(*a*) Reading errors because of faint or fuzzy images of some vessels. These were cases in which the readings were repeated several times and the repetitions are represented by separate data points in Fig. 4. To estimate how much of the scatter is due to this factor we produced Fig. 10 in which the repeated measurements are averaged. The extent of the scatter is not reduced in any significant way. We believe that reading errors were the smallest contributor to the scatter of data points.

(*b*) Reading uncertainties because of curved and nonuniform vessels. This is responsible for a great deal of the scatter and it is an important aspect of the phenomenon in hand. It delivers a useful message to theoretical studies of this subject where it is always assumed that the vessels are straight and uniform. It also suggests that measurements of branching angles and vessel diameters can never be expected to line up neatly along any curve or a straight line without scatter.

(*c*) Genuine departure of some arterial junctions from even the most basic rules, let alone optimality rules. It is a basic rule, for example, that the cross-sectional area must increase through arterial bifurcations to achieve the required total increase of about 1,000-fold from the aorta to the capillaries. Yet, we found many junctions, here and elsewhere, in which the cross-sectional area decreases, i.e., in which $\beta < 1$. It is a basic rule that, in arterial bifurcations, the branches should come off one on each side of the parent artery, yet we found a few cases in which both branches come off on the same side. It is a basic rule that the diameters of the branches be smaller than the diameter of the parent artery, yet we found a number of cases in which this is not so. As in (*b*) above, we believe that the scatter caused by such departures is an integral part of the phenomenon in hand.

We call attention to another important aspect of the scatter of the data points. On theoretical grounds, we have no reason to believe that arterial branching in the cardiovascular system is dictated by only one optimality principle. All four or more principles may be involved collectively, thus giving rise not to a single optimum curve but to an optimum region bound by several curves. The spread of the data points over the optimum regions between the two optimum curves in Figs. 5–7 certainly gives support to the possibility that more than one principle may be involved. Only in Fig. 6, there is some bias in favor of the principles of minimum lumen volume and pumping power.

In general, the data points show a definite qualitative tendency towards the optimum curves, although in some of the figures the tendency is more pronounced than in others. In quantitative terms, if we construct a band of only ±10% deviation from each of the optimum curves in Figures 5–9, these bands would encompass ~ 60% of the data points in Fig. 5, 32% in Fig. 6, 48% in Fig. 7, and 64% in each of Figs. 8 and 9. Now a vertical deviation of ±10% in Figs. 8 and 9 corresponds to a vertical deviation of ~ ±20% in Figs. 4 and 10 because the diameters are squared in the vertical scales of these figures. Thus, in Figs. 4 and 10, if we construct bands of ±20% deviation from the optimum curves, these bands would encompass ~ 55% of the data points in Fig. 4 and 66% in Fig. 10.

After having made these comments we conclude only that our data on arterial branching appear to be in support of at least the two major postulates of theoretical studies in this field. First, that the diameter of an artery is approximately proportional to the cube root of the flow that the artery is designed to convey, and second, that the branching angles in arterial bifurcations are governed by certain optimality principles relating to the physiological function of the cardiovascular system. It must be emphasized, however, that all the biological data of this study came from the retina. Data from other parts of the cardiovascular system will be required before these conclusions can be safely generalized.

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