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Symmorphosis and optimization of biological design: introduction and questions

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Are animals built economically? This seemingly simple question led to the discussions summarized in this volume. Phrased differently it asks whether structures are used sparingly to match functional demand with the result that the *design* of biological organisms would tend to be *optimized* for the functions performed. As reasonable as it seems, the contention that animals should be designed according to strict bioengineering principles raises considerable criticism.

However, there is much evidence that the diversity of species, as it has resulted from evolution by natural selection, represents variations in design suggestive of adaptation to specific tasks, and also of an economic use of resources. Even at the basic level of biological organization, in the cell, economy appears to prevail: although all cells contain the entire genome in their nucleus, only the very small part relevant for the cell's specific functions is expressed. It appears to be a fundamental principle not to load cells with baggage they do not need. But we will have to ask whether the enzyme systems that a particular cell expresses are also *quantitatively* adjusted to the cell's functional needs or whether many of them occur in vast excess.

At the higher levels of biological organization a well-known example of economic design is bone tissue whose fine structure is quantitatively adjusted to the mechanical stresses imposed. This translates into the arrangement of bone trabeculae according to stress lines and into quantitative aspects of the macroscopic design of whole bones such that, for example, the bones of the serving arm of a tennis player are thicker than those of the other arm. Similar effects are known for the quantitative design of musculature where exercise training causes the active muscles to become larger and stronger. Similar differences are found in nature when comparing species that specialize for certain locomotor tasks. Although

the muscle mass of mammals is designed on a basic master plan it shows quantitative differences according to need, as shown by the two cases illustrated in Figure 1.1: the Pronghorn antelope of the Rocky Mountains, a champion high-speed endurance runner, increases the muscle mass at the proximal hind limb with which it achieves the main forward thrust; in contrast, the fossorial mole rat reinforces the muscles of the front limb and neck with which it digs its burrows, and it reduces hind limb musculature which it uses only for balance.

A further well worked-out case is the design of blood vessels where the progression of branch diameters along the vascular trees is such as to minimize both the mass of blood needed to fill the vessels and the energy required to transport blood to the targets against flow resistance. The vasculature also has to ensure that all points in the body are evenly served, a problem that becomes particularly evident in the lung where blood flow must be evenly distributed over a gas exchange area of the size of a tennis court. The solution found by nature is to design the vasculature as fractal trees and adjusting the proportionality factor from one branch generation to the next so as to minimize the cost of transport.

Such case studies suggest that the design of cells, of tissues and of organs is adjusted to functional needs, and that the body uses the materials and the space it has available sparingly. Conversely, if the matching of

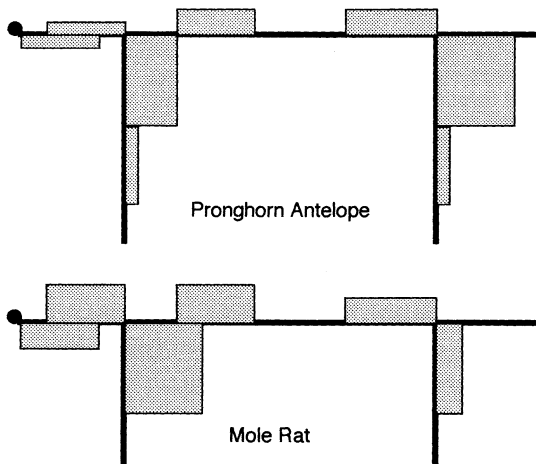


Figure 1.1. Scale models showing the distribution of muscle mass in the Pronghorn antelope of the Rocky Mountains and of the mole rat from Israel (see Chapter 10.4) in accordance with different requirements of locomotion.

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structures to functional needs is combined with strict economy then this implies that the design of biological structures must tend to be optimized for the specific function they serve – a strong statement that must trigger fundamental skepticism.

Optimal design implies perfect matching of structure to functional need, both qualitatively and quantitatively. If design is optimal in the sense that there is no more structure than is needed to fulfill the function, then the structural feature becomes the key factor that sets the limit of functional performance, the functional capacity. The degree of optimality in design can then be tested by estimating how the functional capacity is varied with variations of functional demand.

On the other hand, engineers build their systems with some safety factors that make sure that the system does not “break” when the presumed maximal performance is reached. From an engineering point of view this is “good design” as it considers not only the precise function to be performed but also the risks – to the organism – of exploiting the capacity to the limit. This may, however, be a serious impediment to testing whether optimized design prevails because “safety factors” must appear as excess capacity of which it is hard to say whether it is not simply a wasteful use of resources – unless one can define the potential excess load that must be absorbed by the excess capacity.

Symmorphosis as a hypothesis of optimized integral design

The problems we met in the foregoing discussion resulted largely from focusing on engineering aspects of the design of particular structures. It may, however, be more useful to consider the design of cells and organs in the perspective of the functional systems they serve, rather than as “stand-alone” features. The question then is whether the design of the parts is – quantitatively – adjusted to the overall functional task; in other words, whether the parts are all coadjusted to their common role. It is in view of such questions that we have proposed the hypothesis of *symmorphosis*, which we defined as the “state of structural design commensurate to functional needs resulting from regulated morphogenesis, whereby the formation of structural elements is regulated to satisfy but not exceed the requirements of the functional system” (Taylor and Weibel 1981). This hypothesis has stirred considerable criticism.

Symmorphosis combines three elements: functional performance, functional capacity, and economy of structural design. The hypothesis postulates that capacity is adjusted by design to the (expected) loads on the

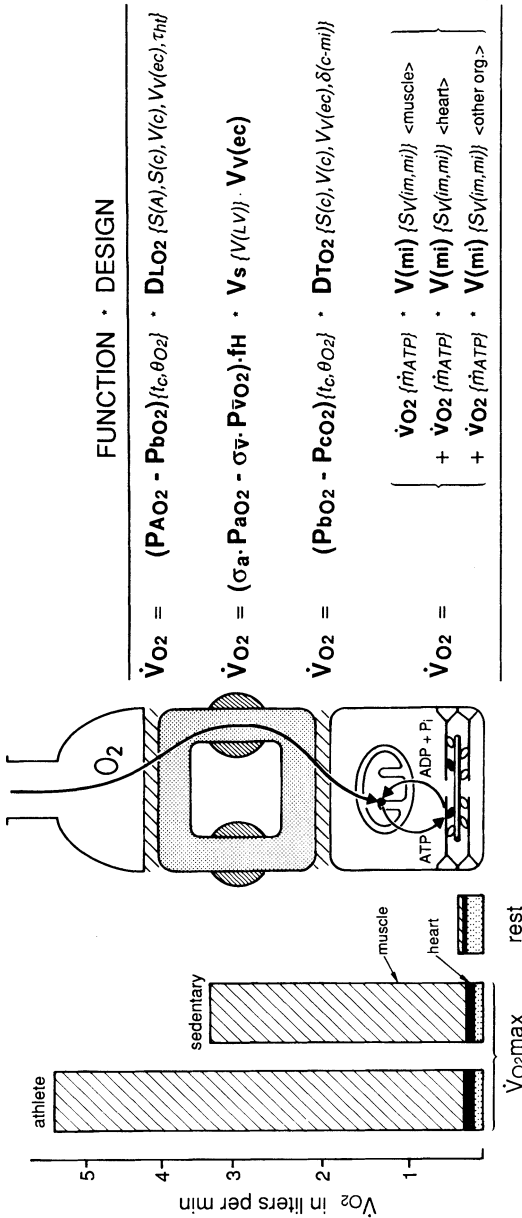


Figure 1.2. Model of the respiratory system. The flow rate \dot{V}_{O_2} is expressed as the product of functional and design parameters shown in bold face; parameters that affect the factors are shown in italics and placed in braces { }. The functional parameters include O_2 partial pressures (P_{O_2}), coefficients of “hematocrit-specific” O_2 capacitance (σ) which depend on O_2 -hemoglobin dissociation, O_2 binding rate (θ), heart frequency (f_H), capillary transit time (t_c), and mitochondrial O_2 consumption rate as function of ATP flux $\dot{v}_{O_2} \{m_{ATP}\}$. Design parameters include diffusion conductances (D) of lung and tissue gas exchangers which depend on alveolar and capillary exchange surface areas ($S(A)$, $S(c)$), capillary volumes ($V(c)$), hematocrit ($V_V(ec)$), harmonic mean barrier thickness (τ_{Ht}), capillary-mitochondrial diffusion distance ($\delta(c-m)$), and mitochondrial volume ($V(mt)$) with inner membrane surface density ($S_V(im, m)$). The histogram to the left shows the distribution of \dot{V}_{O_2} to locomotor muscle, heart and other tissues under resting conditions and at $\dot{V}_{O_{2,max}}$ in sedentary and athletic humans. (Reprinted from *Respiration Physiology*, **87**, E. R. Weibel, C. R. Taylor and H. Hoppeler. Variations in function and design: testing symmorphosis in the respiratory system, 325–48 (1992) with kind permission of Elsevier Science BV, Amsterdam.)

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functional system, and therefore addresses an important question of integrative biology.

Functional processes, such as the supply of oxygen and substrates to cells, are regulated to meet the actual demands of the cells primarily by varying the rates at which enzymes or organs, such as the heart, operate. But these rates very often reach an upper limit: V_{\max} for enzymes, and maximal heart frequency are two examples. These maximal rates determine the *functional capacity*, together with the total quantity of functional units that operate the system: the number of enzyme units or the volume of the heart chambers, to remain with the two examples. If maximal rates are “fixed,” this implies that the overall capacity is, to an important extent, determined by *structural design* properties, and this then means that an adjustment of the functional capacity to altered needs requires morphogenetic processes.

It is now important to note that functional and structural regulation operate with very different time constants. Functional processes are regulated to acute changes in needs in time frames of milliseconds to minutes; structural adaptations to chronic changes in needs typically take at least days to months to be achieved. They also entail different costs: the cost of functional regulation is essentially limited to the incremental energy required to operate the system at higher levels; to make more structure requires not only energy to fuel the morphogenetic processes but also building materials, and space.

The most productive application of the hypothesis of symmorphosis is in the study of integrated functional systems where several organs are joined to serve one specific function. This can be a linear sequence, such as in the supply of oxygen from the lung to the mitochondria of muscle cells; or it can take the form of a branched network, as in the system for substrate supply for oxidative metabolism.

Symmorphosis in the pathway for oxygen

The first case where we tested the hypothesis was the pathway for oxygen, which we considered a good test case for symmorphosis for three main reasons: (1) it serves one dominant vital function; (2) it involves a sequence of linked structures and the effect of design parameters on functional capacity can be defined (Figure 1.2); (3) the overall function has a measurable upper limit, $\dot{V}_{O_2 \max}$, which varies between individuals and species so that the hypothesis can be tested by a comparative approach. This is further aided by the fact that variations in $\dot{V}_{O_2 \max}$

result from three different effects or historical constraints: variations in body size cause body mass specific $\dot{V}_{O_2 \max}$ to increase by sixfold from cows to mice (allometric variation), whereas adaptation to different life styles result in 2.5-fold differences between horses and cows or dogs and goats (adaptive variation); finally, exercise training can increase $\dot{V}_{O_2 \max}$ by about 1.5-fold (induced variation).

These studies attempted to assess the quantitative relations between all parameters listed in Figure 1.2 by studying animals of varying body size and athletic versus sedentary species. The most interesting general result was that the structural parameters were rather precisely adjusted to overall functional capacity at all levels of the system, except for the lung (Figure 1.3), but that this was not achieved in a simple manner (Weibel, Taylor and Hoppeler 1991, 1992). In a broad comparative study from shrews to cows, we found that the volume of mitochondria increased with the same allometric slope as $\dot{V}_{O_2 \max}$, and in comparing athletic with sedentary species the mitochondrial volume was found to be proportional to the differences in $\dot{V}_{O_2 \max}$ (Figure 1.3a). As a result, it was concluded that mitochondria achieve the same rate of oxidative phosphorylation in all mammals, from shrews and mice to cows and horses. This was a simple case: at most levels above the mitochondria (Figure 1.2) we found that several parameters were adjusted part of the way. One example is the design of the muscle capillaries whose volume is adjusted to the muscle cells' need for oxygen only if the variability of the hematocrit, the O_2 carrying capacity of the blood, is taken into account. What is adjusted to the O_2 needs is the volume of capillary erythrocytes; this is achieved by increasing the concentration of erythrocytes *and* by making more capillaries. It appears indeed as eminently economic to split the effort of adaptation to higher needs between the two structures participating in this functional step: blood and vessels. Note, however, that had we looked only at single variables the full adjustment of design to functional demand would not have become apparent. There was one exception to this: the diffusing capacity of the lung was only partly adjusted to $\dot{V}_{O_2 \max}$ both in allometric and adaptive variation (Figure 1.3d) so that some of the species had some excess diffusing capacity, whereas others, mainly athletic and very small species, did not. The general conclusion was that the predictions of symmorphosis were supported for the internal compartments of the body whereas in the lung, the organ of interface to the environment, the hypothesis was not supported unconditionally.

Symmorphosis in complex pathways

The case of the pathway for oxygen is comparatively simple: it constitutes a linear chain of structures connecting the source of O₂ with its target. The situation becomes more difficult when the hypothesis of symmorphosis is used to understand the design principles that govern the performance of complex pathways that have the basic structure of networks rather than a chain. One such example is the system for the supply of fuels for oxidative phosphorylation in muscle cells, which can take different paths by using different substrates from different sources and where some design components, such as the circulation of blood, serve several functions in parallel, one of them being the supply of O₂ for the combustion of these fuels. But, even in this instance, to structure the investigation into the effect of design on functional performance by submitting the hypothesis of symmorphosis turned out to be very productive as it allowed an assessment of the role of specific design properties in the overall perspective of systemic function (Taylor *et al.* 1996). The general conclusion reached was that the pathways for O₂ and fuels were designed to comply to different constraints and that this was compatible with the hypothesis of symmorphosis applied to network structures. Some of this will be discussed in Chapters 9.3 and 9.4 of this volume.

Preparing for the debate

As rational as they seem, the theories of optimal design, and of symmorphosis in particular, have raised much criticism, mainly on the part of evolutionary biologists. It is contested, for example, whether evolution by natural selection can lead to optimal, rather than merely adequate, design. This controversy may be the result of different philosophies prevailing in evolutionary biology and in physiology – perhaps the different interests and the different emphasis in what are called ultimate and proximate causations of design. Can or should one of these be pursued at the exclusion of the other, or are they rather complementary views of nature? These are the fundamental questions we “ultimately” wished to address in order to clarify some of the controversial issues about optimization theory and its validity or heuristic usefulness, bearing in mind the fact that it holds in some instances but breaks down in others.

For this purpose we will first consider the criteria of optimal design under different points of view, and then discuss the processes and conditions of the evolution of species and how these affect the design of

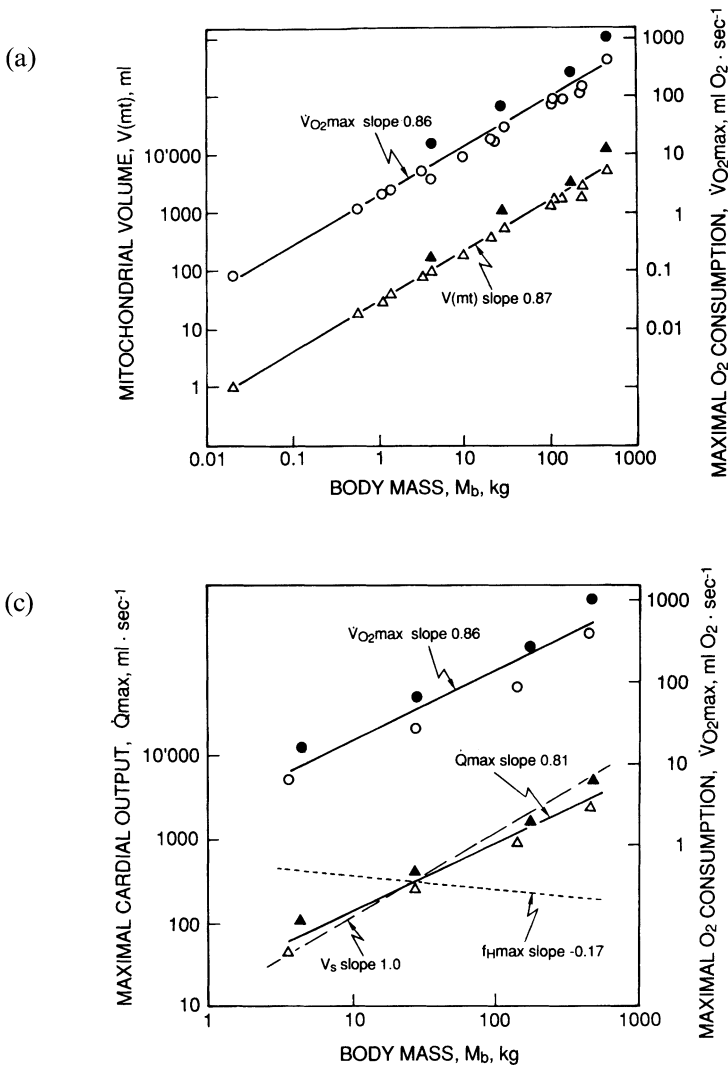


Figure 1.3. Four allometric plots showing the relation to $\dot{V}O_{2max}$ of (a) total mitochondrial volume, (b) capillary volume, (c) cardiac output, and (d) pulmonary diffusing capacity. The open symbols represent sedentary species, and the solid symbols represent athletic species.

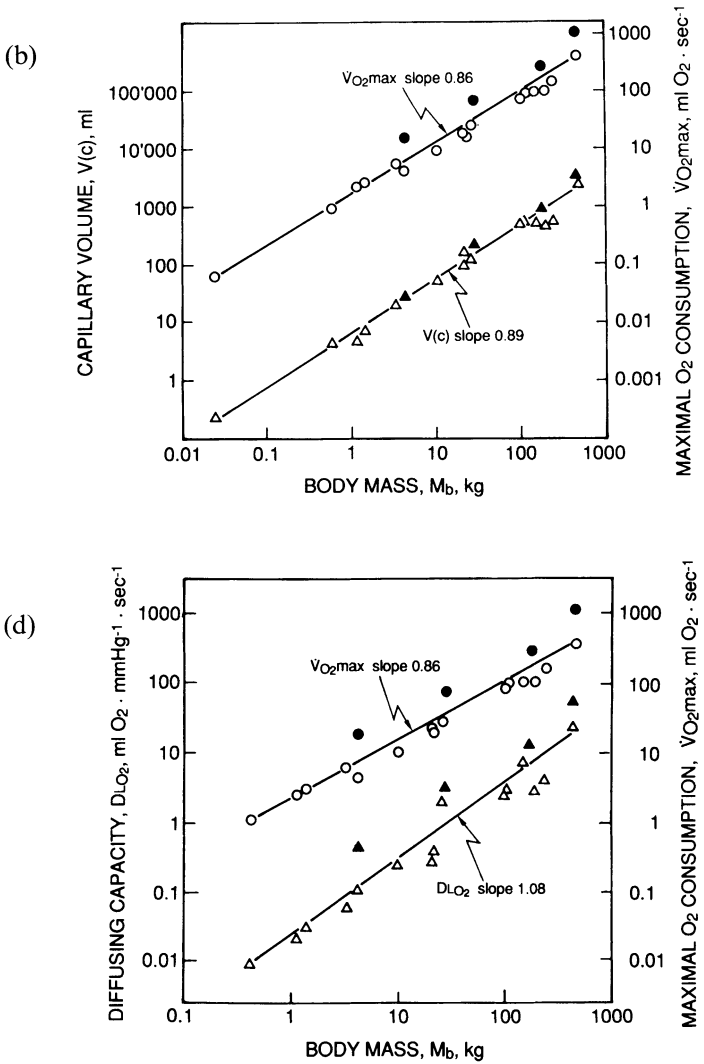


Figure 1.3. (continued)

organisms. This will be followed by a number of case studies at the levels of cells, tissues, and organs, to find instances where optimization of design appears to prevail and where not. A particularly important part will be the discussion of design in complex functional systems for which the hypothesis of symmorphosis has been conceived. The examples used in this discussion range from enzyme systems and muscle cells, and the intestine and lung of different species, to the locomotor and nervous system, and the systems for energy supply.

Further reading

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