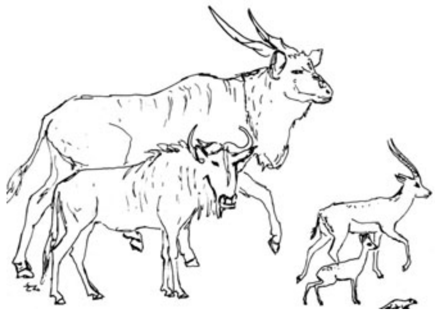
Inside JEB is a twice monthly feature, which highlights the key developments in the *Journal of Experimental Biology*. Written by science journalists, the short reports give the inside view of the science in JEB.

Inside JEB

SIZE MATTERS



How an animal's mass affects its physiology has intrigued scientists for over a century. Animals range in size from tiny shrews weighing in at a few grams up to the truly colossal. Despite countless attempts to define scaling laws that predict how an animal's size affects many aspects of its physiology, from locomotion to lifespan, the debate is far from over. In particular, two rival theories concerning the relationship between metabolic rate and body mass continue to stimulate lively discussion. While some researchers argue that basal metabolic rate scales with body mass raised to the power of 2/3, others staunchly defend a 3/4 scaling exponent. But at present there is no compelling evidence to suggest that either of these is the 'true' value; perhaps it lies somewhere in between, or perhaps there simply isn't a universal scaling law.

There have been many attempts to find a universal law that predicts relationships between an organism's size and physiological functions. But as the theories and data accumulate, it has become ever more difficult to navigate through the controversial field of allometric scaling. To assess our current understanding of scaling laws, Hans Hoppeler and Ewald Weibel from the University of Bern gathered together contributions from physicists, engineers and biologists, discussing their latest ideas and observations on allometric scaling. 'There is a lot of controversy in this field,' Hoppeler says, 'because we still don't have a single scaling theory that predicts everything you see in the data.' Weibel adds, 'the main incentive for this collection was to encourage theoreticians and empiricists to work together to reconsider and possibly revise scaling theories in light of the rapidly accumulating data.'

BASAL METABOLIC RATE AND CELLULAR ENERGETICS

Launching the collection on a controversial note, Geoffrey West and James Brown make their case for a universal scaling law that spans biological systems ranging in size from molecular units of the cells' metabolic machinery to trees and mammals (p. 1575). They propose that the universal fractal-like branching networks of fuel delivery systems, such as animal blood vessels and plant vascular systems, account for the scaling of whole body metabolic rate with body mass to the 3/4 power. They conclude with a 'bold but exciting vision' for the future: 'we see the prospects for the emergence of a general theory of metabolism that will play a role in biology similar to the theory of genetics.'

Moving from the organismal to the cellular level, Anthony Hulbert and Paul Else suggest that the chemical composition of cell membranes has a dramatic effect on a creature's metabolic rate (p. 1593). Knowing that cell membrane fatty acid composition varies with changing body mass in mammals and birds, Hulbert and Else have developed the 'membrane pacemaker' theory of metabolism. They present evidence that animals with higher levels of poly-unsaturated fatty acids in their cell membranes usually have higher metabolic rates, leading to the suggestion that cell membrane composition acts as a pacemaker. Hulbert and Else speculate that, besides regulating the pace of life, differences in cell membrane composition may even be related to lifespan in different-sized animals.

Other metabolic factors that vary with body size are the levels of metabolic enzyme activities in muscle; larger animals have lower mitochondrial enzyme activity and higher glycolytic enzyme activity than smaller animals. Christopher Moyes and Christophe LeMoine survey genetic explanations for this relationship between bioenergetic enzymes and body mass (p. 1601). They comprehensively review the role of various transcriptional regulators that control mitochondrial gene expression in muscle cells. But their attempt to uncover allometric patterns in the enzymes that support metabolic rate reveals that none of these regulators provides a satisfactory explanation for the observed differences between enzyme activity in large and small animals.

Several contributions in this collection argue for a universal scaling law. However, Craig White and Roger Seymour sound a note of caution (p. 1611). Many early studies of the relationship between basal metabolic rate and body mass were based on data sets comprising animals ranging in body mass by 18 orders of magnitude. But White and Seymour suspect that large herbivores were over-represented in these studies, resulting in an inflated mass-scaling exponent because the ruminants' fermenting digestion process makes it impossible to measure 'true' basal metabolic rate. Their re-analyses of these previous data sets indicate that the value of the exponent clearly depends on the conditions under which data are selected, and that truly basal mammalian metabolism does not scale as body mass to the 3/4 power. They recommend that, in future, researchers should carefully consider whether the metabolic rates that they include in their analyses have really been calculated under identical conditions.

ACTIVITY-INDUCED VARIATION OF METABOLISM

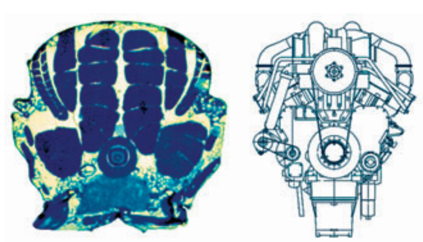
While much effort has been devoted to deriving scaling laws for basal metabolic rate, this may not be the best metabolic measurement to focus on, since most animals routinely function at much higher metabolic rates during their daily chores. Analysing 229 species of birds, mammals and reptiles, Kenneth Nagy suggests that an animal's field metabolic rate – the metabolic rate while it's going about its day-to-day business – may be a more relevant measure of an animal's energy demands (p. 1621). Ewald Weibel and Hans Hoppeler in turn focus on maximal sustained oxygen consumption rate – the upper limit of an organism's aerobic metabolism (p. 1635). Investigating 11 mammalian species, they find that variation of maximal metabolic rate with body size is closely linked to the volume of mitochondria and capillaries in locomotor muscle. They conclude that the scaling of maximal metabolic rate is determined by the energy needs of maximally working muscle cells, and that scaling is determined by variations of this demand with body size.

But deciding which type of metabolic rate has the greatest biological relevance is overshadowed by another problem; analyses of basal, field and maximal metabolic rates all report different scaling exponents. To explain this, Raul Suarez and Charles Darveau argue that simple models based on the assumption that metabolic rates are supply-limited, such as Geoffrey West's model, can only be part of the story (p. 1627). 'Metabolic scaling is such a wonderful, many-splendoured thing that models based on supply-limitation alone fail to do it justice,' they say. Reviewing the evidence from multiple-cause models, Suarez and Darveau conclude that energy supply and demand systems would be better viewed as having co-evolved, ensuring that fuel delivery and consumption rates are matched to each other at any activity level.

LOCOMOTION AND ENERGY DEMAND

Staying with the theme of energy supply and demand, R. McNeill Alexander discusses how muscle efficiency scales with body mass across different modes of locomotion (p. 1645). He highlights how simple locomotion models – birds flying like aircraft, insects hovering like helicopters and fish swimming like submarines – can offer valuable insights into complex physiological and biomechanical functions. He concludes that larger animals, at least those that are running or flying, have more efficient muscles than smaller animals.

James Marden examines another scale effect in locomotion; how net force production relates to body mass (p. 1653). He finds that size-assorted groups of biological and man-made machines – from muscle proteins through animals that are flying, running and swimming, up to piston engines and jets – have similar performance characteristics because they are constrained by fundamental physical limits. This leads Marden to the startling conclusion that a motor's force output is always proportional to its mass raised to a scaling exponent that ranges from 2/3 to 1, depending on the motor's size, and that this holds for both biological and man-made motors.



But all these systems are subject to damaging forces. How have organisms adapted to withstand the ever-increasing forces as they scale up – for example, as animals mature? Andrew Biewener rounds off this section with a review of skeletal scaling in terrestrial animals; how limb bones scale to tolerate the forces that they have to endure during walking and running (p. 1665). Perhaps surprisingly, bone and muscle stresses don't simply increase with body size. By changing their posture and becoming more erect as they grow, animals manage to keep bone and muscle stresses fairly constant over a broad size range from 0.04 to 300 kg.

CIRCULATION AND BODY SIZE

To meet the body's energetic demands, an animal needs to have an efficient fuel supply system, such as the branching delivery network systems found in plants and animals. Building on this concept, Adrian Bejan has constructed a general theory of optimal design for biological systems based on the constructal law, which states that a flow system's architecture will evolve in such a way that it provides easier access to its currents (p. 1677). Applying this design law to living systems, Bejan shows that the constructal law accounts for a 3/4 mass scaling exponent in an astounding variety of situations, ranging from hair diameter in fur to optimal organ sizes. He concludes with the intriguing suggestion that 'biology and natural selection have just been made a part of physics.'

Moving from the large scale to the microscopic, Thomas Dawson focuses on the scaling of animal vascular systems to body mass, and finds that the radius, length and number of blood vessels in microscale capillary networks follow essentially the same pattern in all mammals (p. 1687). Knowing that vascular networks function as oxygen transfer systems, Dawson also finds that oxygen transfer rates vary with mammal body mass raised to the 3/4 power.

Scaling of vascular systems is just as important for birds as it is for mammals; Charles Bishop explains that flight performance depends on well-oxygenated flight muscle fibres. But since heart rate drops with increasing body mass, this may reduce blood flow rate to the flight muscles of larger birds, compromising their performance. Wondering if circulatory constraints limit large birds, Bishop modelled the maximum sustainable flight performance of 15 migrating bird species (p. 1695). These aerodynamic models led Bishop to the conclusion that birds' flight muscle efficiency scales with body mass, and that circulatory constraints may indeed ultimately limit flight performance.

Returning to the basic connection between metabolic rate and body temperature, José Chaui-Berlinck and colleagues note that unusual body temperature patterns have been reported for small mammals. Wondering whether small warm-blooded creatures might be a special case when it comes to body temperature control, they modelled changes in metabolic rate and body temperature over time for a range of mammalian body sizes (p. 1709). The team's models suggest that the body temperature control mechanism itself is subject to size effects, a problem that should not be overlooked in the future.

LIFE SPAN, REPRODUCTION AND ECOLOGY

Why do bigger animals live longer than small ones? John Speakman revisits this age-old observation in his investigation of the scaling relationship between metabolic rate and aging (p. 1717). It seems simple enough: total energy expenditure over a creature's lifetime is fixed, and since a gram of elephant expends its energy more slowly than a gram of shrew, elephants live longer than shrews. 'Live fast, die young' encapsulates this 'rate of living' theory. A possible mechanism that links metabolism to aging is provided by the 'free radical theory', which suggests that oxygen free radicals, a by-product of metabolism, damage cells and cause mortality. But the data don't fit the expectations of these models; clearly, the truth is more complicated than either of these theories suggests. Comparing birds and mammals to test these theories may not be fair, Speakman argues, since these groups will differ in many other biological aspects besides metabolic rate and lifespan. He concludes that a potential avenue for future research is to look at individual variation in the relationship between metabolic rate and lifespan *within* species rather than *between* species.

Also with a view to improving future allometric studies, Robert Martin and colleagues highlight some of the potential methodological problems with allometric scaling analyses (p. 1731). An understanding of these technical problems and how to circumvent them is clearly important for future work in this already contentious field.

While Speakman and Martin consider allometric relationships at the level of the individual organism, Pablo Marquet and colleagues point out that scaling relationships are also found at the ecosystem level (p. 1749). To show how body size scaling relationships 'provide a fresh perspective to tackle ecological complexity' they review the remarkable diversity of these relationships from invertebrates to mammals in marine, freshwater and terrestrial ecosystems. They identify encouraging recent theoretical developments such as the metabolic theory of ecology, which 'attempts to explain material and energetic fluxes, in ecological systems, from first principles of thermodynamics, chemical reaction kinetics, and fractal-like biological structures.' They conclude that 'the way ahead is certainly challenging.'

AT THE CROSSROADS OF THEORY AND EXPERIMENT

So, where do we go from here? Hoppeler and Weibel hope that the scientific community will take up the challenge to understand why experimental data don't always fit the models. 'To make headway and adjust the models to accommodate new data, modellers and experimentalists will have to work together to solve these controversial issues,' Weibel says. 'A universal scaling theory may never be found,' Hoppeler admits. But they are optimistic that this thought-provoking collection of scaling papers will trigger fruitful collaborations between empiricists and theoreticians.

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