METABOLIC CONSTRAINTS AND CURRENCIES IN ANIMAL ECOLOGY

Reconciling theories for metabolic scaling

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Summary

1. Metabolic theory specifies constraints on the metabolic organisation of individual organisms. These constraints have important implications for biological processes ranging from the scale of molecules all the way to the level of populations, communities and ecosystems, with their application to the latter emerging as the field of metabolic ecology. While ecologists continue to use individual metabolism to identify constraints in ecological processes, the topic of metabolic scaling remains controversial.

2. Much of the current interest and controversy in metabolic theory relates to recent ideas about the role of supply networks in constraining energy supply to cells. We show that an alternative explanation for physicochemical constraints on individual metabolism, as formalised by dynamic energy budget (DEB) theory, can contribute to the theoretical underpinning of metabolic ecology, while increasing coherence between intra- and interspecific scaling relationships.

3. In particular, we emphasise how the DEB theory considers constraints on the storage and use of assimilated nutrients and derive an equation for the scaling of metabolic rate for adult heterotrophs without relying on optimisation arguments or implying cellular nutrient supply limitation. Using realistic data on growth and reproduction from the literature, we parameterise the curve for respiration and compare the *a priori* prediction against a mammalian data set for respiration.

4. Because the DEB theory mechanism for metabolic scaling is based on the universal process of acquiring and using pools of stored metabolites (a basal feature of life), it applies to all organisms irrespective of the nature of metabolic transport to cells. Although the DEB mechanism does not necessarily contradict insight from transport-based models, the mechanism offers an explanation for differences between the intra- and interspecific scaling of biological rates with mass, suggesting novel tests of the respective hypotheses.

Key-words: allometry, body-size scaling, dynamic energy budget, Kleiber's law, life history, metabolic theory of ecology, nutrient supply network model, nutrient transport

Introduction

The controversial topic of metabolic scaling has seen a revival in recent years as ecologists have begun to more strongly relate ecological phenomena to constraints on individual metabolism (Brown, Sibly & Kodric-Brown 2012). Renewed interest was sparked by West, Brown & Enquist's (1997) nutrient supply network model (WBE hereafter). This model was subsequently used as a theoretical justification for the widespread application of the empirically observed ¾ power scaling of metabolic rate with individual size to understand ecological patterns more generally – a research agenda now known as the 'The Metabolic Theory of Ecology' (MTE; Brown *et al.* 2004). Other models based on nutrient supply have since emerged (Banavar, Maritan & Rinaldo 1999; Banavar *et al.* 2002, 2010), which also aim to understand how design constraints on the transport of metabolites may be restricting the metabolic organisation of organisms. These 'transport models' have instant appeal as they use simple physical principles about the scaling of vascular supply

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networks to make *a priori* predictions about the general pattern of metabolic scaling that is observed over some 20 orders of magnitude of body size. Other proposed models have also received considerable attention (Darveau *et al.* 2002; Kolokotrones *et al.* 2010), but as West *et al.* (2003), and West & Brown (2005) correctly point out, many 'competing' models make no *a priori* predictions about the scaling of metabolic rate.

While metabolic scaling is ubiquitous in biology, only a small minority of life's diversity is known to possess the equivalent of closed vascular supply systems. In contrast, all organisms must take up, store and mobilise energy and materials as part of their basic metabolism. Emphasising the significance of physicochemical constraints on the build-up and use of stored metabolites, dynamic energy budget (DEB) theory (Kooijman 1986, 2000, 2010) offers a competing explanation for metabolic scaling that has yet to contribute substantially to the debate (but see Van der Meer 2006a; Kearney & White 2012). Like the WBE explanation, the DEB theory explanation also makes *a priori* predictions about metabolic scaling using very simple mechanistic principles and does so without necessarily running contrary to the important insights that physical transport models provide about theoretical properties of vascular supply networks.

The dynamic use of stored metabolites [also known as reserve dynamics (Kooijman 2010)] has been a core conceptual component in DEB theory for almost 30 years (Kooijman 1986). The significance placed on reserve dynamics in DEB theory is motivated by the observation that metabolism depends more on nutritional history than on present feeding conditions – a phenomenon dramatically demonstrated by the Humpback whale, which can travel halfway around the world nursing a 2000 pound pup without feeding. Although best known for its application at the scale of the developing individual, the DEB framework can use its simple physicochemical principles to make *a priori* predictions about broad scaling patterns of many life-history traits between species, including the scaling of metabolic rate (Kooijman 2010).

This paper aims to emphasise and explain how the DEB concept of reserve dynamics can contribute to the debate on metabolic scaling by invoking simple and realistic constraints on the use of stored metabolites, which restrict fluxes of energy and materials through organisms and consequently constrain metabolism. As expressed by Brown and Sibly in a review of recent work in metabolic ecology, 'biological metabolism includes the uptake of resources from the environment, transformation of these substances within the body, allocation of these products to maintenance, growth and reproduction and excretion of wastes into the environment. So, to a first approximation, the metabolic rate sets the pace of life and the rates of all biologically mediated ecological processes' (2012, p. 22). For this reason, understanding constraints on metabolic organisation is important for understanding almost all life processes.

Our broad goal is to encourage further empirical and theoretical comparison between the WBE and DEB theories, something which is practically nonexistent in the literature (but see Van der Meer 2006a; Kearney & White 2012). Brown *et al.* (2004) stated that they 'view the DEB and MTE approaches as complementary. They make different trade-offs between specificity and generality and consequently have different strengths, weaknesses and applications'. We too regard the theories as potentially complementary, but for different reasons. We do not believe the level of specificity (or generality) to be an inherent feature of each theory, but rather a practical consideration that is dependent on the context of the theory's application. To make it clear that DEB theory can be readily applied generally, and at broad scales, we derive an equation for the metabolic scaling of adult heterotrophs that is numerically identical to that of the WBE nutrient supply model, but which rests on a set of profoundly different assumptions. Using realistic values on growth and reproduction from the literature, we estimated the parameters of this equation to make an *a priori* prediction of the scaling of metabolic rate, which is compared against a large mammalian data set.

We show that the DEB explanation does not rely on any arguments of evolutionary optimality. Moreover, the DEB approach clearly distinguishes mechanisms associated with intra- and interspecific variation in rates of respiration, uptake and reproduction and also describes the metabolism of embryos without making any further assumptions. This is an important point of departure from transport-based models and suggests how the respective hypotheses may be tested experimentally (Kearney & White 2012). We also derive other DEB scaling relationships and summarise them as a table of scaling predictions. These results illustrate how DEB theory can contribute to the theoretical underpinning of the emerging field of metabolic ecology.

Constraints on the use of stored nutrients

All organisms take up and store nutrients, either directly or from food. Without nutrient storage, organisms would perish upon the cessation of feeding, unable to cover the basic costs of metabolism. But as soon as assimilated nutrients make their way from the gut into the blood, the task of storage poses immediate problems. Strict limits are placed on the concentration of any substrate in solution. One particularly important example is the maintenance of osmotic pressures; an instantaneous tenfold increase in blood glucose levels would raise osmotic pressure by *c.* 15% (Coulson, Hernandez & Herbert 1977), posing serious physiological risks, familiar to any person suffering from diabetes.

Despite the risks to osmotic balances posed by the simple act of feeding, organisms can process foods at astounding rates. An alligator eats as much as 15 g of protein per kilogram of body weight in one meal which,

for a 70 kg individual, would equate to slightly more than 1 kg of protein or roughly 8·5 moles of amino acids (Coulson, Hernandez & Herbert 1977). Assuming all the protein was absorbed as amino acids in 48 h it would take for digestion and that they were present in the body fluids at the same time, the osmotic pressure would increase by *c*. 59% (Coulson, Hernandez & Herbert 1977). Despite the absorption of this massive amount of substrate over this relatively short period, measured levels of amino acids in plasma and osmotic pressures remain approximately unaltered (Coulson & Hernandez 1970). Moreover, the alligator would only need 18 g or *c*. 2% of the total amino acids absorbed to meet its daily metabolic requirements (Hernandez & Coulson 1952). The majority of the ingested amino acids are used at a later date and so must be stored.

Organisms must simultaneously cope with variable feeding conditions as well as with the problem of maintaining internal osmotic pressures, and they do this by storing absorbed substrates as pools of polymers, which do not affect osmotic pressures. In the case of amino acids, these polymers are proteins, although the same story could be told for carbohydrates as well as lipids. The key point is that, regardless of the organism, most assimilated substrates are best stored as macromolecules. But, because these macromolecules are not well mixed in solution across the body, the periphery of these storage sites becomes more relevant to reaction rates in place of the overall concentration. As a result, simple enzyme kinetics no longer applies.

For animals, DEB theory formalises this notion by partitioning biomass into two compartments: reserve and structure. Reserve represents the sum of all pools of polymers (lipids, carbohydrates, proteins etc.) from which energy and materials are mobilised for the growth and maintenance of structure and reproductive processes. It is assumed that all assimilated materials first enter the reserve compartment (for details see Lika & Kooijman 2011), and that these storage pools do not contribute to overall maintenance costs. For convenience, reserve is typically expressed in units of energy, while structure is expressed as a volume (this is so structure can be easily related to suitable physical measures of size, such as carapace widths in insects or femur length in mammals). However, reserve and structure can just as easily be expressed in terms of mass. Reserve and structure are each assumed to have a constant composition (the strong homoeostasis assumption), which implies stoichiometric constraints on their growth in amounts.

Figure 1 shows how access to reserve through its surface area interface with structure is expected to scale with size. Mobilisation of reserve for metabolism is via enzymes that travel around in the metabolically active structural matrix and do not actually penetrate the pools of reserve, but operate at the interface. The surface area of the pool (such as the membrane of a vacuole) determines how fast a cell can mobilise the enclosed reserve
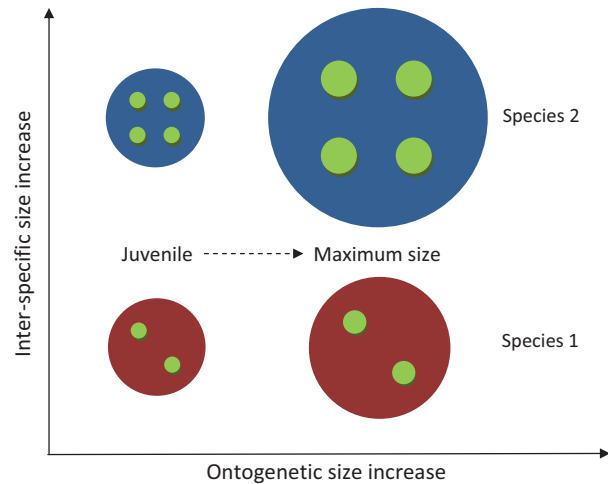
Fig. 1. The body-size scaling of the reserve periphery able to be mobilised for metabolism is determined by assuming a constant proportionality (structural isomorphy) between each reserve pool (small inner circles) to total structure (large outer circles) both within and between species. If the number of reserve pools within a species is constant, ontogenetic size eventually reaches some maximum limit. This is due to the mismatch in scaling between the supply of reserve being mobilised and the demand of structural maintenance. While maintenance scales with structural volume, reserve mobilisation scales with the surface area of reserve sites and thus, scales more slowly within species. Larger adult sizes can be attained by increasing the number of reserve pools, which increases the total surface area and mobilisation rate of reserve per unit structure and hence, the amount of adult structure that can be sustained. Total reserve (E) is equal to the number of reserve pools (n) times the pool size (r) or $E = nr$. The diagram shows that among species total reserve increases both through changes in the size and number (n and r) of reserve sites, while within species, only pool size (r) changes. The reserve interface (I) scales with $nr^{\frac{2}{3}}$. Using the assumption of constant proportionality of reserve pools to structure ($r \propto V$), the interface can also be expressed as, $I \propto E/V^{\frac{1}{3}}$. This argument assumes the individual pools comprising reserve to have identical size, composition and shape, but these are not necessary requirements, and the argument can be extended to cover unequal pools.

substrate. This property is used to derive the equation for metabolic scaling below. The scaling of the surface area interface of reserve rests on the assumption of 'structural isomorphy': that the dimensions of each reserve component, which are subcellular pools of polymers suspended in a matrix of structure, are a fixed proportion of the total amount of structure. The assumption is useful for providing an intuitive mechanism behind DEB theory's reserve dynamics, but can be relaxed in place of the assumption of 'weak homoeostasis' at the cost of increased abstraction (Kooijman 2010).

'Weak homoeostasis' is the assumption that the composition of the individual as a whole does not change during growth in constant food environments. Given that an organism's biomass can be partitioned into compartments of constant, but potentially unique, composition (e.g. structure and reserve), a constant biomass stoichiometry is achieved through maintaining a constant proportionality between the amounts of these

compartments. This assumption is motivated by the observation that stoichiometric homoeostasis is a key life process (Sterner & Elser 2002) and is useful for any metabolic theory that works with metabolic pools of constant composition; else it is not possible to access the amounts and composition of pools in a developing individual. This inability would affect the testability and applicability of such theories substantially. Empirical evidence for weak homoeostasis is voluminous (see e.g. Chilliard, Delavaud & Bonnet 2005; Król *et al.* 2005; Fink, Peters & Von Elert 2006; Ingenbleek 2006; Steenbergen *et al.* 2006) and can considered to be a stylised fact (Sousa, Domingos & Kooijman 2008). The composition of reserve and structure is determined in practice by mapping observed composition of biomass at different constant food levels to their expected relative amounts at these food levels. Metabolic theories that refrain from the delineation of pools need to follow specific metabolites and suffer from the necessity to distinguish the 'important metabolites', where only a few 'important metabolites' can be quantified.

The implication of DEB's reserve dynamics (Fig. 1) is that across species the amount of reserves must increase relative to the amount of structure to compensate for the sublinear scaling of the reserve surface area and mobilisation rate. If the amount of reserves increases sufficiently, the release of reserves will keep pace with the maintenance demands of increasing structure. But, because the relative proportion of structure decreases with size to make room for the reserve, mass-specific maintenance will decrease and the metabolic rate will scale sublinearly with mass interspecifically. Although not strictly reserve, body fat, for example, scales interspecifically as mass$^{1 \cdot 19}$ in mammals (Pitts & Bullard 1968; Calder 1984) and has a very low maintenance costs (Elia 1992).

We now consider the relationship between reserve mobilisation, metabolic rate and body mass under DEB theory (reproduction processes are not considered here, but do not change the result). If structure (V) incurs a maintenance cost of $[\dot{p}_M]$ per unit of structure, the cost of maintenance in energy per time is:

$$\dot{p}_M = V[\dot{p}_M]$$

From Fig. 1, we can see that the interface or periphery of stored reserve scales with $E/V^{\frac{1}{3}}$ where E is expressed in units of energy and V is expressed in units of volume. The reserve mobilisation flux in energy per time is taken to be proportional to this interface:

$$\dot{p}_c = \frac{\dot{v}E}{V^{\frac{1}{3}}}$$

where the proportionality constant $\dot{v}$ has the dimension length per time and thus, has the interpretation of a conductance. For nongrowing organisms at ultimate size (V_m), $E = E_m$ and all mobilised energy is being consumed

by maintenance:

$$\dot{p}_M = \dot{p}_c$$

or after substituting $\dot{p}_M$ and $\dot{p}_C$:

$$V_m[\dot{p}_M] = \frac{\dot{v}E_M}{V_m^{\frac{1}{3}}}.$$

Rearrangement of this equation shows that ultimate reserve scales interspecifically with ultimate structure as:

$$E_m = \frac{V_m^{\frac{4}{3}}[\dot{p}_M]}{\dot{v}}.$$

Adult mass is the sum of the weight of the two biomass compartments, structure and reserve at maximum size, and can be converted to mass using the respective mass density constants, d_v, (wet-mass per volume) and d_E (wet-mass per energy):

$$M = d_v V_m + d_E E_m.$$

Substituting E in this equation we obtain:

$$M = d_v V_m + \frac{d_E V_m^{\frac{4}{3}}[\dot{p}_M]}{\dot{v}}.$$

If basal metabolic rate ($\dot{B}$) of postabsorptive organisms is the rate at which reserve is mobilised for metabolism (and completely consumed by maintenance costs at ultimate size) we have:

$$\dot{B} = V_m[\dot{p}_M].$$

This expression for metabolic rate is a special case, and it should be stressed that metabolic rate cannot always be equated to the rate of respiration contributed by maintenance. In general, respiration would also need to include overheads of growth, assimilation and reproduction, while metabolic rate would also include the energy allocated to product formation (Kooijman 2013). Nevertheless, as we are dealing with postabsorptive animals at ultimate size, we can substitute $\dot{B}$ into the previous equation to arrive at an equation relating metabolic rate to mass:

$$M = \frac{d_V \dot{B}}{[\dot{p}_M]} + \frac{d_E \dot{B}^{\frac{4}{3}}}{\dot{v}[\dot{p}_M]^{\frac{1}{3}}}.$$

Remembering that d_v, d_E, $[p_M]$ and $\dot{v}$ are constants, we can simplify this relationship to:

$$M = C_0 \dot{B} + C_1 \dot{B}^{4/3}.$$

This is precisely the equation that can be derived from the WBE model (see Savage, Deeds & Fontana 2008). As

Table 1. Comparison of the coefficients in DEB and WBE models shows that the same equation for metabolic scaling can emerge from two theories based on different assumptions, leading to a profoundly different interpretation of the metabolic scaling relationship

	DEB	WBE
C_0	$\frac{d_V}{[\dot{p}_M]}$	$C_2\frac{V_{cap}\left(\bar{N}-\frac{1}{n^{1/3}-1}\right)}{B_{cap}}$
C_1	$\frac{d_E}{\dot{v}[\dot{p}_M]^{1/3}}$	$C_2\frac{V_{cap}n^{(1-\bar{N})/3}}{B_{cap}^{4/3}(n^{1/3}-1)}$

d_v, density of structure; $[\dot{p}_M]$, maintenance rate of structure; d_E, density of reserve; $\dot{v}$, conductance; C_2, yield of mass on blood volume; V_{cap}, volume of capillary; $\bar{N}$, transition level to area-preserving branching; n, branching ratio; B_{cap}, metabolic rate of capillary; DEB, dynamic energy budget.

Table 1 below shows, these two coefficients are comprised of very different parameters combinations under the two theories.

Despite the different interpretations of the two constants, the equation converges on Kleiber's law (Kleiber 1932) at the limit of large mass:

$$\lim_{M\to\infty}\dot{B}\propto M^{\frac{3}{4}}.$$

It is important to emphasise that this relationship only holds at the infinite limit of mass and contrary to common perceptions, metabolic rate does not depend on mass as a power function under either of these frameworks. In other words, this function predicts exponents that diverge from ¾ for finite masses when C_0 is positive. Nevertheless, the function approximates the ¾ power relationship well, particularly for small values of C_0. As the constants C_0 and C_1 relate to different physical parameters under each respective framework, this equation has profoundly different interpretations when explaining metabolic scaling. In other words, the two theories lead to equations that are quantitatively identical, but diverge qualitatively. Interestingly, something that has been pointed out in metabolic theory (Isaac & Carbone 2010), but not investigated in any detail, is that different models may be simultaneously valid. Indeed, it is likely that these two frameworks are simultaneously offering useful insight. Without any optimality arguments, DEB's reserve dynamics explains why organisms require less energy per mass with increasing size while for organisms with vascular supply networks, WBE shows how this decreased metabolic demand coincides with a network arrangement that reduces energy losses in transport. Thus, many of the predictions relating to variables of the cardiovascular system are still likely to be relevant approximations, including predicted blood volume, heart rate, stroke volume, blood pressure, radius of the aorta, volume of tissue served by a capillary, number and density of capillaries, dimensions of capillaries and oxygen affinity of haemoglobin (West, Brown & Enquist 1997; Savage, Deeds & Fontana 2008). However,

such transport constraints may not be the causal determinant of the scaling of respiration.

Organisms adapt to and are constrained by physical principles. Without recourse to optimality arguments, predictions can be made of how modes of transport must change as organisms grow larger and cohesion forces becomes less dependable, inertial forces enter the fore, and gravity becomes an increasing concern. Similarly, using only physical principles, we have shown that larger organisms necessitate proportionally more reserve biomass to overcome the mismatched scaling of somatic maintenance and energy mobilisation. The proposed mechanism of reserve dynamics is feasibly more evolutionarily basal (Kooijman & Troost 2007) than other explanations based on network supply constraints, but does not preclude network design optimality where they occur. In this way, the scope of the DEB theory mechanism can be seen to apply to all species, not only those possessing branching vascular supply systems. The dynamics of the use of stored nutrients is a cornerstone of DEB theory and has been used widely and with great success in a variety of applications. This constraint on metabolic organisation can also readily make *a priori* predictions of metabolic scaling and has implications for many life-history traits (incubation times, juvenile periods, life span, reproduction rates, etc.).

An *a priori* respiration calculation

Mathematical descriptions of processes force us to be explicit about all underlying assumptions and provide an objective method for establishing the level of our understanding of a process (Nijhout, Davidowitz & Roff 2006). We have shown how mechanistic theories based on completely different principles can be used to derive the same equations for metabolic scaling, making it impossible to empirically distinguish between models based only on the quality of fits to data on metabolic scaling. However, the coefficients C_0 and C_1 are derived from assumptions about other processes, which are, in principle, measurable and provide an important point of departure.

Dynamic energy budget parameters have been estimated for a large number of animal species from most large phyla and all 13 classes of chordates [this collection is called 'add_my_pet' and is freely available online (see Supporting information)]. At the time of writing this data base, included entries from 12 mammals, including the eastern grey kangaroo, African elephant, common dolphin and brown rat. For each animal in the collection the 'covariation method' (Lika *et al.* 2011a) was applied to simple life-history data to estimate the set of 12 core DEB parameters, which include $\dot{v}$ and $[\dot{p}_M]$. These core parameters specify the unique bioenergetic life cycles of organisms. The intuition behind the estimation procedure is that, although the parameters cannot themselves be measured directly, observational data can be used to restrict the value that these parameters can take. For example, even the trivial observation that all animals dissipate heat

at ultimate size restricts $\dot{v}$ and $[\dot{p}_M]$ to values greater than zero. In a similar way, much more comprehensive data allow the core parameters to be systematically specified with great precision (Lika, Kearney & Kooijman 2011b). Estimated values for the constants d_v and d_E are typical values for mammals that were taken from the literature (Kooijman 2010), while $\dot{v}$ and $[\dot{p}_M]$ are averaged from the 12 mammalian entries in the 'add_my_pet' collection (see Table 2). These separately determined values were used in combination with the derived equation to predict the metabolic scaling relationship for mammals.
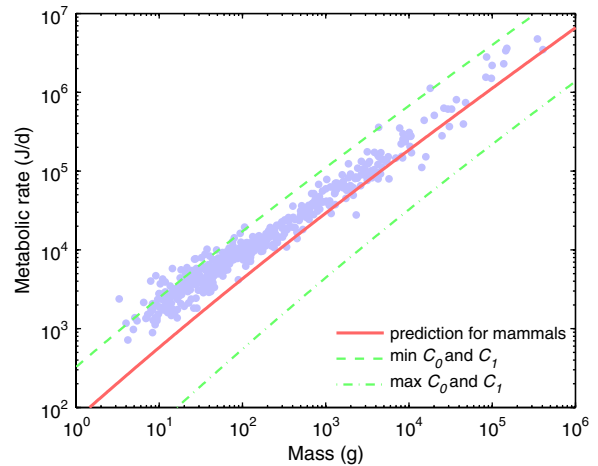
This *a priori* equation is compared against a recently compiled, temperature-corrected mammalian data set (McNab 2008; Kolokotrones *et al.* 2010) in Fig. 2. Although the fit to the data is by no means perfect, the result of the predicted relationship is striking, particularly as no respiration data were used in determining any of the parameter values (except for the tammar wallaby). This approach stands in bold contrast to letting the parameters vary freely and allowing the 'best fit' to decide what value they should take. Letting our knowledge of the physical parameters determine the fit provides a good test of the robustness of model assumptions.

Although the predicted equation follows from simple physicochemical design constraints, consideration of biological and ecological constraints of organisms quickly renders the assumption of constant model parameters as unrealistic (as evidenced by the difference in upper and lower predictions). Population density and trophic level are potentially other important factors not considered here that may be able to account for deviations around the broad pattern of metabolic scaling (Hechinger *et al.* 2011; DeLong, Hanley & Vasseur 2014). In addition to the direct effect of temperature on metabolism through biochemical kinetics (Gillooly *et al.* 2001), environmental temperature may also exert indirect effects on metabolism through the modification of competitive outcomes that produce interactions with body size (Reuman, Holt & Yvon-Durocher 2013). Indeed, the evolution of life histories optimised to a wide range of selective environments must be considered to make any sense of deviations from our simple prediction. Smaller mammals, for example are

Fig. 2. Rather than letting the 'best fit' determine the parameters, dynamic energy budget (DEB) theory was used to specify an *a priori* prediction of the metabolic scaling relationship for mammals using the mean DEB parameters of 12 mammals in the 'add_my_pet' collection and typical values for the caloric content of mammalian biomass. Metabolic rates are temperature corrected using an Arrhenius function with the Arrhenius temperature estimated to be 8627 Kelvin. The effect of variation in the coefficients C_0 and C_1 is represented by upper and lower predictions based on the lowest and highest values of $\dot{v}$ and $[\dot{p}_M]$ that were observed for mammals in the 'add_my_pet' collection (see supplementary data). Variation in the mass, density and energy density coefficients (d_v and d_E) of mammalian biomass was assumed to be insignificant compared to the observed variation in the dynamic energy budget (DEB) parameters $\dot{v}$ and $[\dot{p}_M]$, which can differ by some two orders of magnitude for different mammals. The nonallometric DEB function predicts metabolic rate to scale with mass$^{0.767}$ for the largest observed masses in the data set and with mass$^{0.915}$ for the smallest. Data from McNab (2008) and Kolokotrones *et al.* (2010).

likely to be more frequently exposed to conditions below their thermal-neutral zone and may thus have higher resting metabolic rates as a correlated response to higher heat-generating capacity overall (Rezende, Bozinovic & Garland 2004). Indeed, the previously mentioned add_my_pet collection of eco-physiological data and DEB parameters revealed a deviation from the expected pattern in parameter values that extends outside mammals: small-bodied species that live off blooming resources have a much higher somatic maintenance than expected (Kooijman 2013). This eco-physiological adaptation was hypothesised to result from the wasting of resources in order to boost production (growth and reproduction), while keeping adult body size small.

DeLong *et al.* (2010) recently tested Kleiber's law across a size range inclusive of unicellular eukaryotes and prokaryotes and supported deviations from Kleiber's law at the extreme of small sizes. The linear scaling of unicellular eukaryotes was argued to be a response of the linear increase in the membrane-bound sites of ATP synthesis located in organelles, concordant with the linear scaling of structure with mass predicted by DEB theory at very small sizes. This steeper linear scaling of smaller

Table 2. The parameters required to specify the metabolic scaling relationship for mammals were estimated separately (see Supporting information) from the literature and 'plugged in' to the derived DEB equation. The rate parameters are given for 20 °C and are obtained from averages for the mammal entries of 'add my pet'

Parameter	Units	Description	Value
d_v	g (wet) cm^{-3}	Density of structure	1·0
d_E	g(wet) J^{-1}	Energy-to-mass coefficient of reserve	$1·45 \times 10^{-4}$
$\dot{v}$	cm d^{-1}	Conductance	0·043
$[\dot{p}_M]$	J cm^{-3}	Somatic maintenance	90·4

DEB, dynamic energy budget.

organisms is also supported by Huete-Ortega *et al.* (2012) in a study on the metabolic scaling of unicellular autotrophic protists where they highlight the importance of changing surface-to-volume ratios. Indeed, changing surface-to-volume ratios slow growth down during the cell cycle in a way that is well-captured by DEB theory, which successfully describes microbial growth, respiration and product formation (Kooijman 1986, 2010; Evers 1991; Hanegraaf & Muller 2001; Brandt, Van Leeuwen & Kooijman 2003; Brandt *et al.* 2004; Eichinger *et al.* 2010). The DEB explanation has particular, and experimentally confirmed, implications for population growth (Ratsak 1995; Ratsak, Maarsen & Kooijman 1996 on ciliates, Kooijman & Kooi 1996 on myxamoebae, Hanegraaf, Stouthamer & Kooijman 2000; Muller 2011; Muller *et al.* 2011 on yeasts, Lorena *et al.* 2010 on microalgae) and readily explains the difference between flocculated growth and growth in cell suspension (Brandt & Kooijman 2000) and the effect of genome size on population growth (Stouthamer & Kooijman 1993).

Implications, extensions and limitations

Dynamic energy budget theory considers the interspecific relationship between metabolic rate and mass as being mediated by two compartments (structure and reserve), each with separate dynamics. But, just as metabolic rate can be expressed as a function of reserve and structure, so can many other life-history traits. In contrast to the WBE approach, which uses the theoretical scaling of oxygen delivery to derive other life-history scaling relationships, DEB theory views reserve dynamics as fundamental to these relationships, including how the rate of oxygen consumption scales with body size. Knowledge of how the relative contribution of reserve to biomass varies with size allows the calculation of simple scaling relationships of life-history traits.

Table 3 provides DEB theory equations for some other important interspecific scaling relationships in terms of mass (see Supporting information for derivations). These equations are not all strict power functions but, at the infinite limit of mass, many converge on the quarter-power scaling relationships frequently observed in biology. However, even in finite mass ranges these nonallometric functions can approximate quarter-power scaling.

There are theoretically sound reasons for the expression of biomass in terms of reserve and structural mass, not least of all because this distinction helps to increase the coherence of intra- vs. interspecific scaling (Kooijman 2010; Sousa *et al.* 2010). Zeuthen (1947) was the first to point to the fundamental difference between these scaling relationships, an important warning that went almost lost in recent discussions. Reproductive rate, for example increases with mass intraspecifically but decreases interspecifically; the reason being that the cost per neonate is expected to be constant within species, but varying between species. Under food restriction, adult reserve can

Table 3. Dynamic energy budget theory was used to derive equations for the scaling of a number of important life-history traits. When expressed in terms of total mass, rather than structure and reserve, the well-known quarter-power scaling relationships emerge at the infinite limit of mass. For derivations of the relationships, see Supporting information

Trait	Interspecific scaling of traits	
	In terms of V_m and E_m	Limit as mass $(M) \to \infty$
Body mass	$M = d_V V_m + d_E E_m$	∞
Metabolic rate	$\dot{B} = [\dot{p}_M] V_m$	$\dot{B} \propto M^{\frac{3}{4}}$
Growth rate[a]	$\dot{r}_B = \frac{[\dot{p}_M]}{3[E_G] + 3E_m/V_m}$	$\dot{r}_B \propto M^{-\frac{1}{4}}$
Food uptake rate[b]	$\dot{p}_A = [\dot{p}_A] V_m$	$\dot{p}_A \propto M^{\frac{3}{4}}$
Starvation time	$t_S = \frac{E_m}{V_m [\dot{p}_M]}$	$t_S \propto M^{\frac{1}{4}}$
Mass at birth[c]	$M_b = \frac{V_b}{V_m}(d_v V_m + d_E E_m)$	$M_b \propto M^1$
Development time to V_p	$t_P = \frac{1}{\dot{r}_B} \ln \frac{V_{3m}^{\frac{1}{3}} - V_{3b}^{\frac{1}{3}}}{V_{3m}^{\frac{1}{3}} - V_p^{\frac{1}{3}}}$	$t_P \propto M^{\frac{1}{4}}$
Egg mass	$M_e \simeq d_E \left(\frac{V_b}{V_m}\right)^{\frac{1}{3}} E_m \left(1 - \frac{1}{4}\left(\frac{V_b}{V_m}\right)^{\frac{1}{3}}\right)^{-3}$	$M_e \propto M^1$
Reproductive rate[d]	$R = \frac{(1-\kappa)d_E \dot{v} E_m}{V_m^{\frac{1}{3}} M_e}$	$R \propto M^{-\frac{1}{4}}$

[a]$[E_G]$ is the cost per unit of structure. This growth rate coefficient is identical to the von Bertalanffy growth rate.
[b]$\dot{p}_A$ is volume specific uptake rate.
[c]V_b is structure at birth and must be less than some arbitrary structural volume, V_p.
[d]$1 - \kappa$ is the proportion of the mobilisation flux allocated to reproduction, assuming the remaining proportion κ is being allocated to maintenance at full size. Prior to reproductive age this energy is assumed to be dissipated as a cost of development.

decrease intraspecifically, so the amount of resources available for reproduction decreases, and reproductive rate declines with size. This reduction in adult reserve also occurs for interspecific size decreases (see Fig. 1), but is accompanied by a greater decrease in offspring size (see Table 3), which has the net effect of increasing reproductive rate.

This distinction also leads to different expectations of the scaling of uptake rates. Table 3 shows that assimilation is expected to scale interspecifically with mass^3/4 at the infinite limit of mass (higher exponents for finite masses). During ontogeny, however, assimilated energy needs to match the rate of reserve mobilisation and so only scales with mass^2/3 (Kooijman 1986, 2010). Indeed, uptake rates have been found to scale interspecifically with an exponent significantly larger than 2/3 and 3/4 (Pawar, Dell & Savage 2012), which is the DEB expectation for finite sizes.

Perhaps most relevant to the topic at hand, thinking of biomass in terms of structure and reserve also leads to a very different interpretation of inter- vs. intraspecific scaling of respiration – an area of metabolic theory that has attracted much criticism in the past. Studies investigating the intraspecific scaling of respiration rate frequently find the relationship is best approximated by a mass exponent

significantly different from ¾ (Glazier 2005, 2006; Caruso *et al.* 2010), while others question the appropriateness of fitting a simple power law altogether (Glazier 2005, 2006; Sears *et al.* 2012). Intraspecifically and under constant food, DEB theory predicts that maintenance costs would scale proportionally to mass. The decrease in mass-specific respiration that is frequently observed through ontogenetic development is explained by the decreasing contribution of growth overheads to respiration. Under DEB theory, the changing relative contributions from growth, assimilation and maintenance to intraspecific respiration explains variation in the estimated exponent. This important distinction between intra- and interspecific cases has been used to successfully predict the ontogenetic respiration of bryozoans, which scaled with mass$^{1/2}$ (White *et al.* 2011). The reserve concept also captures the time course of respiration rates during embryonic development. At the beginning of embryonic development, the egg consists almost entirely of reserve and hardly respires but, as the embryo grows, somatic maintenance and growth overheads contribute more and more to respiration until hatching. This frequently observed pattern is shown in Fig. 3.

The previous examples illustrate how the biological quantities of reserve and structure can be more informative than the total body mass of an organism. Unlike body mass, however, these abstract quantities can be difficult to measure in practice. If reserve was defined as something easily measurable, such as fat storage, an elephant weighing roughly 200 000 times more than a mouse would have *c.* 200 000$^{1/4}$ ~ 21 times more fat storage per mass than a mouse. As such a simplistic interpretation would lead to incongruities with empirical knowledge, constituents of reserve and structure are best defined by their dynamics: reserve consists of those elements of biomass that have a finite turnover, while those elements that are maintained indefinitely comprise structure. Both
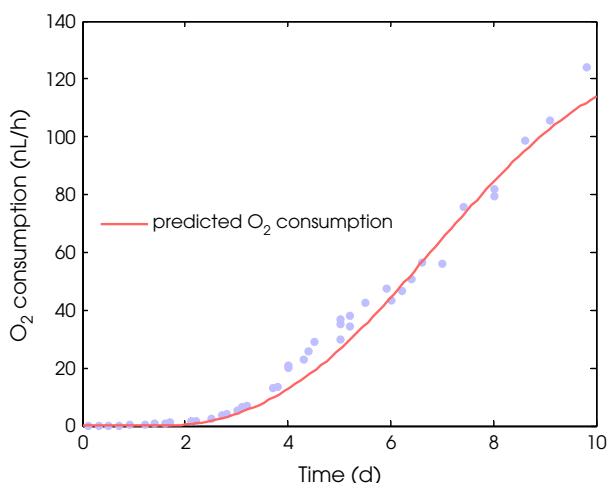
reserve and structure are treated as generalised compounds: mixtures mainly consisting of carbohydrates, protein and lipids, with potentially different weight coefficients. The utility of the concepts of reserve and structure should not be seen in the ease of their measurement but in their theoretical implications. Allele frequencies in a population, for example were initially very difficult to measure but have conceptually revolutionised evolutionary biology. In a similar vein, Houston & McNamara (2014) take the theoretical currencies of animal condition and reserve, in addition to energy and time, to create a more nuanced model for foraging behaviour, suggesting ways in which the DEB state variables of reserve and structure could be further extended.

Discussion

The discussed theories for metabolic scaling each offer idealised 'canonical' models. The similarity in the predicted interspecific scaling of metabolic rate with body mass can be interpreted intuitively as design constraints on the rate of energy and material flows within organisms. In 'transport models', nutrients are delivered through a network to 'terminal units' (WBE) or 'service volumes' (Banavar *et al.* 2002), each with an invariant metabolic rate (i.e. maintenance cost). Network design constraints imply that the volume of animal associated with each terminal unit increases with body mass, and that there is a matching between supply and demand. Because terminal units have fixed metabolic rates, metabolic rate per unit mass decreases with body mass. In DEB theory, metabolic rate is constrained by the utilisation process of storable metabolites (reserve) and the regulation of their concentration within an organism. Assimilate is eventually transformed into structural biomass with an invariant specific maintenance cost, where the chemical intermediate of this process is defined as reserve. Constraints on reserve utilisation require that the ratio of structure to reserve decreases interspecifically with body mass. Because structure has a fixed maintenance requirement, metabolic rate per unit mass for a nongrowing animal decreases with body mass.

Interestingly, in both the DEB and WBE theory, metabolic scaling is explained by the scaling of the relevant metabolite interface (exposed periphery of reserve pools in DEB theory, and the terminal unit in the supply network in the WBE), but neither of these metabolite interfaces scale with mass$^{2/3}$, as one might naively expect from simple Euclidean geometry. If these important interfaces really are scaling in unison then, taken together, these theories show how optimal nutrient transport designs can coincide with the decreased metabolic demands resulting from simple reserve dynamics. There are, however, some clear areas of divergence, particularly regarding the relationship between inter- and intraspecific scaling of biological rates, which suggest fruitful tests to further refine the current theories of metabolism.

Fig. 3. Dynamic energy budget (DEB)-based equation modelling embryonic respiration in the pond snail *Lymnaea stagnalis* (adapted from Kooijman 2010). Respiration increases until hatching as embryonic structure accumulates.

We end by noting that mechanistic models are built from a small set of core assumptions or first principles that are causally linked and capture something fundamental about a physical reality. The explanatory capacity of mechanistic models is based on the fundamental processes they consider. This provides robust predictive power, especially under novel circumstances. However, because these models only focus on a small number of processes, deviations from their predictions by specific organisms may be as instructive as congruence. When a particular species deviates from the patterns that were predicted, we can look to that organism's life history for explanations. With DEB theory, this is typically done by looking for the minimum set of modifications to the standard DEB model, such that a 'phylogeny' of model variants emerge (Van der Meer 2006b); there is no need to start from scratch with each new focal organism. With the growing body of data on DEB parameters, the DEB theory of interspecific scaling is thus not only of fundamental scientific interest, but also of considerable practical value.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Data S1. DEB parameter database.

Data S2. Mammalian respiration dataset (from Kolokotrones *et al.* 2010; McNab 2008).

Data S3. Detailed derivation of *a priori* predictions.