dynamic system whose structure and function are driven by a system of such coincident events, and we can identify such a system with an organism, unicellular or multicellular. Viewed in this manner, cells and their higher-order systems whose structure and properties ultimately depend on enzymes can be naturally associated with a 4-dimensional space. In other words, living systems are 4-dimensional and can be projected onto either the traditional 3-dimensional space of Euclid at a given time (span) or the one-dimensional space of time under a given spatial arrangement.

15.11 Allometry

Allometry is the study of the effect of the size of an organism, either unicellular or multicellular, on its function. For example, the linear relation between metabolic rates and body mass of different organisms shown in Fig. 15.13 is the subject of intense studies in the field of allometry. Whitfield defines allometry as follows (2006, p. 58):

![Graph showing allometric relationship between metabolic rate and mass of various organisms](image-url)

Fig. 15.13 The relationship between the metabolic rate of various organisms and their body mass (Reproduced from Whitfield 2006, p. 77 with kind permission from Novo Nordisk, Inc.)
The relationship between metabolic rate and body weight is an example of a biological pattern called allometry, which compares how the value of any biological trait, such as metabolic rate or leg length, changes with the total size of a plant or animal. (15.7)

The so-called quarter-power scaling laws (Whitfield 2006, pp. 78–79) stating that many biological traits scale as body mass raised to the power of one or more quarters may be derived from the postulate that the phenomenon of life is 4-dimensional because enzymes are coincidence detectors (see Sect. 7.2.2). The allometry equation has the following deceptively simple form:

\[ y = ax^b \]  

(15.8)

where \( y \) is biological trait, either processes or structures, \( x \) is the total size of a cell, a plant or animal, and \( a \) is the allometric coefficient, and \( b \) is the allometric exponent which can be greater or less than 1. If \( b \) is greater than 1, for example, as in the case of deer antlers, the trait grows proportionately larger, and, if \( b \) is less than 1 as is the case with metabolic rate, it gets proportionately smaller so that, when the body size doubles, the metabolic rate increases by less than twofold.

During the past one and a half century, it has been found that, over a very wide range of body sizes of organisms (covering 27 orders of magnitude from unicellular organisms to whales), the metabolic rate scales as (or is proportional to) the body mass raised to the power of approximately \( (\text{White and Seymour 2005}). \) In Fig. 15.13, the metabolic rates of organisms from single cells to the elephant are plotted against their body masses on a log–log scale. The figure has three parallel lines, one each for homeotherms, poikilotherms (also called ectotherms), and unicellular organisms. They all have the same slope, that is, \( b = 3/4 \) but intercept the \( y \)-axis at different points, resulting in different values for \( a \): The lower the intercept, the lower the average metabolic rate for each group. The allosteric exponent of shown in this figure is not the only possibility. There are many cases where it differs from and hovers around 2/3 (see Table 1 in White and Seymour 2005). It will be assumed here that the power law reflects at least some of the principles underlying the scaling phenomena in biology and that even the allometric exponent of 2/3 may be viewed as an example of the quarter-power scaling since 2/3 is equal to 2.666/4. Thus, any viable theory of allometric scaling should be able to provide a reasonable theoretical basis to account for the numerical values of both \( a \) and \( b \) in Eq. 15.8. It should be noted here that certain traits such as life span, heart beats, blood circulation time, and unicellular genome length scale as the body mass raised to the power of \( 1/4 \), and the radii of aortas and tree trunks scale as body mass raised to the power of 3/8 or 1.5/4 (West and Brown 2004). These are examples of “quarter-power scaling,” and the key question that has been challenging theoretical biologists for more than a century is why these exponents are multiples of 1/4, not 1/3 as expected on the basis of the scaling in the Euclidean space.

One of the currently most widely discussed and intensely debated theories to account for the 3/4 allometric exponent of the power law relating metabolic rate \( (y) \) to body mass \( (x) \) is the one proposed by West and Brown (2004, Whitfield 2006). Their theory accounts for the 3/4th scale exponent on the basis of the assumption that natural selection evolved hierarchical fractal-like branching networks that distribute energy, metabolites, and information from macroscopic reservoirs to microscopic sites.

(West and Brown 2004) (15.9)
They further postulated that the hierarchical branching networks provided the following constraints:

1. Networks service all local biologically active regions in both mature and growing biological systems. Such networks are called space filling.
2. The networks’ terminal units are invariant within a class or taxon.
3. Organisms evolve toward an optimal state in which the energy required for resource distribution is minimized.

It is interesting to note that the concept of networks employed by West and his coworkers (e.g., animal circulatory systems, plant vascular systems) focuses on the static spatial and geometric aspect of bionetworks, which may be viewed as belonging to the class of the equilibrium structures of Prigogine (Sect. 3.1.5). Since living systems are dynamic and better described in terms of dissipative structures (Prigogine 1977, 1980, Ji 1985a, b), and since living processes are almost always mediated by enzymes whose behaviors can be best characterized in terms of “temporal networks” in contrast to “spatial networks” as pointed out in Sect. 7.2.3, it may be reasonable to formulate an alternative theory of allometric scaling based on the notion of dissipative network, which are at least 4-dimensional in the sense that it takes four coordinates to characterize them, namely, x, y, z, and t.

Therefore, a simple explanation for the quarter-power scaling laws may be derived on the basis of the following assumptions:

1. The body mass (x) of an organism is not a geometric object (i.e., equilibrium structure) but a 4-dimensional entity, because it can be viewed as an organized system of cells and processes catalyzed by enzymes (acting as coincidence detectors) (see Fig. 7.8 in Sect. 7.2.3).
2. The number of cells (n) of an organism can be viewed as the projection of organisms on to the 3-dimensional Euclidean space (i.e., devoid of the time dimension).
3. The metabolic rate (y) of an organism is directly proportional to the number of cells constituting that organism (whose Euclidean volume is v), the proportionality constant increasing with both body temperature (T) and cell density, d = n/v, defined as the number of cells per unit body volume. (For simplicity, it will be assumed that the mitochondrial contents, or better the average respiratory activities, of cells are invariant among individual organisms and across species.)

Based on Assumptions (1) and (2), we can write:

\[ n \sim x^{3/4} \Rightarrow n = ax^{3/4} \quad (15.10) \]

Based on Assumption (3), we can write:

\[ y \sim n \quad (15.11) \]

Combining Eqs. (15.10) and (15.11) leads to:

\[ y_i = a_i x_i^{3/4} \quad (15.12) \]
where $y_i$, $a_i$, and $x_i$ are, respectively, the metabolic rate, the proportionality constant and the body size of the $i$th species with a distinct cell density, $d_i$, and habitat temperature, $T_i$. Because of Assumption (3), $a_i$ is a function of both $T_i$ and $d_i$:

$$a_i = f(d_i, T_i)$$  \hspace{1cm} (15.13)

Taking the logarithm of both sides of Eq. (15.12) leads to:

$$\log y_i = \frac{3}{5} \log x_i + \log a_i$$  \hspace{1cm} (15.14)

Equation (15.14) predicts that, when the $i$th metabolic rate, $y_i$, is plotted against the $i$th body mass, $x_i$, on a double logarithmic coordinate system, a straight line with slope $3/4$ would be obtained with different $y$-intercepts for different species, consistent with Fig. 15.13. Designating unicellular organisms as 1, poikilotherms as 2, and homeotherms as 3, the data in Fig. 15.13 make it clear that $a_1 < a_2 < a_3$, indicating that the metabolic rates per unit mass increase from unicellular organisms to poikilotherms to homeotherms. This observation is consistent with the FERFAC (Free energy requirement for Active complexity) hypothesis, Statement 15.20, which predicts that organisms with higher active complexities require higher energy expenditures, since the active complexity (Sect. 5.2.3) of the groups of the organisms considered here most likely increases in the same order as their intercept values, $a_i$.

The life span (LS) of an organism can be viewed as the projection of the living processes embodied in $x$ on to the time dimension, which leads to:

$$LS_i = a_i x^{1/4}$$  \hspace{1cm} (15.15)

where $LS_i$ and $a_i$ are, respectively, the life span and the proportionality constant of the $i$th species. Equation (15.15) is qualitatively consistent with the life span vs. body-mass plots found in the literature (e.g., see http://www.senescence.info/comparative.html) and (West and Brown 2004).

The key difference between the West–Brown–Enquist (WME) approach to developing a theory of allometric scaling and the one proposed in this book is that the former assumes that the $3/4$ exponent can be derived mathematically from the species-specific physical characteristics of organisms (e.g., vascular trees of mammals, diffusion paths within cells in unicellular organisms), whereas the present approach regards the exponent as resulting from the universal property of all living systems, i.e., enzymic activity, regardless of differences in distribution networks among different individuals and species. It is possible that both approaches are relevant, since living systems embody two distinct processes – transport of matter between micro-meso (e.g., cells) and macro-sites (e.g., lung) and transformation of matter within cells. Based on the structural information of all living systems (e.g., role of mitochondrial membranes and lung alveoli membranes), it is likely that transport processes scale as the body mass raised to the power of $2/3$ as was first suggested by Rubner in 1883 (White and Seymour 2005), and, based on the idea that
enzymes are coincidence detectors serving as the nodes of temporal branching networks (Fig. 7.7), it can be suggested that transformation of matter in cells scale as the body mass raised to the power of 3/4, as proposed above. It is also possible that certain dynamic traits are rate-limited by transport of matter and that of certain others by transformation of matter, depending on the evolutionary, ontogenic, and physiological conditions of the organisms under consideration, thereby exhibiting either the 2/3 or 3/4 allometric exponents or some values in between as seems to be the case (see Tables 1 and 2 in White and Seymour 2005). These ideas are summarized in Fig. 15.14.

As evident in Fig. 15.15, the level of non-protein-coding DNA (i.e., dr-genome defined in Sect. 11.2.4) relative to protein-coding DNA (drp-genome, Sect. 11.2.4) is found to increase rapidly with increasing biological complexity, for example, from unicellular to multicellular organisms. The ratio of noncoding DNA to the total DNA does not change much from Nanoarchaeum equitans through Rickettsia conorii (spanning 67 unicellular species) but begins to rise sharply with Rickettsia prowazekii, continuing to rise through 19 species (multicellular species), reaching the maximum ratio with Homo sapiens (Mattick 2004). One plausible interpretation of the data in Fig. 15.15 is that the noncoding portions of DNA encode the information needed to organize in space and time the cells in multicellular organisms in order to maintain their functions. This idea can be expressed using the language of network sciences (Sect. 2.4) (Barabasi 2002, 2009):

The coding regions of the DNA of a multicellular organism determine the intrinsic properties of the nodes of a biocomplex and the noncoding DNA regions determine both the interactions among the nodes and the space- and time-dependent control of their interactions in order to accomplish evolutionarily selected functions of the organism.
ncDNA/tgDNA ratios vs. species plot

Fig. 15.15 The ratio of non-protein-coding (dr-genes, Sect. 11.2.4) to protein-coding DNA (drp-genes) in various species. The ratio does not change much from *Nanoarchaeum equitans* through *Rickettsia conorii* (spanning 67 species) but begins to rise sharply with *Rickettsia prowazekii*, continuing to rise through 19 species, reaching the maximum ratio of 0.983 with *Homo sapiens*.

The data were downloaded from Taft and Mattick 2012. ncDNA = noncoding DNA; tgDNA = total genomic DNA. The ncDNA/tgDNA ratio values were obtained from (Taft and Mattick, arXiv.org/ftp/q-bio/papers/0401/0401020.pdf, downloaded on 01/04/2012; see also Mattick 2004).

In Sect. 2.4.1, a bionetwork was defined as a network of nodes (\(n\)), such as proteins, RNA, and DNA, connected by edges (\(e\)) according to some topology (\(T\)) so as to accomplish a biological function (\(F\)), that is, \(F = T(n,e)\). Statement 15.16 satisfies all the requirements of the definition of a bionetwork with the following identifications:

1. \(F = \) “evolutionarily selected functions of the organism”
2. \(T = \) “the noncoding DNA regions determine ... the space- and time-dependent control of their interactions...”
3. \(n = \) “...coding regions of the DNA ...determine the intrinsic properties of the nodes ...”
4. \(e = \) “the noncoding DNA regions determine ... the interactions among the nodes”

Therefore, based on the empirical data shown in Fig. 15.15 and the bionetwork theory described in Sect. 2.4.1, it is possible to make the following equivalent or related generalizations:

- DNA of an organism encodes a bionetwork. [15.17]
- DNA is a molecular representation of a bionetwork. [15.18]

Since DNA is a molecular representation of a bionetwork and since a bionetwork is a graph-theoretical representation of an organism, DNA is a molecular representation of an organism. [15.19]

Statement 15.19 may be referred to as the Bionetwork Theory of DNA (BTD), and it is here suggested that BTD complements the Watson-Crick theory of DNA (Watson and Crick 1953) which is mostly structural (or node-centered, in the language of network sciences).

At least 50% of the non-protein-coding DNA of the human genome has been found to code for RNA molecules that are not translated into proteins (Mattick 2004). Hence, Fig. 15.15 indicates that the level of RNA in cells most likely increases with biological complexity, making RNA levels inside the cell (and associated non-protein-coding DNA, or dr-genes; Sect. 11.2.4) a reliable index of the complexity (the active kind; see Sect. 5.2.4) of the phenotype of multicellular organism. Since maintaining complex structures of organisms would entail free energy dissipation, the following generalization follows:

The more complex an organism is, the more energy the organism needs to survive. [15.20]

We will refer to Statement 15.20 as the Hypothesis of the Free Energy Requirement for Active Complexity of Living Systems or more briefly as the Free Energy Requirement for Active Complexity (FERFAC) (for the definition of “active complexity”, see Sect. 5.2.3). As discussed in connection with Fig. 15.13, the allometric data on the log–log relation between the body weight vs. the metabolic rate of various species, i.e., Eq. (15.14), strongly support the validity of the FERFAC hypothesis.