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Comparative Physiology of Fatigue

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ABSTRACT

JONES, J. H. Comparative Physiology of Fatigue. *Med. Sci. Sports Exerc.*, Vol. 48, No. 11, pp. 2257–2269, 2016. This review attempts to provide insights into factors associated with fatigue in human and nonhuman animals by using the two fundamental approaches of comparative physiology: determining common principles that govern structure and function in animals that are relatively invariant between animals and evaluating animals that have been highly adapted by natural selection to demonstrate extreme performance. In this review, I approach the topic of fatigue by considering factors that are associated with its reciprocal or inverse or duration of sustained performance before fatigue sets in to end the performance. The two general factors that I consider that affect endurance time more than any other are body temperature and body mass. The former affects endurance time because of thermodynamic effects on chemical reaction rates and metabolism; the latter acts through the mechanism of allometry or scaling. The examples of extreme animal performance that I discuss are two examples of bird migration, the diving performance of marine mammals, and the unique relationship that governs energy cost of locomotion in hopping kangaroos. **Key Words:** BODY TEMPERATURE, ALLOMETRY, SCALING, BIRD MIGRATION, DIVING MAMMALS, KANGAROO

Comparative physiology is a discipline highly influenced by a phrase written by August Krogh, the 1920 Nobel Laureate in Physiology or Medicine for his work on capillaries and the only comparative physiologist to ever be so honored. In 1929, he wrote (38):

For a large number of problems there will be some animal of choice or a few such animals on which it can be most conveniently studied.

Numerous examples come to mind of studies for which those words are applicable, from the study cited by Krogh in that article of the work he did as a student in Christian Bohr's laboratory that capitalized on the proximal bifurcation of the tortoise's trachea to enable him to sample gas independently from each lung to studies of the squid giant axon that resulted in breakthroughs in understanding neural conduction. The term "August Krogh Principle" was coined by Hans Krebs in 1975 (37), although, in reality, the concept of using animal models with particularly useful traits for a given experiment dated back nearly 60 yr before Krogh wrote those words to Claude Bernard (8).

Krogh's words and the principle attributed to him define the concept that, as physiologists and zoologists, we should use our knowledge of the diversity of animals resulting from natural selection to choose animals for our studies that will

maximize the signal-to-noise ratio of our results. However, in a sense, Krogh anticipated the development of modern molecular genetic techniques that enable investigators to create phenotypes that can also maximize the information return from experiments by modifying the genome by artificial methods. Part of Krogh's legacy is that modern comparative physiologists tend to take two interdependent approaches to studying animal adaptation. One approach is to study factors that remain relatively invariant between different animals, e.g., mitochondria, to understand what "building blocks" are fixed in terms of their function and have little or no plasticity. The second approach is to study animals that demonstrate the limits of adaptation in that they are able to survive in extreme environments or perform physiological feats that appear remarkable in comparison with those possible for a species, e.g., *Homo sapiens*, which is more highly selected presumably for cognitive abilities rather than physical adaptations, e.g., finger dexterity or endurance. In this review, I will consider both of these approaches, first by discussing two general factors that affect physiological function in vertebrate animals more than any others, body temperature and body size, and then by applying some of those principles to consideration of three examples of the Krogh Principle that result in extreme animal performance: bird migrations, deep-diving marine mammals, and hopping of kangaroos. In the context of this article, I will address the issue of animal fatigue by discussing it in terms of its reciprocal or inverse, endurance time.

BODY TEMPERATURE

Birds and mammals are homeothermic (derived from the Greek roots *homoios* [like or same] and *thermē* [heat] and

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frequently called by laypeople “warm-blooded”), i.e., they regulate their body temperatures usually narrowly around a fixed set point, typically within a broader range of 38°C–43°C for birds and 30°C–39°C for mammals. However, that set point may vary at times, e.g., during hibernation, periods when the animal is febrile, or during torpor, which is a reduction in body temperature of small vertebrates during the night to reduce the temperature difference between their body and surrounding air and, hence, their rate of heat loss by conduction and radiation. Uniquely among vertebrates, both birds and mammals have external insulation (feathers or fur) that allow them to retain heat produced by metabolism as well as having completely divided circulatory systems that enable them to develop higher systemic blood pressure, cardiac output, oxygen delivery, and mass-specific (per kilogram) metabolic rates. As a result, they are capable of generating sufficient metabolic heat to offset the rate at which their (usually) higher than ambient body temperatures lose heat to the environment. By contrast, the other vertebrate classes (fish, amphibians, and reptiles) are poikilothermic (derived from the Greek roots *poikilos* [variable] and *thermē* [heat] and often called by laypeople ectothermic or “cold-blooded”), i.e., they have variable body temperatures that usually are close to being at equilibrium with their surrounding environments, although some poikilotherms use either anatomical or behavioral adaptations to maintain higher than ambient body temperatures.

An important consequence of animals having different body temperatures stems from the fact that metabolism is fundamentally a series of chemical reactions, and elevated temperature provides more activation energy for those reactions and increases their rates. When we use the term “body temperature,” we should keep in mind that different parts of any animal’s body may be at different temperatures depending on the temperature of the surrounding environment as well as how active are the animal’s muscles, given that most of the energy used in muscular contractions is released in the form of heat and may provide localized warming of tissues. Hence, even in humans, moderate heterogeneity of temperatures may exist within the body, e.g., between working muscles and gut.

Keeping these principles in mind, changes in body temperature alter the amount of energy activating the chemical reactions of metabolism and their rates, including enzyme activities. Among the enzyme activities affected by temperature is that of myosin-ATPase, the enzyme catalyzing the interaction of actin and myosin myofilaments in skeletal muscle sarcomeres that determines the speed at which crossbridges form and break and, ultimately, the speed of muscle shortening and ATP utilization. The metabolic rate of an animal and the functions that contribute to determining it, e.g., muscle shortening rate (velocity), increase with higher temperature and decrease with lower temperature. The relationship of the effect of temperature on chemical reaction and metabolic

rates is quantified by the variable Q_{10} , described by the following equation:

$$Q_{10} = \left(\frac{R_2}{R_1} \right)^{\frac{10}{T_2 - T_1}}, \quad [1]$$

where Q_{10} is the quantitative value of the effect of temperature on reaction rate, R_1 is the rate of reaction at the initial temperature in degree Celsius, R_2 is the reaction rate after a temperature change in degree Celsius, and T_1 and T_2 are the initial and final temperatures in degree Celsius causing the change in reaction rates. The relationship between temperature and reaction rate is shown in Figure 1.

It is easier to interpret the relationship between temperature and reaction rate if we rearrange equation 1 and logarithmically transform it to express $\log R_2$ as a function of $\log R_1$, $\log Q_{10}$, and the inverse of the temperature relationship:

$$\log R_2 = \log R_1 + \left(\log Q_{10} \frac{T_2 - T_1}{10} \right) \quad [2]$$

with all symbols having the same meanings as they did for equation (1). This transformation linearizes the relationship when plotted as $\log R_2$ versus $\left(\frac{T_2 - T_1}{10} \right)$ (linear abscissa and logarithmic ordinate), yielding a line with slope equal to $\log Q_{10}$ and intercept of $\log R_1$, making it easy to see differences between groups of animals (Fig. 2). For most vertebrates, both homeotherms and poikilotherms, the fundamental effect of Q_{10} is that it changes metabolic rate (determined by chemical reaction rates throughout the body) by an average of approximately 2.3-fold for every 10°C change in body temperature with higher temperatures elevating rates. The Q_{10} value is therefore the factor by which metabolic rate changes with each 10°C change in body temperature. Given that vertebrate animals have body temperatures ranging from

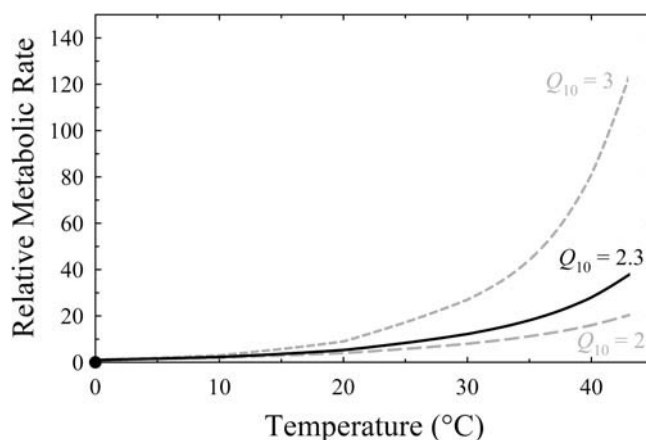


FIGURE 1—The Q_{10} effect is the relationship between temperature (°C) and chemical reaction rate that determines metabolic rate. Short dashed gray curve is the relationship when $Q_{10} = 3$; long dashed gray curve is the relationship when $Q_{10} = 2$; solid black curve is the relationship when $Q_{10} = 2.3$, the average value for most vertebrates. Metabolic rates have been standardized so the value is 1 at 0°C.

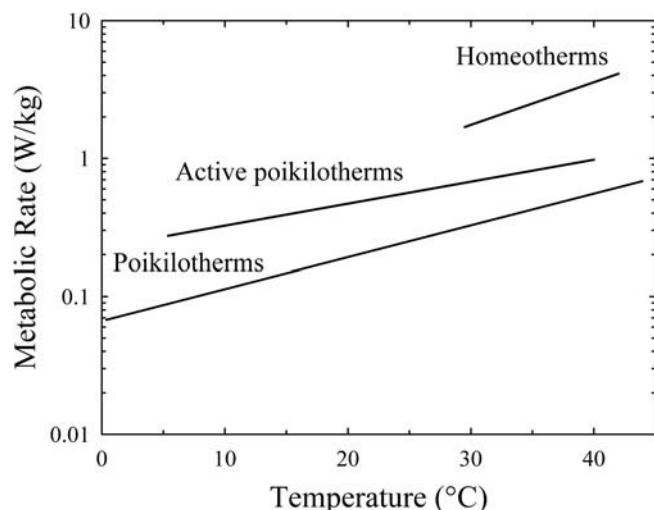


FIGURE 2— Q_{10} effect on metabolic rates of vertebrate homeotherms (top), active poikilotherms (middle), and poikilotherms (bottom). Q_{10} effect (slope of line) is similar for each group, although intercepts vary with inherent metabolic rate of each group. Note that abscissa is linear and ordinate is logarithmic.

slightly lower than 0°C (poikilothermic Antarctic ice fish of the suborder Notothenioidei) to approximately 43°C (homeothermic song birds of the order Passeriformes)—a range exceeding four spans of 10°C—the Q_{10} effect can vary rates of chemical reactions, speed of muscle shortening, and metabolic rate by a factor of nearly 30-fold ($>2.3^4$).

The effect of Q_{10} has been shown to directly influence endurance times of aquatic poikilothermic animals in terms of their duration of diving (30), with higher temperatures reducing dive duration. In this situation, the Q_{10} effect plays a major role in determining the rate at which the animal uses up its available oxygen stores. A contributing factor to extending dive times at lower temperatures for some animals is the increasing role, as temperature decreases, of cutaneous gas exchange in helping animals meet their oxidative metabolic demand. This is because the solubility of oxygen in water increases as water temperature decreases.

A key factor for the athletic performance of animal athletes, including human animals, is warming up sufficiently before a competition. This enables the athlete to capitalize on the Q_{10} effect that can ultimately provide slightly more speed to their movements than without adequate warm-up. Although the differences in muscle temperature are slight after warming up, the Q_{10} effect increases speed in situations, e.g., at elite levels of competition, in which milliseconds can make the difference between winning and losing. Schmidt-Nielsen (67) provides an excellent summary of these relationships in his chapter on “Temperature effects.”

BODY SIZE

Although a vertebrate’s body temperature can theoretically elicit differences in metabolic rate and speed of

movement by as much as 30-fold, differences in body size can result in even greater differences. The area of comparative physiology that investigates the effects of body size on structure and function is called *allometry* or *scaling*. Allometry stems from the Greek words *alloios* meaning “different” and *metros* meaning “measure,” taken together meaning “by a different measure.” The term is based on the fact that small and large animals cannot be built identically because dimensions of an animal change size heterogeneously as body size changes because different elements are governed by different exponential relationships as explained in the following paragraph.

Allometric relationships take the form of a power function, e.g.,

$$Y = a M^b, \quad [3]$$

where Y is a structural or functional variable, a is a constant dictated by the shape of the animal, M is the animal’s body mass, and b is an exponent that describes how the variable Y changes with size. When plotted on linear axes, this relationship for most exponents yields a curvilinear relationship that can be difficult to interpret visually (Figs. 3A and 3B), although such a graph directly conveys the magnitude of changes in a variable with body size. The allometric relationship can be simplified for visual analysis by logarithmically transforming each side:

$$\log Y = \log a + (b \log M), \quad [4]$$

with symbols having the same meanings as for equation 3. This transformation allows the relationship to be plotted on logarithmic axes with the slope of the resulting straight line indicating the value of the mass exponent b (Fig. 3C). Although the shape factor or coefficient, a , influences the final value of the relationship by determining the intercept, the mass exponent, b , is the term that describes the effect of body size on the variable.

If we consider a part of an animal’s body with a given length (L), e.g., 1 cm, then $L = L^1 = 1$ cm. We would calculate that the area (A) of a square of this unit length would be $L^2 = 1$ cm², and the volume (V) of a cube with 1-cm edges must be $L^3 = 1$ cm³. This will be the volume of an animal’s body after multiplying by a shape factor variable. However, because the exponents of these different geometrical elements of the animal’s body differ (=1, 2, or 3), this means that lengths, areas (both surface and cross-sectional), and volumes of an animal change disproportionately as body size changes. For instance, considering how area and volume are related, $A \propto L^2$ and $V \propto L^3$, these relationships can be rearranged to show that $A \propto V^{2/3}$. In this case, the 2 in the numerator of the exponent indicates that a characteristic length of the animal is squared to determine the area, whereas the 3 in the denominator indicates that characteristic length is cubed to determine the animal’s volume. As a consequence of the fact that all vertebrates have bodies of

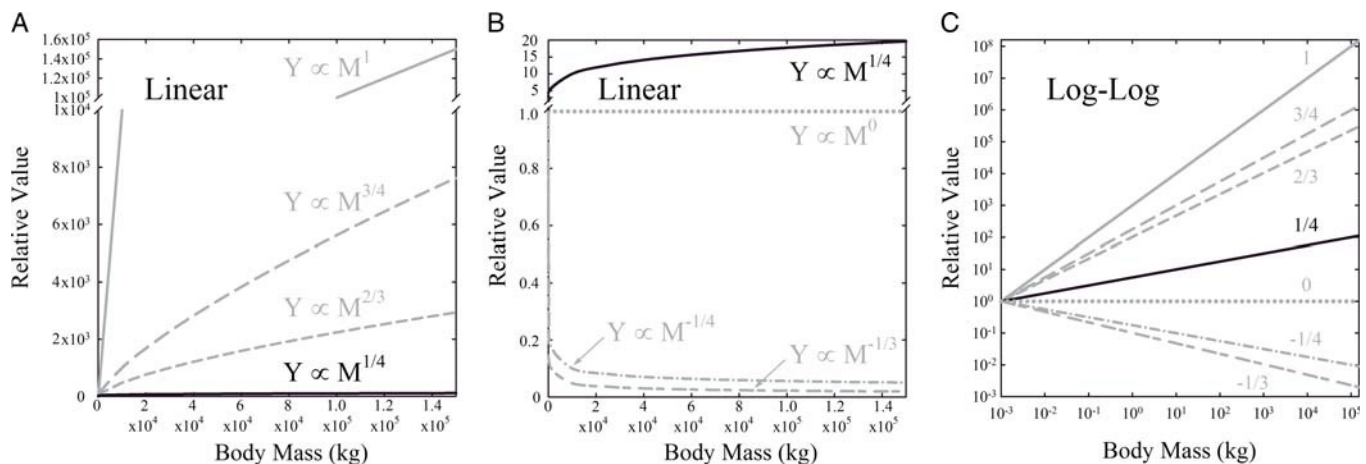


FIGURE 3—Allometric relationships as functions of body mass when abscissa is plotted with a logarithmic scale and ordinate is plotted with a linear scale (A and B) or a logarithmic scale (C). The curvilinear relationships observed for most exponents when data are plotted with a linearly scaled ordinate (A and B) reflect the magnitude of the mass exponent in the power function ($Y = aM^b$) but are difficult to interpret visually. If the data are plotted on the log-log axes (C), the curvilinear power function relationships are transformed into straight lines with slopes equal to the mass exponents of the original power functions and can be easily compared and interpreted visually. Curves and lines shown in gray are for allometric relationships described in the text; curves and line shown in black show the relationship for *physiological time* ($Y \propto M^{1/4}$). Redrawn from Pypendop and Jones (60).

nearly identical density, we can substitute body mass (M) for V and state that

$$A \propto M^{2/3}. \quad [5]$$

By convention, allometric exponents are usually depicted as a fraction when they denote an underlying theoretical relationship but are shown as decimal values when they are derived from empirical measurements.

Equation 5 shows that areas of an animal's body ($\propto L^2$ and $M^{2/3}$) increase at a slower rate as body size increases than does body mass ($\propto V = L^3$ or $M^{3/3} = M^1$); hence, area per unit volume (or mass) increases in proportion to L^2/L^3 . Areas that increase with size are not only surface areas of structures but also cross-sectional areas, e.g., the cross-sectional area of skeletal muscle. Because the peak stress (force/area) that vertebrate skeletal muscle can generate is dictated by the number of actin-myosin crossbridges within a given cross-sectional area of muscle and the packing of myofibrils in sarcomeres is relatively fixed, the maximal force that can be generated by a skeletal muscle (3–4 kg force·cm⁻²) for all vertebrates is directly related to its cross-sectional area. As shown in equation 5, smaller animals can generate a greater amount of force relative to their body mass than can larger animals, and hence, smaller animals are relatively stronger than larger ones. This means that smaller animals are capable of performing feats such as exerting sufficient force to pull and raise their body mass vertically against gravity when climbing a tree, whereas larger animals cannot. Among mammals, that limit appears to be reached at about the size of the American black bear (*Ursus amercianus*) that typically weighs less than 400 kg and can climb trees, whereas its larger cousin, the grizzly bear (*Ursus arctos*), may approach 700 kg in body mass and is incapable of climbing trees. At the other end of the size spectrum, ants that weigh only 1 mg are capable of lifting 20 times their body weight in

their jaws and pulling loads of 50 times their body weight on the ground behind them.

Additional evidence demonstrating the extent to which allometry governs animal strength stems from the fact that before the advent of the use of anabolic steroids in sports, world weight lifting records for humans by (body mass) size class fit almost perfectly an allometric regression with a mass exponent of 2/3, the ratio by which muscle cross-sectional area changes with body mass. However, because the use of anabolic steroids has become prevalent in sports, variance around such regression equations has increased dramatically (47).

Figure 3 shows several allometric relationships that commonly govern changes in structures and functions in animals as body size changes. All three panels (Figs. 3A, 3B, and 3C) are plotted with logarithmic scales for body mass on the abscissa. Figures 3A and 3B are plotted with linear scales for the ordinate, whereas Figure 3C uses a logarithmic scale for the ordinate. The relationships shown by the curves or lines in Figure 3 include such scaling factors as those describing direct proportionality ($Y \propto M^1$) (e.g., body mass and volume), interspecific metabolic rate in mammals ($Y \propto M^{3/4}$), intraspecific metabolic rate or surface or cross-sectional areas ($Y \propto M^{2/3}$), variables that are independent of body size ($Y \propto M^0$) and invariant among mammals (e.g., hematocrit), resting heart rate or mass-specific (per kilogram) interspecific metabolic rate ($Y \propto M^{-1/4}$), and mass-specific (per kilogram) surface or cross-sectional areas ($Y \propto M^{-1/3}$ = surface-to-volume ratio). Rates or frequencies, e.g., heart rate ($Y \propto M^{-1/4}$), have units of 1/time, and their inverse relationship ($= Y \propto M^{1/4}$) has the units of time.

In each of the panels in Figure 3, the allometric curves or lines are shown in gray except for one that is plotted in black, the relationship $Y \propto M^{1/4}$ (or $M^{0.25}$ if derived empirically). This scaling factor is of particular significance

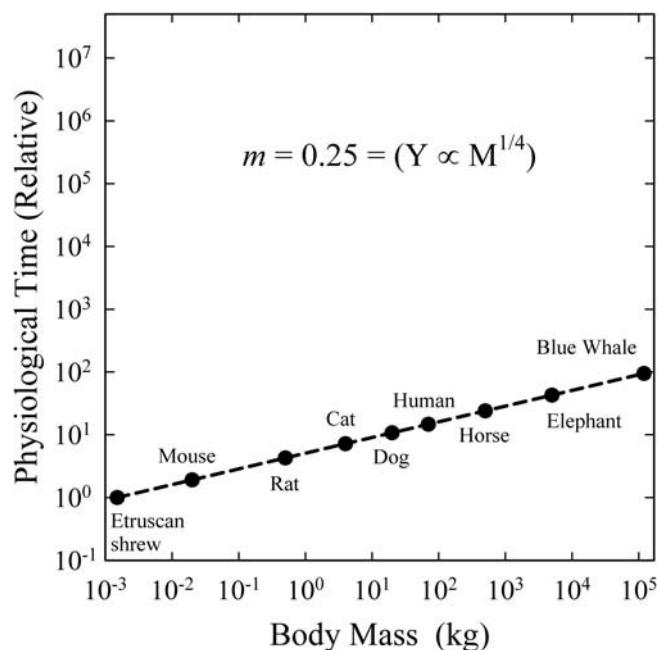


FIGURE 4—Log-log plot of body mass (abscissa) versus physiological time (ordinate) for mammalian species spanning the mammalian size range from smallest (Etruscan shrew, *Suncus etruscus*, 0.0015 kg) to largest (blue whale, *Balaenoptera musculus*, 1.5×10^5 kg), a size range of 10^8 . Because physiological time scales $\propto M^{1/4}$, across the mammalian size range, physiological time changes by two factors of 10- or 100-fold.

because it denotes a relationship called *physiological time* (Fig. 4). Physiological time refers to the amount of time required for a given event to occur in mammals of different sizes. Mammals span a size range of 10^8 - or 100-million-fold from the smallest mammal, the Etruscan shrew (*Suncus etruscus*), which weighs 0.0015 kg (1.5 g), to the blue whale (*Balaenoptera musculus*), which weighs more than 150,000 kg. The scaling factor of $M^{1/4}$ indicates that every time body mass increases by 10^4 , the time required for a similar event to occur in a larger animal will increase by a factor of 10^1 , i.e., it will take 10 times longer. This is because the exponent of $1/4$ indicates the ratio of time change (10^1) in the numerator to that of body mass (10^4) in the denominator. A simple example of this relationship is the manner in which resting heart rate (determined by the duration of time between heartbeats) changes with body size, given that the time it takes for a heartbeat to occur is governed by physiological time. As mentioned previously, mammalian heart rate scales as $Y \propto M^{-1/4}$, the negative exponent indicating that as mammals increase in size, their resting heart rate decreases. The 1.5-g Etruscan shrew has a resting heart rate of approximately 800 bpm, whereas the 150-ton blue whale, being 10^8 times larger, has a resting heart rate of approximately 11 bpm, a difference of nearly 100-fold (11). This reduction in heart rate as body size increases results from the initial increase in body mass of 10^4 , reducing heart rate by a factor of 10, then the second increase of an additional 10^4 in body mass multiplying that initial 10-fold reduction by an additional factor of 10, for a total reduction in heart rate of 100-fold. It

is essential that the whale's heart beat so slowly given that its heart is approximately the size of a Volkswagen Beetle, and the equivalent scaling of cardiac output and the cross-sectional areas of aorta and vena cava result in all mammals having nearly identical velocities of blood flow in aorta and vena cava (11) at any equivalent exercise intensity from resting to maximal. However, if the whale had a higher heart rate than allometrically predicted, the increased velocity of the venous return blood entering the heart could potentially damage the myocardium when that higher velocity blood decelerated abruptly. This relationship is theoretically true for all mammals and demonstrates how allometric relationships can govern animal design.

Physiological time, as a general principle, dictates the time required for any particular event in an animal's life to occur, including the single longest event, the animal's life span. Perhaps the earliest recognition of the relationship between body size and longevity was Aristotle's observation in a manuscript written in 350 BC titled "*On Longevity and the Shortness of Life*" that large animals live longer than small ones (in 70). Examining this relationship in homeotherms, Lindstedt and Calder (11,43,44) noted that recorded maximal life spans of birds and mammals kept in captivity scale approximately as $Y \propto M^{1/4}$. However, they found that birds tend to live over twice as long as mammals of the same body mass on average. This observation indicates that for the allometry of lifetime duration, the coefficient a in the allometric equation is more than twice as large for birds as for mammals. Certain anomalous situations appear to exist in these generalizations, e.g., the fact that giant breeds of domestic dogs, *Canis familiaris*, tend to have life spans of only 7 to 8 yr, whereas smaller breeds may live twice as long. However, paleontological evidence suggests that the progenitors of the domestic canid were smaller animals, and that in artificially selecting for giant breed dogs, humans may have inadvertently used selective breeding for other factors to give these dogs traits that tend to kill them at younger ages, e.g., the tendency to develop gastric dilatation and volvulus (twisting that causes ischemia and necrosis) that fatally bloats them or a high frequency of occurrence of long-bone osteosarcomas.

For mammals, the allometric relationship for life span scales as $Y = 11.6 M^{0.2}$, where Y is lifetime in years (11). It is notable that this equation predicts the life span of a 70-kg human as slightly more than 27 yr, approximately one-third what average Americans attain. However, it must be remembered that modern Americans benefit from a variety of research advances in medicine and nutrition that have increased life spans considerably for the past century, as well as the fact that because allometric relationships are plotted on log-log scales, residuals that fall slightly above a regression line may translate into differences of two- to three-fold in the raw data.

As a consequence of the allometric relationship between body size and physiological time, it is almost inevitable that time to fatigue would be related to body mass as nearly all

physiological functions take more time to occur in larger mammals. This relationship will be considered more thoroughly (and demonstrably) in the Diving section. However, in considering the relationship between exercise power output and time to exhaustion in humans, Wilkie (79) showed that there was a nearly hyperbolic relationship between the two variables, contributing to the development of the concept of “critical power” that was introduced in 1965 (49). A key aspect of the critical power model is that critical power is the highest rate of aerobic energy transduction that can be sustained without drawing on anaerobic energy stores. Critical power is the asymptote for power or velocity and there is a curvature constant (W'), composed partially of sources of anaerobic energy, that limits the time that exercise can be sustained as those sources become depleted. The critical power concept has been extensively discussed in the literature and reviewed and likely plays a role in dictating when fatigue occurs in exercising animals (29,31,34,50,77). One could hypothesize that there might even be a link between muscle temperature and fatigue as well. The onset of fatigue could occur when proteins begin to denature, given the observation that between 40°C and 45°C, the denaturation of proteins in mammals is dose dependent on temperature and time of exposure (42). Fatigue in this circumstance might be acting as a protective mechanism in animals.

Allometric relationships govern numerous aspects of function in mammals, including in humans. For instance, because of their body size, smaller human athletes live on an inherently faster time scale than larger ones. Smaller athletes have intrinsically faster rates of myosin ATPase cycling (3,45), resulting in smaller competitors being theoretically capable of moving faster than larger ones, although factors, e.g., genotype and/or training, may influence this. These differences in speeds may be measured in milliseconds; however, at elite levels of competition, such differences can influence outcomes. A recent review of the application of allometric principles was published by Pypendop and Jones (60), and an excellent and easily understandable introduction to the effects of allometry and scaling on animal function was conducted by Schmidt-Nielsen (66).

An interesting and enjoyable article that applies principles of allometry and physiological time to animal performance was written in 1950 by A. V. Hill, the 1922 Nobel Laureate in Physiology or Medicine for his work on skeletal muscle. The article was based on an evening lecture he had given in 1949 at the Royal Institution and was titled “The Dimensions of Animals and Their Muscular Dynamics” (28). In this article, Hill considers the scaling of structures in animals and comes to two remarkable conclusions: that mammals of different body sizes should be able to run at the same maximal speed and that mammals of different sizes should all be capable of raising their centers of mass by the same amount when they jump.

As it turns out, Hill was wrong about the maximal running speeds of mammals being the same based on an incorrect assumption he made for which he had only few empirical

data available to use in his calculations. Hill knew that smaller animals move their limbs at higher stride frequencies than do larger animals; however, he assumed this rate is faster than it really is (26,55). Furthermore, Hill did not realize that because the cross-sectional area of bones in the limbs of mammals scales with an exponent of approximately $Y \propto M^{1.1}$ (2), the area of bone and its strength in compression that supports an animal’s weight does not increase in proportion to the mass that is loading the bone; for it to do so, the cross-sectional area of the bones would need to scale as $Y \propto M^{1.33}$. As a result, larger mammals have relatively weaker skeletons than those of smaller animals; more than 20% of an elephant’s body mass is made up of bone, whereas only approximately 2% of a mouse’s body mass is skeleton, yet the mouse has a relatively stronger skeleton than the elephant. This inherent weakness of the limbs means that very large mammals, e.g., elephants, are constrained to adopt a graviportal posture with the legs placed nearly vertically beneath their bodies to support their body mass on columns beneath their bodies. This results in their being unable to trot or gallop as can most mammals because of the risk of placing too much shearing force on a limb that was extended at a large angle from vertical. Indeed, the limb excursions of running quadrupedal mammals scale allometrically such that those of larger animals undergo much smaller excursions than those of smaller mammals (46). As a result of these factors, very small mammals do not move their limbs at sufficiently high frequencies to make up for their short strides, and very large mammals must take shorter strides to avoid damaging their skeletons. This combination of factors results in the fastest terrestrial running mammals all having body masses of approximately 50 kg, including the cheetah (*Acinonyx jubatus*), the Indian blackbuck (*Antilope cervicapra*), and the pronghorn antelope (*Antilocapra americana*) (16,32).

Although Hill was wrong about the maximal speeds of mammals of different sizes being the same, he was remarkably accurate in his prediction of jumping ability. He based his hypothesis on consideration of the volume of muscle in the legs and speed of contraction to conclude that mammals of different body sizes should have the same acceleration at takeoff and, hence, should be capable of raising their body mass the same distance. Hill’s prediction was uncannily accurate given that the world record for high-jumping in a 500-kg horse was set by a thoroughbred named Huaso in Santiago, Chile, in 1949 at 2.47 m (19); the world record for high jumping was set by an 82-kg human, Javier Sotomayor of Cuba, in 1992 at 2.45 m (19); and a 0.25-kg lesser galago (*Galago senegalensis*) was documented to jump vertically 2.25 m (21). Given the galago’s small size relative to the other record holders (approximately 13 cm in body length), it seems likely that it raised its center of mass by at least as much as the larger animals. It seems nonintuitive that mammals differing in body mass by 2000-fold should be able to jump to the same height. Allometry can clearly be used to assess and predict performance of athletes in a variety of contexts.

THE KROGH PRINCIPLE AND EXTREMES IN ADAPTATION

I have briefly reviewed two major factors that govern how animals perform and contribute to how quickly they fatigue: body temperature and scaling with body size. The consideration of these factors constitutes one fundamental approach used in comparative physiology—determining general invariant principles that determine how animals function. The remainder of this review will focus on three cases of “problems [for which] there will be some animal of choice or a few such animals on which [they] can be most conveniently studied,” as stated by Krogh and defined by Krebs as constituting the essence of the Krogh Principle (37,38). In an interesting article, Poole and Erickson (59) have reviewed performances of mammals that have been highly selected for extreme exercise performance and compare them with human performance. In the remainder of this article, I will discuss two extreme cases of adaptation related to fatigue in nonhuman animals: migratory bird flight and diving durations of marine mammals, as well as a case of extreme adaptation for locomotor economy and potentially staving off fatigue—the hopping kangaroo.

BIRD MIGRATION

Numerous species of birds migrate seasonally to take advantage of greater availability of food resources as well as to avoid the metabolic cost of having to generate large quantities of heat to maintain their homeothermic body temperature when ambient temperatures drop during the winter. Energy savings from going into torpor are insufficient when dealing with such great temperature differentials. Because flying birds tend to be relatively small in size, they inherently have high surface-to-volume ratios and, as a result, high thermal conductances that cause them to rapidly lose heat to the surrounding air. Migration provides a solution to both of these problems by transporting the bird to an environment that is warmer during the winter months and in which there is more food available to meet the demands of its high mass-specific metabolic rate.

A remarkable feat of avian migration is that of the ruby-throated hummingbird (*Archilochus colubris*), a population of which spends the warm months of the year living in the Gulf coast states of the southeastern United States. These animals average approximately 8 cm in body length and weigh between 0.003 and 0.004 kg (3–4 g) in body mass. The smallest hummingbirds can attain maximal mass-specific rates of oxygen consumption that are 10-fold higher than those of the most elite human athletes (71). Endocrine changes triggered by shortening day length in the fall cause hyperphagia in the birds, which results in their doubling their fat mass of 1 g, after which they fly nonstop over the Caribbean Sea for 20 h or more to reach the Yucatan Peninsula in Mexico (23). The oxidation of adipose provides the energy for the flight and water generated as a waste product of that oxidation keeps the birds hydrated;

they lose approximately half of their starting body mass during the flight. The ruby-throated hummingbird's metabolic performance during migration is impressive, particularly if one considers that in relation to the physiological time scale on which the birds live, their performance is equivalent to a human athlete performing sustained exercise continuously (nonstop) at energy cost equivalent to flying, approximately 8 to 10 times his or her resting power output (41) for a period of 10 d.

Perhaps even more remarkable than the migratory feat of the ruby-throated hummingbird is that of the bar-tailed godwit (*Limosa lapponica baueri*). The bar-tailed godwit is a shorebird that averages approximately 40 cm in body length with males having a maximal body mass of 400 g and migratory females usually less than 500 g. Godwits spend the boreal summer months breeding in Alaska between late May and August then fly to spend the austral summer months in New Zealand and Australia; approximately 70,000 birds annually migrate between these locations. Godwits typically leave New Zealand around the end of March or early April and fly northward to the Korean Peninsula to refuel then continue onward to their breeding grounds in Alaska (4).

Studies of migrating bar-tailed godwits fitted with satellite telemetry transmitters have shown that these birds can fly nonstop for distances up to 11,680 km for a period of 9.4 d (17,18). Considering the difference in physiological time scales, this would be equivalent to a human athlete exercising nonstop at eight to 10 times his or her resting metabolic rate for 32.5 d.

This degree of sustained effort represents an unprecedented combination of metabolic intensity and duration (22,57,58). In turn, it raises questions about several associated physiological processes that would be expected to be altered dramatically during such a flight, including body composition (5,24,39,56,57), dehydration (33,40,64), sleep deprivation (62), and navigation (63,80). Indeed, studies are being conducted on several of these questions to better understand how these birds are able to achieve such extreme endurance performance. By determining the physiological mechanisms that permit godwits to accomplish feats that are unimaginable by human standards, it may be possible to gain insights into principles that can be applied to enhancing human endurance performance. In every respect, the sustained metabolic performance of the bar-tailed godwit during its migration is likely an unparalleled feat of endurance among animal athletes.

DIVING

The aquatic medium presents numerous challenges to homeotherms trying to survive in it. The most obvious is the lack of oxygen available to meet aerobic metabolic demand. Because marine mammals do not have access to an external source of oxygen to breathe, they must take their oxygen supply with them when they dive. In deep-diving marine mammals, e.g., whales and seals, two adaptations provide

solutions to this problem. The first is that, unlike terrestrial mammals in which the blood typically makes up approximately 7% of their body mass (i.e., blood volume $\propto 0.07 \times M^0$), marine mammals typically have twice that volume of blood, approximately 15% (35). Furthermore, whereas most mammals have hematocrits of approximately 40%, splenic contraction in diving mammals may raise theirs to approximately 65% (25), near the crossover point at which the facilitation of oxygen transport exceeds the cost of pumping blood because of increased viscosity. Although these adaptations for blood oxygen storage are important, the most prevalent adaptation found in diving mammals is an increase in muscle myoglobin concentration (35) that is correlated with dive duration capacity (52). When summed, the total volume of oxygen contained in the blood and myoglobin of diving mammals can be three to four times greater than in terrestrial mammals.

A second problem faced by deep-diving mammals is caused by the fact that hydrostatic pressure increases by 1 atmosphere with every 10 m in depth that an animal descends. This increased pressure can create problems directly with gas spaces in the body, e.g., pressure on sinuses or eardrums, as well as affecting the quantity of gases that are dissolved in the blood. Because the air in the lungs of a diving animal is compressed by the surrounding hydrostatic pressure, the partial pressure of the gases in the lungs increases. As the partial pressure of nitrogen increases, more of it dissolves in the blood that is flowing through the alveolar capillaries. If diving mammals breathed in a manner similar to human scuba divers who breathe compressed gas from a tank through a regulator that delivers gas for breathing at pressure equal to the surrounding hydrostatic pressure, they would have the same problem as scuba divers do when ascending from a deep dive. That problem originates from the nitrogen dissolved in their blood at equilibrium with the high nitrogen partial pressure in the lungs becoming supersaturated during ascent and resulting in the formation of bubbles in the blood creating downstream ischemia. In humans, this condition is called the bends, primarily because the bubbles tend to form in joints and cause severe pain leading to the afflicted individual bending over. Scuba divers can be affected even when they dive to modest depths for extended durations of time.

Because deep-diving marine mammals dive to depths far greater than human divers can survive, it would be impossible for diving mammals to have air in their lungs being pressurized so as to generate very high partial pressures of nitrogen that would dissolve in the blood. To avoid this problem, deep-diving mammals exhale completely before diving. The complete exhalation of a highly adapted diving mammal is beyond the capacity of any terrestrial mammal. This is because both seals and whales have cartilage in their bronchioles extending down to their alveoli (10,27,51,78). As a result, the surface tension of the airway lining fluid that in terrestrial mammals causes compliant small airways to close and trap a volume of high-pressure gas inside the lungs

does not do so in diving mammals. Instead, the cartilage prevents the collapse of the airways, and the animals can exhale their entire lung volume before diving, thereby leaving no gas in the alveoli to be pressurized. Although diving mammals carry no gas in their lungs when they dive, their total body oxygen stored far exceeds those of a terrestrial mammal because of the aforementioned higher values of blood volume, hematocrit, and muscle myoglobin concentration.

Compared with air, water has nearly 3400 times greater thermal capacitance, and it conducts heat nearly 25 times better than air, presenting challenges to homeotherms that are immersed to maintain body temperature. Fur and feathers that trap air may provide some insulation to shallow divers; however, they offer no benefit to deep divers. For deep divers, layers of blubber 5 cm or more thick may be the only effective mechanism to retain body heat. For very large divers, e.g., whales, hypothermia is not a problem because of the discordant allometric scaling of metabolic rate ($Y \propto M^{3/4}$) and body surface area ($Y \propto M^{2/3}$). This same relationship of the scaling of heat production increasing faster than the surface area through which it can be lost to the environment results in larger terrestrial mammals having difficulty dissipating heat compared with smaller ones. As a result, large mammals in warm climates, e.g., hippopotamuses and elephants, frequently reside in or near bodies of water into which they can transfer body heat to cooler water or spray themselves with water to facilitate evaporative cooling. Because flippers or flukes have relatively high surface-to-volume ratios that facilitate heat loss, marine mammals have evolved effective countercurrent heat exchangers in the circulations to their appendages. The countercurrent heat exchanger functions to retain heat in the animal's body because of the anatomical arrangement of the arteries and veins in the limbs (68). These vessels lie directly adjacent to one another so that as arteries carry warm blood to the appendage, they run alongside veins returning cooler blood from the periphery where the blood was cooled by surrounding water. Because the arterial blood is warmer than the venous, heat flows from artery to vein; as this thermal gradient is maintained along the entire length of the vessels, a substantial portion of heat that would have been lost to the surrounding water is instead returned to the body in the venous blood.

A factor that affects dive duration in mammals is the energy cost of locomotion, which is set by the medium in which an animal is locomoting. It is not inherently apparent to a member of a species, e.g., a human, that is not streamlined and adapted for aquatic locomotion, but the energy cost of locomotion for animals of any given size is lowest for swimming, greater for flying, and highest for running (65). This relationship illustrates that the neutral buoyancy of a mammal in water plays a dominant role in minimizing the energy required to support the body's mass and is a key factor in reducing energy cost of locomotion—the energy required to move a unit of body mass a unit distance. By contrast, a significant amount of energy is required to

overcome hydrodynamic drag associated with the water's high density (approximately 800 times that of air) through which they move, their large size that increases the area of contact with the water and generates friction, and by their ability to move at relatively high speeds. All of these factors—density, length, and speed—contribute to these animals having very high Reynolds numbers, which is a factor in the generation of turbulent flow that increases energy cost of locomotion.

Flying vertebrates can generate aerodynamic lift to support their body mass but have to contend with aerodynamic drag, whereas terrestrial mammals must actively generate muscle tension to support their body mass above the substrate, making it the most costly form of locomotion (72). In addition, the allometric relationships for energy cost of locomotion for all three modes of locomotion have significant negative slopes, and because deep-diving mammals are among the largest in body size, this means they inherently have the lowest mass-specific energy cost of locomotion of all vertebrates (65). Because energy cost of locomotion in diving mammals is low, the oxygen stored in their blood and myoglobin can sustain them for dives of long duration.

One other factor that significantly extends dive duration is the diving reflex (54). The response to submersion is highly pronounced in diving mammals and elicits bradycardia and peripheral vasoconstriction, resulting in the large supply of oxygen stored in the blood being slowly recirculated primarily between the heart and the brain, the two organs that have an absolute metabolic requirement for oxygen and aerobic metabolism. Very high concentrations of myoglobin provide oxygen to the minimally (because of the low mass-specific energy cost of locomotion) working skeletal muscles, and because of the nearly nonexistent peripheral blood flow, any lactate that forms accumulates in the muscles and is only washed out when perfusion is reinstated after the dive (13,20).

Figure 5 is a log-log plot of body mass versus dive duration for birds and mammals that are aquatic-adapted (*divers*) (upper regression) or are not aquatic-adapted (*nondivers*) (lower regression)

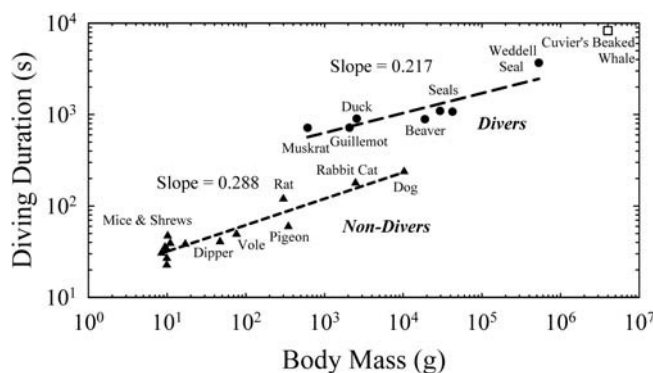


FIGURE 5—Log-log plot of body mass (abscissa) versus dive duration (ordinate) for species highly adapted by natural selection for aquatic life (*Divers*, upper curve) and those not highly adapted for aquatic life (*Nondivers*, lower curve). Note that dive durations of both groups fit slopes nearly equal to the relationship governing physiological time ($Y \propto M^{0.25}$). Also shown (open square) is the record dive duration for Cuvier's beaked whale. Redrawn from Calder (11).

(lower regression). Both regression lines have slopes that fall around the value that defines the allometric relationship for physiological time ($Y \propto M^{0.25}$). This relationship between dive duration and the scaling of physiological time also appears in data recently published on diving capacity and myoglobin (48). The recurrence of the slope of the physiological time relationship in these analyses of diving duration argues for its significant role in determining dive duration.

The extremes for depth descended by a diving mammal as well as the duration of dive have recently been reported for record-breaking dives by Cuvier's Beaked Whales (*Ziphius cavirostris*) (69). Researchers collecting more than 3700 h of diving data on these animals recorded a dive to a depth of 2992 m (nearly 300 atmospheres of hydrostatic pressure), eclipsing the previous record of a sperm whale (*Physeter microcephalus*) that had dived to a depth of 2035 m. Another Cuvier's beaked whale was recorded making a dive that lasted for 137.5 min. These are astonishing numbers which indicate that natural selection has the capacity to imbue animals with truly remarkable physiological capacities. As the 19th century Swiss-born naturalist Louis Agassiz, a professor at Harvard University and founder of its Museum of Comparative Zoology, said, "Study nature, not books."

HOPPING IN KANGAROOS

Kangaroos (genus *Macropus*; the term "macropod" refers to members of the marsupial family Macropodidae that includes kangaroos and wallabies) are among a small group of mammalian species that locomote using saltatory locomotion, or hopping. Forty years ago, it was reported that like other mammals, when red kangaroos (*Macropus rufus*) locomote at low speeds on a treadmill while wearing an open-flow calorimetry mask, their rate of oxygen consumption increases linearly with speed, although at a higher rate with increasing speed than is typical for quadrupedal mammals (15,73,75). This low-speed locomotion is described as being pentapedal because the kangaroo drags its tail on the ground. However, unlike other mammals, when the kangaroo begins hopping at higher speeds, it can go from the lowest speed at which it starts hopping ($\sim 6 \text{ km}\cdot\text{h}^{-1}$; $1.7 \text{ m}\cdot\text{s}^{-1}$) and triple that speed without increasing its rate of oxygen consumption; in fact, there is a negative slope to the linear regression of oxygen consumption versus speed, indicating it has a lower rate of oxygen consumption at higher speeds (15) (Fig. 6). The rate of oxygen consumption at $6 \text{ km}\cdot\text{h}^{-1}$ was 20 times the resting value and over twice as high as it would be for a quadruped of the same size at that speed, and the oxygen consumption did not decrease to less than that predicted for a running quadruped until the kangaroo reached a speed of $18 \text{ km}\cdot\text{h}^{-1}$. However, one animal reached a speed of $25 \text{ km}\cdot\text{h}^{-1}$ ($7 \text{ m}\cdot\text{s}^{-1}$) while wearing the mask, and the authors reported that in the wild red kangaroos maintain speeds of $40 \text{ km}\cdot\text{h}^{-1}$ ($11 \text{ m}\cdot\text{s}^{-1}$) for several kilometers and may reach speeds of $50\text{--}65 \text{ km}\cdot\text{h}^{-1}$ ($14\text{--}18 \text{ m}\cdot\text{s}^{-1}$) for short bursts. Kangaroos increase speed almost exclusively by increasing

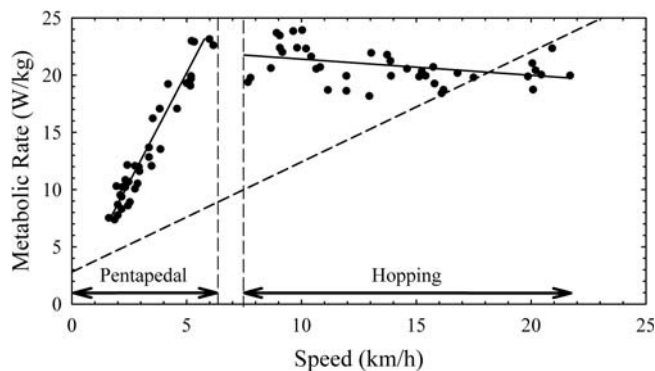


FIGURE 6—Rate of oxygen consumption as a function of speed for a red kangaroo (*Macropus rufus*) when walking pentapedally at slow speeds with its tail in contact with the ground and when hopping at higher speeds. Linear regressions (solid lines) of mass-specific energy cost of locomotion show pentapedal locomotion ($1.5\text{--}6\text{ km}\cdot\text{h}^{-1}$) requires much more energy at low speeds than quadrupedal locomotion, whereas energy cost when hopping has a negative slope and is very low at high speeds. Dashed line shows predicted energy cost of locomotion for a quadruped of the same size (73–75). Hopping becomes cheaper than quadrupedal running when the kangaroo's speed exceeds $18\text{ km}\cdot\text{h}^{-1}$. Redrawn from Taylor et al. (15,74,75).

stride length while keeping stride frequency fairly constant. The authors suggested that kangaroos may store elastic energy in structures, e.g., their Achilles tendons, and that stored energy may then be recovered in the following hop. Given that their acceleration at takeoff is greater at faster speeds, increased recovery of stored elastic energy might account for the decrease in oxygen consumption at higher speeds.

Studies of 5-kg tammar wallabies (*Macropus eugenii*) (6) found that when the animals moved pentapedally up to the speed at which they began hopping ($\sim 2\text{ m}\cdot\text{s}^{-1}$), they had equivalent rates of mass-specific oxygen consumption as quadrupeds (74). However, once they began hopping, there was no increase in the rate of oxygen consumption up to the maximum speed measured, approximately $9.5\text{ m}\cdot\text{s}^{-1}$, suggesting that smaller hoppers use a similar mechanism of elastic energy storage and recovery as do larger ones. However, measurements made of the 37-g Australian fawn hopping mouse (*Notomys cervinus*) showed that as it increased speed, its mass-specific rate of oxygen consumption increased at about half the rate of a quadrupedal mammal even when the animal was hopping with nearly constant stride frequency but increased stride length at faster speeds (14). This raised a question whether smaller hopping animals can recover elastic energy as effectively as larger ones do. This question was answered in a study of a 3-kg rodent springhare (*Pedestes capensis*), a 1.1-kg marsupial rat kangaroo (*Bettongia pencillata*), a 104-g rodent desert kangaroo rat (*Dipodomys deserti*), and a 32-g rodent Merriam's kangaroo rat (*Dipodomys merriami*) (76). For all four species, the rates of oxygen consumption increased linearly with speed and did not differ from the predicted cost of locomotion for a running quadruped (74,75), suggesting that smaller animals might not have their elastic structures scaled effectively for storing and recovering elastic strain energy.

Several research groups have undertaken studies to better understand the mechanism by which kangaroos and wallabies achieve their unique disconnect between locomotor speed and metabolic rate. Different investigators have used various combinations of treadmill measurements of oxygen consumption, force platform measurements, high-speed film or video kinematic analyses, electromyography, *ex vivo* tendon displacement, strain measurements, and *in vivo* tendon force-buckle measurements to estimate the percentage savings of energy provided by storage of elastic strain energy. These investigations have shown that estimated energy savings due to elastic storage increases with speed in the wallaby from 23% at $2.7\text{ m}\cdot\text{s}^{-1}$ to 70% at $6.2\text{ m}\cdot\text{s}^{-1}$ (1). However, others (9) have noted that those investigators overestimated the density of the tendon and this likely biased high their energy savings estimate by 27%.

Calculations of the power provided by elastic recoil were made by taking the ratio of external power output (power to raise and reaccelerate the center of mass) and metabolic power input as an index of efficiency. The investigators considered values exceeding 0.25, the maximum efficiency with which chemical energy can be converted by muscle into mechanical work, as a minimum value of the elastic recoil power given that muscles usually do not operate at 0.25 efficiency. Those investigators calculated estimated values of efficiency for the 2.5-kg springhare as increasing from 0.16 to 0.26 as speed increased from 10 to $25\text{ km}\cdot\text{h}^{-1}$, whereas for the 18-kg kangaroo, they increased from 0.25 to 0.75 for the same range in speeds, indicating substantial contributions of elastic recoil (7,12).

Measurements of the energetics of red kangaroos hopping uphill on a treadmill were made to measure the efficiency of their muscles working against gravity to determine whether their muscles are unusually efficient. That study measured limb angles of kangaroos hopping over a wide speed range to evaluate if a more upright limb posture (i.e., joints flexed less) allows them to operate with greater effective mechanical advantage (EMA). The study estimated peak tendon stresses to evaluate if these might limit maximal hopping speed or set preferred speeds (36). Hopping uphill resulted in oxygen consumption increasing linearly with speed, with a maximal mass-specific value of $180\text{ mL O}_2\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$, approximately 250% of the rate kangaroos normally have when hopping on the level and nearly twice the value of the most elite human athlete measured. It is also about the same as a racing-fit thoroughbred race horse, but only 45% of the most highly aerobic mammal known, the 1.5-g Etruscan shrew. The efficiencies with which kangaroos hopped uphill were equivalent to those of dogs running up an equivalent grade (61). The EMA of kangaroos was constant at all speeds and has been shown to be constant and invariant with body size (7) in macropods, which is different than that in eutherians (members of the mammalian clade Eutheria, of which all living members are placental mammals, unlike marsupials) in which it changes regularly with size. This factor contributed to the aforementioned graviportal posture

of elephants that Hill did not consider when he predicted uniform maximal running speeds for mammals of different sizes. Other authors noted that the high value for tendon stress in hopping kangaroos of 79 MPa (7,9) is very near the ultimate breaking stress for tendons (100 MPa), indicating that kangaroos hop with very small safety margins. This may indicate why they tend to hop at lower speeds even though hopping at faster speeds would use less energy to transport them over any distance.

It has been shown that when kangaroos move pentapedally, their tails function as a “leg” and provide as much propulsive force as the fore- and hindlimbs combined as well as supplying approximately 14% of the vertical force that supports the body off the ground during a stride (53). The kangaroo performs as much mass-specific work with its tail as a human does with one of his or her legs while walking. Furthermore, because kangaroos swing both hind legs and both front legs in tandem when moving pentapedally, they can have relatively small forelimbs that reduce the kinetic energy cost when hopping as both forelimbs and hindlimbs need not move the same distance with each stride as is the case with quadrupeds.

Anatomical components (cross-sectional areas of muscles and attached tendons as well as stress-strain curves for tensile loading of tendons) of hind limbs of macropods ranging in body mass from 0.5 to 38 kg have been dissected, measured, and analyzed to determine their allometric relationship (7). Investigators found that the potential for elastic strain energy storage in macropods scales $\propto M^{1.73}$, whereas for eutherian quadrupeds, it scales $\propto M^{1.28}$. This finding indicates that a 1.6-kg macropod or eutherian could store the same amount of strain energy, whereas a 50-kg macropod can store 6.5 times as much as a eutherian quadruped of the same size. As mentioned previously, investigators also found that the EMA of macropods is constant and independent of body size, unlike eutherian mammals. These findings might help to explain the observation that small hopping

mammals do not demonstrate independence of energy cost and speed.

The results of these varied studies do not completely answer the question as to how hopping kangaroos and wallabies can separate hopping speed from energy cost, but they provide some insights into factors that are likely involved. Furthermore, the unique ability of kangaroos and wallabies to hop at faster speeds with decreasing rates of oxygen consumption suggests a mechanism by which they potentially could delay onset of fatigue.

SUMMARY

In this review, I have used the two complementary approaches of comparative physiology—identifying general principles that broadly govern how animals function as well as considering extremes of adaptation that enable highly selected animals to perform feats that are impossible for humans. I first examined two of the most ubiquitous factors that influence metabolism and exercise performance in animals—body temperature and body size. Both play major roles in determining endurance times in animal (including human) athletes, the former via Q_{10} effects and the latter via the scaling of physiological time. I also reviewed two examples of extreme endurance performance in animals, migratory flights of the ruby-throated hummingbird and bar-tailed godwit, and diving durations in marine mammals. Finally, I discussed the unique ability of the kangaroo to increase hopping speed without increasing its rate of oxygen consumption, and even reducing it at higher speeds. Using these approaches in combination can provide unique insights into understanding how animals perform and function and capitalize on using their adaptations as an experimental tool.

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REFERENCES

- Alexander RM, Vernon A. The mechanics of hopping by kangaroos (Macropodidae). *J Zool Lond.* 1975;177:265–303.
- Anderson JF, Rahn H, Prange HD. Scaling of skeletal mass to body mass in birds and mammals. *Am Nat.* 1979;113:103–22.
- Barany M. ATPase activity of myosin correlated with speed of muscle shortening. *J Gen Physiol.* 1967;50(Suppl):197–218.
- Battley PF. Consistent annual schedules in a migratory shorebird. *Biol Lett.* 2006;2:517–20.
- Battley PF, Piersma T, Dietz MW, Tang S, Dekinga A, Hulsman K. Empirical evidence for differential organ reductions during trans-oceanic bird flight. *Proc Biol Sci.* 2000;267:191–5.
- Baudinette RV, Snyder GK, Frappell PB. Energetic cost of locomotion in the tammar wallaby. *Am J Physiol.* 1992;262:R771–8.
- Bennett MB, Taylor GC. Scaling of elastic strain energy in kangaroos and the benefits of being big. *Nature.* 1995;378:56–9.
- Bernard C. *Introduction à l'étude de la médecine expérimentale (Introduction to the study of experimental medicine)*. Paris: J.B. Baillière et Fils; 1865. p. 400.
- Biewener AA, Baudinette RV. In vivo muscle force and elastic energy storage during steady-speed hopping of tammar wallabies (*Macropus eugenii*). *J Exp Biol.* 1995;198:1829–41.
- Boyd RB. A gross and microscopic study of the respiratory anatomy of the Antarctic Weddell seal *Leptonychotes weddelli*. *J Morphol.* 1975;147:309–36.
- Calder WA. *Size, Function, and Life History*. Cambridge (MA): Harvard University Press; 1984. p. 431.
- Cavagna GA, Heglund NC, Taylor CR. Mechanical work in terrestrial locomotion: two basic mechanisms for minimizing energy expenditure. *Am J Physiol.* 1977;233:R243–61.
- Davis RW. Lactate and glucose metabolism in the resting and diving harbor seal (*Phoca vitulina*). *J Comp Physiol.* 1983;153:275–88.
- Dawson TJ. Energetic cost of locomotion in Australian hopping mice. *Nature.* 1976;259:305–7.
- Dawson TJ, Taylor CR. Energetic cost of locomotion in kangaroos. *Nature.* 1973;246:313–4.

16. Garland T. The relation between maximal running speed and body mass in terrestrial mammals. *J Zool Lond.* 1983;199:157–70.
17. Gill RE, Piersma T, Hufford G, Servranckx R, Riegers A. Crossing the ultimate ecological barrier: evidence for an 11 000-km-long nonstop flight from Alaska to New Zealand and Eastern Australia by bar-tailed godwits. *Condor.* 2005;107:1–20.
18. Gill RE, Tibbitts TL, Douglas DC, et al. Extreme endurance flights by landbirds crossing the Pacific Ocean: ecological corridor rather than barrier? *Proc R Soc B.* 2009;276:447–57.
19. *Guinness World Records 2015.* London: Guinness World Records; 2014, 256 p.
20. Guppy M, Hill RD, Schneider RC, et al. Microcomputer-assisted metabolic studies of voluntary diving of Weddell seals. *Am J Physiol.* 1986;250:R175–87.
21. Hall-Craggs ECB. An analysis of the jump of the lesser galago (*Galago senegalensis*). *J Zool.* 1965;147:20–9.
22. Hammond KA, Diamond J. Maximal sustained energy budgets in humans and animals. *Nature.* 1997;396:457–62.
23. Hargrove JL. Adipose energy stores, physical work, and the metabolic syndrome: lessons from hummingbirds. *Nutr J.* 2005;4:36.
24. Hedenstrom A, Alerstam T. Optimum fuel loads in migratory birds: distinguishing between time and energy minimization. *J Theor Biol.* 1997;189:227–34.
25. Hedrick MS, Duffield DA, Cornell LH. Blood viscosity and optimal hematocrit in a deep-diving mammal, the northern elephant seal (*Mirounga angustirostris*). *Can J Zool.* 1986;64:2081–5.
26. Heglund NC, Taylor CR, McMahon TA. Scaling stride frequency and gait to animal size: mice to horses. *Science.* 1974;186:1112–3.
27. Henk WG, Haldiman JT. Microanatomy of the lung of the bowhead whale *Balaena mysticetus*. *Anat Rec.* 1990;226:187–97.
28. Hill AV. The dimensions of animals and their muscular dynamics. *Sci Prog.* 1950;38:209–30.
29. Hill DW. The critical power concept. A review. *Sports Med.* 1993;16:237–54.
30. Jackson DC. Temperature and hypoxia in ectothermic tetrapods. *J Therm Biol.* 2007;32:125–33.
31. Jones AM, Vanhatolol A, Burnley M, Morton RH, Poole DC. Critical power: implications for determination of $\dot{V}O_{2max}$ and exercise tolerance. *Med Sci Sports Exer.* 2010;42:1876–90.
32. Jones JH, Lindstedt SL. Limits to maximal performance. *Annu Rev Physiol.* 1993;55:547–69.
33. Klaassen M. May hydration risk govern long-distance migratory behaviour? *J Avian Biol.* 2004;35:4–6.
34. Kolbe T, Dennis SC, Selley E, Noakes TD, Lambert MI. The relationship between critical power and running performance. *J Sports Sci.* 1995;13:265–9.
35. Kooyman GL, Castellini MA, Davis RW. Physiology of diving in marine mammals. *Annu Rev Physiol.* 1981;43:343–56.
36. Kram R, Dawson TJ. Energetics and biomechanics of locomotion by red kangaroos (*Macropus rufus*). *Comp Biochem Physiol B.* 1998;120:41–9.
37. Krebs HA. The August Krogh Principle: “for many problems there is an animal on which it can be most conveniently studied.” *J Exp Biol.* 1975;194:221–6.
38. Krogh A. The progress of physiology. *Science.* 1929;70:200–4.
39. Kvist A, Lindstrom A, Green M, Piersma T, Visser GH. Carrying large fuel loads during sustained bird flight is cheaper than expected. *Nature.* 2001;413:730–2.
40. Landys MM, Piersma T, Visser GH, Jukema J, Wijk A. Water balance during real and simulated long-distance migratory flight in the bar-tailed godwit. *Condor.* 2000;102:645–52.
41. Lasiewski RC. Oxygen consumption of torpid, resting, active, and flying hummingbirds. *Physiol Zool.* 1963;36:122–40.
42. Lepock JR. Cellular effects of hyperthermia: relevance to the minimum dose for thermal damage. *Int J Hyperthermia.* 2003;19:252–66.
43. Lindstedt SL, Calder WA. Body size and longevity in birds. *Condor.* 1976;78:91–4.
44. Lindstedt SL, Calder WA. Body size, physiological time, and longevity of homeothermic animals. *Quart Rev Biol.* 1981;56:1–15.
45. Lindstedt SL, Hoppeler H, Bard KM, Thronson HA Jr. Estimate of muscle-shortening rate during locomotion. *Am J Physiol.* 1985;249:R699–703.
46. McMahon TA. Using body size to understand the structural design of animals: quadrupedal locomotion. *J Appl Physiol.* 1975;39:619–27.
47. McMahon TA, Bonner JT. *On Size and Life.* New York: W.H. Freeman; 1983. p. 255.
48. Mirceta S, Signore AV, Burns JM, Cossins AR, Campbell KL, Berenbrink M. Evolution of mammalian diving capacity traced by myoglobin net surface charge. *Science.* 2013;340:1234192.
49. Monod H, Scherrer J. The work capacity of a synergic muscular group. *Ergonomics.* 1965;8:329–38.
50. Morton RH. The critical power and related whole-body bioenergetic models. *Eur J Appl Physiol.* 2006;96:339–54.
51. Ninomiya H, Inomata T, Shirouzu H, Katsumata E. Microanatomy of the terminal air spaces of Baird’s beaked whale (*Berardius bairdii*) lungs. *J Vet Med Sci.* 2005;67:473–9.
52. Noren SR, Williams TM. Body size and skeletal muscle myoglobin of cetaceans: adaptations for maximizing dive duration. *Comp Biochem Physiol A.* 2000;126:181–91.
53. O’Connor SM, Dawson TJ, Kram R, Donelan JM. The kangaroo’s tail propels and powers pentapedal locomotion. *Biol Lett* [Internet]. 2014. doi:http://dx.doi.org/10.1098/rsbl.2014.0381.
54. Panneton WM. The mammalian diving response: an enigmatic reflex to preserve life? *Physiology.* 2013;28:284–97.
55. Pennycuik CJ. *Newton Rules Biology: A Physical Approach to Biological Problems.* Oxford: Oxford University Press; 1992. p. 111.
56. Pennycuik CJ. Computer simulation of fat and muscle burn in long-distance bird migration. *J Theor Biol.* 1998;191:47–61.
57. Pennycuik CJ, Battley PF. Burning the engine: a time-marching computation of fat and protein consumption in a 5420-km non-stop flight by great knots, *Calidris tenuirostris*. *Oikos.* 2003;103:323–32.
58. Peterson CC, Nagy KA, Diamond J. Sustained metabolic scope. *Proc Natl Acad Sci USA.* 1990;87:2324–8.
59. Poole DC, Erickson HH. Highly athletic terrestrial mammals: horses and dogs. *Compr Physiol.* 2011;1:1–37.
60. Pypendop BH, Jones JH. Indexing cardiovascular and respiratory variables: allometric scaling principles. *Vet Anaesth Analg.* 2015;42:343–9.
61. Raab JL, Eng P, Waschler RA. Metabolic cost of grade running in dogs. *J Appl Physiol.* 1976;41:532–5.
62. Rattenborg NC, Mandt BH, Obermeyer WH, et al. Migratory sleeplessness in the white-crowned sparrow (*Zonotrichia leucophrys gambelii*). *PLoS Biol.* 2004;2:924–36.
63. Sandberg R, Holmquist B. Orientation and long distance migration routes: an attempt to evaluate compass cue limitations and required precision. *J Avian Biol.* 1998;29:626–36.
64. Schmaljohann H, Bruderer B, Liechti F. Sustained bird flights occur at temperatures beyond expected limits of water loss. *Anim Behav.* 2008;76:1133–8.
65. Schmidt-Nielsen K. Locomotion: energy cost of swimming, flying, and running. *Science.* 1972;177:222–8.
66. Schmidt-Nielsen K. *Scaling: Why Is Animal Size so Important?* New York: Cambridge University Press; 1984. p. 245.
67. Schmidt-Nielsen K. *Animal Physiology: Adaptation and Environment.* 5th ed. New York: Cambridge University Press; 1997. p. 607.
68. Scholander PF, Schevill WE. Counter-current vascular heat exchange in the fins of whales. *J Appl Physiol.* 1955;8:279–82.
69. Schorr GS, Falcone EA, Moretti DJ, Andrews RD. First long-term behavioral records from Cuvier’s beaked whales (*Ziphius cavirostris*) reveal record-breaking dives. *PloS One.* 2014;9(3):e92633.
70. Speakman JR. Body size, energy metabolism and lifespan. *J Exp Biol.* 2005;208:1717–30.

71. Suarez RK. Hummingbird flight: sustaining the highest mass-specific metabolic rates among vertebrates. *Experientia*. 1992;48:565–70.
72. Taylor CR. Relating mechanics and energetics during exercise. *Adv Vet Sci Comp Med*. 1994;38a:181–215.
73. Taylor CR, Caldwell SL, Rowntree VJ. Running up and down hills: some consequences of size. *Science*. 1972;178:1096–7.
74. Taylor CR, Heglund NC. Energetics and mechanics of terrestrial locomotion. *Annu Rev Physiol*. 1982;44:97–107.
75. Taylor CR, Schmidt-Nielsen K, Raab JL. Scaling of energetic cost of running to body size in mammals. *Am J Physiol*. 1970;219:1104–7.
76. Thompson SD, MacMillen RE, Burke EM, Taylor CR. The energetic cost of bipedal hopping in small mammals. *Nature*. 1980;287:223–4.
77. Vandewalle H, Vautier JF, Kachouri M, Lechevalier JM, Monod H. Work-exhaustion time relationships and the critical power concept. A critical review. *J Sports Med Phys Fitness*. 1997;37:89–102.
78. Wessels JC, Chase CC. Light and electron microscopical observations on the terminal airways and alveoli of the lung of the SA (Cape) fur seal *Arctocephalus pusillus*. *The Onderstepoort J Vet Res*. 1998;65:253–62.
79. Wilkie DR. Man as a source of mechanical power. *Ergonomics*. 1960;3:1–8.
80. Williams TC, Williams JM. The migration of birds over the Pacific Ocean. In: N Adams, R Slotow, editors. *Acta XXII Congressus Internationalis Ornithologici, Durban, South Africa*. Johannesburg (South Africa): Bird Life South Africa; 1999. pp. 1948–57.