

Scaling laws for capillary vessels of mammals at rest and in exercise

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A general derivation is presented for the scaling laws governing the size and number of capillary blood vessels in mammals. The derivation is based on the assumption of three idealized similarity principles known to apply, *at least approximately*, to resting mammals: (i) size-invariant blood pressure; (ii) size-invariant fraction of blood in the capillaries; and (iii) size-invariant oxygen consumption and uptake, per unit of body mass, during each heart cycle. Results indicate that the radius and length of capillaries, and the number that are open and active in the resting state, should scale with mammal mass to the powers $1/12$, $5/24$ and $5/8$, respectively, consistent with earlier work by the author. Measurements are presented supporting the results. Physiological changes accompanying strenuous exercise are accounted for by a change in the scaling law for capillary number, from scaling exponent $5/8$ to $3/4$.

Keywords: capillaries; blood vessels; scaling laws; allometric reactions; mammals

1. INTRODUCTION

The discovery of the minute blood vessels connecting the arterial and venous sides of the circulation is attributable to Marcello Malpighi who first identified them in 1661 with the aid of the newly invented microscope. The existence of the capillaries, as they are now called, was anticipated some 30 years earlier by William Harvey in the form of 'porosities of the flesh' associated with his general theory of blood circulation. Since that time, the capillaries have become recognized as essential elements in the life process through which all exchanges take place between the blood and the tissues.

In spite of the long-recognized importance of the capillaries to the cardiovascular system of humans, in particular, and mammals in general, very little progress was made in understanding their physiology until the early part of the 20th century when August Krogh reported extensive experimental studies on the system. This work addressed the number and distribution of capillaries in muscles and the manner of oxygen transfer from capillaries to surrounding tissue (Krogh 1919). The work also revealed the existence of both active and inactive capillaries in resting muscle tissue and illustrated the fact that the latter could become active during exercise (Krogh 1920). Later fundamental work of interest here includes: Pappenheimer *et al.* (1951) on the manner of fluid transfer across capillary walls; Schmidt-Nielsen & Larimer (1958) on measurements of scale variation of the oxygen pressure in the blood of mammals and its relation to oxygen transfer from the capillaries; Schmidt-Nielsen & Pennycuik (1961) and Hoppeler *et al.* (1981) on measurements of scale variation in capillary density in the muscle tissue of mammals; and Gehr *et al.* (1981) on measurements of scale variation in the volume and surface area of the pulmonary capillaries of mammals.

Consistent with the subject of the present paper, the latter measurements of capillary volume and area indicate orderly variation in capillary size as attention is shifted from the human to other mammals. The author (Dawson 1991) discussed these measurements and such variations

some years ago in connection with the scaling laws and design aspects of the cardiovascular system. Unfortunately, however, that work has not received wide attention. Indeed, in recent works by West *et al.* (1997) and Banavar *et al.* (1999) on cardiovascular function, a contrary assumption was made that the capillary dimensions do not vary with mammal size. The matter has been addressed further (Dawson 1998, 2001) in terms of general design considerations of the cardiovascular system, but additional clarification is needed, including the consideration of recent work by Dodds *et al.* (2001) on possible transitions in scaling laws associated with small and large mammals. An extension of the earlier work is also required in view of the increased understanding of the exercise state of mammals provided by the works of Baudinette (1978), Taylor *et al.* (1981), Weibel *et al.* (1991), Bishop (1997, 1999) and Darveau *et al.* (2002), among others. The present work accordingly involves a reconsideration of the capillary system of mammals and provides a new general derivation of the scaling laws for capillary size and number, together with a critical assessment of the assumptions and new results on capillary physiology associated with both resting and exercise states.

2. EXISTENCE OF SIMILARITY AND SCALING LAWS

First, consider the fundamental basis for possible scaling laws governing capillary characteristics on both the systemic and the pulmonary sides of the circulation. The *resting* state of mammals is considered, and the entire vascular system is envisioned on the systemic side, with all its branching from the aorta to the large and small arteries and onward to the many capillaries spread throughout the body and open to blood flow. Likewise, the vascular system on the pulmonary side is considered, with its various branchings from the pulmonary arteries to the capillary beds of the lungs. The characteristic radius of these capillaries, for any specific mammal, is denoted by R_C , their characteristic length by L_C and their characteristic *operative* number in the resting state by N_C . It is the scaling of

these quantities with mammal mass M that is of interest in the present work, together with any modification of the characteristic number that may be needed as a result of strenuous exercise and the opening of additional capillaries in muscle tissue.

Whether such scaling laws exist at all depends, of course, on whether sufficient similarity exists in the capillary systems of mammals to allow correlation of properties from one mammal size to another. Evidence that this is the case has already been given in connection with the author's earlier work and with the measurements of Gehr *et al.* (1981) on the volume and surface area of the pulmonary capillaries. Further evidence can be found in the various other physiological measurements on resting mammals that have been carried out. For example, early experimental work by Rubner (1883) on dogs indicated that their resting oxygen consumption rates varied in an orderly manner, being proportional to body mass raised to the power $2/3$. Work by Kleiber (1932) and Brody & Procter (1932) on mammals in the mouse to elephant range indicated a similar orderly variation, but with mammal mass raised to a power closer to $3/4$. In addition, measurements by Rihl (1926) and Clark (1927) indicated that the resting heart rate of mammals varies with mammal mass raised to a power of approximately $-1/4$, and measurements by Woodbury & Hamilton (1937) and Gregg *et al.* (1937) demonstrated that the systolic and diastolic blood pressures of resting mammals are essentially independent of mammal size. Holt *et al.* (1968) showed, moreover, that resting cardiac output varies with mammal mass raised to a power of approximately $3/4$, and measurements by Schmidt-Nielsen & Larimer (1958) revealed that oxygen partial pressure in the blood of mammals varies approximately with mammal mass to the power $-1/12$. These many results therefore indicate that appreciable similarity exists in the measured physiological variables of resting mammals, as well as in the underlying capillary processes responsible for them.

The extent of the similarity that actually exists among mammals has, in fact, become a subject of increased interest in recent times. Dodds *et al.* (2001) have studied the scaling law for the oxygen consumption rate of resting mammals in considerable detail and have shown, consistent with the earlier work of Bartels (1982) and Heusner (1991), that existing datasets show a transition in power-law representation at a mammal mass of *ca.* 10 kg. For data from mammals with body masses below this level, a scaling law with mammal mass raised to a power of approximately $2/3$ appears preferable, while for the combination of these data with those for larger mammals, a power of approximately $3/4$ is indicated. The work is important in that it indicates the possibility of some basic physiological differences between small and large mammals. It also suggests that the latter $3/4$ relation may not be a fundamental feature of the physiology of mammals, but instead simply a convenient representation for oxygen consumption rate over a wide range of mammal sizes. Weibel (2002) has provided additional insight into the matter of power-law description of oxygen consumption rate.

At present, it is not known whether differences between small and large mammals can be identified in power-law representations of physiological variables associated

Table 1. Idealized scaling relations for resting mammals, where variable Y is proportional to (mammal mass)^b.

variable Y	symbol	exponent b^a
oxygen consumption rate	\dot{V}_{O_2}	$3/4$
heart rate	ω	$-1/4$
blood pressure	—	0
cardiac output	Q_B	$3/4$
oxygen partial pressure in blood	P_O	$-1/12$

^a Details and references noted in text. Additional references are Schmidt-Nielsen (1984) and Dawson (1991).

directly with capillary size or number. It may be that the transition described above is associated only with the process of oxygen transfer across the capillary walls and that the capillaries' characteristics themselves are independent of any such divided representation. The matter is of obvious importance to a general understanding of capillary physiology and will be addressed in the present paper.

In respect of the overall representation of physiological measurements by single empirical scaling relations, it has long been recognized that they are experimental generalizations and that predictions for any specific mammal are likely to be somewhat deficient when compared with the actual measurement for that mammal. The idea in such representations is not so much the precise prediction of values for particular mammals, as these can be determined better from measurements, but rather the establishment of idealized relations, illustrative of the general similarity indicated by the measurements, and amenable ultimately, it is hoped, to a theoretical description in terms of broadly applicable physiological processes. In this sense then, the traditional scaling laws for oxygen consumption rate, heart rate and the many others identified earlier, can serve as a useful reference for theoretical investigation and for more detailed consideration of any departure from these broad general concepts. This is the view adopted in the present work.

The scaling relations of importance in the present investigation of capillaries are listed in table 1, with the understanding that they denote idealized (nominal) representations for mammals ranging in size from the mouse to the elephant and that they provide a convenient baseline for further discussion of observed differences between theory and measurement.

The nominal value of $3/4$ for resting oxygen consumption rate in table 1 may be compared with the value of 0.74 found by Kleiber (1932); the nominal value of $-1/4$ for resting heart rate may be compared with the value of -0.27 found by Clark (1927); and the nominal value of $3/4$ for cardiac output may be compared with the value of 0.78 found by Holt *et al.* (1968). Likewise, the nominal value of $-1/12$ for oxygen partial pressure in the blood may be compared with the value of -0.06 found by Schmidt-Nielsen & Larimer (1958) and the modified value of -0.09 found by Dawson (1991).

3. DERIVATION OF SCALING LAWS AND CRITICAL REVIEW

It is notable that the net flow of blood through all the systemic and pulmonary capillaries of the body must equal

that from the heart, that is to say, it must equal the cardiac output, Q_B , from the left and right ventricles, respectively. Notable also is the generally accepted fact (table 1) that blood pressures in mammals in the resting state are essentially invariant with respect to mammal size. The pressure associated with pushing the blood through the entire set of capillaries can therefore also be expected to be invariant with respect to mammal size. This condition is assumed here.

The famous Poiseuille equation for viscous flow in small tubes (Poiseuille 1846) provides a connection between pressure, cardiac output and capillary dimensions. The relation, developed originally with capillary blood flow in mind, requires the driving pressure ΔP for flow in a single capillary vessel of length L_C and radius R_C to be proportional to blood viscosity μ according to the relation $\Delta P = 8\mu L_C V_C / R_C^2$ where V_C denotes the average blood velocity in the vessel. For a number of identical parallel vessels N_C , the velocity V_C is equal to the total average blood flow Q_B divided by the net sectional area $N_C \pi R_C^2$ so that the relation is $\Delta P = 8\mu L_C Q_B / N_C \pi R_C^2$.

The viscosity of the blood may be assumed to be independent of mammal size, in agreement with laboratory measurements of Amin & Sirs (1985) on the blood of mammals ranging in size from rabbit to horse. The proportional relation for the condition of size-independent driving pressure ΔP is then expressible in the form of the similarity relation $\Delta P \propto L_C Q_B / N_C R_C^2 \propto M^0$, where the symbol \propto denotes proportionality under change of scale and M denotes mammal mass. Moreover, the cardiac output of resting mammals varies with mammal mass to the nominal power $3/4$, so that this relation is expressible finally as

$$L_C M^{3/4} \propto N_C R_C^2. \quad (3.1)$$

Next, consider the fraction of total blood that is in the capillaries of the body and assume that this fraction is the same for all mammals. Total blood volume in mammals is known to be proportional to mammal mass (Brody 1945), therefore this similarity condition provides the relation $N_C L_C R_C^2 / M \propto M^0$, which may be written as

$$N_C L_C R_C^2 \propto M. \quad (3.2)$$

As to the physical basis for this last relation, the extensive measurements of capillary volume in the lungs by Gehr *et al.* (1981) may be considered. In a group of African mammals they discovered that the volume of the pulmonary capillaries varied with mammal mass to the power 0.97. For these and other more familiar mammals, ranging in size from shrew to cow, they determined that the variation was directly proportional to mammal mass. The difference between the two cases is not significant, and equation (3.2) may be considered representative of these measurements. Interestingly, a reanalysis of the data in connection with the present work shows that, for mammals with body mass no greater than 10.1 kg, the capillary volume varies with mammal mass to the power 1.007 ± 0.022 ($n = 22$, $r^2 = 0.991$; \pm values indicate standard errors) while for all the mammals in the study the power is found to be 1.015 ± 0.014 ($n = 37$, $r^2 = 0.993$). Accordingly, no significant difference between small and large mammals is revealed by these measurements.

Next, consider the final relation needed to establish the scaling laws for the capillaries. Here, the conditions (table 1) used are that the rate of oxygen consumption (and also uptake) of resting mammals \dot{V}_{O_2} varies, like cardiac output, as mammal mass to the nominal power $3/4$, and that the heart rate ω of resting mammals varies with mammal mass to the nominal power $-1/4$. The similarity relation $\dot{V}_{O_2} / M\omega \propto M^0$ can then easily be seen to apply. This condition states that the oxygen consumption (and uptake) per unit of body mass during a heart cycle is invariant with respect to mammal size.

In order to relate this last condition to capillary dimensions, it should be noted that the oxygen consumption rate must equal the rate at which it is transferred through the capillary walls. This latter process is one of diffusion (Krogh 1919), and it can therefore be expected to follow the general law requiring rate of transfer to be proportional to the product of the differential oxygen partial pressure $P_O - P'_O$ and the capillary area $2\pi R_C L_C$ and to be inversely proportional to the capillary-wall thickness, say H_C . Here, P_O denotes the oxygen partial pressure in the blood and P'_O the pressure immediately outside the capillary.

The differential oxygen partial pressure $P_O - P'_O$ can be expressed as $P_O(1 - P'_O/P_O)$, but unfortunately no information exists on the variation of the ratio of these two pressures P'_O/P_O with change in mammal size. It can be expected, however, that any percentage change in one pressure from change in scale will be accompanied by a similar, or near similar, change in the other. The ratio P'_O/P_O will therefore be assumed to be constant for all mammals. It may be noted, however, that variation in the ratio could provide a source for the divided representation of the oxygen consumption rate indicated in measurements for small and large mammals, as noted by Dodds *et al.* (2001) and discussed earlier. The matter will be addressed further in a later section of this paper. Assuming, for the present, that the ratio is constant and considering all systemic or pulmonary capillaries of the body, we may then write the proportional relation for the rate of oxygen consumption, or uptake, as $\dot{V}_{O_2} \propto N_C P_O R_C L_C / H_C$.

The question now is what to do with the capillary thickness in this last relation? Again, as in the case of the above pressure ratio, there are no explicit measurements to guide the answer. There are two simple possibilities: either it is size invariant, or it varies directly as the radius varies. Support for the latter over the former is found in the condition (for rupture prevention) that the mechanical stress in the capillary wall from blood pressure is size invariant in accordance with the Laplace formula for stress (net blood pressure times radius divided by wall thickness). Thus, accepting this condition, the oxygen condition may be written as $\dot{V}_{O_2} \propto N_C P_O L_C$, and the size-invariant condition as $N_C P_O L_C / M\omega \propto M^0$. Oxygen partial pressure in the blood is known, from measurement, to vary with mammal mass to the nominal power $-1/12$ (Dawson 1991). The final relation is then expressible as $N_C M^{-1/12} L_C \propto M\omega \propto M^{3/4}$ or

$$N_C L_C \propto M^{5/6}. \quad (3.3)$$

The scaling laws can now be established for the dimensions and number of capillary vessels using the above three

conditions. From equations (3.2) and (3.3) it can easily be seen that $M^{5/6}R_C^2 \propto M$, so that R_C^2 must be proportional to $M^{1/6}$ and hence the radius R_C must be proportional to $M^{1/12}$. Equations (3.2) and (3.3) alone therefore determine the scaling laws for capillary radius R_C and net length $N_C L_C$. In order to determine the separate scaling laws for capillary length and number, equation (3.1) may be multiplied by L_C and written as $L_C^2 M^{3/4} \propto N_C L_C R_C^4$. Utilizing equation (3.2), this may also be written as $L_C^2 M^{3/4} \propto M R_C^2$. Using the previously established condition for R_C , we thus find that the capillary length L_C must be proportional to mammal mass to the power $5/24$. Finally, equation (3.3) therefore illustrates that capillary number N_C must be proportional to mammal mass to the power $5/8$. Collating these results, we thus have the scaling laws for the capillary dimensions and number expressible as

$$R_C \propto M^{1/12}, \quad L_C \propto M^{5/24}, \quad N_C \propto M^{5/8}. \quad (3.4)$$

These relations are in agreement with those of the author's earlier work (Dawson 1991, 2001). They have been derived here in a relatively direct manner, using the idealized properties of mammals tabulated in table 1 and additional assumptions as critically discussed.

4. EXPERIMENTAL DEMONSTRATION

In this section, the experimental demonstration of the scaling laws of equation (3.4) is considered. The discussion is partly one of review, since the author (Dawson 1991, 2001) has already discussed the matter in considerable detail. The assumption is that the scaling laws for characteristic capillary dimensions and number apply to all capillaries within any well-defined part of a mammal where consistent measurements can be made.

For example, if the radius of the capillaries in a certain organ of a human, with a body mass of 70 kg, is found to equal 0.0040 mm, then we would expect the radius of corresponding capillaries in an elephant, with a body mass of 3000 kg, to be 0.0055 mm, as determined by the product $0.004 (3000/70)^{1/12}$ from the first relation of equation (3.4). Similarly, if the number of capillaries in an organ of the human is estimated to equal a certain value, this number may also be scaled to the elephant using the third relation in equation (3.4). Of course, in this last example, the capillaries in question must be only those active in the resting state, since resting conditions are assumed in the development of equation (3.4). All capillaries in the kidneys and lungs, for example, are active in the resting state, in contrast with the various muscles of the body, which generally have both active and inactive capillaries during resting.

First, the capillary number N_C is considered and reliable measurements sought for confirmation of the $5/8$ power law of equation (3.4) for this variable. Fortunately, as noted earlier (Dawson 1991), such data are available from the extensive study of the fundamental nephron units of the kidneys by Kunkel (1930). These units consist of a cluster of capillaries, encased in the renal capsule, through which fluid is discharged, and also additional capillaries through which it is partially reabsorbed. In the human, there are approximately one million such units in each kidney. Assuming a similar architecture of the units among mammals, with the same total number of capillaries per

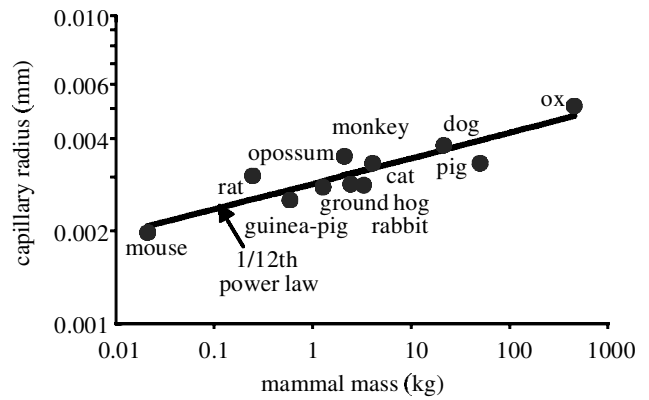


Figure 1. Illustration of variation of capillary radius with mammal mass and comparison with $1/12$ power law. Data are determined from those of Kunkel (1930) by assuming a capillary radius equal to 2% of the diameter of the renal capsule.

unit, the number of units should scale with mammal size exactly as the scaling law of equation (3.4) for the number of capillaries. Detailed measurements of nephra number by Kunkel for mammals ranging in size from mouse to ox were analysed by Adolph (1949) and the number was found to scale with mammal mass to the power 0.62, in excellent agreement with the power $5/8$ (0.625) required by equation (3.4). A reanalysis of the measurements in connection with the present work reveals a power of 0.617 ± 0.021 ($n = 17$, $r^2 = 0.983$), thus confirming the close agreement with the theory.

Also, because of the flexibility of the lengths of the capillaries relative to their diameters, the size (or diameter) of the renal capsules should scale with the radius of the capillaries. Measurements of the diameters of the renal capsules by Kunkel were also analysed by Adolph and found to vary with mammal mass to the power 0.08. This is in excellent agreement with the power $1/12$ (0.083) required by equation (3.4) for the capillary radius. A reanalysis of the data for the present work indicates, in fact, a power of 0.083 ± 0.013 ($n = 15$, $r^2 = 0.752$) consistent with the earlier result of Adolph.

These data have not been discussed previously in this connection, and the implied variation of capillary radius with mammal mass is thus shown explicitly in figure 1. Here, use has been made of Kunkel's measurements, assuming a capillary radius of 2% of the diameter of the renal capsule, consistent with a capillary radius of *ca.* 0.004 mm for the human. Predictions from the $1/12$ power law from equation (3.4), with the proportional coefficient (0.002 86) determined from the data, are also shown. The overall agreement is remarkably good.

Next, consider measurements demonstrating the scaling law for the capillary length L_C . Direct measurements are unavailable. However, indirect measurements of the product $N_C L_C$ are available from data on fluid discharge across capillary walls. In particular, fluid output must, like oxygen transfer discussed in § 3, vary as the product of driving pressure and net capillary length $N_C L_C$, at least for a capillary-wall thickness proportional to radius under scale change. In this case, however, the driving pressure is the difference between the scale-invariant blood pressure and the (assumed) scale-invariant pressure external to

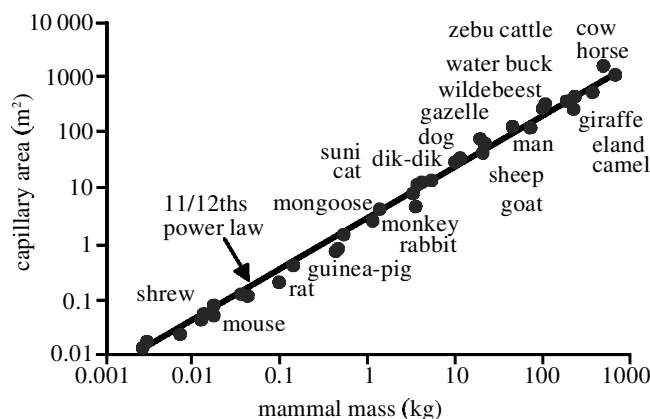


Figure 2. Measurements of Gehr *et al.* (1981) for net surface area of pulmonary capillaries compared with predictions from scaling theory.

the capillary (Pappenheimer *et al.* 1951). Fluid output is therefore expected to scale simply as the product $N_C L_C$, that is, as mammal mass to the power 5/6 (0.83) according to equation (3.4). As noted previously (Dawson 1991), this value is in excellent agreement with classic measurements for the mouse to elephant range, which showed urine output of mammals to vary as mammal mass to the power 0.82 (Adolph 1943, 1949). Reanalysis of the data for the present work provides the power 0.819 ± 0.040 ($n = 12$, $r^2 = 0.977$), thus confirming the excellent agreement indicated.

Experimental support for the scaling relations (equation (3.4)) is now considered for the pulmonary side of the circulation. The basic measurements to be considered are those for the net capillary surface area of mammals. This area should scale as the product $N_C L_C R_C$ scales, that is, as mammal mass to the power 11/12 (0.92) according to equation (3.4). This value is in excellent agreement with extensive measurements reported by Gehr *et al.* (1981). In particular, for a group of African mammals they report a scaling value of 0.92, and for these and more familiar mammals, they report a scaling value of 0.95.

The latter results of Gehr *et al.* (1981) are from the same investigation as the measurements of capillary volume quoted in § 3 in connection with equation (3.2). As in the case of the volume measurements, no significant difference is found between the scalings of the capillary surface area for smaller and larger mammals. Analysis carried out for the present work indicates that for mammals used in the study with a body mass no greater than 10.1 kg, the scaling power is 0.920 ± 0.023 ($n = 22$, $r^2 = 0.988$) and for all mammals considered in the study the power is 0.946 ± 0.013 ($n = 37$, $r^2 = 0.993$). In figure 2, data are compared with predictions from the theory requiring proportional variation with mammal mass raised to the power 11/12. The proportional coefficient (2.98) was determined from the data. The agreement is seen to be remarkably good over the entire range of mammals considered, from the shrew of mass 0.0026 kg to the cow of mass 700 kg.

A major conclusion from the results illustrated in figure 2, and the earlier results noted for capillary volume for the same range of mammals, is that no transitions exist in the power-law representations of capillary dimensions and

Table 2. Comparisons of theory with measurement for scaling powers b in the relation $Y \propto (\text{mammal mass})^b$ for quantity Y .

quantity y	b theory	b measurement ^a
capillary number	0.625	0.62
capillary radius	0.083	0.08
fluid transfer	0.833	0.82
capillary surface	0.917	0.92–0.95
capillary volume	1.000	0.97–1.00
oxygen transfer	0.750	0.74

^a Details and references noted in text.

number. The entire discussion of this section also demonstrates that the theoretical scaling laws of equation (3.4) provide impressive agreement with measurements over a wide range of mammal sizes.

The scaling laws associated with capillary dimensions and number are summarized in table 2, together with predictions and comparisons with the measurements just discussed. Also included are the scaling results for oxygen transfer rate and capillary volume, as referred to in the derivation of equation (3.4).

5. POSSIBLE SOURCE FOR THE TRANSITION IN THE OXYGEN CONSUMPTION RATE LAW

In using the 3/4 power law for oxygen consumption rate \dot{V}_{O_2} of resting mammals in the derivation (see § 3) of the scaling laws for capillary dimensions and operative number, we may, in fact, be considering an average relation for both small and large mammals. In the relation $\dot{V}_{O_2} \propto N_C P_O (1 - P'_O/P_O) L_C$, stated in § 3 in connection with the development of equation (3.3), an average on the left side implies an average on the right side. The successful scaling laws of equation (3.4) were derived by using the 3/4 power law for oxygen consumption rate and an assumed scale invariance for the pressure factor $(1 - P'_O/P_O)$, as associated with the oxygen pressures P_O and P'_O inside and immediately outside a capillary, respectively. The latter may, of course, be interpreted as replacing the oxygen consumption rate and pressure factor in the relation by their average (or smoothed) variations.

Suppose now that the relation is reconsidered using the successful scaling laws for capillary length L_C , number N_C and oxygen pressure P_O , but with the factor $(1 - P'_O/P_O)$ now considered variable and the oxygen consumption rate unspecified. The following relation can be given:

$$\dot{V}_{O_2} \propto N_C P_O (1 - P'_O/P_O) L_C \propto (1 - P'_O/P_O) M^{3/4}. \quad (5.1)$$

It can be seen from this result that the 2/3 power law for smaller mammals, indicated by Dodds *et al.* (2001) in the dataset of Heusner (1991), could simply arise from the factor $(1 - P'_O/P_O)$ having an actual variation with mammal mass to the power -0.08 . By contrast, for large mammals, the variation would need to be different, with mammal mass to the power $+0.13$, in order to provide the 0.88 power law indicated by Dodds *et al.* (2001) for larger mammals in the same dataset.

Insofar as the scaling laws for capillary variation are concerned, the situation may therefore be as follows: the use of the 'average' 3/4 power law for oxygen consumption

rate for a wide range of mammal sizes and the assumption of an average scale-invariant value for the pressure factor $(1 - P'_0/P_0)$ leads to the same correct scaling laws for capillary dimensions and number as would be found from the use of 'actual' laws of oxygen consumption rate for small and large mammals, together with the 'actual' variations in the pressure factor for the small and large mammals.

These observations are speculative, but they indicate how the divided power-law representations described recently by Dodds *et al.* (2001) for oxygen consumption rate could arise from the physiology of the oxygen transfer across the capillaries, without having a corresponding divided representation in the power-law description for the capillary characteristics. The latter is of course consistent with results found here. The entire matter requires further experimental study.

6. CHANGES WITH STRENUOUS EXERCISE

It can be seen from the present work that the scaling laws for capillary dimensions and active number (in the resting state) are based on resting, or near resting, conditions. For a number of years, it was generally thought that scaling relations for mammals were the same for both resting and exercise states. This could be the case if physiological variables such as oxygen consumption rate and heart rate increased by the same factor in all mammals during strenuous exercise. Based on work by Baudinette (1978), Taylor *et al.* (1981), Weibel *et al.* (1991) and Bishop (1997, 1999), among others, this is now known to be untrue.

In particular, the oxygen consumption rate and cardiac output of mammals (bat to steer range) in strenuous exercise have recently been shown by Bishop (1997, 1999) to vary closely with mammal mass raised to the power 0.88, in contrast with the corresponding value of 0.73 for the rest state. In this same work, the heart rate was estimated to vary with mammal mass to the approximate power -0.12 , in contrast with the approximate power of -0.27 for the resting state. These results are in general agreement with the earlier work of Baudinette (1978) and Weibel *et al.* (1991) on scaling of heart rate and oxygen consumption rate during intense exercise.

In respect of the actual conditions existing for mammals in strenuous exercise, the recent work by Darveau *et al.* (2002) and the discussion by Weibel (2002) have emphasized the weighted average involved in the oxygen law from various physiological processes, and have provided insight into the increased scaling exponent that applies for the exercise state. It remains to relate this change under exercise to the broader characteristics of the capillary system, as provided by the general scaling theory. This may, in fact, be done by retaining the scaling laws for capillary radius and length, as determined from the resting state, and adjusting the scaling law for the *number* of capillaries in mammals.

It is, of course, well known from the work of Krogh (1920) that additional capillaries are opened to blood flow during exercise. It is, indeed, this very control mechanism that allows increased blood and oxygen to be delivered to organs in need during exercise. In this regard, therefore, the design of the capillary system is governed by the

intense-exercise conditions, as it is these conditions that determine the number of reserve capillaries required for service during exercise. The matter is in general agreement with the concept of *symmorphosis* (Taylor & Weibel 1981; Weibel *et al.* 1991; Hoppeler & Weibel 1998), that nothing more is provided in the design of mammals than is needed for their purposes.

In order to determine the number of capillaries open and operating during strenuous exercise, we may return to the three broad similarity principles used in establishing equations (3.1) and (3.3) for the resting state. One relation has to be relaxed with the new requirement on capillary number, and this evidently must be that associated with equation (3.2), expressing the scale-invariant fraction of total blood volume in the capillaries. In this relation, the capillary radius and length are fixed by the resting conditions, and hence only the capillary number can be varied. When it is varied, as in the present case, the only alternative is to relax the condition.

Disregarding equation (3.2), it is still possible to examine the remaining two similarity conditions. The first, on which equation (3.1) is based, is the requirement that the blood pressure needed to push blood through the entire capillary network must be independent of mammal size. As noted in § 3, this is a critical condition regarding stress and failure of capillary walls and is likely to be maintained during strenuous exercise. The earlier general relation expressing this condition, namely $L_C Q_B / N_C R_C^4 \propto M^0$, now takes the form

$$M^{5/24} Q_B(\max) \propto N'_C M^{4/12}, \quad (6.1)$$

where N'_C denotes the modified capillary number for strenuous exercise, and where the relations in equation (3.4) for the resting state have been used for capillary radius R_C and length L_C . From earlier remarks, the cardiac output $Q_B(\max)$ is known to vary with mammal mass to the power 0.88 (Bishop 1997, 1999). Equation (6.1) accordingly requires that the capillary number N'_C for the exercise state vary with mammal mass to the power 0.75, that is that $N'_C \propto M^{3/4}$.

The relation for the net oxygen transfer rate, as used in § 3 in rest conditions, is now expressible as

$$\dot{V}_{O_2}(\max) \propto P_0 N'_C L_C, \quad (6.2)$$

and this provides the relation $\dot{V}_{O_2}(\max) \propto M^{0.88}$, in agreement with measurements for the exercise state. Here, oxygen partial pressure P_0 is required to vary with mammal mass to the power $-1/12$, as in the rest case, and capillary length L_C is required to vary according to the second relation in equation (3.4), also based on rest conditions.

The remaining similarity condition on which equation (3.3) is based, namely, the condition that the oxygen consumption, or uptake, per unit of body mass during a heart cycle is independent of mammal size, is satisfied by this last result and the previously noted variation of maximum heart rate with mammal mass to the power -0.12 , that is, $\dot{V}_{O_2}(\max)/M\omega(\max) \propto M^0$.

Thus, the two fundamental similarity relations, on which equations (3.1) and (3.3) are based, remain valid during intense exercise. The basic similarity equation (3.2) ceases, of course, to apply under exercise conditions; that is, the fraction of blood in the capillaries is no longer invariant during strenuous exercise, but rather increases

with increasing mammal size. The increase, moreover, is proportional to the ratio of revised to original capillary number N'_C/N_C , which varies as mammal mass to the power 0.13.

7. CONSIDERATION OF CAPILLARY DENSITY

In addition to the above considerations for capillary number, it is interesting to consider capillary density, which typically involves the number of capillaries per unit of area in muscle tissue. The subject was originally studied by Krogh (1919) who demonstrated, using measurements from muscles of the horse, dog and guinea-pig, that capillary density increases with decreasing mammal size. More recently, Schmidt-Nielsen & Pennycuik (1961) and Hoppeler *et al.* (1981) have performed further detailed measurements for a wider range of mammals and have reached the same general result, although with some qualifications.

Some idealized observations may be made with respect to the present theory. Assuming the mass of any particular muscle varies directly with mammal mass M , its sectional area will vary as $M^{2/3}$ for a similar shape. The total number of capillaries in the section will then be expressible in proportional terms as the product of the capillary density, say γ , and this variation, that is, as $\gamma M^{2/3}$. In addition, the length of the muscle will vary as $M^{1/3}$, and the number of independent sections in the muscle will be proportional to the ratio of this length to the capillary length L_C , that is $M^{1/3}/M^{5/24}$, where the scaling law for capillary length is that given by the second relation in equation (3.4). Using these results, the total number of capillaries in the muscle, say N , is expressible as $\gamma M^{2/3} M^{1/3}/M^{5/24}$, that is, as

$$N \propto \gamma M^{9/24}. \quad (7.1)$$

From equation (7.1) the expected capillary density for the resting number of total capillaries in the muscle can be considered. Thus, setting $N \propto N_C \propto M^{5/8}$ from equation (3.4) gives $\gamma \propto M^{-1/6}$. This is an interesting result and is equivalent to requiring that capillary spacing in the muscle be proportional to capillary radius R_C . The latter was assumed independently of equation (7.1) in the author's earlier work (Dawson 1991) and shown to apply to measurements of capillary density of the masseter muscle reported by Schmidt-Nielsen & Pennycuik (1961). The conclusion, as evident from the extended work here, is that these measurements were probably mainly concerned with the capillaries that are open and active in the resting state.

In addition to measurements of the masseter muscle, Schmidt-Nielsen & Pennycuik (1961) reported capillary density values for the gastrocnemius muscle. The measurements were divided into those for red and white muscle fibres, with the idea that these fibres represented different muscle characteristics. Fortunately, enough data were provided to allow consolidation of the two for present purposes. This has been carried out and the results are plotted in figure 3, together with the above theoretical $-1/6$ scaling law with the proportional coefficient (725) determined from the data. The agreement is generally good, considering the nature of the measurements. Detailed regression analysis of the data indicates, in fact, an exponent of -0.155 ± 0.044 ($n = 10$, $r^2 =$

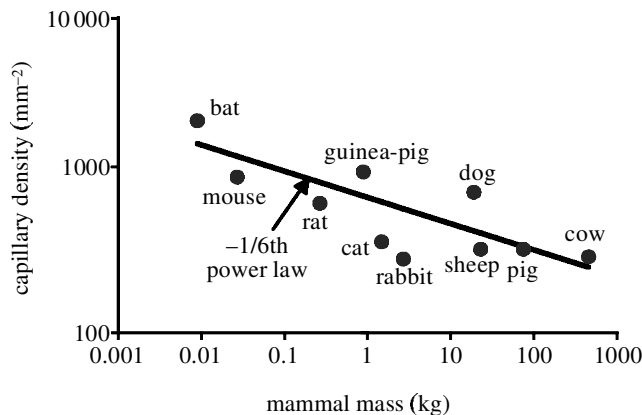


Figure 3. Capillary density (number mm^{-2}) variation with mammal size as measured by Schmidt-Nielsen & Pennycuik (1961) for the gastrocnemius (leg) muscle.

0.609), which is in surprisingly good agreement with the theoretical value of $-1/6$ (-0.167) required by equation (7.1) and the present theory. As in the case of the measurements for the masseter muscle, it is therefore probable that these measurements mainly involved those capillaries open and active in the resting state.

The measurements of Schmidt-Nielsen & Pennycuik (1961) were made using light microscopy, and, in view of the experimental difficulties noted by Krogh (1920) in detecting inactive capillaries in the resting state, it is not surprising that they were probably missed in the investigation.

The more recent measurements of capillary density in muscle tissue by Hoppeler *et al.* (1981) employed electron microscopy and provided a better opportunity to detect inactive (reserve) capillaries in tissue. When such capillaries are included in the determination of capillary density, we can no longer expect the $-1/6$ scaling law (based on resting conditions) to apply. Neither can we expect the capillary density to follow the scaling relation from equation (7.1) when the capillary-number variation ($3/4$ power law) for strenuous exercise is used on the left side of this relation. This variation represents a net variation for the entire body, some parts having no reserve capillaries and some with both active and reserve capillaries. We can, however, use equation (7.1) to determine the number of active and reserve capillaries in a muscle when the capillary density in that muscle has been measured.

Using the measurements of Hoppeler *et al.* (1981) for the four muscles of the body studied (semitendinosus, longissimus, vastus medialis and diaphragm), the capillary density is found to vary with mammal mass to the average power -0.073 . Equation (7.1) demonstrates that the average number of capillaries in these muscles varies with mammal mass to the power 0.72. This is greater than the resting case (0.63), but not perhaps as large as might be expected. The case of the diaphragm by itself is noteworthy in that its capillary density was found to vary with mammal mass to the power $+0.045$. Equation (7.1) then requires the total number of capillaries in the diaphragm to vary with mammal mass to the power 0.84, which is appreciably larger than for the average and the resting cases. The matter requires more experimental investigation, but the indications are favourable and provide sup-

port for the theoretical results of the present work regarding scaling of capillary number for strenuous exercise.

8. DISCUSSION AND CONCLUSIONS

In summary, the present work has demonstrated that there can be little doubt that the minute capillary vessels of mammals vary in size and number with mammal body mass. There can also be little doubt about the general validity of the scaling laws developed here for describing these variations. The basic similarity assumptions from which they were derived, while idealized in table 1, rest on a firm experimental foundation. The additional measurements used in this work to confirm the scaling laws combine to provide strong independent evidence for their general validity as derived here, and as presented earlier by the author (Dawson 1991, 2001) on different grounds.

With regard to the latter, it may be worthwhile to observe that the basic data of Gehr *et al.* (1981) for capillary volume V_C and surface area S_C can also be used to estimate the scaling laws for capillary radius R_C and net capillary length $N_C L_C$ directly from the geometric conditions $R_C \propto V_C/S_C$ and $N_C L_C \propto S_C^2/V_C$. It has been shown, by analysis of the data, that V_C and S_C vary with mammal mass to the powers 1.015 ± 0.014 and 0.946 ± 0.013 , respectively. The capillary radius and net capillary length are accordingly indicated by these results to vary with mammal mass to the powers 0.069 ± 0.027 , and 0.877 ± 0.040 , respectively. These results are likewise in good agreement with the scaling laws of equation (3.4), which provide predictions of 0.083 and 0.833, respectively, based on the idealized representations of related physiological variables in table 1. The following conclusions can therefore be reached.

Capillary radius and length in mammals vary in an idealized sense with mammal mass to the powers 1/12 and 5/24, respectively. Measurements provide general agreement.

The entire number of capillaries in the body that are open and active in the resting state varies, in an idealized sense, as mammal mass to the power 5/8. Moreover, for organs whose entire capillary networks are open and active in the resting state, the latter scaling law applies also to the total number of capillaries in these individual organs. Measurements support the prediction.

Recent work (Dodds *et al.* 2001) has identified a transition in the power-law (scaling) representation of oxygen consumption rate between small and large mammals. However, no such difference has been found in the present work for power-law representations of measurements (Gehr *et al.* 1981) of capillary volume and surface area. This matter has been addressed here in terms of the basic process of oxygen transfer across capillaries. A plausible explanation is offered that attributes the different representations for the oxygen consumption rate to actual differences in the oxygen transfer process for small and large mammals, thus leaving the capillary representations unaffected.

By considering an average power-law representation (traditional 3/4 power law) for oxygen consumption rate for all mammal sizes, and an average of the oxygen-

transfer process across capillaries, reasonably accurate scaling laws for capillary size and resting number are obtained, even though differences presumably exist between small and large mammals regarding both the oxygen-consumption-rate law and the oxygen process.

The scaling theory for the capillary system of mammals at rest has been extended to include the intense-exercise state. The capillary system for this state involves an increased number of operative capillaries in muscle tissue. The measured scaling laws for oxygen consumption rate and heart rate are accounted for by this shift, but similarity of the system that exists in the resting state is lost. Larger mammals have greater increases in capillary number during exercise than do smaller ones. The fraction of blood in the total number of capillaries in the body is accordingly no longer size invariant, but rather increases with increasing mammal size, in proportion to the ratio of the total number of capillaries in exercise to the total number at rest.

During strenuous exercise, the scaling laws for capillary radius and length remain the same as for the resting state, but the scaling law for the *total* number of capillaries in the body is changed from the theoretical 5/8 power law for resting to a 3/4 power law. For individual organs where all capillaries are active in the resting state, the 5/8 power law continues to apply, but for muscles and other organs where an increased number of capillaries are active in exercise, neither the 5/8 nor the 3/4 law is applicable.

Theory indicates that, with respect to actual capillary count in the cross-section of muscles, the density of operative capillaries in the resting state should vary with mammal mass to the power $-1/6$. Measurements confirm this general relation for (presumably) open and active capillaries of the resting state. Theory and measurements also indicate decreased scale variation for capillary density when both active and reserve capillaries are included in the counting.

Capillary density in muscle and other tissue varies in an idealized sense with mammal mass to the power $-1/6$ when only capillaries that are active in the resting state are considered. For muscles where both active and reserve capillaries are considered, the scaling exponent can be expected to be nearer to zero, or even positive.

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