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SCALING MITOCHONDRIAL VOLUME IN HEART TO BODY MASS

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Abstract. The heart mass was measured and the volume density of mitochondria, V_V(mt,f), morphometrically estimated in 11 mammalian species ranging from shrew (3 g) to cattle (920 kg). The mass or the volume of the heart muscle (Vh) was found to scale as $Mb^{0.970}$ whereas V_V(mt,f) scaled as $Mb^{-0.044}$. Hence, the total volume of mitochondria in heart, V(mt), scaled as $Mb^{0.927}$ ($V(mt) = V_V(mt,f) \times Vh$). The volume of heart mitochondria was found to scale disproportionately to $\dot{V}_{O_2}max$ ($Mb^{0.75}$) but in proportion to resting cardiac work rate ($Mb^{0.9}$).

Allometric relation	Fox	Myocardium
Cardiac muscle	Heart mass	Rat
Cat	Heart size	Shrew
Cattle	Horse	Skeletal muscle
Coyote	Maximal oxygen consumption	Wolf
Dog	Mitochondrion	Woodmouse

Maximal (and resting) metabolic rate increases with the 3/4 power of body mass (Taylor *et al.*, 1981; Kleiber, 1932), whereas the volume of many organs, including the heart, changes in linear proportion to body mass (Stahl, 1950). This scaling of metabolic rate results in an O_2 consumption per unit body mass that is 20 times larger in an Etruscan shrew weighing 2 g than in a 900 kg cow. As the heart generates the force to transport O_2 convectively through the blood, and as the O_2 capacity of the blood varies in a narrow range, it follows that the heart must perform considerably more work per unit time and body mass in a small than in a large animal.

In a previous allometric study we found the scaling of the total volume of mitochondria in three skeletal muscles to be nearly identical to the scaling of $\dot{V}_{O_2}max$

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measured on the same animals (Mathieu *et al.*, 1981). This finding suggested a constant (body mass independent) relationship between the total volume of mitochondria and $\dot{V}_{O_2}$max. In this earlier study no morphometric information on heart was obtained. For this study, we hypothesized that, everything else being equal, the total volume of mitochondria in heart would also scale close to $\dot{V}_{O_2}$max. To test this hypothesis we estimated the mitochondrial content in hearts of 11 animal species by stereological methods.

Materials and methods

Hearts were obtained from 11 mammalian species (n = 1) used in various experimental procedures not related to this investigation. They were removed within minutes after the death of the animals, cleaned and weighed; heart mass included ventricles and atria. Transmural muscle samples were taken from the tip of the left ventricle and processed for electron microscopy as previously described (fig. 1; Hoppeler *et al.*, 1981).

For the stereological analysis we used four independent randomly chosen tissue sections from each animal. Each section was subsampled by taking 10 micrographs in consecutive frames of 200-square mesh grids, hence, 40 micrographs at a final magnification of × 24000 were analysed in each animal to estimate the volume density of mitochondria, V_V(mt,f). The surface of inner mitochondrial membranes per unit volume of mitochondrion, S_V(im,mt), was estimated in the hearts of the woodmouse, cat and cow only. In each animal 20 micrographs of randomly chosen mitochondria were analysed at a final magnification of × 120000. The stereological variables were obtained by applying standard stereological procedures (Weibel, 1979). The inner mitochondrial membranes were assumed to be randomly oriented with regard to the muscle fiber axis. No corrections were made for effects of section thickness or compression.

Results and Discussion

Table 1 reports species data of the physical and morphological variables used to calculate the allometric regressions. We found a scaling factor of 0.97 for the relationship of the heart mass to body mass (fig. 2). This is very close to the scaling factor of 0.98 reported for this variable by Stahl (1950) for a much larger animal population (n > 100).

The volume density of mitochondria was found to scale to the body mass to the power −0.044 (fig. 2). The 95% confidence interval for this scaling factor does not include zero which means that small animals do have higher mitochondrial densities in their hearts. Mitochondrial densities seem not to vary much from one location in the heart to another (Anversa *et al.*, 1978; Olivetti *et al.*, 1980) and

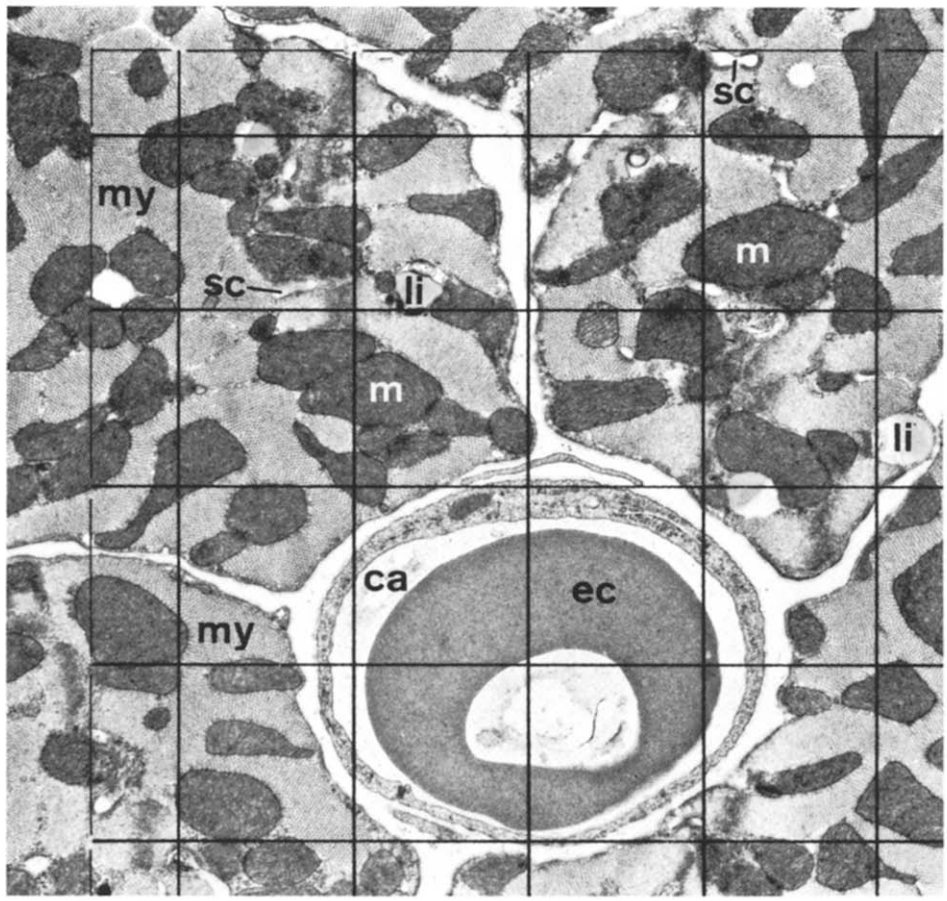

Fig. 1. Cross-sections of portions of adjacent muscle fibers of the heart of European woodmouse *(Apodemus sylvaticus)*. Within the muscle cells numerous mitochondria (m) lay between the myofibrils (my). Further noticeable components of the heart cells are the sarcoplasmic reticulum (sc) and intracellular lipid deposits (li). The electron micrograph also shows the profile of a capillary (ca) containing an erythrocyte (ec). Part of a morphometric test grid is superimposed.

the interindividual error variance for this variable is reportedly very low (SE typically $< 5\%$ of the estimate of the mean) for any group of control or experimental animals (Anversa *et al.*, 1978; Olivetti *et al.*, 1980; Page and McCallister, 1973; Smith and Page, 1976).

The volume of mitochondria in three skeletal muscles in a series of African mammals was shown to be an adequate measure of their potential for oxidative metabolism as the surface of inner mitochondrial membranes per unit of mitochondrial volume, $S_V(im,mt)$, was not found to systematically change with body size (Mathieu *et al.*, 1981; Hoppeler *et al.*, 1981). Likewise no systematic size dependent difference for $S_V(im,mt)$ was found in hearts of woodmouse, cat and cattle (41.4, 30.9 and 45.5 $m^2 \cdot cm^{-3}$, respectively).

TABLE 1

Individual data for body mass (Mb), heart mass (Mh), volume density of heart mitochondria, V_V(mt,f) and absolute volume of heart mitochondria, V(mt), in 11 species of mammals. For V_V(mt,f) the standard error was typically less than 5% of the estimated mean

		Mb (kg)	Mh (g)	V_V(mt,f) ($cm^3 \cdot cm^{-3}$)	V(mt) (cm^3)
Shrew	*(Suncus etruscus)*	0.0024	0.0307	0.361	0.0104
Woodmouse	*(Apodemus sylvaticus)*	0.0207	0.135	0.364	0.0463
Rat	*(Rattus rattus)*	0.245	0.978	0.335	0.291
Cat	*(Felis catus)*	2.2	8.10	0.245	1.87
Fox	*(Vulpes vulpes)*	4.16	23.0	0.252	5.46
Coyote	*(Canis latrans)*	12.6	114	0.254	27.4
Wolf	*(Canis lupus)*	20.7	173	0.239	39.0
Dog	*(Canis familiaris)*	31.8	263	0.222	55.0
Goat	*(Capra hircus)*	32.2	181	0.219	37.4
Horse	*(Equus caballus)*	520	3750	0.259	917
Cattle	*(Bos taurus)*	920	3560	0.211	707

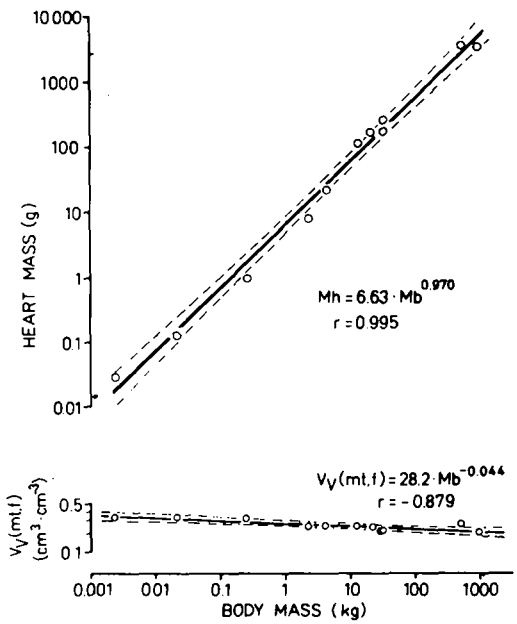

Fig. 2. Allometric plots of heart mass (Mh) and volume density of mitochondria, V_V(mt,f), against body mass (Mb) for 11 animal species. The dashed lines in the figure enclose the 95% confidence band for each line. The 95% confidence intervals for the scaling factors are 0.898, 1.04 and −0.062, −0.026 for Mh and V_V(mt,f), respectively.

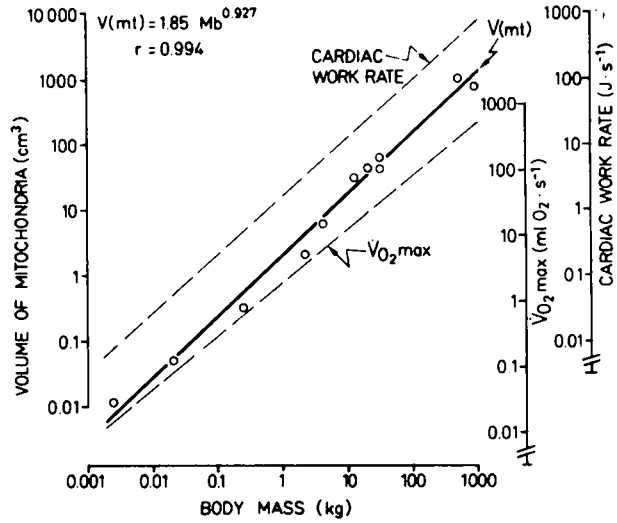

Fig. 3. Regression line of logV(mt) (total volume of heart mitochondria) *vs* logMb for the 11 species analysed. The regression lines of log$\dot{V}_{O_2}$max (Taylor *et al.*, 1981) and log(resting cardiac work rate) (Calder, 1981) *vs* logMb are added for comparison (dashed lines). The 95% confidence interval for the scaling factor of V(mt) is 0.852, 1.00; for $\dot{V}_{O_2}$max it is 0.747, 0.870 (Taylor *et al.*, 1981).

The absolute volume of heart mitochondria, V(mt), for any one species was obtained by multiplying the volume density of mitochondria with the heart mass and dividing it by the density of muscle tissue (1.06 $g \cdot cm^{-3}$; Méndez and Keys, 1960). V(mt) was found to scale to the body mass to the power 0.927 (fig. 3).

We initiated this study in the belief that the absolute volume of heart mitochondria would be adjusted to the rate of energy expenditure of the heart needed to move the blood and consequently to move oxygen under conditions of $\dot{V}_{O_2}$max, and that V(mt), therefore, should scale as $\dot{V}_{O_2}$max. Figure 3 shows that this is not the case. The slope for the allometric regression for V(mt) is significantly steeper than the regression for $\dot{V}_{O_2}$max (Taylor *et al.*, 1981). To account for the apparent difference between the scaling of V(mt) and $\dot{V}_{O_2}$max we had to identify a size-dependent factor which would explain why shrew hearts only need some 10 × rather than 20 × more mitochondria per unit body mass than cattle hearts to cover their weight specific energy requirements. A possible answer can be found by looking at the scaling of circulatory variables (Calder, 1981). Under resting conditions work per stroke was found to scale as $Mb^{1.15}$ and heart frequency as $Mb^{-0.25}$ (Holt *et al.*, 1968). Work per stroke times heart frequency gives cardiac work rate (power):

$$Mb^{1.15} \times Mb^{-0.25} = Mb^{0.90}$$

which increases disproportionately to metabolic power and scales similarly to the total volume of mitochondria in heart. Under conditions of $\dot{V}_{O_2}$max, however, allometric data seems to be available for the maximal heart rate only, which is reported to scale as $Mb^{-0.19}$ (Baudinette, 1978).

By determining the scaling of work per stroke under conditions of $\dot{V}_{O_2}$max it will be possible to see whether, in proportion to $\dot{V}_{O_2}$max, big animals have a larger mitochondrial compartment in their hearts in order to provide the additional power required to produce an identical blood pressure as in small animals under the unfavorable condition of a larger ventricle. By Laplace's law larger hearts would have to maintain a higher tension in the muscle to produce the same systolic pressure resulting in their relatively larger energy requirements (Burton, 1957).

The validity of the statistical derivation of Kleiber's 3/4 inter-specific mass exponent for basic metabolism has recently been challenged by Heusner (1982). It has subsequently been shown by Feldman and McMahon (1983) using the same data but a different statistical analysis that the 3/4 mass exponent still appears as a valid numerical estimator for inter-specific variation. Until the current debate on the statistical correctness and on the physiological meaning of allometric descriptors is settled we feel legitimate to continue to use generally accepted allometric procedures (Yates, 1983; Calder and Braun, 1983).

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