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Multiphasic allometry: the reality and significance of ontogenetic shifts in the body-mass scaling of metabolic rate

Douglas S. Glazier[1,*]

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Abstract

Commonly observed multiphasic ontogenetic scaling of the rate of metabolism with body mass deserves increased attention because metabolism fuels all biological processes, including growth and development. Traditionally, developmental biologists have largely overlooked how ontogenetic transitions are powered by metabolic energy. The reality of multiphasic allometry in some species has also been challenged based on statistical grounds. Therefore, this article attempts to provide helpful perspectives about the reality and significance of multiphasic ontogenetic allometry in three ways. First, it is argued that recent statistical criticisms of multiphasic allometry are problematic because they are based on data that were not properly scaled in geometric (log–log) space and/or on results of analyses of covariance that were distorted by unequal sample sizes and/or unequal/nonoverlapping body-size ranges of the different developmental stages analyzed. Second, it is recommended that the existence of nonlinear (multiphasic or curvilinear) allometry should be tested by comparing linear versus curvilinear regression models or body-size scaling slopes (and their 95% confidence intervals) of different developmental stages, each analyzed with separate, statistically independent log–log regression lines. Third, ontogenetic shifts in metabolic scaling are related to other fundamental developmental changes, thus highlighting the significance of multiphasic allometry for understanding organismal development. Ontogenetic metabolic allometry should be given a more central (general) place in the field of developmental biology.

Keywords: *body size, developmental stages, log-transformation, metabolic rate, multiple age-related allometric relationships, statistical methods*

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1. Introduction

Development of individual multicellular organisms is a dynamic process involving fundamental changes in body form and function. Many of these changes have been related to increases in body size. During ontogeny, diverse morphological, anatomical, and physiological traits (T) vary in magnitude with body mass (M) with such regularity that they can often be described by simple power functions ($T = aM^b$, where a is the scaling coefficient or antilog of the intercept in a log–log plot and b is the scaling exponent or slope). Often the exponent (b) is ≠ 1, which is called "allometric" [1]. Allometric relationships have been studied not only across species (see reviews in [2–4]) but also within species (e.g., [1, 5, 6]). Intraspecific allometric analyses may involve comparisons of individuals of the same or different ages or developmental stages (i.e., "static" versus "ontogenetic' allometry": see, e.g., [7]).

This article focuses on the ontogenetic allometry of the rate of metabolism. This is an important topic because metabolism fuels all biological processes, and therefore, an understanding of its variation during organismal ontogeny may provide important insight into the energetic demands of various developmental processes. Furthermore, numerous studies have reported that the ontogenetic relationship between metabolic rate and body size may shift significantly as organisms transition from one major developmental stage to another. For example, the metabolic scaling exponent is often positively allometric ($b > 1$) during embryonic development, isometric or nearly so during larval development ($b \approx 1$), and negatively allometric ($b < 1$) during later juvenile development toward adulthood (reviewed in [5, 8]). Ontogenetic shifts in metabolic scaling exponents (b) and/or intercepts (a) (i.e., multiphasic allometry) have been observed in diverse species, including plants (e.g., [9, 10]), various aquatic and terrestrial animals (e.g., [5, 6, 8, 11–27]), and even humans [28, 29].

Three major aims are pursued. First, an assessment is made about whether multiphasic allometry of metabolic rate during ontogeny is real or statistically spurious, as claimed in some recent critiques

[1]Department of Biology, Juniata College, Huntingdon, PA 16652, USA.
*email: glazier@juniata.edu

[30–34]. As a result, specific statistical methodologies are recommended for analyzing nonlinear (multiphasic or curvilinear) allometry. Second, some major hypotheses explaining the existence of multiphasic ontogenetic metabolic scaling are outlined. Third, further research is encouraged regarding the existence and mechanistic basis of multiphasic ontogenetic metabolic scaling and its incorporation into general theories of organismal development. Currently, ontogenetic allometry of metabolic rate receives no attention in leading textbooks on developmental biology (see, e.g., [35, 36]). Developmental energetics is an old topic [37–40] that deserves resuscitation, as recently noted by some developmental physiologists and molecular biologists (e.g., [6, 41–45]). A field of "metabo-devo" is now emerging and shows much promise for deepening our understanding of developmental processes [43].

This article aims to provide useful perspectives on current studies of multiphasic metabolic allometry that can be applied by students, beginning researchers, and established scientists working within various biological disciplines, including ecology, physiology, developmental biology, and the evolutionary biology of life histories. Because of space limitations, this article does not provide a comprehensive review of the various kinds of ontogenetic allometry nor of the statistical and scientific methodologies used to analyze them. Further background can be found in the literature cited herein.

2. Is multiphasic ontogenetic metabolic scaling real or statistically spurious?

2.1. Two major kinds of critiques

Although examples of ontogenetic shifts in metabolic scaling abound in the literature and have been known for decades, their existence has been recently disputed in two ways. First, it has been asserted that they are artifacts of using log-transformed data because ontogenetic shifts (i.e., distinct phases) in the allometry of various traits "disappear" when linear or nonlinear statistical analyses based on the original arithmetic data are used [30–32]. Second, it has been claimed that some examples of ontogenetic shifts in metabolic allometry based on log-transformed data "disappear" as well when fitted to single regression lines and analyzed by an analysis of covariance (ANCOVA) after the removal of supposed outliers [33, 34]. If generally true and applicable, these criticisms would necessitate a significant revamping of our knowledge of ontogenetic metabolic scaling. A major aim of this article is to challenge both these criticisms and argue that multiphasic ontogenetic metabolic scaling relationships are not merely statistical artifacts, but rather are real phenomena intimately tied to fundamental developmental changes in body form and composition, rate and cellular mode of growth, and other biochemical, physiological, and behavioral processes.

2.2. Is multiphasic ontogenetic metabolic scaling an artifact of logarithmic transformation?

Some studies [30–32, 46] have asserted that biphasic patterns of ontogenetic allometry are merely artifacts of using log-transformed data, as traditionally done for body-size scaling analyses for over a century (e.g., [1–5, 47]), because they allegedly "distort" relationships between the magnitude of traits and body size as observed in arithmetic space. Unfortunately, this viewpoint represents a misunderstanding of the value of carrying out scaling analyses in geometric (log–log) space because they allow the ready discernment of proportional relationships not easily analyzed in arithmetic space, as noted by many leaders in the field of allometry (e.g., [48–51]). Proper scaling in allometric analyses requires a focus on proportions (relative values), not absolute values. Some studies [46, 52–54] have continued not to recognize this critical point and others reviewed by [51] showing the value of using log-transformed data in scaling analyses.

In addition, some studies [52–54] have not fully appreciated the many observations that indicate that allometric scaling analyses are distorted by using unscaled arithmetic data (see, e.g., [50, 51, 55–60]). In arithmetic analyses, large organisms have larger variation of absolute trait sizes and broader body-size ranges that outweigh the smaller variation of absolute trait sizes and narrower body-size ranges in small organisms, thus producing distorted linear (or nonlinear) regressions that do not evenly represent relative (proportional) trait variation at different body sizes. Logarithmic analyses prevent this kind of distortion. As one example also discussed in Section 2.3, the phyllosoma larvae of the spiny lobster (*Sagmariasus verreauxi*) exhibit significantly steeper metabolic scaling in log–log space than do older juveniles [25]. However, when the effect of body size on metabolic rate is examined in arithmetic space for both developmental stages analyzed together, an ontogenetic shift is obscured by the overwhelming effect of the larger body-size range of the juveniles, which reduces the effect of the phyllosomas on the overall scaling relationship, because they occupy a relatively small body-mass range [51]. Therefore, it is not surprising that the use of unscaled arithmetic data results in a single highly significant regression line dominated by the juvenile variation in metabolic rate and body mass. The resulting "disappearance" of biphasic ontogenetic metabolic scaling is a statistical artifact resulting from not scaling the data evenly in geometric space, as is made possible with log-transformation.

2.3. Is multiphasic ontogenetic metabolic scaling an artifact of inadequate statistical analysis?

It has been proposed that biphasic ontogenetic metabolic scaling may not only be an artifact of log-transformation but also that ontogenetic metabolic scaling, even when based on log-transformed data, is better understood in terms of single linear regressions rather than multiple discontinuous scaling relationships [33, 34]. Attempts to support this point [33, 34] have involved re-analyzing three datasets [25, 27, 61].

First, one critique [33] argued that the biphasic ontogenetic allometry reported by [27] for the American eel (*Anguilla rostrata*) is an artifact of not eliminating a data point for the smallest thinnest eel analyzed, which was regarded as an outlier. However, the data point for this eel was not a statistical outlier in the original biphasic analysis using log-transformed data for metabolic rate and body mass [27]. It only becomes an outlier when a single regression line is forced through all the data for both juvenile and subadult eels. Other justifiable statistical and biological reasons are given by [61] for why [27] did not remove the point in question from their analysis, for which [34] has provided no counterarguments. Therefore, [61] concluded that the existence of an outlier was an artifact of an attempt by [33] to fit a single regression line to two developmental stages showing significantly different metabolic scaling with or without the point in question.

Second, [61] presented an additional scaling analysis showing significantly different ontogenetic scaling slopes for the metabolic rates of juvenile and subadult eels in relation to their body lengths, notably without outliers. In this analysis, the thinness of an individual eel that concerned [33] is clearly not a critical factor in causing the biphasic scaling observed. Nevertheless, [34] has argued that this finding of biphasic metabolic scaling in relation to body length is invalid because an ANCOVA reveals a barely nonsignificant interaction between body length and developmental stage (p = 0.06) on metabolic rate. Two counterarguments are possible. First, leading statisticians have disputed the value of strict dichotomous significance testing. As Rosnow and Rosenthal [62] once famously remarked, "surely, God loves the .06 nearly as much as the .05" (also see [63]). Even Fisher [64], who advocated $p \leq 0.05$ as a critical value for rejecting a null hypothesis, claimed that this value was arbitrary and based on no theoretical foundation. Second, [34] offers no adequate explanation for why an ANCOVA based on all the eel data analyzed together indicated only a marginally significant difference between the scaling slopes for juveniles and adults ($p < 0.10$), whereas a comparison of the 95% confidence limits of the slopes of the separately calculated regression lines for these developmental stages did show a significant difference ($p < 0.05$). The study of [34] asserts that the 95% confidence interval (CI) method used by [27, 61] is unreliable without saying why and despite it being commonly used to compare scaling slopes in the metabolic scaling literature (e.g., [2, 5, 9, 20, 23, 26, 55, 65–69]), as well as it being justified in the statistical literature (e.g., [70–74]). This criticism is apparently based on the mistaken belief that slopes with partially overlapping 95% CIs are not significantly different. However, this need not be true: when the values of each slope compared do not overlap with the 95% CI of the other, they can be considered significantly different at the $p \leq 0.05$ level [63, 70, 72, 74]. Many investigators do not realize that the complete nonoverlap of the 95% CIs of the slopes or other mean values being compared indicates significance at the $p < 0.01$ level [72, 74]. Using these criteria, the body-mass scaling slopes for metabolic rate differed at the $p < 0.01$ level for the developmental stages of the American eels (see [27]), whereas the body-length scaling slopes of the eels and the body-mass scaling slopes of the spiny lobsters at different developmental stages differed significantly at the $p \leq 0.05$ level (see [25, 61]). Although the 95% CI method has been criticized [75], the highly cited study by Cumming [74] showed that it is generally useful. Therefore, an alternative explanation for why the ANCOVA results reported by [33, 34] differed somewhat from those of [27, 61] is needed. A plausible answer is that an ANCOVA may, at least in some cases, be a less sensitive approach for detecting significantly different metabolic scaling slopes between developmental stages, compared to the 95% CI method.

This article provides credible reasons for why an ANCOVA should not be considered the "gold standard" for determining the existence of multiphasic ontogenetic metabolic scaling, as apparently assumed by [33, 34]. The ANCOVA was originally devised to allow the calculation of a factor's effect on a variable of interest, while controlling for the influential effect of a covariate such as body size [76]. In comparative biology, an ANCOVA is most reliable when comparing the elevations of parallel scaling relationships with similar sample sizes and equal, overlapping body-size ranges. However, it becomes less reliable when comparing scaling relationships that have different slopes and/or different sample sizes and/or unequal, nonoverlapping body-size ranges. The difficulty of correcting for body-size effects when the slopes of the scaling relationships being compared differ significantly has been recently reviewed [77]. Although ANCOVA allows the estimation of whether scaling slopes differ (as revealed by whether an interaction between the effects of body size and a factor of interest is significant), this estimation becomes increasingly unreliable when the sample sizes and body-size ranges of the scaling relationships being compared become increasingly different. This is especially true for comparisons of the metabolic scaling slopes of different developmental stages, which often have unequal and/or nonoverlapping body-size ranges. The rest of this section discusses examples supporting these points.

Consider the ontogenetic metabolic allometry of American eels in relation to body length examined by [27, 61]. A likely reason why the ANCOVA used by [34] revealed only a marginally significant difference in scaling slopes between juveniles and subadults is that the approximately 10-fold greater body size range of the subadults (see Figure 1 in [61] and Figure 1 in [34]) reduced the power of this method to detect a significantly shallower slope for the juveniles, as observed when each developmental group is analyzed separately [61]. This biased effect of the subadults on the results generated by an ANCOVA is evidenced by the scaling slope of the overall regression line (b = 2.52) being much closer to that for the subadults analyzed separately (b = 2.71) than that for the juveniles analyzed separately (b = 1.47). In short, the narrower body-size range of the juveniles reduced the ability of an ANCOVA to detect the significantly shallower scaling slope of this developmental stage.

A similar pattern is seen in an ontogenetic metabolic scaling analysis involving larvae of the Tobacco hornworm *Manduca sexta* [22]. In this case, as reported by [22], the metabolic scaling slope is significantly steeper for the third instar (b = 1.313 ± 0.304 [95% CI]) than for the fourth (b = 0.930 ± 0.168; $p < 0.05$) and fifth instars (b = 0.902 ± 0.051; $p < 0.01$) (**Figure 1a**). These scaling relationships excluded data for individuals that had reached their "critical mass" near the end of an instar when respiration rate asymptotes because of tracheal oxygen supply limits [22]. If all data are used, the metabolic scaling slope is still significantly steeper for the third instar (b = 0.924 ± 0.109) than for the fourth (b = 0.779 ± 0.095; $p < 0.05$) and fifth instars (b = 0.706 ± 0.051; $p < 0.01$) (**Figure 1b**). Critically, the body-mass range is much larger for the fourth and fifth instars grouped together than for the third instar. As a result, the scaling slope of the regression line for all data taken together (b = 0.792) is much closer to that for the fourth and fifth instars only than that for the third instar only (**Figure 1c**; also see Figure 1 in [22]). As seen for the American eels, the developmental stages with large body-size ranges obscure the significantly different scaling relationship for a stage having a smaller body-size range. Nevertheless, four kinds of statistical analyses confirm the multiphasic (polyphasic) allometry originally reported by [22]. First, the scaling slope for the third instar is significantly different from those of the fourth and fifth instars, as shown by the 95% CI method (and confirmed by using a similar method proposed by [71]). Second, an ANCOVA reveals a significant interactive effect of instar and body mass on metabolic rate, thus indicating distinct instar-specific scaling slopes (p = 0.001). Third, a quadratic regression analysis reveals a significantly curvilinear relationship between metabolic rate and body mass for all instars taken together ($p <$ 0.001; **Figure 1d**). This analysis shows that the instantaneous

slope shifts significantly from 1.009 at the smallest mass to 0.624 at the largest mass, thus corroborating the age-related decline in scaling exponent shown by comparing the scaling relationships of each instar calculated separately. Fourth, quadratic regression for each instar analyzed separately reveals significantly curvilinear relationships clearly showing developmental discontinuities (inset of **Figure 1b**; also see Figure 2 in [22]), thus providing further support for multiphasic allometry.

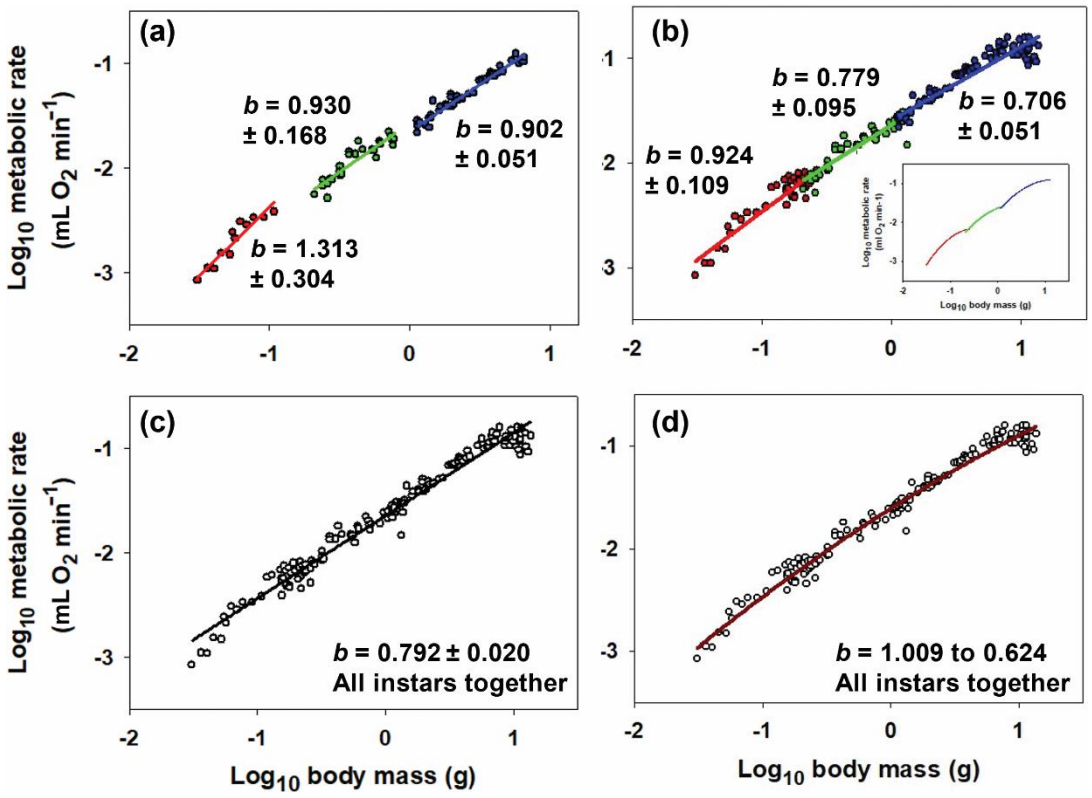

Figure 1 • Metabolic scaling relationships for the third, fourth, and fifth larval instars of the Tobacco hornworm *Manduca sexta* (adapted from [22], under a Creative Commons Attribution 4.0 International (CC BY) license). The scaling exponent (log–log slope = *b*) is shown for each line, along with the ±95% confidence intervals. (a) Least squares regression lines shown separately for each instar (not including individuals that have reached their critical mass): third instar ($Y = 1.313(X) - 1.061$; $r = 0.949$; $p < 0.001$; $N = 12$); fourth instar ($Y = 0.930(X) - 1.570$; $r = 0.916$; $p < 0.001$; $N = 27$); and fifth instar ($Y = 0.902(X) - 1.651$; $r = 0.979$; $p < 0.001$; $N = 43$). (b) Regression lines shown separately for each instar (including individuals that have reached their critical mass): third instar ($Y = 0.924(X) - 1.544$; $r = 0.937$; $p < 0.001$; $N = 43$); fourth instar ($Y = 0.779(X) - 1.637$; $r = 0.934$; $p < 0.001$; $N = 43$); and fifth instar ($Y = 0.706(X) - 1.593$; $r = 0.951$; $p < 0.001$; $N = 84$). The inset graph shows curvilinear (quadratic) lines for each instar: third instar ($Y = -0.880(X) - 0.897(X^2) - 2.375$; $r = 0.958$; $p = 0.038$ for X term; $p < 0.001$ for X^2 term; $N = 43$); fourth instar ($Y = 0.460(X) - 0.677(X^2) - 1.628$; $r = 0.948$; $p < 0.001$ for X term; $p = 0.003$ for X^2 term; $N = 43$); and fifth instar ($Y = 1.410(X) - 0.608(X^2) - 1.716$; $r = 0.975$; $p < 0.001$ for X term; $p < 0.001$ for X^2 term; $N = 84$). (c) A single linear regression shown for all three instars taken together ($Y = 0.792(X) + 1.644$; $r = 0.987$; $p < 0.001$; $N = 170$). Note how using a single linear regression analysis obscures the scaling differences between instars. (d) A single curvilinear regression shown for all three instars taken together ($Y = 0.787(X) - 0.074(X^2) - 1.610$; $r = 0.989$; $p < 0.001$ for X term; $p < 0.001$ for X^2 term; $N = 170$). The instantaneous slopes for the smallest to largest individuals were calculated as the first derivative = $2aX + b$, where $Y = aX^2 + bX + c$. Symbols defined: r = Pearson's product moment correlation coefficient; p = probability that r is due to chance; and N = sample size.

Unequal sample sizes may also reduce the reliability of an ANCOVA in detecting different scaling slopes. This concern applies to the Tobacco hornworm data (see **Figure 1a** and **b**) and the third dataset analyzed by [34], i.e., the ontogenetic metabolic allometry of spiny lobsters. In this case, the sample size for the phyllosoma larvae (7 points each based on 4–11 replicate measurements) was nearly twice as large as the sample size for the juveniles (4). The body-mass range of the phyllosomas was also larger than that for the juveniles (see Figure 3 in [25]; and Figure 2 in [34]). Again, the results of an ANCOVA are biased, due to a greater statistical impact of the scaling relationship for the phyllosomas compared to that for the juveniles. In this case, the scaling slope of the overall regression line ($b = 0.93$) was somewhat closer to that for the phyllosomas analyzed separately ($b = 1.01$) than that for the juveniles analyzed separately ($b = 0.83$). Nevertheless, an ANCOVA still yields a significant interaction term ($p = 0.01$), which should not be discounted as [34] does.

An ANCOVA is also not well suited for detecting significant slope differences between developmental stages with nonoverlapping body-size ranges. Extrapolating regression lines or their influence in a statistical analysis beyond that of the range of the empirical data is fraught with uncertainty [76, 78]. This is especially true for the American eel and spiny lobster datasets where there are large gaps between the body-size ranges of different developmental stages. Given this problem and the additional problems of unequal samples sizes and body-size ranges described above, a more reliable method would seem to be to calculate a regression line separately for each developmental stage and then compare their slopes using the 95% CI method, as has been carried out in many studies of multiphasic ontogenetic allometry (e.g., [9, 20, 23, 25–27, 61]). In this way, the

scaling relationship for each developmental stage is estimated in a statistically independent way, which ensures an unbiased comparison of their slopes unconfounded by the influence of the scaling relationships of other developmental stages. In cases where developmental stages are not easily distinguished, other methods of identifying break points in broken-line regressions of ontogenetic metabolic allometry could be used (see, e.g., [79–81]).

3. The reality and significance of multiphasic ontogenetic metabolic allometry

Both types of criticism of multiphasic ontogenetic metabolic scaling analyses discussed in Section 2 are handicapped by serious statistical problems. Using unscaled arithmetic data prevents a proper estimation of scaling slopes because they are biased by the greater effects of larger body-size ranges and absolute trait-size variation in larger organisms. A single linear regression across ontogeny may deceptively seem to be a good fit because it is "swamped" by the overwhelming effects of the large organisms in the sample, thus preventing different scaling relationships in the smaller organisms from being discerned. Log-transformation prevents this problem by evenly spacing out relative body-size differences and by making trait-size variation across different size classes statistically equivalent in geometric space. This problem is well illustrated by statistical analyses of ontogenetic metabolic allometry in spiny lobsters [25, 51].

Similarly, using single linear regression analyses (and an associated ANCOVA or other mixed effects models) based on log-transformed data to represent ontogenetic metabolic scaling may also be problematic if the body-size ranges of various developmental stages are unequal and nonoverlapping. Developmental stages with relatively large sample sizes and/or body-size ranges have inordinately large effects on the results of an ANCOVA and single linear regression analyses, thus outweighing the influence of developmental stages with smaller sample sizes and/or body-size ranges. This problem is well illustrated by statistical analyses of ontogenetic metabolic allometry in American eels [27, 61] and Tobacco hornworms [22] (see Section 2.3).

Therefore, the statistical approaches of [30–34, 53] do not invalidate observations of multiphasic ontogenetic metabolic scaling, because they may not adequately detect discontinuous metabolic scaling during ontogeny. Instead, it is recommended that log–linear regressions be calculated separately for each developmental stage of interest (thus ensuring statistical independence), and then comparing their slopes and intercepts by using the 95% CI method (following [55, 70–74]). Only if differences between the slopes and intercepts are statistically insignificant, should one consider representing ontogenetic metabolic allometry by a single regression line. In addition, even if no discontinuities in metabolic scaling exist, one should also test whether metabolic scaling relationships change continuously in a curvilinear way throughout ontogeny, as revealed by curvilinear regression (as shown in **Figure 1d** and [82–84]).

Note that the above approach largely follows in principle the recommendation of [52]. First, visually examine the data to judge whether single linear, curvilinear, or multiphasic regression analyses are needed to best represent the variation observed. If multiple trends for different developmental stages are apparent, as seen for the datasets discussed in this article, then it would seem to be prudent to fit these divergent trends with separate regression lines. Attempting to fit such data to a single regression line and then removing outliers caused by this procedure or by ignoring resulting nonrandom, body-size-dependent residual variation associated with specific developmental stages can be highly misleading [61].

The validity (significance) of multiphasic ontogenetic metabolic scaling is further supported by the frequent observation of parallel, theoretically predictable ontogenetic shifts in metabolic scaling in diverse species. For example, in many plant and animal species, early developmental stages often show steeper metabolic scaling than later stages (e.g., [5, 8–18, 20–23, 25, 26, 28, 29, 80, 82–87]). This widespread pattern can be explained, at least in part, by rapid, metabolically expensive growth rates associated with chiefly cell multiplication (and thus relatively steep scaling of metabolically relevant cell surface area) during early developmental stages and slower growth rates associated with chiefly cell expansion (and thus relatively shallow scaling of cell surface area) during later developmental stages (for further details about the possible mechanisms involved, see, e.g., [5, 8, 26, 84, 87, 88]). Notably, in rare cases where growth rates are faster in later developmental stages, metabolic scaling also shifts from being relatively shallow to steeper, as expected (see, e.g., [5, 89]).

In addition, in many aquatic larval animals that respire largely through their skin, steep metabolic scaling is associated with growth chiefly in the longest or two longest dimensions (i.e., body growth occurs chiefly via elongation or flattening, respectively), whereas shallower metabolic scaling occurs during later developmental stages when growth is more three-dimensional, as predicted by surface-area models [25, 90]. These recurrent patterns observed in diverse aquatic species further dispel the claim [34] that multiphasic ontogenetic metabolic scaling is dubious for statistical reasons (see, e.g., Figures 1 and 2 in [25] showing that the scaling exponents of six species are consistently significantly higher during early versus later developmental stages). Remarkably, in rare cases where early life stages grow chiefly along the shortest dimension (i.e., body growth occurs chiefly via thickening), metabolic scaling is shallower than during later developmental stages when growth is more three-dimensional, again as predicted by surface-area models [27, 90]. Significant ontogenetic shifts in metabolic scaling have also been related to changes in body composition [17, 22, 28, 85], modes of locomotion [18, 91] and thermoregulation [5, 15], and other factors [5]. Some proximate (functional) and ultimate (evolutionary) mechanisms proposed to explain multiphasic ontogenetic metabolic scaling are summarized in **Table 1**, but we have much to learn.

Although multiphasic ontogenetic metabolic scaling is common in nature, linear or curvilinear relationships in log–log space may also occur (see [5, 82–84] and **Figure 1b** and **d**). In addition, nonlinear (mixed power) scaling may occur for interspecific relationships between log metabolic rate and log body mass (e.g., [5, 12, 93–98], but also see [99]), as well as for the intra- and interspecific allometry of other traits (e.g., [1, 7, 22, 60, 100–111]). In short, biological scaling is often complex and need not follow simple power functions as conventionally thought.

Table 1 • Proximate (functional) and ultimate (evolutionary) mechanisms proposed to explain ontogenetic shifts in metabolic scaling exponents (b)

Ontogenetic shift		Sources
	Proximate explanation	
$b_E > b_{EP}$ (Often hypermetric vs. isometric)	Metabolically significant cellular surface area increases faster than body volume during E vs. EP developmental stages because cell multiplication results in smaller cells during E, but relatively equal-sized cells during EP.	[8]
$b_{EP} > b_{LP}$ (Often isometric vs. hypometric)	Faster rates of metabolically expensive growth during the EP vs. LP developmental stages.	[5, 8, 11, 13, 14, 19, 21, 26, 80, 87, 88]
$b_{EP} > b_{LP}$ (Often isometric vs. hypometric)	Metabolically significant cellular surface area increases at the same rate as body volume during the EP developmental stage, but slower during the LP developmental stage because cell multiplication prevails during EP, whereas cell expansion prevails during LP.	[8, 84]
$b_{EP} > b_{LP}$ (Often isometric vs. hypometric)	In skin-breathing organisms, shifts in body shape (and thus respiratory surface area relative to body volume) occur due to elongation or flattening of the body during the EP developmental stage (i.e., growth occurs primarily along the longest or two longest dimensions), whereas three-dimensional growth more nearly occurs during the LP developmental stage.	[25, 86]
$b_{EP} > b_{LP}$ (Often isometric vs. hypometric)	Shifts in body composition: organs/tissues that are relatively metabolically active grow relatively rapidly during the EP developmental stage, whereas less metabolically active organs/tissues grow relatively rapidly during the LP developmental stage.	[17, 22, 28, 85, 87]
$b_{EP} > b_{LP}$ (Often isometric vs. hypometric)	Shifts in mode of metabolically expensive locomotion from EP to LP developmental stages.	[14, 18, 91]
$b_{EP} > b_{LP}$ (Often isometric vs. hypometric)	In endothermic birds and mammals, more rapid development of metabolically expensive heat production during the EP vs. LP developmental stages.	[5, 15]
$b_{EP} < b_{LP}$	Faster rates of metabolically expensive growth during the LP vs. EP developmental stages.	[5, 89]
$b_{EP} < b_{LP}$	In skin-breathing eels, shifts in body shape (and thus respiratory surface area relative to body volume) occur due to thickening of the body during the EP developmental stage (i.e., growth primarily along the shortest dimension), whereas three-dimensional growth more nearly occurs during the LP developmental stage.	[27, 61]
	Ultimate explanation	
$b_{EP} > b_{LP}$ (Often isometric vs. hypometric)	Higher mortality rates in relatively vulnerable juveniles vs. more protected adults may select for more rapid metabolically expensive growth and maturation that causes steeper metabolic scaling during EP vs. LP developmental stages. This is especially evident for aquatic animals with pelagic larvae that are more exposed to predation than benthic adults.	[5, 14, 92]

Note: The exponents b_E, b_{EP}, and b_{LP} refer to embryonic (E), early postembryonic (EP), and late postembryonic (LP) developmental stages, respectively. Hypermetric ($b > 1$), isometric ($b = 1$), and hypometric ($b < 1$).

4. Conclusions

Strong empirical and theoretical support exists for the widespread existence of multiphasic ontogenetic allometry of metabolic rate in nature. The discussion in Sections 2 and 3 also affirms a conclusion made previously by [51], i.e., biological scaling analyses are more than just statistical line-fitting. Scaling analyses should be carried out in biologically and theoretically meaningful ways. By doing so, ontogenetic shifts in metabolic scaling (whether continuous or discontinuous) can be shown to be intimately tied to fundamental developmental changes in theoretically predictable ways. Accordingly, a synthetic theory should be formulated that links multiphasic or curvilinear ontogenetic metabolic scaling with the dynamics of various developmental processes at the cellular, organ, and whole organism levels, as well as biochemically, physiologically, morphologically, and behaviorally. Doing so should enhance our understanding of both biological scaling and developmental biology in mutually beneficial ways (also see [8]). Traditional approaches in developmental biology that are gene (information) centered would benefit from integration with metabolic (energy) approaches that have for too long been neglected (also see [43–45]). As one example, ontogenetic shifts in metabolic scaling may provide new insight into trade-offs between growth and differentiation, a classic pattern in developmental biology [8]. Developmental shifts from rapid somatic growth and cell multiplication to slower somatic growth and cell differentiation appear to coincide with decreases in the ontogenetic scaling slopes for cell surface area and metabolic rate (**Table 1** and [8]). The importance of metabolic energy in supporting shifts from cell multiplication to differentiation is supported by not only correlations between metabolic changes and cell differentiation, but also evidence for their co-regulation [112] and experimental studies showing that these fundamental developmental transitions are

sensitive to the availability of energy and nutrients (e.g., [113, 114]). Other notable recent studies promoting integrative studies of metabolism and development include [115–117].

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