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The Pace of Life: Metabolic Energy, Biological Time, and Life History

James H. Brown^{*,†}, Joseph R. Burger[†], Chen Hou and Charles A.S. Hall[§]

^{*}Department of Biology, University of New Mexico, Albuquerque, NM 87131, USA; [†]Department of Biology, University of Kentucky, Lexington, KY 40506, USA; [‡]Department of Biological Science, Missouri University of Science and Technology, Rolla, MO 65409, USA; [§]Department of Environmental and Forest Biology and Program in Environmental Science, State University of New York, College of Environmental Science and Forestry, Syracuse NY, 13210, USA

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¹E-mail: jhbrown@unm.edu

Synopsis New biophysical theory and electronic databases raise the prospect of deriving fundamental rules of life, a conceptual framework for how the structures and functions of molecules, cells, and individual organisms give rise to emergent patterns and processes of ecology, evolution, and biodiversity. This framework is very general, applying across taxa of animals from 10^{-10} g protists to 10^8 g whales, and across environments from deserts and abyssal depths to rain forests and coral reefs. It has several hallmarks:

- (1) Energy is the ultimate limiting resource for organisms and the currency of biological fitness.
- (2) Most organisms are nearly equally fit, because in each generation at steady state they transfer an equal quantity of energy (~ 22.4 kJ/g) and biomass (~ 1 g/g) to surviving offspring. This is the equal fitness paradigm (EFP).
- (3) The enormous diversity of life histories is due largely to variation in metabolic rates (e.g., energy uptake and expenditure via assimilation, respiration, and production) and biological times (e.g., generation time). As in standard allometric and metabolic theory, most physiological and life history traits scale approximately as quarter-power functions of body mass, m (rates as $\sim m^{-1/4}$ and times as $\sim m^{1/4}$), and as exponential functions of temperature.
- (4) Time is the fourth dimension of life. Generation time is the pace of life.
- (5) There is, however, considerable variation not accounted for by the above scalings and existing theories. Much of this “unexplained” variation is due to natural selection on life history traits to adapt the biological times of generations to the clock times of geochronological environmental cycles.
- (6) Most work on biological scaling and metabolic ecology has focused on respiration rate. The emerging synthesis applies conceptual foundations of energetics and the EFP to shift the focus to production rate and generation time.

Introduction

Recent advances in theory and data raise the prospect of a new synthesis for ecology. This synthesis is based explicitly on energy and metabolism, on laws of physics, and first principles of biology. It shows how the structure and function of molecules, cells, and individual organisms give rise to emergent patterns and processes of populations, communities, and ecosystems. It scales up and down: (i) across space and time, from microns

and nanoseconds at the molecular level to kilometers and millennia at the biosphere level; (ii) across body sizes and taxa of animals, from 10^{-10} g protists to 10^8 g whales; and (iii) across environments, from sparsely inhabited deserts and abyssal depths to biologically rich tropical forests and coral reefs (Hutchinson 1959; Van Valen 1973, 1980; Brown 1981, 1995; Brown et al. 2004, 2018; Loreau, M. 2010; Sibly et al. 2012; Worm and Titensor 2018; Burger et al. 2021).

This new ecological synthesis is based on unifying themes of metabolic energy and biological time:

Metabolism. It is the uptake, processing, and release of energy and materials by organisms. The rates of metabolic processes link biochemistry and physiology to emergent patterns and processes of ecology and evolution (e.g., [Hutchinson 1959](#); [Brown 1981, 1995](#); [Peters 1983](#); [Brown et al. 2004](#); [Marquet et al. 2005](#); [Schramski et al. 2015](#); [Hatton et al. 2015, 2019](#)). The most relevant metabolic rate is the rate of biomass production: the rate at which biomass energy assimilated from the environment is passed on to surviving offspring.

Biological time. It is the pace of life—the speed of living—plays out in biological time rather than clock or geochronological time (e.g., [Winfree 1980](#); [Calder 1984](#); [Gillooly et al. 2002](#)). The most relevant biological time is generation time. At all levels from molecules to ecosystems, generation time rescales the pace of life, adjusting metabolic processes to intrinsic biological constraints of body size and temperature and to extrinsic environmental conditions of abiotic stress, biotic interactions, and diel, lunar and annual cycles.

Energy is the currency of biological fitness, the ultimate limiting resource for living things. As [Boltzmann \(1886\)](#) pointed out “The ‘struggle for existence’ of living beings is . . . for the possession of the free energy obtained, chiefly by means of the green plant, from the transfer of radiant energy from the hot sun to the cold earth.” See also [Lotka \(1922\)](#), [Odum \(1971\)](#), [Van Valen \(1980\)](#), [Brown \(1981, 1995, Brown et al. \(2004, 2018\)\)](#). Solar energy, captured in organic molecules by net primary production of photosynthetic plants, is transformed by metabolic processes, used by individual organisms to synthesize ATP and produce offspring, and passed through the food chains of ecosystems. Biophysical laws govern the fluxes and stocks of energy, and the resulting patterns of structure and function reflect universal rules of life. This paper focuses on animals, from unicellular protists to giant invertebrates and vertebrates, but the biophysical laws and basic metabolic theory should apply to all organisms, including plants and microbes.

One cornerstone of the emerging synthesis is the equal fitness paradigm (EFP; [Brown et al. 2018](#), [Burger et al. 2021](#)). When populations are stable, which usually is approximated over modest scales of space and time, parents pass an equal quantity of energy (22.4 kJ/g) and mass (1 g/g) to surviving offspring in the next generation. This unifying commonality underlies the amazing diversity of living things, which span many orders of magnitude in body mass, physiological rates, and biological times, from unicellular microbes to giant clams, fish, whales, dinosaurs, and trees. Another cornerstone is the systematic scaling of life history traits with body

size and temperature. These “scaling laws” reflect powerful biophysical constraints, but they are not absolute ([Peters 1983](#); [Calder 1984](#); [Schmidt-Neilson 1984](#); [Brown et al. 2004](#); [Sibly et al. 2012](#); [Uyeda et al. 2017](#)). In large part, this is because anatomical, physiological, and life history traits have been modified by natural selection to adapt the intrinsic biological times of generations to the extrinsic clock times of geochronological cycles.

The goal of this paper and the emerging metabolic theory of life history is to explain both the common themes and the patterns of variation based on a small number of well-established “scientific laws” and “empirical facts.” In this synthesis paper, we focus on how energy balance constrains the allocation of assimilated energy between respiration and production, and how this allocation affects variation in life history traits, including the pervasive quarter-power scaling with body mass and Q_{10} scaling with temperature.

Energy and fitness

The EFP

We start with Boltzmann’s foundational principle that energy, the ultimate limiting resource for living things, is the currency of biological fitness. Energy allocation to fitness can be quantified as

$$E = P_{coh} GFQ, \quad (1)$$

where E is energetic fitness, the quantity of biomass energy passed from a parent to a surviving offspring in one generation, P_{coh} is mass-specific rate of cohort biomass production amortized over a generation, G is the generation time from birth to death, F is the fraction of production that is passed through to *surviving* offspring, and Q is the energy density of biomass (≈ 22.4 kJ/g dry weight). Q is essentially constant, because protoplasm of most organisms has similar chemical and energy content. Consequently, the above equation can be simplified and rewritten as

$$M = 1 = P_{coh} GF, \quad (2)$$

where M is the quantity of biomass passed from a parent to surviving offspring in units of mass per body mass per generation (e.g., g/g per generation), P_{coh} is the mass-specific rate of cohort biomass production in units of mass per body mass per time (e.g., g/g/y), G is the generation time in units of time (e.g., y), and F is the unitless fraction of production passed on to the *surviving* offspring that replaces its parent. This simplification allows quantification of fitness and metabolic parameters in units of mass, and it facilitates empirical tests of the theory using large electronic databases on diverse organisms.

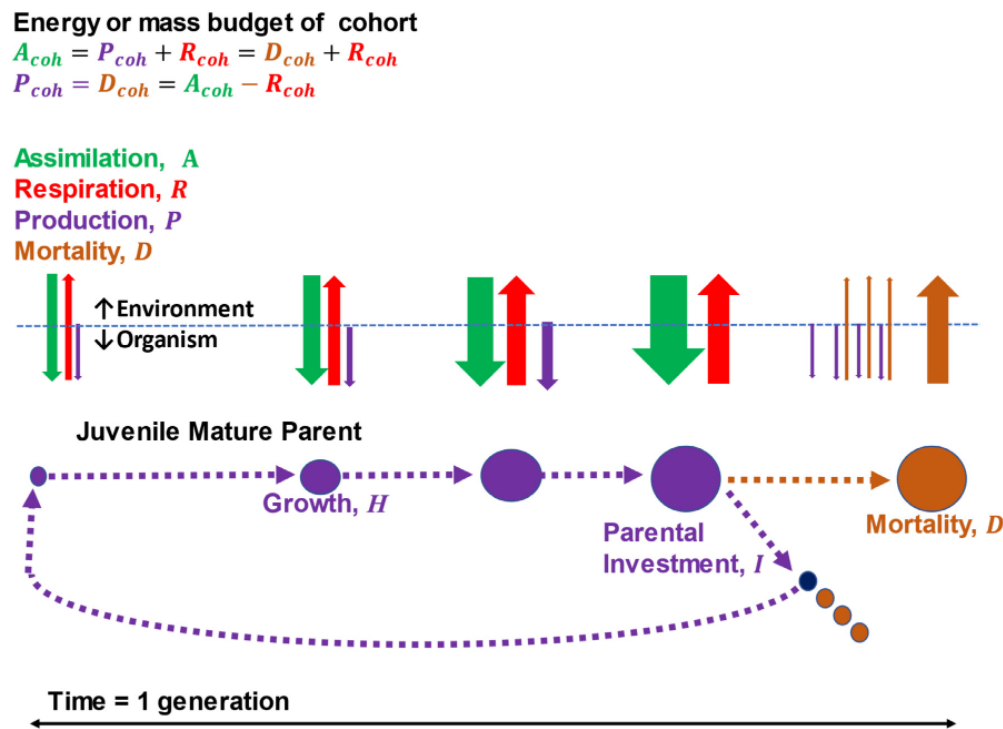


Fig. 1 Energy and mass balance for an animal population (the cohort of offspring produced at steady state by an average parent over its lifespan). A newly independent juvenile assimilates biomass from the environment, allocates it between production and respiration, grows to mature size, and dies after investing in offspring, most of which die before maturing, but one survives to replace the parent. There is energy and mass balance, because all biomass energy taken in from the environment as assimilation is ultimately returned to the environment as respiration plus mortality. This diagram is for a simple life history with determinate growth and semelparous reproduction, but more complicated ones could easily be constructed.

Equation (1) is the seminal equation of the EFP. It is a tautology in the sense that at steady state organisms are equally fit because each generation parents replace themselves—joule-per-joule, gram-per-gram, and individual-per-individual—with surviving offspring (Brown et al. 2018; Burger et al. 2021). The EFP is also a law of nature. Given its assumption of steady state and definition of parameters, there can be no exceptions. In this respect, it is similar to the Hardy–Weinberg equilibrium (HWE) of genetics. By making the assumption of steady state, the HWE predicts the frequencies of alleles and genotypes for Mendelian traits and provides a quantitative theoretical basis for much of population genetics and evolutionary biology (Hartl and Clarke 2007). Similarly, by making the assumption of steady state, the EFP predicts allocations of energy and mass to basic life history traits. Both the HWE and the EFP can be extended to account for cases when the steady state assumption no longer holds, such as responses to natural selection and environmental change.

Energy and mass balance

The foundational principle that biological fitness can be quantified in physical terms marks a departure from tra-

ditional evolutionary biology, where fitness has been defined in terms of differential survival and reproduction of genes or phenotypes. The biophysical laws of thermodynamics and energetics allow the contribution of a gene, quantitative trait, or individual organism to the next generation—its fitness—to be reformulated from biological units of survival and reproduction to physical units of energy and mass. This reformulation is important, because it explicitly shows how the biological laws of population dynamics and evolution by natural selection arise from the physical laws of thermodynamics and the underlying processes of molecular-, cellular-, and individual organism-level biology. Interestingly, the modern synthesis of evolution in the 20th Century focused on mathematical theory and the molecular mechanisms of inheritance and largely ignored energetics and metabolism.

The First Law of Thermodynamics dictates that energy and mass are conserved. For an animal population, this can be quantified in an energy- or mass-balance diagram (Fig. 1). Biomass energy in food is taken into the body from the environment by assimilation, A , transformed by biochemical and physiological processes to perform the work of survival and reproduction, and ultimately returned to the environment. The Second

Law of Thermodynamics dictates that such transformations are always inefficient; some of the energy is dissipated as heat. Most assimilated energy is expended on oxidative respiration, R . Organic molecules of food are catabolized and some of the energy is transferred to ATP molecules, which are transported around the body and used to fuel the biological work of maintenance and activity. The end products of respiratory metabolism (carbon dioxide, water, and heat) are released back into the environment. However, some assimilated organic molecules are not catabolized; they are passed on to the next generation with energy intact as production, P , in the form of growth and reproduction. One fraction, F , of production is passed on to *surviving* offspring and realized as fitness. The remaining fraction, $(1 - F)$, is dissipated in the ecosystem, mostly as mortality of offspring which die without reproducing.

The EPF is a direct consequence of energy balance of a population at steady state:

$$\begin{aligned} A_{coh}G &= R_{coh}G + P_{coh}G \\ &= R_{coh} + FP_{coh}G + (1 - F)P_{coh}G, \end{aligned} \quad (3)$$

where A_{coh} is the rate of cohort biomass energy assimilation from the environment, R_{coh} is the rate of cohort energy expenditure on respiration, P_{coh} is the rate of cohort energy production, and F is the fraction of cohort production passed on to the offspring that survive to reproduce and replace their parents, all amortized over generation time, G . Energy and mass balance (Equations 1 and 2) dictate that at steady state all organisms are equally fit, because on a mass-specific basis and a time scale of one generation, they all pass the same quantities of energy ($E = 22.4$ kJ/g) and biomass ($M = 1$ g/g) to their surviving offspring.

Steady state and demographic balance

The steady state assumption of the EFP requires that the population is in demographic as well as energy balance. Population size remains constant when an average parent exactly replaces itself in one generation with one mature reproducing offspring. So,

$$\frac{dN}{dt} = r = 0, \quad b = d, \quad R_0 = 1, \quad (4)$$

where $\frac{dN}{dt}$, r , b and d , are, respectively, the rates of population growth, increase, birth, and death, and R_0 is the net replacement per generation. As addressed in more detail elsewhere (Burger et al. 2019; Gaillard and Lemaître 2020; Kearney et al. 2021), the demographic balance constraint is important for linking production to mortality, explaining the tradeoff between number

and size of offspring, and accounting for the magnitude of F :

$$F = \frac{m_A}{2m_A + D_{mor}}, \quad (5)$$

where $D_{mor} = \sum_{x=0}^{x=G} m_x d_x$ is the biomass of offspring of mass m_x and age x , which die d_x , before maturing; m_A is the mass of a parent which dies after reproducing; and the 2 reflects the two-for-two replacement of male and female parents at demographic steady state in a sexual animal.

Scaling relations

Correlations with body size and temperature

There can be no exceptions to the EFP, given the above assumptions and definitions. Energetic fitness is constant because of the precise and pervasive tradeoff between net production rate, $P_{coh}F$, and generation time, G (Fig. 2). Although the product, E or M , in Equations (1) and (2) is invariant, there is wide variation in the underlying variables, P_{coh} , G , and F . Much of this variation is correlated with body size and temperature. Body sizes of animals vary by many orders of magnitude, from 10^{-10} g protists to 10^8 g whales and dinosaurs (McMahon and Bonner 1983; Peters 1983; Smith 2021). Body temperatures typically vary about 40-fold over the typical temperature range of 0–40°C. The correlations of most biological traits with body size and temperature can be quantified by statistical analyses and fitted by analytical equations of the form

$$Y = Y_0 m^\alpha e^{\frac{E_a}{kT}}, \quad (6)$$

where Y is the value of the trait, Y_0 is the normalization coefficient, m is the body mass, α is the mass-scaling exponent, e is the root of the natural logarithm, E_a is the “activation energy” which gives the temperature dependence, k is the Boltzmann’s constant, and T is the temperature in Kelvin (e.g., Kleiber 1932; Lindstedt and Calder 1981; McMahon and Bonner 1983; Peters 1983; Calder 1984; Schmidt-Nielsen 1984; Brown 1995; Brown et al. 2004; Gillooly et al. 2001, 2002; White and Kearney 2011; Sibly et al. 2012). Many empirical studies (e.g., Figs. 3 and 4) have shown that for mass-specific metabolic and many other rates $\alpha \approx -1/4$ and $E_a \approx -0.65$ eV ($\approx Q_{10} \sim 2.5$). Signs of the exponents are reversed for biological times, so $\alpha \approx 1/4$ and $E_a \approx 0.65$ eV (Brown et al. 2004; Sibly et al. 2012; Hatton et al. 2019). These scaling relations generally apply both over ontogeny within species where body mass, m_x , varies with age, x , and across species, which differ in adult body size, m_A .

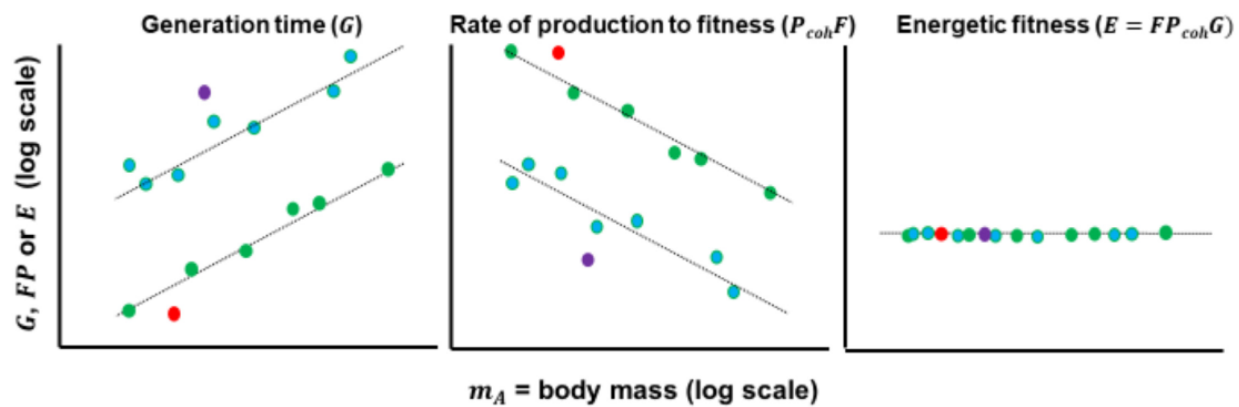


Fig. 2 Cartoons showing hypothetical patterns of variation in allocation of energy to fitness, $P_{coh}F$, generation time, G , and energetic fitness, $E = P_{coh}GF$, as functions of body mass. Shown are data for multiple species in two taxa (green and blue) and single deviant individuals (red and purple). Because of the tradeoff between $P_{coh}F$ and G , the product, E , is invariant and fitness is equal across species at steady state.

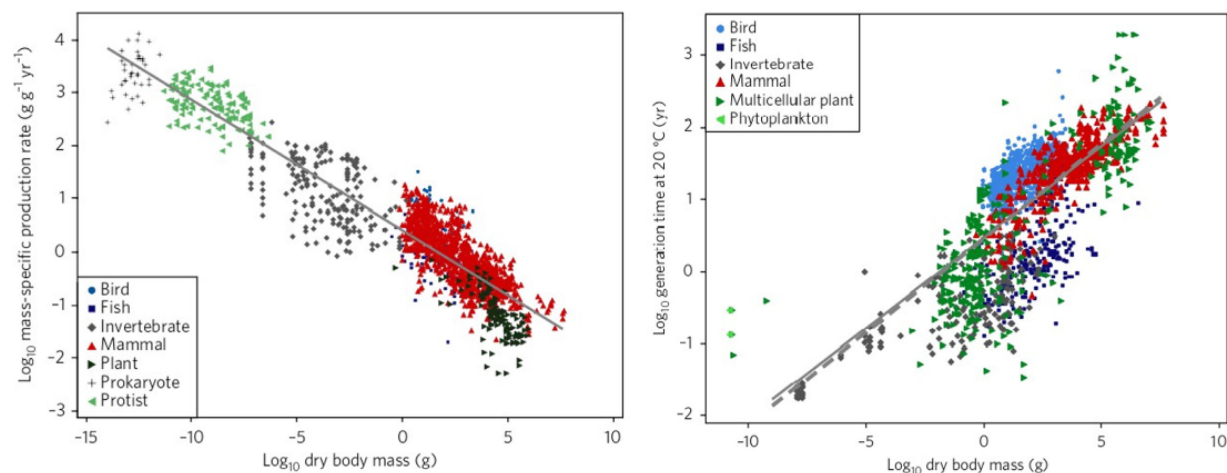


Fig. 3 Variation in individual production rate and lifespan as functions of body mass (from Brown et al. 2018). Note that the overall scaling relations, plotted on logarithmic axes, have equal but opposite slopes: $B = 2.54m^{-0.25}$ and $G = 2.97m^{0.26}$; and exponents very similar to $-1/4$ and $1/4$, respectively, as predicted for standard metabolic scaling, but there is considerable variation within and between taxa. Some of this is undoubtedly because the traits plotted here are not defined and measured the same as the cohort production rate, P_{coh} , and the generation time, G , of the EFP (Equation 1). Sufficiently detailed and accurate metabolic life tables are only available for a very few species. Temperature dependence gives similar equal but opposite scaling relations (e.g., Gillooly et al. 2001, 2002).

In many empirical and theoretical studies, it has been assumed that the relevant body size is the mass of a mature reproducing individual, m_A . The robustness and usefulness of this assumption depends on the relative size of offspring at independence, whether growth is determinate (asymptotic as in many birds and mammals) or indeterminate (continuous throughout life as in many fish), and whether reproduction is semelparous (a single bout as in salmon and many invertebrates) or iteroparous (multiple bouts as in most vertebrates). These complications are addressed in more detail elsewhere (Burger et al. 2019; Burger et al. 2021)

Dimensional analysis and the principle of similitude

Relationships among variables follow from dimensional analysis. Metabolism, life history, and demography all

involve transformations of molecules, so turnover rates of energy, ATP, oxygen, carbon dioxide, water, biomass, and individuals can all be expressed in units of mass per time. The rates of cohort assimilation, respiration, and production are mass-specific, the relevant mass is body mass, m . The relevant time scale is generation time, G , the time for turnover of energy, biomass, and individuals in a complete life cycle from independence of an offspring to death of its parents. So, at steady state, mass-specific and population-level rates are proportional:

$$A_{coh} \quad R_{coh} \quad P_{coh} \quad \frac{dN}{dt} \quad \frac{1}{G}, \quad (7)$$

and the net population replacement rate per generation $R_0 = 1$.

We can express the scalings of metabolic and other rates with body mass and temperature using Equation

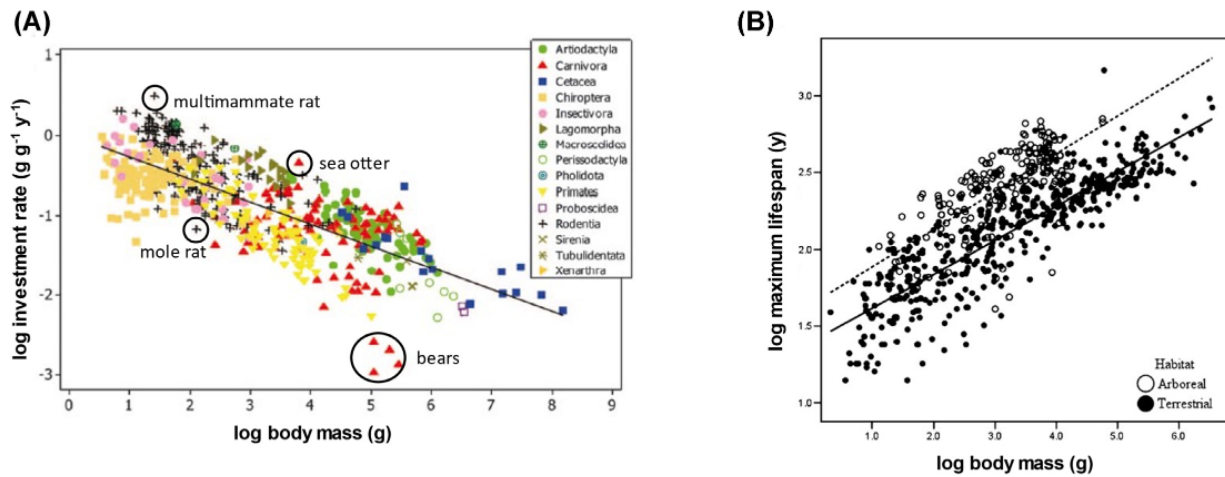


Fig. 4 Scalings of life history traits with body mass among taxa and lifestyles of placental mammals: **(A)** Variation in rate of maternal investment (in g/g/y) as a function of body mass (in g) plotted on logarithmic axes. Overall, across 637 species, the exponent ($\alpha = -0.27$) is close to the predicted scaling ($\alpha = m^{-1/4}$). But scalings of some orders are offset with different normalization constants (i.e., conspicuously lower in bats and primates and higher in rodents, lagomorphs, artiodactyls, and some carnivores). In addition, some taxa (four are circled) deviate conspicuously from the vast majority of other mammals. Note, the rate of “maternal investment” plotted here (mass of newborn times number per litter times number of litters per year) does not include allocations to growth and lactation, so it not the same as the production rate (P_{coh}) in Equations (1) and (2). Replotted from Sibly and Brown (2007). **(B)** Variation in maximum lifespan (in year) as a function of body mass (in gram) across 776 species as a function of habitat. When analyzed separately, arboreal (unfilled symbols) and terrestrial (filled symbols) mammals have similar scaling exponents ($\alpha = 0.25$ and 0.22 , respectively, and both close to the predicted $\alpha = 0.25$). But the scalings of the two groups are offset—i.e., with significantly different normalization coefficients; arboreal species on average live about 25% longer than terrestrial species of the same size. Note (i) the arboreal species include bats and primates, which are among the mammals with the lowest rates of maternal investment in Fig. 5A; and (ii) the maximum lifespan plotted here is not the same as the generation time, G , in Equations (1) and (2). From Shattuck and Williams (2010).

(6) for the cohort or population level as

$$A_{coh} = m^{-\alpha} e^{-\frac{E_a}{kT}} \text{ and } G = m^{\alpha} e^{\frac{E_a}{kT}}, \quad (8)$$

and for the individual- or whole-organism levels as

$$B_{ind} = R_{coh} e^{-\frac{E_a}{kT}} = m^{-\alpha} e^{-\frac{E_a}{kT}} = m^{1-\alpha} e^{-\frac{E_a}{kT}} \quad (9)$$

The pioneers of biological allometry recognized that most biological rates scale with the same exponents, and biological times with the same values but opposite signs. D’Arcy Thompson termed this “the principle of similitude” (Thompson 1961; Kleiber 1961; Peters 1983; for temperature dependence see Gillooly et al. (2001, 2002). It is straightforward to extend this principle and dimensional analysis to all levels of biological organization (i.e., molecular, cellular, whole-organism, population, ecosystem, and biosphere). This begs the question, however, of what determines the values of the exponents. The temperature dependence, with $E_a \approx 65$ eV and $Q_{10} \approx 2.5$, is consistent with Arrhenius–Boltzmann kinetics of biochemical processes. But a general explanation for the pervasive “quarter-power” scaling with body mass has proven more elusive.

The fourth dimension of life is time

Ever since Kleiber’s pioneering work almost a century ago, the vast majority of empirical studies have found

body mass-scaling exponents very close to simple multiples of $1/4$ (e.g., Kleiber 1932; Lindstedt and Calder 1981; McMahon and Bonner 1983; Peters 1983; Calder 1984; Schmidt-Nielsen 1984; Brown 1995; Sibly et al. 2012; Hatton et al. 2019). So much so that the $m^{3/4}$ scaling of whole-organism respiration rate (Equation 9) has come to be called “Kleiber’s rule,” and there have been many efforts to account for the pervasive “quarter-power” exponents.

Most studies have focused on respiration rate, usually referred to simply as “metabolic rate.” Many of them are based on models of the vascular or respiratory systems which supply the resources and remove the wastes of respiratory metabolism. Many—but by no means all—of these models assume or predict fractal-like branching consistent with power-law scaling with quarter-power exponents. However, there is enormous variation across the diversity of animals in the structural and function of resource supply networks, not only among different taxonomic and functional groups of species, such as aquatic invertebrates, insects, fish, and mammals, but also among different organ systems within individual animals, such as arterial, venous, pulmonary, renal, and digestive systems of a mammal (e.g., West et al. 1997; Banavar et al. 1999, 2010; Aitkenhead et al. 2020). Consequently many of the models based on resource supply

are consistent with quarter-power scaling, but they are not definitive. There is currently no general theory that can encompass the diversity and account for the pervasiveness of Kleiber's rule.

Recently, we (Burger et al. 2021) have followed others (e.g., Blum 1977; Winfree 1980; Ginzburg and Damuth 2008) in proposing that the four in the denominator of the body mass scaling exponents reflects the dimension of biological time.

The static features of organisms can be measured by the three standard dimensions of geometry (length, L , surface area, A , and volume, V), which scale with third powers $L \propto V^{1/3}$, $A \propto V^{2/3}$; because the composition and density of protoplasm is similar across organisms, $V \propto m$. A fourth dimension, time, t , is required to capture dynamics. As eminent physicist Murray Gell-Mann remarked to James Brown, "Every physicist knows that the fourth dimension is always time." Indeed, this is well-established in physics, where Riemann (1868) and Minkowski (1909) and others used it to lay the foundations for Einstein's theory of relativity (Møller 1923). And in engineering, where, for example, "The fourth-power law has been used for >40 years to assist the modeling of the damage that accumulates in pavements due to different traffic load levels and differing numbers of load applications" (Dawson 2008). Also, directly relevant is the well-established empirical evidence that a wide variety of biological times, from small-scale molecular and cellular processes to large-scale population and ecosystem phenomena, all scale approximately as $m^{1/4}$ (e.g., Lindstedt and Calder 1981; Calder 1984; Brown 1995; West et al. 1999; Noujaim et al. 2004; Brown et al. 2004; Savage et al. 2004; Brown et al. 2018). Intuitively, times of ontogenetic development and population dynamics scale positively with body mass for thermodynamic reasons: it takes longer to build larger, more complicated bodies, so to be fit they must last longer.

If we accept the empirical evidence that $t \propto m^{1/4}$ and tentatively assume that biological time is the fourth dimension, then the above dimensional analysis and principle of similitude provide a unifying explanation for the pervasive quarter-power scalings: time is the reciprocal of rate, so if generation time sets the pace of life and other biological times scale as $m^{1/4}$, then mass-specific metabolic rate and most other rates must scale as $m^{-1/4}$ (Equations 7 and 8). Previous authors have made similar or somewhat different conjectures that the fourth dimension is time (e.g., Blum 1977; Winfree 1980; Ginzburg and Damuth 2008). Our argument is novel in invoking the equal fitness paradigm and highlighting the importance of generation time, G , in Equations (1) and (2), as the fundamental time scale of fitness and the pace of life.

Senescence and mortality

The quarter-power scaling of biological time and the tradeoff between $P_{coh}F$ and G in Equations (1) and (2) call attention to the importance of generation time and its reciprocal, mortality rate. All animals are mortal. This appears to be a uniquely biological consequence of the Second Law of Thermodynamics. As the body ages, entropic damage and disfunction accumulate, and death ultimately ensues. Sexual reproduction—the joining of sperm and egg to form a zygote and create a new individual—restarts the biological clock.

Metabolism causes aging. Free radicals and other reactive compounds produced in oxidative respiration cause molecular and cellular damage that accumulates over the lifespan, increasingly impairing function. Because generation time scales as $\sim m^{1/4}$ and mass-specific respiration rate as $\sim m^{-1/4}$, all animals age at approximately the same rate after adjusting for the pace of life. Smaller and warmer animals live faster and die younger than larger and cooler ones, but they all have an approximately equal number, $\sim m^{1/4} m^{-1/4} \sim m^0$, of ATP turnovers, cell divisions, and heartbeats in a lifetime. This empirical observation led to the formulation of rate of living theories (ROL: e.g., Rubner 1908; Pearl 1928; Speakman 2005; Furness and Speakman 2008). It has become increasingly clear, however, that although metabolic aging can be an important cause of senescence and death in modern humans and animals in captivity, other causes predominate in natural populations where few individuals live long enough to become senescent. We conjecture that although the correlations among lifespan, respiration rate, and body mass reflect mechanistic linkages between the oxidative metabolism and processes of aging, senescence, and mortality, the scaling of mortality rate and resulting pace of life in wild animal populations is not set by molecular and cellular damage due to oxidative respiration, but by the energetics of fitness and the pervasive relationship between production rate and generation time.

Exponential growth, density-dependence, and the Red Queen

The ecological and evolutionary dynamics of natural populations play out in the context of ecosystems, such as Darwin's (1859) iconic tangled bank: "It is interesting to contemplate a tangled bank, clothed with many plants of many kinds, with birds singing on the bushes, with various insects flitting about, and with worms crawling through the damp earth, and to reflect that these elaborately constructed forms, so different from each other, and dependent upon each other in so complex a manner, have all been produced by laws

acting around us.” The most relevant are the laws of Malthusian population dynamics, Darwinian evolution by natural selection, and Red Queen zero sum game for energy.

The Malthusian–Darwinian dynamic. At small scales of space and time, the steady-state assumption of demographic equilibrium and the EFP is continually violated: individuals leave varying numbers of descendants, and populations fluctuate. The ecology and evolution of populations are governed by the Malthusian law of population growth and the Darwinian law of evolution by natural selection (MDD; Brown 1995; Nekola et al. 2013). When sufficient resources are available and other environmental conditions are favorable, populations grow exponentially. There is “r-selection” for high production rate and associated traits such as fast growth, rapid maturity, and high fecundity. However, exponential population growth cannot continue indefinitely in a limited environment. Increases are checked by resource limitation and density-dependent processes: proximally by competitive, predatory, parasitic, pathogenic, and mutualistic interactions within and among species, and ultimately by the limited supply of net primary production (e.g., Van Valen 1973, 1980; Boltzmann 1886; Brown et al. 2004, 2018; Burger et al. 2021). As populations stop growing, there is a shift toward “K-selection” for traits that trade off the high production rate for greater survival and reproduction in crowded, resource-limited environments: for traits such as slower growth, delayed maturity, increased longevity, and enhanced competitive ability (Pianka 1970; Sibly and Calow 1987).

The Red Queen. As a population increases in abundance, so does the number and strength of interactions with other species: competition, predation, parasitism, and disease. The niches of coexisting species are in constant flux as abundances fluctuate and traits respond to selection. At larger scales of space and time, the net result of the many small-scale compensatory dynamics is a zero sum game for the limited energy of net primary production at the larger scales of ecosystems and the biosphere (e.g., Boltzmann 1886; Van Valen 1977, 1980; Brown et al. 2018; Burger et al. 2021). Van Valen called this the Red Queen phenomenon, by analogy to Lewis Carroll’s character who had to keep running just to stay in the race. The Red Queen limits dominance of populations, facilitates coexistence of species, and maintains biodiversity. The Red Queen runs at the speed of metabolism (Equation 6). Smaller and warmer animals grow, live, and die, and evolve faster, and are more numerous and diverse in ecosystems and the biosphere than larger and colder species (e.g., Hutchinson 1959; Brown 1981, 1995, 2014; Worm and Tittensor 2018). But to keep pace in the Malthusian–Darwinian–Red

Queen struggle for existence, each species must conform to the EFP and assimilate enough biomass in a generation for parents to produce 22.4 kJ/g and 1 g/g of surviving offspring.

The “residual” variation and the role of natural selection

The patterns of constrained variation with body size and temperature (Equation 6 and above) have often been termed biological scaling laws. This is a misnomer; they are not invariant laws of nature. They still beg for theoretical explanation. They are empirical correlations that can be quantified statistically in terms of central values and residual variation. Some of the variation is undoubtedly due to error: including inconsistent definitions, inaccurate measurements, and different statistical methods (e.g., White and Kearney 2011). Issues of data quality and comparability notwithstanding, much of the variation is undoubtedly real. Some of it is the essentially random or unexplained scatter about the central tendency in any empirical dataset. In addition, however, three patterns of variation are relevant to any theory of biological scaling and life history (Figs. 4–6).

Similar exponents, different normalization coefficients. There are many examples of different taxonomic and functional groups with similar exponents but different normalization coefficients, resulting in approximately parallel but offset distributions on logarithmic axes (e.g., Figs. 4 and 5). Many of these cases conform to the principle of similitude (Thompson’s 1961) and standard metabolic theory, with $\alpha \approx -1/4$ and $E_a \approx -0.65$ eV (e.g., Peters 1983; Brown 1995; Sibly and Brown 2007; Hamilton et al. 2011; Sibly et al. 2012). For example, primates and bats have slower life histories—lower production rates and correspondingly longer lifespans—than similar-sized rodents, lagomorphs, and artiodactyls (Figs. 4 and 5).

Deviant values. Some species and taxonomic or functional groups have trait values that deviate substantially from the statistically fitted regression line based on group membership or the value predicted from standard scaling theory (see examples in Fig. 4A). Often the variation is modest, within one or two standard deviations from the mean value. An extreme case is the more than two orders of magnitude variation in generation times of insects weighing approximately 2 g: from 3 or 4 months in some tropical locusts to 204 months in 17-year cicadas (Fig. 5).

Variation in F and life history tradeoffs. Some of the variation that is not “explained” by body size (or temperature) may be associated with life history traits. Figure 6 shows preliminary data for a small sample of ani-

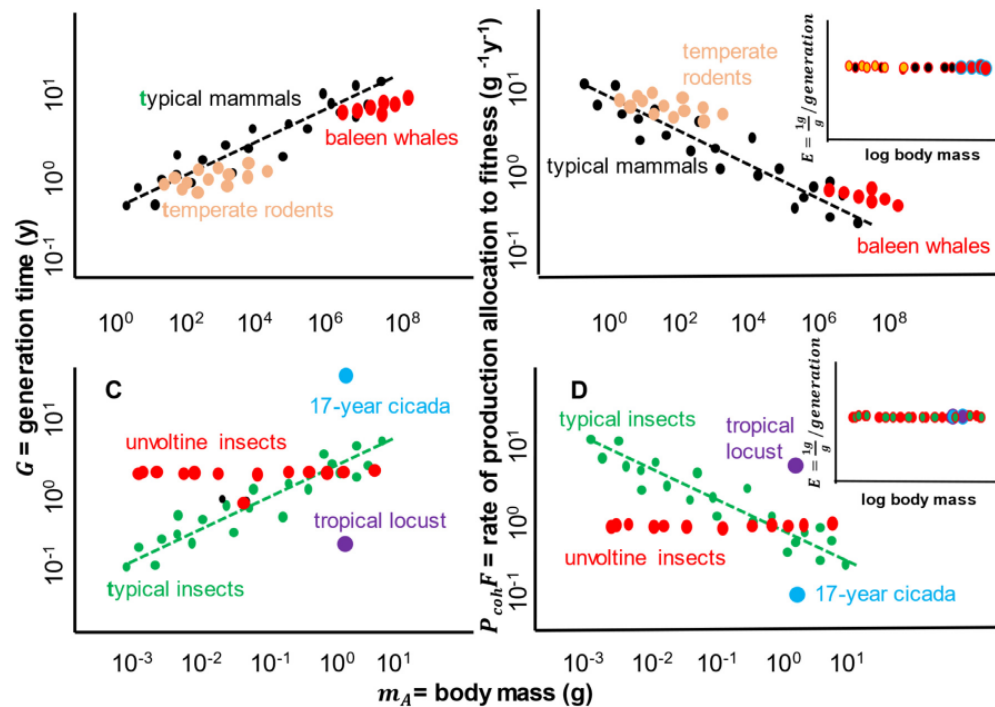


Fig. 5 Cartoons showing examples of large deviations from group-wide scaling relations due to selection to adjust the biological time of the life history to the clock time of geochronological events. Above, in mammals: many species have generation times (left) and production rates (right) that scale with body mass approximately as predicted by metabolic theory (black symbols) with quarter-power exponents (dashed lines); but baleen whales (red symbols) and temperate rodents (tan symbols) deviate in having generation times of ~ 3 – 5 years and 1 year, respectively, to fit biological cycles of reproduction and survival to annual cycles of favorable environmental conditions. Below, in insects: many species have generation times (left) and production rates (right) that scale with body mass approximately as predicted by metabolic theory (green symbols); but many other insects are univoltine, one generation per year (red symbols), reflecting adaptations to use diapause and other strategies to fit growth, reproduction, and survival within favorable seasons of an annual cycle. Species that weigh ~ 2 g exhibit extreme variation, with some tropical locusts having 4 or 5 generations per year and 17-year cicadas living almost two decades. Note, however, as shown in the inserts, that at steady state, all mammals, insects (and other taxa as well) have equal energetic fitness and pass 1 g/g of biomass to surviving offspring each generation.

mals on variation in F , the fraction of cohort production passed through to surviving offspring (Equations 1, 2, and 5). Interestingly, F does not appear to scale with body mass of either adult or offspring, but to vary systematically with the number and relative size of offspring. Animals that produce just a few large offspring allocate a large fraction of production to them and have relatively high values of F . Those that produce enormous numbers of miniscule offspring have high values of $(1-F)$, lose larger fractions of cohort production to pre-reproductive mortality, and contribute more “secondary productivity” to energy flow in ecosystems (Fig. 6). More data and theory will be required to address how F may depend on whether growth is determinate (asymptotic as in many birds and mammals) or indeterminate (continuous throughout life as in many fish), and whether reproduction is semelparous (a single bout as in salmon and many invertebrates) or iteroparous (multiple bouts as in most vertebrates). Such complications are beyond the scope of this paper (but see Brown et al. 2018; Burger et al. 2019, 2021).

The role of natural selection

The variation and deviations warrant more attention than they have received to date—and more than we give them here. Many are due to natural selection. As ancestors of lineages speciated and interacted with diverse abiotic conditions and coexisting species, they evolved diverse life histories. The result is an interesting duality. On the one hand, biophysical limits have powerfully constrained the possible space of physiological and life history traits (e.g., Charnov 1993; Brown 1995; Brown et al. 2004, 2018; Babich Morrow et al. 2021). On the other hand, natural selection has acted powerfully to fill the space within the limits, not only with scalings with body size, temperature, and other factors but also with adaptive deviations from these scalings (e.g., Peters 1983; Calder 1984; Enquist et al. 2015; Burger et al. 2019).

Many deviations from the standard scaling relations are due to selection on generation time. The schedules of births and deaths, production and mortality have evolved to adaptively adjust the biological time

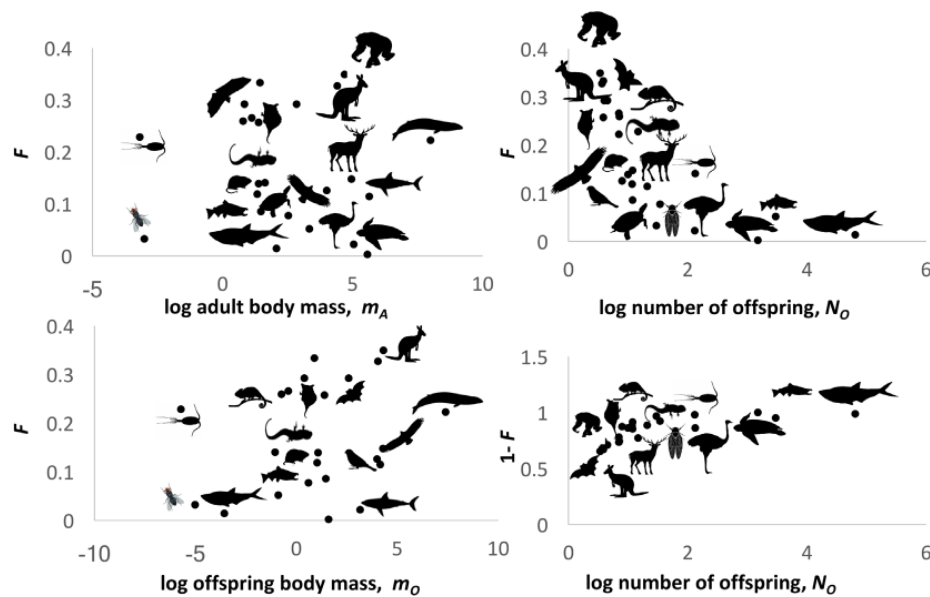


Fig. 6 Variation in F , the fraction of cohort production passed on to surviving offspring in the next generation, as a function of body mass of adult, m_A , body mass of offspring, m_O , and number of offspring, N_O , and variation in $(1 - F)$, the fraction of cohort production dissipated as pre-reproductive mortality of offspring, as a function of number of offspring, N_O . Note that F is not correlated with adult or offspring body size, but F and $(1 - F)$ vary closely with number of offspring. Animals that produce large numbers of offspring, leave most of their production (sometimes >95%) in the ecosystem.

scale, measured in generations, to the scales of extrinsic astronomical and environmental cycles measured in clock time of milliseconds to millennia. An extensive literature on circadian rhythms documents how biological activities have been modified to fit diel cycles (e.g., Winfree 1980; Bernhardt et al. 2020). Plankton migrate vertically through changing water depths, temperatures, and light regimes to feed, avoid predators and regulate their metabolic rates. The smallest diurnal birds and nocturnal mammals forage voraciously during their active periods and budget the stored fat reserves—sometimes abandoning temperature regulation and entering torpor—to last through the period of inactivity and fasting. Gut microbiota activities are synchronized with diel cycles and circadian rhythms of host activity and feeding (Thaiss et al. 2015). Many intertidal animals are attuned to lunar cycles. A wide array of animals from diverse taxa and habitats have life histories adapted to annual cycles and seasonal rhythms. The annual life histories of many insects and small vertebrates concentrate assimilation and production in favorable warmer or wetter seasons and reduce metabolic activity during colder or drier periods (Kong et al. 2019). In contrast, the extremely long prime-number generation times of 13- and 17-year cicadas appear to be adaptations to overwhelm predators that have not coevolved similarly synchronized multiannual life cycles (Williams and Simon 1995). Similarly, the 4-year semelparous life histories of sea-run salmon, together with large variations in abundance be-

tween years, have been interpreted as adaptations to reduce predation (Quinn 2018). All 16 species of baleen whales have reduced times of gestation and lactation to just one year to match the annual cycle of production in temperate oceans (Lockyer 1984). Their fast life histories allowed populations of baleen whales to recover more rapidly than predicted for mammals of similar size after the 1970s whaling ban (Estes et al. 2006; Lotze et al. 2011).

Concluding remarks

This review, synthesis, and commentary on the energetic basis of life history highlights a fundamental dichotomy in biology. On the one hand, living things are amazingly diverse—with millions of species that differ enormously in anatomical structure, physiological function, ecological interactions, and evolutionary histories. On the other hand, these same organisms exhibit common features that can be quantified by statistical correlations and mathematical equations: variation with body size and temperature, tradeoffs in life history traits, and patterns of biodiversity over geographic space and evolutionary time. For well over a century, biologists have been intrigued by this dichotomy, assembled and analyzed empirical data, and produced theories and models to account for both the shared features and the deviations. Here, we have focused on how commonalities of structure and function at molecular, cellular and individual levels of organization give rise to both

unifying themes and pervasive diversity at population, ecosystem, and biosphere levels.

Our emphasis differs from most traditional physiological ecology and allometry, which has focused on respiratory metabolism and sought a theoretical explanation for Kleiber's rule. For decades biologists measured basal, resting, active, and field respiration rates, and explored linkages between metabolic performance of individual organisms and emergent patterns of scaling relations, tradeoffs, ecological interactions, and biodiversity. Such studies are well represented in this symposium.

In contrast, our synthesis is based on the energetic basis of fitness and the implications of Boltzmann's (1886) insight that biomass produced by photosynthetic plants is the ultimate limiting resource for living things. We explore how the struggle for this net primary production in the zero-sum, Red Queen processes of ecological and coevolutionary interactions has shaped the life history traits of organisms—and in particular, how the tradeoff between cohort production rate and generation time allows all organisms to be equally fit, even while they vary by orders of magnitude in body mass, rates of growth and mortality, and number and relative sizes of offspring. Our framework emphasizes the central role of generation time in scaling the pace of life, adjusting biological times of intrinsic biological processes to the clock times of extrinsic geochronology.

A complete metabolic theory of ecology and evolution is still a work in progress. The topics considered above—the energetic basis of fitness, correlations with body size and temperature, and the central importance of generation time—will be important ingredients of the synthesis. Others not addressed here include (i) how allocation of production between growth, parental investment, and survival leads to the traditional life history tradeoffs (e.g., between determinate and indeterminate growth, semelparous and iteroparous reproduction, and number and size of offspring); and (ii) how the efficiency of allocation of assimilated energy between production for growth and reproduction, and respiration for maintenance and survival, constrains fitness of individuals, growth of populations, and energy fluxes in ecosystems. Ultimately the theory should address other topics, such as the two-fold cost of sexual reproduction, the energetic basis of inclusive fitness and sociality, and the role of sexual selection in the evolution of “exaggerated” traits. It is a large and challenging agenda, but recent progress is ground for optimism.

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References

- Aitkenhead IJ, Duffy GA, Devendran C, Kearney MR, Neild A, Chown SL. 2020. Tracheal branching in ants is area-decreasing, violating a central assumption of network transport models. *PLoS Comput Biol* 16:e1007853.
- Babich Morrow C, Ernest SM, Kerkhoff AJ. 2021. Macroevolution of dimensionless life-history metrics in tetrapods. *Proc R Soc B* 288:20210200.
- Banavar JR, Maritan A, Rinaldo A. 1999. Size and form in efficient transportation networks. *Nature* 399:130–2.
- Banavar JR, Moses ME, Brown JH, Damuth J, Rinaldo A, Sibly RM, Maritan A. 2010. A general basis for quarter-power scaling in animals. *Proc Natl Acad Sci* 107:15816–20.
- Bernhardt JR, O'Connor MI, Sunday JM, Gonzalez A. 2020. Life in fluctuating environments. *Philos Trans R Soc B* 375:20190454.
- Blum JJ. 1977. On the geometry of four-dimensions and the relationship between metabolism and body mass. *J Theor Biol* 64:599–601.
- Boltzmann L. 1886. “The second law of thermodynamics” in: *In: Populare Schriften. Essay No. 3 (Address to Imperial Academy of Science, 1886); reprinted in English in Theoretical Physics and Philosophical Problems (D. Riedel, Dordrecht, Netherlands, 1905).*
- Brown JH. 1995. In: *Macroecology*, Chicago, Illinois, USA: University of Chicago Press. p. 269.
- Brown JH, Gillooly JF, Allen AP, Savage VM, West GB. 2004. Toward a metabolic theory of ecology. *Ecology* 85, 1771–89.
- Brown JH, Hall CA, Sibly RM. 2018. Equal fitness paradigm explained by a trade-off between generation time and energy production rate. *Nat Ecol Evol* 2:262–8.
- Brown JH. 1981. Two decades of homage to Santa Rosalia: toward a general theory of diversity. *Am Zool* 21:877–88.
- Brown JH. 2014. Why are there so many species in the tropics? *J Biogeogr* 41:8–22.
- Burger JR, Hou C, AS Hall C, Brown JH. 2021. Universal rules of life: metabolic rates, biological times and the equal fitness paradigm. *Ecol Lett* 24:1262–81.
- Burger JR, Hou C, Brown JH. 2019. Toward a metabolic theory of life history. *Proc Natl Acad Sci* 116:26653–61.
- Calder WA. 1984. *Size, function, and life history*. Cambridge (MA): Harvard University Press.
- Charnov EL. 1993. *Life history invariants*. Oxford: Oxford University Press.
- Darwin C. 1859. *On the Origin of Species by Means of Natural Selection, or Preservation of Favoured Races in the Struggle for Life.*, London: John Murray.
- Dawson AR. 2008. Rut accumulation and power law models for low-volume pavements under mixed traffic. *Transp Res Rec* 2068:78–86.
- Enquist BJ, Norberg J, Bonser SP, Violle C, Webb CT, Henderson A, Sloat LL, Savage VM. 2015. Scaling from traits

- to ecosystems: developing a general trait driver theory via integrating trait-based and metabolic scaling theories. *Adv Ecol Res* 52:249–318.
- Estes JA, Williams TM, Doak D, DeMaster D, Brownell RL (eds.) 2006. Whales, whaling and ocean ecosystems. Berkeley (CA): University of California Press.
- Furness LJ, Speakman JR. 2008. Energetics and longevity in birds. *Age* 30:75–87.
- Gaillard JM, Lemaître JF. 2020. An integrative view of senescence in nature. *Funct Ecol* 34:4–16.
- Gillooly JF, Brown JH, West GB, Savage VM, Charnov EL. 2001. Effects of size and temperature on metabolic rate. *Science* 293: 2248–51.
- Gillooly JF, Charnov EL, West GB, Savage VM, Brown JH. 2002. Effects of size and temperature on developmental time. *Nature* 417:70–3.
- Ginzburg L, Damuth J. 2008. The space-lifetime hypothesis: viewing organisms in four dimensions, literally. *Am Nat* 171:125–31.
- Hamilton MJ, Davidson AD, Sibly RM, Brown JH. 2011. Universal scaling of production rates across mammalian lineages. *Proc R Soc B* 278:560–6.
- Hartl DL, Clarke AG. 2007. Principles of population genetics. Sunderland (MA): Sinauer.
- Hatton IA, Dobson AP, Storch D, Galbraith ED, Loreau M. 2019. Linking scaling laws across eukaryotes. *Proc Natl Acad Sci* 116:21616–22.
- Hatton IA, McCann KS, Fryxell JM, Davies TJ, Smerlak M, Sinclair AR, Loreau M. 2015. The predator–prey power law: Biomass scaling across terrestrial and aquatic biomes. *Science* 349.
- Hutchinson GE. 1959. Homage to Santa Rosalia or why are there so many kinds of animals?. *Am Nat* 93:145–59.
- Kearney MR, Jusup M, McGeoch MA, Kooijman SA, Chown SL. 2021. Where do functional traits come from? The role of theory and models. *Funct Ecol* 35:1385–96.
- Kleiber M. 1932. Body size and metabolism. *Hilgardia* 6:315–353.
- Kleiber M. 1961. The fire of life. New York (NY): Wiley.
- Kong JD, Hoffmann AA, Kearney MR. 2019. Linking thermal adaptation and life-history theory explains latitudinal patterns of voltinism. *Philos Trans R Soc B* 374:20180547.
- Lindstedt SL, Calder WA, III. 1981. Body size, physiological time, and longevity of homeothermic animals. *Q Rev Biol* 56: 1–16.
- Lockyer CH. 1984. Review of baleen whale (Mysticeti) reproduction and implications for management. *Rep Int Whal Commn* 6:27–50.
- Loreau M. 2010. From populations to ecosystems: theoretical foundations for a new ecological synthesis. Princeton (NJ): Princeton University Press.
- Lotka AJ. 1922. Contribution to the energetics of evolution. *Proc Natl Acad Sci USA* 8:147–51.
- Lotze HK, Coll M, Magera AM, Ward-Paige C, Airoldi L. 2011. Recovery of marine animal populations and ecosystems. *Trends Ecol Evol* 26:595–605.
- Marquet PA, Quiñones RA, Abades S, Labra F, Tognelli M, Arim M, Rivadeneira M. 2005. Scaling and power-laws in ecological systems. *J Exp Biol* 208:1749–69.
- McMahon TA, Bonner JT. 1983. On Size and Life. New York: Scientific American Library.
- Minkowski H. 1909. “Raum und zeit.” *Jahresber Deutsch Math-Verein* 18:75–88.
- Møller C. 1923. The theory of relativity. 2nd ed. Oxford: Clarendon Press. p. 93.
- Nekola JC, Allen CD, Brown JH, Burger JR, Davidson AD, Fristoe TS, Hamilton MJ, Hammond ST, Kodric-Brown A, Mercado-Silva N et al. 2013. The Malthusian–Darwinian dynamic and the trajectory of civilization. *Trends Ecol Evol* 28:127–30.
- Noujaim SF, Lucca E, Munoz V, Persaud D, Berenfeld O, Meijler FL, Jalife J. 2004. From mouse to whale: a universal scaling relation for the PR interval of the electrocardiogram of mammals. *Circulation* 110:2802–2808.
- Odum HT. 1971. Environment, power, and society. New York (NY): Wiley-Interscience.
- Pearl R. 1928. The Rate of Living. New York: Knopf.
- Peters RM. 1983. The ecological implications of body size. Cambridge (MA): Cambridge University Press.
- Pianka ER. 1970. On r-and K-selection. *Am Nat* 104:592–7.
- Quinn TP. 2018. The behavior and ecology of Pacific salmon and trout. Seattle University of Washington Press.
- Riemann B. 1868. On the hypotheses which lie at the foundation of geometry. *Nature* 8: 14–17.
- Rubner M, editors. 1908. Das Problem der Lebensdauer und seiner beziehung zur zum Wachstum und Ernahrung. Munich: Oldenberg.
- Savage VM, Gillooly J, Woodruff W, West G, Allen A, Enquist B, Brown J. 2004. The predominance of quarter-power scaling in biology. *Funct Ecol* 18:257–82.
- Schmidt-Nielsen K. 1984. Scaling: why is animal size so important? Cambridge (MA): Cambridge University Press.
- Schramski JR, Dell AI, Grady JM, Sibly RM, Brown JH. 2015. Metabolic theory predicts whole-ecosystem properties. *Proc Natl Acad Sci* 112:2617–22.
- Shattuck MR, Williams SA. 2010. Arboreality has allowed for the evolution of increased longevity in mammals. *Proc Natl Acad Sci* 107:4635–9.
- Sibly R, Calow P. 1987. Ecological compensation—a complication for testing life-history theory. *J Theor Biol* 125:177–86.
- Sibly RM, Brown JH, Kodric-Brown A, editors. 2012. Metabolic ecology: a scaling approach, New York: Wiley-Blackwell.
- Sibly RM, Brown JH. 2007. Effects of body size and lifestyle on evolution of mammal life histories. *Proc Natl Acad Sci* 104:17707–12.
- Smith FA. 2021. Mammalian paleoecology: using the past to study the present. Baltimore (MD): JHU Press.
- Speakman JR. 2005. Body size energy metabolism and lifespan. *Journal of Experimental Biology* 208:1717–1730.
- Thaiss CA, Zeevi D, Levy M, Segal E, Elinav E. 2015. A day in the life of the meta-organism: diurnal rhythms of the intestinal microbiome and its host. *Gut Microbes* 6:137–42.
- Thompson DW. 1961. On growth and form. Cambridge (MA): Cambridge University Press.
- Uyeda JC, Pennell MW, Miller ET, Maia R, McClain CR. 2017. The evolution of energetic scaling across the vertebrate tree of life. *Am Nat* 190:185–99.
- Van Valen L. 1973. A new evolutionary law. *Evol Theor* 1:1–30.

- Van Valen L. 1977. The Red Queen. *The American Naturalist* 111:809–810.
- Van Valen L. 1980. Evolution as a zero-sum game for energy. *Evol Theor* 4:289–300.
- West GB, Brown JH, Enquist BJ. 1997. A general model for the origin of allometric scaling laws in biology. *Science* 276: 122–6.
- West GB, Brown JH, Enquist BJ. 1999. The fourth dimension of life: fractal geometry and allometric scaling of organisms. *Science* 284:1677–9.
- White CR, Kearney MR. 2011. Metabolic scaling in animals: methods, empirical results, and theoretical explanations. *Compr Physiol* 4:231–56.
- Williams KS, Simon C. 1995. The ecology, behavior, and evolution of periodical cicadas. *Annu Rev Entomol* 40: 269–95.
- Winfree AT. 1980. *The geometry of biological time*. New York (NY): Springer.
- Worm B, Tittensor DP. 2018. *A theory of global biodiversity (MPB-60)*. Princeton (NJ): Princeton University Press.