

Growth models based on first principles or phenomenology?

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Summary

1. Most models of growth are simply mathematical descriptions of growth trajectories. They are evaluated empirically based on goodness of statistical fit.
2. Recently we (West *et al.* 2001) presented a theory of growth based on first principles of energy conservation and allocation. The critical parameters are defined precisely and operationally in terms of measurable fundamental parameters not directly connected to growth, so the mechanistic basis of the model can be evaluated by testing both the assumptions and the predictions. To the extent that available data permit such evaluation, they generally support the model for many classes of organisms including mammals, birds, fish and crustacea.
3. Our model provides a basis for understanding the general and fundamental features governing ontogenetic growth. It is intended to explain the major patterns in terms of first principles of energy allocation to production (of new cells) and maintenance (of existing cells) that are applicable to all organisms. While the model is not intended to account for all of the observed variation in growth rates and life histories it does provide a baseline for developing more detailed treatments of ontogenetic growth.
4. Ricklefs (2003) has criticized the conceptual foundation of our theory as it applies to birds and asserts that it cannot account for many of their growth and life-history attributes.
5. He correctly points to similarities in mathematical form and statistical fit between our growth model and that of von Bertalanffy 1938, but fails to point out the fundamental conceptual differences between the two models.
6. With respect to birds, our model suggests a new hypothesis based on water balance, for the difference in growth allometry between altricial and precocial species. In particular we show that ours is the only model discussed by Ricklefs that correctly predicts the absolute value and scaling characteristics of the total energy metabolized by altricial birds from hatching to fledging.
7. In contrast, Ricklefs's models are of limited utility since they are primarily designed for birds, and are based on qualitative concepts such as 'growth potential' and 'functionality' of tissues and therefore do not readily lead to quantitative predictions.
8. Our model does not imply that mature or asymptotic size is determined simply by resource supply. It allows for a mature body size that is set by natural selection and that results in a balance of energy allocation between production of new biomass and maintenance of existing biomass.

Key-words: allometry, energy allocation, growth model, postnatal development

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Introduction

Even though ontogenetic growth is one of the most fundamental processes in biology, there is little in the way of a general theory of growth. There is a rich liter-

ature on the control of cell proliferation and differentiation, on the one hand, and on the evolution of life history attributes, on the other. Still largely missing, however, is a theoretical framework for understanding the mechanisms that affect whole-organism growth trajectories. So questions such as why growth curves are almost universally sigmoidal, what controls the final or mature body size, and what affects the allocation

of energy and materials to growth and development remain largely unanswered. Since the seminal work of Huxley (1932), however, some biologists have obtained valuable insights into these big questions by focusing on allometric or body size-dependent variation both within individuals, as body size changes over ontogeny, and between species that differ greatly in mature body size.

In this spirit, West, Brown & Enquist (2001) have recently taken an allometric approach to produce a general theoretical model that explicitly addresses the allocation of energetic and material resources to biosynthesis and whole-organism growth. This model is potentially very general and is able to account for the major features of ontogenetic growth in all multicellular animals, including determinate and indeterminate growers. Ricklefs (2003) has criticized this model, claiming that it is inadequate to account for much of the variation in patterns of post-hatching growth that he and colleagues have documented in birds. Ricklefs makes several points that are critical of or alternatives to our model. Here, we respond to the most salient points raised by Ricklefs and use this opportunity to offer a more complete explanation of our model, and to show how it erects a general theoretical framework, based on first principles of energy balance and allometric scaling of metabolism and biosynthesis, that offers new quantitative insights into the kinds of variation in growth patterns that have been documented in birds and other organisms.

Growth models and the $3/4$ allometric scaling exponent

As we had already emphasized in our paper, Ricklefs correctly points out that there is a plethora of growth models. Many give such good fits to empirically measured growth trajectories that there is little or no basis for choosing among them on statistical grounds alone. Usually good fits are simply obtained by adjusting parameters, and no attempt is made to understand the values of the parameters or the functions in the equations from any underlying theory of growth. There are several classes of growth models, one of which, attributed by Ricklefs to Pütter (1920), is of the general form

$$dm/dt = am^y - bm^z. \quad \text{eqn 1}$$

The rate of change in body mass, m , with time, t , is related to the difference between two power functions, each with a characteristic coefficient or normalization constant, a or b , and a characteristic allometric scaling exponent, y or z . In almost all versions $y < z$, and the growth trajectory has the characteristic sigmoidal shape that is observed empirically.

Most growth models are simply descriptive and make no implicit or explicit assumptions about the biological processes that regulate growth and development. Consequently, neither the coefficients, a and b , nor the exponents, y and z , are predicted but instead are obtained

by curve fitting. This is true of most versions of the Pütter equation. An exception is the model of von Bertalanffy (1938, 1957), which characterizes growth as the difference between rates of anabolism and catabolism. von Bertalanffy suggested a version of the Pütter equation in which $y = 2/3$ and $z = 1$, justifying this choice of exponents on biological grounds, but leaving a and b undetermined. He assumed that $y = 2/3$ because 'anabolism' or production scaled with metabolic rate, which he took to be a surface phenomenon and therefore to scale as $m^{2/3}$. He further assumed that $z = 1$ because 'catabolism' or maintenance simply scaled linearly with body mass. Even for the von Bertalanffy model, however, the coefficients, a and b , are not derived from any underlying theory but must instead be obtained by curve fitting.

We derived a general model for growth based on first principles of mass and energy balance which incorporates the allometric scaling for the cost of producing and maintaining cells. Our derivation naturally leads to a version of the Pütter equation in which

$$dm/dt = am^{3/4} - bm. \quad \text{eqn 2}$$

Our model differs from that of von Bertalanffy in two important respects. First, the exponent $y = 3/4$ instead of $2/3$. This reflects the widespread consensus that whole-organism metabolic rate scales as $m^{3/4}$. This consensus, originally based solely on empirical grounds, did not emerge until after von Bertalanffy's work (Peters 1983; Calder 1984; Schmidt-Nielsen 1984). We have recently derived a theoretical explanation for the $m^{3/4}$ scaling of whole organism metabolic rate, based on design constraints that limit the supply of energy and materials to cells through fractal-like networks (West *et al.* 1997; West *et al.* 1999). Our model predicts $y = 3/4$ because our equation links growth directly to the rate of metabolism, which must generate the energy that fuels growth. We were well aware (West *et al.*, 2002b), and Banavar *et al.* (2002) and Ricklefs have subsequently pointed out, that the difference between the $3/4$ and $2/3$ scaling exponent results in only a small change in the shape of predicted growth curves. Because the data are not sufficiently precise, it is often difficult to choose between our model and von Bertalanffy's solely on statistical grounds and a best fit analysis.

Second, and more importantly, our model differs fundamentally from von Bertalanffy's, because it characterizes growth in terms of underlying biological processes, thereby leading to expressions for a and b in terms of more fundamental quantities. Contrary to the impression given by Ricklefs, the difference is much more than just a matter of bookkeeping: it is not, for example, because we express body size in terms of number of cells rather than overall mass, or because we simply substitute $3/4$ for the $2/3$ in von Bertalanffy's model. We derive equation 2 from first principles of mass and energy balance and the energetic costs of building new cells and maintaining existing ones. At

any time during ontogeny, the rate at which oxygen and metabolites are delivered to cells via the respiratory and circulatory systems is directly proportional to the total whole-body metabolic rate, B . In the absence of growth, conservation of energy necessarily requires that this is the sum of the metabolic rates of all of the cells in the body. Thus, if the organism is assumed to be composed of N_c identical 'average' cells each having a metabolic rate, B_c then, clearly, $B = N_c B_c$. During growth, however, a portion of the available metabolic power delivered via the network is devoted to net biosynthesis to build additional cells, thereby increasing the total body mass. So, regardless of the details of the process, conservation of energy requires $B = N_c B_c + E_c dN_c/dt$, where E_c is the energy required to produce a new cell.

Ricklefs did not mention that our equation 2 is derived from this more fundamental and complete equation, which expresses the conservation of energy. By further imposing the conservation of mass, namely that, at any growth stage, the total mass of the organism is the sum of the masses of all the cells: $m = N_c m_c$, where m_c is the average mass of a cell, this can be re-expressed as

$$\frac{dm}{dt} = \left(\frac{m_c}{E_c}\right)B - \left(\frac{B_c}{E_c}\right)m \quad \text{eqn 3}$$

Assuming that whole-organism metabolic rate, $B = B_0 m^{3/4}$, equation 3 can then be rewritten as equation 2. Obviously, if B were a more complex function of mass or had a different or varying exponent, this could be used in equation 3. Indeed, for sufficiently small $m < \mu$, (~ 1 g for mammals), we have shown that B is linear in m , rather than scaling as $m^{3/4}$, in which case $dm/dt \propto m$ (West *et al.* 1997, 2002a). Thus, for small times until m reaches $\sim \mu$, this leads to an exponential growth rather than the t^4 behaviour of equation 3. In any case, this derivation makes it clear that the two terms on the right-hand sides of equations 2 and 3 do not simply represent 'anabolism' and 'catabolism.' The growth process that we model is more realistic and complicated than von Bertalanffy envisaged. The energetic cost of creating a new cell, E_c , which is energy devoted to 'anabolism' or biosynthesis, appears in *both* terms. The reason that growth slows and ultimately ceases as body size increases is that the energetic cost of maintaining existing biomass increases more rapidly than the energetic capacity to synthesize new biomass. As discussed below, however, this does not necessarily mean that the cessation of growth is due to whole-body vascular resource supply proximally limiting biosynthesis and cell proliferation.

More importantly, because our equation is derived from underlying principles, it contains no 'arbitrary' parameters. All the parameters occurring in our model are determined in terms of more fundamental quantities that can be measured independently of ontogenetic growth. For example, E_c , the energy cost of biosynthesis per gram to produce a new cell, has been estimated

empirically to be ~ 7 kJ g^{-1} (Peters 1983). Our derivation leads to expressions for the two parameters $a \equiv B_0 m_c / E_c$ and $b \equiv B_c / E_c$ and determines the values for the two exponents $y = 3/4$ and $z = 1$. In all other models, including von Bertalanffy's, the values of a and b are simply estimated by fitting the observed growth curve rather than by deriving them from first principles. Indeed, several authors have criticized statistically fitting ontogenetic growth 'models' that have no theoretical basis. This practice provides little insight into the mechanisms that produce the characteristic shape of growth curves and cause variability in the fitted parameters a and b (Roff 1980; Zullinger *et al.* 1984; Day & Taylor 1997).

In contrast, our model provides an explicit framework for predicting growth trajectories based on fundamental attributes of whole-organism and cellular energetics reflected in the values of a and b . Because these coefficients have explicit mechanistic definitions, we can understand how variations in these quantities are related to variation in growth rates and asymptotic body sizes among different kinds of organisms. For example, our theory gives an explicit prediction for the asymptotic mass, M , in terms of the basic underlying parameters: $M = (B_0 m_c / E_c)^4$. Alternatively, we can determine how a and b scale with asymptotic mass, M : a is approximately invariant, whereas b decreases as $M^{-1/4}$, reflecting the behaviour of B_c . The coefficient a relates the rate of energy allocation to produce a cell to the rate of the whole-organism metabolic rate that must fuel this biosynthesis in terms of normalization constant, B_0 . In our paper, we showed that the predicted values of $a = B_0 m_c / E_c$ are in good agreement with physiological data. The other coefficient $b \equiv B_c / E_c$ represents the ratio of the power required to maintain a cell relative to the energy required to produce a new cell. So b is directly related to the size at maturity, M , and hence to the time required to grow to asymptotic size.

We have subsequently shown that in ectothermic organisms, where temperature is a primary determinant of metabolic rate and other biological rates and times, a can be related to temperature via the Boltzmann factor or the van't Hoff-Arrhenius relation, $e^{-E/kT}$, where E is the activation energy for the rate-limiting biochemical reactions of metabolism, k is Boltzmann's constant and T is temperature in K (Gillooly *et al.* 2001; Gillooly *et al.* 2002). Note that in Table 1 of our paper the values of a are similar across species of endothermic birds and mammals (mean value = 0.38 $g^{1/4} \text{ day}^{-1}$, except for altricial birds which will be explained below), whereas the value for an ectothermic tropical fish, the guppy, is somewhat lower (0.10 $g^{1/4} \text{ day}^{-1}$), and the values for the colder-water ectotherms, salmon, cod and shrimp are almost an order of magnitude lower still (0.017 – 0.027 $g^{1/4} \text{ day}^{-1}$). Application of our model to embryonic (prehatching) development in diverse kinds of organisms showed that adjustment for temperature accurately predicts times to hatching for birds' eggs in relation to those of oviparous ectotherms (Gillooly *et al.* 2002).

The prediction of absolute normalizations as a model discriminator

Our theory not only predicts the shape of the growth curve but also its absolute normalization and how that scales with M . It is this property, rather than the goodness of fits to empirical growth curves, that distinguishes our model from previous ones, including Ricklefs' own models of ontogenetic growth (Ricklefs 1969, 1979).

Several examples of quantitative predictions for absolute values are given in our paper. Here we present a particularly powerful example that can be used to rule out most of the variants of the Pütter equation discussed by Ricklefs. Consider the question of how much metabolic energy, E_m , is used by the organism in reaching maturity, defined as when its mass reaches within a given fraction, ϵ , of its asymptotic mass: that is, when $m = m_m = (1 - \epsilon)M$. This was derived in our paper and found to be

$$E_m = \int_0^{t_m} B(m) dt = -\left(\frac{4B_0}{a}\right) M \left[\ln\left(\frac{\epsilon}{4}\right) + \frac{11}{6} \right] \quad \text{eqn 4}$$

where t_m is the time to maturity (which we showed scales as $M^{1/4}$, in agreement with data). This is rederived in the Appendix in the context of water loss for altricial hatchlings. Note that the coefficient $4B_0/a = 4E_c/m_c$. Our theory therefore predicts that E_m should scale linearly with asymptotic mass, M , so that $E_m = E_0 M$ with E_0 a constant given by equation 4. Now, the energy content of tissue per unit mass is $\sim 7 \text{ kJ g}^{-1}$ (Peters 1983), which we identify with the energy content per cell, E_c/m_c . Taking $\epsilon = 0.15$, we therefore predict from equation 4 that $E_0 \approx 40.6 \text{ kJ g}^{-1}$. Data on E_m for birds have been collected by Weathers (1992); these are primarily for altricial birds (discussed in more detail below and in the Appendix) and represent the energy metabolized from hatching to fledging. For 31 birds covering a range of mature masses from 9.7 g to 3700 g he finds $E_m = 28.43 M^{1.06} \text{ kJ}$ and states that 'the scaling exponent is not significantly different from 1'. In Fig. 1 we show Weathers' data for E_m plotted as a function of M together with his best fit and our prediction. Given the uncertainty in the value of the basic parameter E_c/m_c the agreement with our prediction is remarkably good. The closeness of agreement between the theoretical prediction and data should not be taken too seriously because there are significant uncertainties in the basic parameters. Rather, this should be viewed as illustrating the power of the model (based on first principles of cellular metabolism) to understand quantitatively the general features of growth phenomena. This is particularly true given that none of the alternative proposals for growth equations predicts this behaviour, as we now show.

The linearity prediction for E_m is a deceptively simple but nontrivial result. For, if E_m is calculated using an arbitrary Pütter equation for growth, equation 1, it leads to

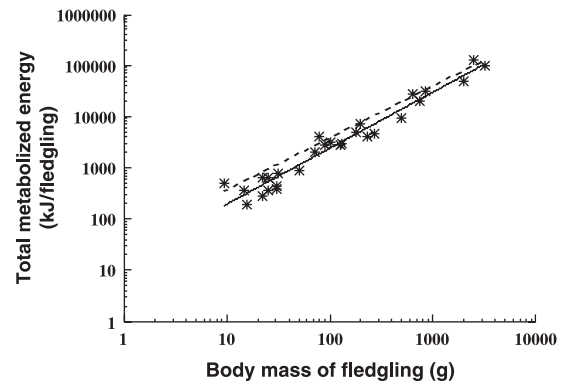


Fig. 1. Log-log plot of total metabolized energy from hatching to fledging as a function of fledgling mass; data taken from Weathers (1992). The solid line represents Weathers' best fit (whose slope is 1.06, consistent with unity) while the dotted line represents the absolute prediction of our model (both the linear slope and the normalization); see equation 4. No other growth models predict agreement with this data; see equation 5.

$$E_m = -\left(\frac{B_0}{a(z-y)}\right) M^{1+a-y} \left[\ln\left(\frac{\epsilon}{4}\right) + C \right] \quad \text{eqn 5}$$

where $B = B_0 m^\alpha$ and C is a calculable constant. When $\alpha = y = 3/4$ and $z = 1$ (as in our model) this reduces to equation 4 with $C = 11/6$. However, for an arbitrary Pütter model, equation 5 shows that the dependence on M is only linear when $\alpha = y$. Since $\alpha = 3/4$, it is clear that this rules out *all* models considered by Ricklefs (2003) in his Table 2, except for ours and that of von Bertalanffy (which also predicts a linear dependence since he would have $\alpha = y = 2/3$). However, in addition to the deficiencies already mentioned concerning von Bertalanffy's model, it suffers from not giving a prescription for determining the parameters a and b and therefore cannot predict absolute values of quantities such as E_m .

As another example we discuss below the related issue of water use in altricial birds growing from hatching to fledging and its effect on the apparent value of the metabolic rate exponent, α . Details can be found in the Appendix.

Variation in growth rates among birds

Ricklefs claims that our model cannot account for all of the variation in patterns of growth measured in birds in different taxonomic groups or with different life histories. On the one hand, we agree. As is customary with allometric relationships, the model is intended to explain universal phenomena that are most apparent when body size varies over several orders of magnitude. It provides a quantitative explanation for growth based on first principles of energy conservation and allocation. It is intended to apply to all multicellular eukaryotes in which: (i) whole-organism metabolic rates scale as $m^{3/4}$, and (ii) biosyntheses have a near-constant cost because they are performed by the same basic biochemical reactions.

In providing a simple theoretical explanation for major trends, our model deliberately leaves out the detail required to explain all the variations on these themes. Nevertheless, it provides a basis for building potentially more detailed models that incorporate phenomena that play a secondary role in determining growth. In saying this, we do not mean to imply that this variation is uninteresting or that it cannot be explained, at least in part, by more specific models or hypotheses which incorporate additional variables and processes. We do mean to imply, however, that most taxon-, functional group- or environment-specific variation is, by definition, secondary to the main themes of biological variation that are related to body size, temperature and stoichiometric composition. Indeed, general models that incorporate universal scientific principles and biological processes that can be expected to hold across all (or nearly all) organisms provide a predicted baseline for assessing the influence of other variables and processes. Variation takes on additional and insightful meaning when it can be measured as quantitative deviation from a theoretical prediction. We suggest that most of the variations in avian growth trajectories noted by Ricklefs are of this type. Doesn't it make more sense to first ask to what extent growth of birds can be understood in terms of principles and processes that apply to the vast majority of organisms, before focusing on the details of differences among species or functional or taxonomic groups of related species?

We believe that evaluating our model in this way would enhance understanding of avian life histories by integrating them into a general theoretical framework: one that emphasizes the common features of living things, rather than the enormous and often idiosyncratic differences among them. In this regard, Ricklefs cites analyses of scaling of postnatal growth rates at different levels of the taxonomic or phylogenetic hierarchy that give quite different estimates of allometric exponents, from 0.18 to 0.39 (Derrickson & Ricklefs 1988; Ricklefs & Nealen 1998). Ricklefs argues that differences at species, genus, family and order levels reflect historical patterns of life-history diversification, presumably in response to evolutionary innovations and selective pressures. We find these arguments unconvincing. They are based on the assumptions that the Sibley & Ahlquist (1990) taxonomy that the authors used accurately reflects phylogenetic relationships, and that taxa of the same rank had similar times or rates of evolutionary divergence. Furthermore, results of such analyses – including the statistics that Ricklefs reports for small taxonomic subsets of birds – are subject to biases influencing OLS regression statistics and consequently are likely to yield spuriously different allometric exponents (see Pagel & Harvey 1988; Harvey & Pagel 1991). Most importantly, however, the authors' explanations for different allometric scaling exponents at different taxonomic levels are *ad hoc*. Without a theoretical framework to make and test empirical predictions, it is difficult to assess whether

these apparent differences are artefacts of sampling or statistical analysis and/or whether they do indeed represent important evolutionary changes in the patterns and processes of avian growth and development.

Differences of tissue water content and 'functionality' between altricial and precocial species

We develop this point further by considering two kinds of variation to which Ricklefs has called attention. First he emphasizes the difference in the allometric scaling of growth and the cost of biosynthesis between precocial and altricial birds. He correctly notes that this difference is apparent only, or at least primarily, when body size is measured as wet mass. Altricial birds are hatched with unusually high quantities of water in their tissues and this water is used up as development proceeds. So when body size is measured as dry mass, the difference disappears: for both altricial and precocial birds, growth rates scales as $m^{3/4}$ and the whole-organism cost of producing new tissue scales linearly with mass – meaning that the energy cost of production per cell or per unit mass is essentially constant, independent of body size (Weathers & Siegel 1995; West *et al.* 2001). These results for dry body mass are exactly what are predicted by our model.

So the question now becomes, is the model flawed because in its original form it does not directly predict the wet mass growth trajectories of altricial birds, or is the model fundamentally correct but there is something special about the way that water content changes over the ontogeny of altricial birds? Ricklefs would suggest that it is the former. He argues that the 'functional maturity' or 'functional capacity' of tissues during ontogeny is omitted from our model. We note that the 'functionality' of tissue is difficult to define rigorously and mechanistically. We suggest that such terms are *ad hoc* phenomenological characterizations with little basis in first principles or biological mechanism. The special nature of the phenomenon is suggested by the fact that it appears to be restricted to altricial and semiprecocial birds.

We hypothesize that the high water content of tissues in hatchling altricial birds is a special feature of their physiological ecology. Altricial birds are incapable of foraging. They are fed by their parents a diet that is usually composed of insects or vertebrate flesh. Since the diet is essentially the same osmotic concentration as the adult tissues, and the nestlings lose water by evaporation and in the urine and faeces, they will experience a net loss of body water until their kidneys are able to produce sufficiently concentrated urine to compensate. We hypothesize that the high water content of altricial birds at hatching represents a store of water supplied by the mother in the egg to defray water loss during post-hatching development. (Avian physiologists have documented the provision of water in the egg to compensate for evaporative water loss during

incubation, which is a size-invariant quantity approximately 15% of total egg mass, e.g. Rahn & Ar 1974; Calder 1984.) In the Appendix we show how these ideas can be incorporated naturally into our model to modify the equations and to generate quantitative predictions that generally agree with observations. In particular, we show that the allometric exponent of metabolic rate for altricial birds as a function of wet mass should be a varying function with a value of order unity after hatching and decreasing to 0.75 at maturity, in agreement with the trends of the data (Weathers 1992).

Our hypothesis accounts not only for the observed water loss during nestling growth and development in altricial birds, but also for two other observations. First, as Ricklefs points out, 'semiprecocial' birds, such as gulls and terns, also hatch with reduced tissue 'functional maturity' and presumably with high tissue water content. Even though these semiprecocial birds hatch with downy plumage, open eyes and well-developed capacity to locomote and thermoregulate, they usually do not have access to drinking water and are fed flesh by their parents. Hence, they still require a store of body water to last them until they can produce concentrated urine. In contrast, truly precocial birds, such as ducks, chickens and quail, which do not have tissues of reduced 'functional maturity' and high water content at hatching, are able to travel to drinking water to meet their osmoregulatory requirements. Second, even though many mammals resemble altricial birds in being blind, naked and helpless at birth, investigators have not commented on their tissues exhibiting reduced 'functional maturity.' Altricial mammals are supplied with water in their mothers' milk. This, then, seems to be a simple explanation for why altricial mammals are not born with excessive quantities of water in their tissues and why they do have postembryonic growth rates that scale with wet body mass as $m^{3/4}$. Thus, we disagree both that 'it is premature to proclaim a general model for postnatal growth' and that our model cannot account for some of the subtle, but important, patterns of growth described by Ricklefs.

Is growth rate limited by resource supply or targeted adult size?

Ricklefs incorrectly characterizes our model as describing the situation where growth is limited directly by resource supply. We find this somewhat ironic, because a recent paper criticized our original model for the $M^{3/4}$ allometric scaling of whole-organism metabolic rate (West *et al.* 1997) for attributing the critical rate-limiting constraints to the whole-organism level rather than to the cellular and subcellular levels where the metabolic reactions actually occur (Darveau *et al.* 2002). We addressed this criticism in part by showing that constraints on the functional design of the whole organism dictate how processes at the cellular and subcellular level must scale allometrically with adult body size, rather than the other way round (West *et al.*

2002a,c; see also Banavar *et al.* 2003). Additionally, we note that the quarter-power allometries across species of different sizes are indeed rate-limited by the design of vascular and other resource supply networks. Within an individual that will grow to a given adult size, however, the absolute rate of resource flow and power output is clearly rate-limited by the network. As in any transport system, changes in supply and demand cause the flow through the network to change accordingly. This allows for sufficient production to fuel growth during ontogeny and also for changes in adult metabolic rate (metabolic scope) to accommodate the temporally varying demands of activity, reproduction, thermoregulation, moult and other energy-requiring processes. A simplified analogy is the power output of automobile engines: this scales with vehicle size, but the power of any given auto can be varied on demand by varying fuel supply.

Ricklefs incorrectly characterizes our model as predicting that increasing energy supply during growth should inevitably result in larger offspring. Having raised this straw man, he then cites evidence that changing resource supply by supplemental feeding of hatchlings has only a modest effect in accelerating growth rates. We are well aware of this, and of similar evidence that increasing nutritional status of female mammals has only modest effects on size of offspring at both birth and weaning. On the other hand, there is abundant evidence that in many organisms, from fruit flies to humans, severe restriction of food supply during development can prolong time to maturity and result in smaller adult size (Emlen *et al.* 1991; Lurling & van Donk 1997; Davidovitz *et al.* 2003). The variation in growth trajectories, even among littermates, as shown in Ricklefs' Fig. 2 by the standard deviation peaking well before asymptotic mass is attained, may reflect variation in environmental conditions (e.g. competition among offspring within a brood and variation in parental quality among broods) as well as convergence toward some targeted adult size. Of more direct relevance to our model would be plots of the actual growth trajectories of the individual offspring. Do the littermates each follow the predicted universal growth curve but have somewhat different growth rates and/or asymptotic sizes, or are the shapes of their growth curves fundamentally different?

Our model does, in principle, apply to cases where final size may be limited directly by resource supply, such as limitations of vascular supply on growth of malignant tumours (Guiot *et al.* 2003). In fact, this example indicates the hazard of inferring the existence of some inherent 'tissue growth potential' that always causes growth to cease at some relatively constant size. Our model is also meant to apply, however, to cases where the 'mature' or asymptotic size, is a relatively fixed target. This includes not only postnatal growth and development in determinate growers such as birds and mammals, but also prenatal or embryonic growth from zygote to hatching or birth within a bird egg or mammal

uterus. In these cases there is a substantial heritable influence on final size, both within and between species, and the large differences in body size between some species is the result of evolution by natural selection. The targeted adult size is set well below the size where the capacity of the vascular network to supply energy and nutrients directly limits cellular metabolism and biosyntheses. The reason is obvious. Adult organisms require considerable reserve metabolic capacity to fuel activity and reproduction. Indeed, metabolic rates during flight and other brief bouts of activity (i.e. metabolic scope) can be more than 10 times higher than resting or basal metabolic rates, and during periods of reproduction, cold stress, or moulting can be several times higher than field metabolic rates at other times.

Coda

Ricklefs ends by saying that ‘the search for (scientific) understanding must navigate a narrow path between the desire to have general laws and the empirical complexity of nature.’ We agree, but would respond with three comments. First, biologists have devoted much more attention to documenting the empirical complexities than to searching for general laws. Many biologists, seemingly as an article of faith, categorically reject the possible existence of any new general laws.

Second, the empirical observations have little value unless there are conceptual frameworks to organize the enormous variation among living things. The most powerful unifying concepts are general law-like mechanisms that reflect the operation of fundamental, generally accepted principles. Biology has such laws. Examples include the common evolutionary origin of life, the molecular mechanisms of inheritance, and the process of natural selection. Although these laws provide enormously powerful explanations for many empirical patterns, none of them can explain all of the enormously detailed, seemingly idiosyncratic variation among organisms. Let us not dismiss efforts to discover additional laws because they, too, do not provide a theoretical explanation for everything.

Third, much of our disagreement with Ricklefs seems to revolve around what constitutes ‘the essential features of variation in growth rate among species’. Growth is fundamentally a dynamical process of energy and material transformation that must obey the first principles of physics, chemistry and biology. Across all organisms ontogenetic growth rates are directly tied to metabolic rates, because biosynthesis is fuelled by the biochemical reactions of metabolism. Our theoretical explorations are based on the premise that much can be learned by probing deeply how body size, temperature and material (stoichiometric) resource requirements, which together determine most of the variation in metabolic rates, also affect growth rates and other biological rate processes. Our metabolic theory of growth is not intended to account for all of the variation. It is intended

to predict the major patterns of growth as manifestations of fundamental metabolic processes. If this can be done, then it should be easier to interpret and investigate the remaining variation. We see no reason why this theoretical approach in general, and our model of growth in particular, should not be as applicable to post-hatching growth of birds as it is to other biological growth processes, including tumour growth (Guiot *et al.* 2003) and population growth (Savage *et al.* 2003).

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Appendix: altricial birds

The growth of altricial birds presents an interesting variant on our growth model. Here we show that, for this case, the model naturally predicts that the allometric exponent for metabolic rate, α , is itself a function of the mass of the chick, as observed. The discussion presented here is a simplified version of a more complete analysis; details will be presented elsewhere. Generally speaking we show that α is predicted to be greater than the canonical $3/4$ until maturity when it asymptotes to $3/4$, in agreement with observation.

As discussed in the text, we assume that the predominant difference between precocial and altricial birds is that the latter hatch with an additional supply of water that lasts until they fledge and leave the nest. Up until that time altricial nestlings have no access to external water beyond that contained in food supplied by the mother and therefore have to rely on an excess repository acquired prior to hatching. Precocial birds do not need such an excess internal supply since they procure the requisite amount of water directly from the environment by drinking. Their development is therefore expected to follow the growth curve described by equation 2 with m as their total body mass. As remarked in our paper, altricial birds are also expected to follow the same growth curve but with m interpreted as their 'dry' mass, that is, the difference between their total body mass,

m_{tot} , and the mass of excess water, m_w , remaining in their bodies at time t after hatching; thus, $m_{\text{tot}} = m + m_w$. In support of this is the observation that metabolic rates of altricial nestlings scale as $m^{3/4}$ as a function of dry mass, whereas they scale as m_{tot}^α as a function of total body 'wet' mass, with α varying between 0.8 and 1.6 and with mean value of 1.1 (Weathers & Siegel 1995).

We assume that the excess water, like any metabolite, is consumed at a rate that is proportional to overall metabolic rate, B . Thus, if m_w^e is the mass of the excess water consumed at time t after hatching, then $dm_w^e/dt = fB$, where f is a proportionality constant. With $B = B_0 m^{3/4}$ this can be straightforwardly integrated to give

$$m_w^e = -f \left(\frac{4E_c}{m_c} \right) M \left[\frac{r^3}{3} + \frac{r^2}{2} + r + \ln(1-r) - \frac{r_0^4}{4} \right] \quad \text{A1}$$

where $r = (m/M)^{1/4}$, $r_0 = (m_0/M)^{1/4}$, M the mass at maturity and m_0 the mass at hatching. Notice that in this equation m_w^e is expressed as a function of the dry mass, m , whose dependence on time is determined by equation 2.

The total excess water used between hatching and fledging is given by the value of m_w^e when $m = m_f$, the mass at fledging. But, this is just the total amount of excess water, m_w^{tot} , that the chick had to have when it hatched at time $t = 0$. Since $m_f \approx M$ (the asymptotic mass), $r \approx 1$ at fledging. Using these in equation A1 and introducing $\varepsilon = (M - m_f)/M$ then leads to

$$m_w^{\text{tot}} = -f \left(\frac{4B_0}{a} \right) M \left[\ln \left(\frac{\epsilon}{4} \right) + \frac{11}{6} \right] \quad \text{eqn A2}$$

Thus, the mass of excess water at hatching is predicted to be a constant fraction of the mature mass. A comparison of these predictions with data will be presented elsewhere. Suffice it to say here that this calculation is essentially identical to a calculation of E_m , the total metabolic energy used from hatching to fledging, which is given in equation 4; the only difference is the presence of the factor f in equations A1 and A2. In the text we show how the prediction of linearity of E_m with M and the value of the overall normalization are in good agreement with data.

Since $m_{\text{tot}} = m + m_w$, the expression for the total body mass $m_{\text{tot}}(t)$ as a function of time t is quite complicated: $m_{\text{tot}}(t) = m(t) + m_w^{\text{tot}} - m_w^c[m(t)]$. The first term $m(t)$ is the solution to equation 2 and can be found in West *et al.* (2001); the second term is a constant and given by equation A2; and the last term is given by equation A1 with the time dependence implicit in $r = [m(t)/M]^{1/4}$. The allometric exponent of B as a function of total body mass (α) can be determined by first expressing B in terms of dry mass, $B = B_0 m^{3/4}$, and then

inverting the above expression to write m as a function of m_{tot} ; α is then given by $\alpha = \partial \ln B / \partial \ln m_{\text{tot}}$. Though it is straightforward in principle to derive the exact expression, it is a somewhat involved and tedious procedure. For the present purposes it is more transparent to approximate B in order to expose the general features of the result. We first rewrite B as $B_0(m_{\text{tot}} - m_w)^{3/4}$ which, when $m_w \ll m_{\text{tot}}$, reduces to $B \approx B_0 m_{\text{tot}}^{3/4} [1 - (3/4)m_w/m_{\text{tot}}]$ leading to $\alpha \approx 3/4(1 + m_w/m_{\text{tot}} - \partial m_w / \partial m_{\text{tot}})$. Now, m_w is expected to be a monotonically decreasing function of m_w^{tot} , that is, $\partial m_w / \partial m_{\text{tot}} < 0$ so $\alpha > 3/4$ and is generally expected to be a decreasing function of chick mass. Furthermore, the magnitude of $\partial m_w / \partial m_{\text{tot}}$ is expected to be no larger than m_w/m_{tot} , so a rough estimate is $\alpha \approx 3/4(1 + c m_w/m_{\text{tot}})$ with $2 \geq c \geq 1$. Thus, if $m_w/m_{\text{tot}} \sim 0.2$ in early growth, then $\alpha \sim 1$, decreasing to 0.75 at fledging. These general trends are in agreement with data (Weathers & Siegel 1995); however, there is quite a spread in values of α (including values < 0.75) and a detailed analysis is clearly called for based on the exact solutions. Here, we are simply using this to stress the potential power of our theory and the methodology that can be brought to bear on 'special cases' such as the growth of altricial birds.