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Variation and Evolution of Function-Valued Traits

Richard Gomulkiewicz,[1] Joel G. Kingsolver,[2] Patrick A. Carter,[3] and Nancy Heckman[4]

[1]School of Biological Sciences, Washington State University, Pullman, Washington 99164, USA; email: gomulki@wsu.edu

[2]Department of Biology, University of North Carolina, Chapel Hill, North Carolina 27599, USA

[3]School of Biological Sciences, Washington State University, Pullman, Washington 99164, USA

[4]Department of Statistics, University of British Columbia, Vancouver, British Columbia V6T 1Z4, Canada

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Abstract

Function-valued traits—phenotypes whose expression depends on a continuous index (such as age, temperature, or space)—occur throughout biology and, like any trait, it is important to understand how they vary and evolve. Although methods for analyzing variation and evolution of function-valued traits are well developed, they have been underutilized by evolutionists, especially those who study natural populations. We seek to summarize advances in the study of function-valued traits and to make their analyses more approachable and accessible to biologists who could benefit greatly from their use. To that end, we explain how curve thinking benefits conceptual understanding and statistical analysis of functional data. We provide a detailed guide to the most flexible and statistically powerful methods and include worked examples (with R code) as supplemental material. We review ways to characterize variation in function-valued traits and analyze consequences for evolution, including constraint. We also discuss how selection on function-valued traits can be estimated and combined with estimates of heritable variation to project evolutionary dynamics.

1. INTRODUCTION

Variation in phenotypes is critically important to both the ecology and evolution of species. Phenotypes range in complexity from simple traits such as body mass to highly intricate traits such as morphology, metabolic networks, and behavior. Among the more elaborate phenotypes are the so-called function-valued traits. Function-valued traits are phenotypes that are described as a trajectory over a continuous index (time, space, temperature, etc.). Such traits include an extensive array of evolutionary and ecologically relevant ones including developmental trajectories, gene expression profiles, movement patterns, mating calls, reaction norms, physiological processes, and morphological shapes. Studies of these biologically ubiquitous and important traits are significantly less common than those of simpler traits, however, presumably because of the challenges posed by their inescapable complexity.

Our capacity to study function-valued traits in empirical systems has improved dramatically over the past two decades. This is largely due to the rapid development and increasing use of statistical methods that have been specifically designed to analyze data collected from function-valued traits in evolutionary biology and agricultural breeding programs. A primary goal here is to review these advances. Despite the ready availability of these powerful tools, function-valued analyses are not performed as often as they could be. We suspect that their underutilization is primarily because function-valued trait methods are unfamiliar and, indeed, seem intimidating to the uninitiated. To help overcome such obstacles, we introduce some of the central concepts and methods that are used to study function-valued trait data in evolutionary biology. To that end, we work through three examples in detail; one example, in **Supplemental Appendix 1**, uses real data. The other examples, in **Supplemental Appendixes 2** and **3**, use realistic but hypothetical data. More information about the **Supplemental Appendixes** can be found in the sidebar Worked Examples with R Code.

Supplemental Material >

1.1. What Is a Function-Valued Trait?

Function-valued traits are logical extensions of multivariate or vector-valued traits.[1] Recall that a multivariate trait is a finite list (vector) of phenotypic values that are ordered by a discrete set of index values, say, integers from 1 to k. For example, the bivariate trait of stature could be represented as a vector with two entries, $\mathbf{s} = (s_1, s_2)$, where s_1 is the height and s_2 the weight of an individual. A function-valued trait, by comparison, is an infinite list of phenotypic values that is ordered by a continuous index (argument, independent variable). Function-valued traits are most conveniently represented in the mathematical form of a function and usually visualized as a curve. For example, a growth trajectory is a function-valued trait described by a function, m, with $m(t)$ equal to the body mass at age t, which is a continuous argument. Though its index is continuous, the function can be smooth, kinked, or even discontinuous. For an example of the latter, consider a host whose immune system responds to a pathogen only when the pathogen's density exceeds a detection threshold. The host's immune response profile can be represented by a discontinuous indicator function that takes the value zero for pathogen densities below the threshold (no immune response) and the value one for densities above it (immune response active). However, the pathogen's density takes values on a continuum.

[1] This close connection provides a way to think about function-valued traits: Concepts and results from matrix algebra and multivariate statistics apply to function-valued traits; the functional analogs often involve only a formal change from vector and matrix notation.

WORKED EXAMPLES WITH R CODE

Supplemental Appendixes 1, 2, and **3** contain step-by-step worked examples of the methods reviewed here. The three documents were generated by knitting `R Markdown` (`.Rmd`) files (RStudio 2016). Each R Markdown file is a text file that contains commentary and the R code used to produce all analyses and plots for the appendix.

Supplemental Material >

There are many types of continuous indices of interest to biologists. These include univariate indices such as time of day or year (diurnal or annual life cycles, seasonal phenologies), age (ontogenies), temperature, concentration, red:far-red light ratio (reaction norms), distance from a spatial reference point (geographic location, locomotion), and angle (leaf or wing shape). In some cases, the continuous indices of interest are multivariate. Examples include 2D and 3D coordinates (spatial location, 2D or 3D morphological shapes) and combinations of univariate indices (e.g., age and temperature for a temperature-dependent ontogeny).

1.2. Curve Thinking

For biologists, the first question is often about how best to construe the trait of interest for an individual or genotype: Is it the function or the parameters? In some cases one will choose functions whose parameters have a biological interpretation, so it is useful to think about variation among individuals and genotypes in terms of those parameter values. In that sense, this approach treats parameters as traits rather than treating functions as traits.[2] In many other situations, biologists will treat a multivariate set of empirical measurements of a function-valued trait (such as the sizes of an individual at different ages or the performance measures of a single clone replicated over a set of discrete temperatures) as the trait of interest and make biological interpretations in terms of the means, variances, and covariances of those measurements. This approach treats measurements as traits rather than treating functions as traits.

Kingsolver et al. (2015a) introduced the term "curve thinking" to mean taking the perspective that the function itself is the biological sine qua non. Curve thinking is rather different from regarding parameters or measurements as traits in that it compels one to relegate those descriptions to supporting roles: The parameters or measurements are considered entities that help describe the function and need not have biological significance beyond that.

A pure curve-first focus, however, poses mathematical and empirical challenges because a function-valued trait can require an infinity of values to be characterized completely. The mathematical challenge is to describe a function-valued trait and its variation in quantitatively tractable forms. The empirical challenge stems from the fact that without a specific model, estimation of an infinite number of unknowns is impossible with a finite data set. We are then led to consider how to model and collect data from function-valued traits to allow statistically meaningful estimates and inferences. Both challenges are surmountable, and indeed, the statistical study of curves has spurred the development of practical, efficient, and powerful data analytic methods, collectively called functional data analysis (e.g., Ramsay & Silverman 1997). In statistical terms, then, curve thinking is a feature that aids design of informative experiments, rather than a problem.

Recognizing that the function is the biology is key to curve thinking in evolutionary biology. In some contexts, the biologically interesting characteristics of a function may well consist of only a

[2] A common problem with the parameters as traits approach is that, in practice, investigators wrongly treat parameter measures as exact rather than as estimates, that is, they ignore sampling error in estimates of particular parameters and/or correlations among parameters.

few quantities, such as the slope and intercept in the case of a line. But in many other contexts (the majority, we submit) these summary numbers have no significance beyond their mathematical role in representing the curve. A line, for example, could be described equally well mathematically by its slope and intercept or by any two points it contains. This means that one should not automatically assume that parameters and summary statistics of curves have intrinsic biological significance simply because they can be defined and measured. Without explicit biological justifications, it is difficult to discern the biological implications, if any, of differences of opinion about how best to analyze intercepts, slopes, and curvatures or other mathematically familiar properties of function-valued traits, such as nonlinear thermal reaction norms (e.g., Rocha & Klaczko 2012, Liefting et al. 2014, Rocha & Klaczko 2014, Morrissey & Liefting 2016). Curve thinking expands the biologist's vantage well past the narrow confines of a particular function's attributes, and toward consideration of the curve as a whole. It also inspires creative rethinking of empirical approaches, including novel study designs with significant practical benefits.

Data collected from function-valued traits—functional data—can take a variety of forms. For traits like growth trajectories and reaction norms, empiricists can generally measure only a handful of values per individual or genotype. While it may be tempting to treat a finite set of measurements as a multivariate trait, we explain below why doing so is not only unnecessary but might also underutilize the data. In contrast, traits that are recorded as images or audio or using data loggers (e.g., morphological shapes, vocalizations, daily patterns of nest box use, respiration profiles) have so much data that the challenge is to find manageable ways to store, analyze, and interpret the information. Fortunately, curve thinking–based statistical methods provide a well-grounded and systematic way to address both data analysis challenges.

We see that, in many contexts, curve thinking is a natural biological approach. However, the advantage goes beyond that because curve thinking provides a framework for valid statistical inference and, typically, leads to increased statistical efficiency and power—getting more bang for the buck from the data. Curve thinking, at its most fundamental level, forces one to treat data from the same individual or genotype as related and, at a bare minimum, as a set of correlated measurements. This sets the foundation for statistically valid assessment of variability in the data from all individuals or genotypes, with standard errors that correctly describe uncertainty in parameter estimates and *p*-values that do not overstate the case against a null hypothesis, as we see in our first example (**Figures 1–3**).

Treating measurements as related is not exclusive to curve thinking and, indeed, forms the core of multivariate statistical analysis, where measurements from one individual or genotype form a vector. But the concept of the curve itself offers additional, uniquely powerful advantages, essentially because of its continuous index. For example, consider a growth curve for body mass in the flour beetle, *Tribolium castaneum* (see **Supplemental Appendix 1**). Because a beetle's body mass depends on a continuous index (age), it is reasonable to expect that masses expressed at ages separated by a day should be more similar than masses at ages one week apart. Standard multivariate approaches, in comparison, utilize the correlations but do not account for information provided by the discrete index. In a multivariate approach, the index order, once set, is irrelevant to the multivariate analysis.

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1.3. When to Use Function-Valued Methods

We have hinted that curve thinking offers advantages to biologists who study function-valued traits. In the next two subsections, we elaborate on some of the main conceptual and statistical reasons to prefer function-valued methods over other approaches for describing variation of function-valued traits and predicting their evolution.

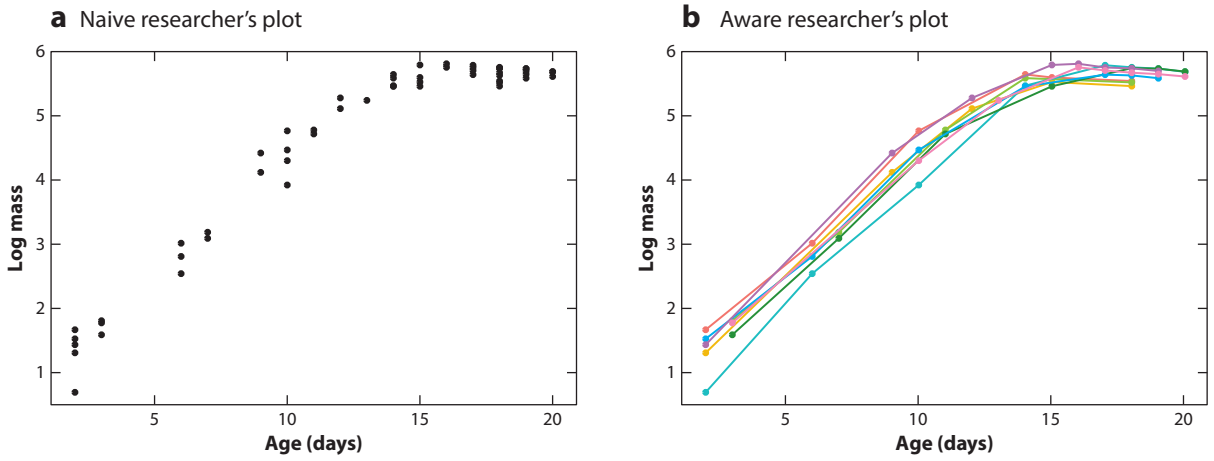

Figure 1

Ignoring and accounting for individuals in functional data set. Both panels, as well as those in **Figure 2**, show the same growth trajectory data, described in **Supplemental Appendix 1**, which consists of mass measurements collected from eight full siblings who were included in a study population of the flour beetle *Tribolium castaneum* (for details, see Irwin & Carter 2014). **Supplemental Appendix 1** also details the analyses step by step and includes the R code used to generate the plots displayed in this figure and in **Figures 2** and **3**. (*a*) Perspective of a naive researcher, who ignores the identities of the eight subjects and views all 54 measurements as independent samples. (*b*) Perspective of an aware researcher, who plots the data points and then connects the dots to account for the fact that the measurements come from 8 individuals. This researcher knows it is important to consider the relationship among measurements collected from the same individual, but it is unclear how to compare the sets of measurements from different individuals (see **Figure 2**).

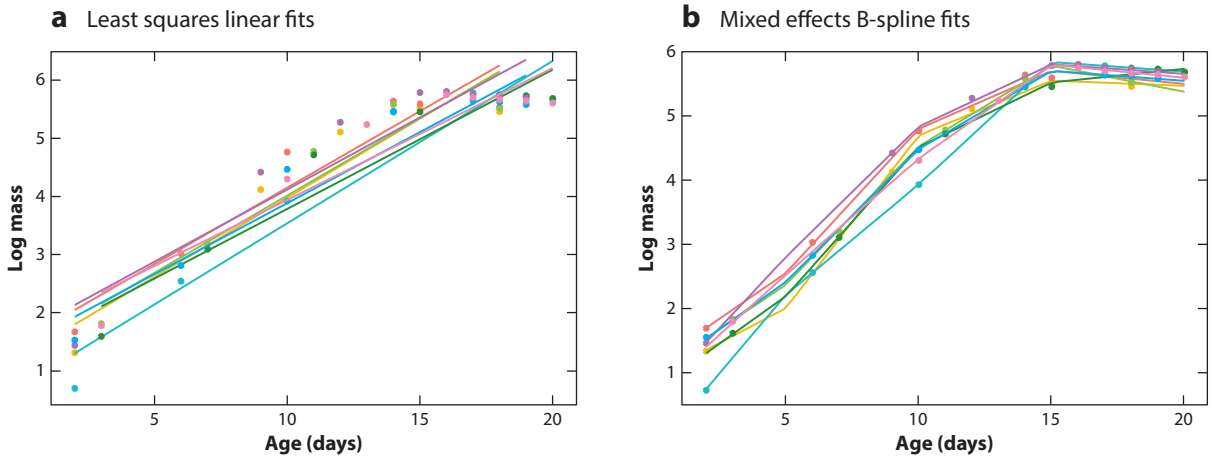

Figure 2

Individual fits based on curve thinking for the *Tribolium* mass measurement data used in **Figure 1**. In both panels, the curve thinker accounts for the identities of the subjects (unlike in **Figure 1*a***) and the ages at which each was weighed (unlike in **Figure 1*b***). (*a*) A straight-line growth trajectory is fitted via standard least squares to each individual separately; the slopes and intercepts of different individuals can be directly compared. However, the curve thinker has not made any inference about the population and, indeed, has not used the fact that individuals are sampled from a population. And, clearly, the lines are crude fits of the data. (*b*) Random regression (i.e., linear mixed effects modeling) and a flexible B-spline basis function expansion are used to fit a curve for each individual.

Supplemental Material >

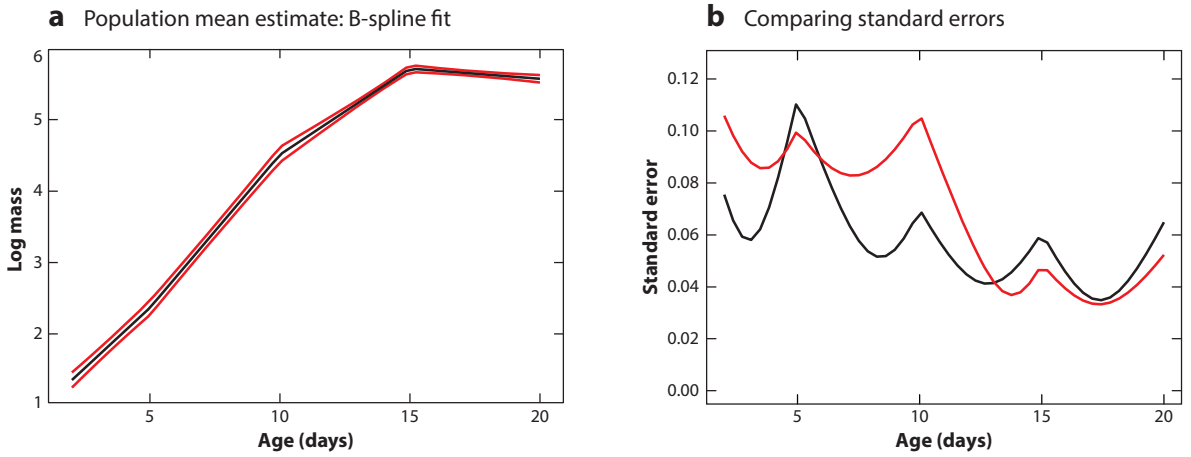

Figure 3

Mean growth curve with standard errors for the *Tribolium* mass measurement data used in **Figure 1**. (*a*) Estimate of the population mean growth trajectory (*black curve*) and uncertainty of the estimate at each age (*red curves* are one standard error above and below the estimated mean) using random regression and a flexible B-spline basis function expansion as in **Figure 2*b***. (*b*) A comparison of standard errors computed with versus without accounting for individual identities. The standard errors in panel *a*, shown here by the red curve, indicate correct levels of uncertainty because they account for the identities of the eight subjects, sampled from a single population. The standard errors computed by ignoring individual identities as in **Figure 1*a*** (*black curve*) effectively treat every size measurement as an independent sample; this tends to understate the uncertainty of the estimate at different ages.

1.3.1. Statistical reasons. Functional data in evolutionary biology are often collected and analyzed either in a way that is oblivious to curve thinking or without using functional data analysis methods. It is natural to ask whether the relatively unfamiliar and seemingly complicated statistical methods designed for functional data are worth the trouble. At the extreme, suppose a trait (size, say) is measured at the exact same two index values (ages) on different subjects (individuals, genotypes). In that case, the two index values provide essentially no information beyond that subsumed in a bivariate statistical analysis. One might be tempted to make a similar argument if measurements are taken at the exact same three index values on all subjects, but even then, a function-valued approach might be preferable if one is interested in, say, estimating the curvature of responses over the index (as in, e.g., studies of phenotypic plasticity; Murren et al. 2015). If measurements are taken at four or more index values, the main issue becomes how best to summarize the data for subjects, both individually and collectively. Although one could define ad hoc summaries of such multivariate data, function-valued approaches provide natural summaries of function-valued data for both the individual and sample.

Finally, function-valued methods are clearly superior whenever measurements are taken at different index values on different individuals. If the discrepancy among individuals is minor, that is, if individuals are meant to be measured at the same index values but some data points are missing, one could use multivariate missing data techniques, calculating relevant statistics by either imputing or ignoring the missing data, then assessing variability using a technique such as bootstrapping (see, for instance, Efron 1994). However, in more extreme situations where the index values vary greatly among individuals, using the functional nature of the data is a crucial part of the analysis. Common, but ad hoc, function-valued approaches include adding pseudo-data via interpolation between measurements and binning measurements at different index values. Both types of adjustment may lend themselves to bootstrap techniques of assessing variability, but interpolation does not incorporate measurement error, and binning is inefficient, throwing away

information in the data. The function-valued approaches described in this article, in contrast, provide an efficient and structured way to analyze data when measurements are not taken at the same argument value, explicitly using the continuous nature of the index. Indeed, there is no need to devote effort and expense to ensuring that measurements are collected at exactly the same index values, or even the same number of index values on different subjects. (**Supplemental Appendixes 1** and **2** walk the reader through step-by-step analyses of two such data sets.)

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1.3.2. Conceptual reasons. Curve thinking applied to evolutionary biology provides conceptual advantages that are completely separate from its value for statistical purposes. Although this review emphasizes the latter, it is well worth noting the former, which by themselves provide a host of convincing reasons to adopt and apply curve thinking. For example, genetic constraints on evolutionary responses to selection are an important issue for multivariate traits (e.g., Houle 2001, Kirkpatrick 2009). Variation in traits that are continuous curves, such as growth trajectories or performance curves, are necessarily constrained: The correlation between trait values approaches one as the difference in index values approaches zero. As a result, any multivariate representation of a continuous curve that consists of a finite subset of its points will underestimate the magnitude of constraints for function-valued traits. Along these lines, after comparing functional and multivariate data sets, Kirkpatrick (2009) concluded that the function-valued traits were more constrained than the multivariate traits.

Similarly, most abiotic and biotic environmental factors—for example, temperature, light intensity, soil moisture, and the density of predators or competitors—vary continuously in time and space in natural populations. Intuition suggests, and theoretical models show, that the strength and patterns of selection on reaction norms and performance curves—traits that vary with some environmental index—depend quantitatively on the frequency distribution or temporal pattern of environmental variation (Levins 1968, Via & Lande 1985, Gomulkiewicz & Kirkpatrick 1992, Kingsolver & Gomulkiewicz 2003; see also Section 3.3). Describing environmental variation in terms of a pair or handful of discrete environmental levels will badly misrepresent selection in natural environments. Likewise, quantifying the full fitness consequences of an ontogenetic trait (e.g., size) by considering just one or a few ages could provide a seriously deficient understanding of how fitness depends on the entire course of individual development (see Section 3.1 and **Supplemental Appendix 3**). Moreover, failure to consider selection over all environments or, more generally, across all index values could lead to poor predictions of adaptive evolutionary dynamics because one would, in effect, be ignoring the contributions of a continuum of correlated evolutionary responses to selection (see Section 3.2).

Finally, curve thinking, at its most fundamental level, serves as a constant reminder that the function, no matter how simple or complex, is the ultimate biological object of interest. By adopting this perspective, any biologist interested in studying the evolution of function-valued traits will retain a healthy degree of skepticism that any simplifications they decide to make for purposes of convenience, analysis, or interpretation could limit the accuracy, precision, or scope of their conclusions.

In sum, one should always use curve thinking when investigating questions that involve function-valued traits. Function-valued methods of data analysis deserve serious consideration for any study that involves measurements taken at more than two index values.

1.4. Basis Function Expansions and Random Regression: The Basics

In this section, we introduce two fundamental concepts of functional data analysis: basis function expansions and random regression. To understand these, it is useful to start by considering the

simple case of fitting straight lines to data from a sample of n individuals, each with a separate intercept and slope. This analysis, familiar from elementary statistics textbooks, is a type of function-valued analysis. Indeed, a simple individual-by-individual linear regression yields estimates $\hat{\alpha}_j$ and $\hat{\beta}_j$ of the intercept α_j and the slope β_j of the jth individual, which in turn provide an estimate of that individual's curve m_j for data that lie close to a line: $\hat{m}_j(t) = \hat{\alpha}_j + \hat{\beta}_j t$. However, fitting the regression lines individual-by-individual does not provide a unified framework for statistical analysis and so does not make the most of the data. Instead, it is better to fit via random regression, which is a type of linear mixed effects model (Demidenko 2004).

In a random regression analysis that uses straight-line fits (e.g., Dingemanse et al. 2010, Martin et al. 2011), the individual-level intercepts and slopes are viewed as a sample of intercept-slope pairs drawn from a population, that is, $\{(\alpha_1, \beta_1), \ldots, (\alpha_n, \beta_n)\}$ is a random sample of intercept-slope pairs from a population with mean intercept α and slope β. This view allows us to borrow information across individuals to infer properties of the population mean slope and intercept and of the population mean line $\alpha + \beta t$. It also reduces the number of parameters from $3n$ for n individual intercepts, slopes and regression error variances to six in total for any sample size: a population mean intercept and slope, population variances of the slopes and intercepts, population covariance between the slopes and intercepts, and one regression error variance. We can still infer individual-level intercepts and slopes using the random regression framework.

In many cases, straight-line fits are egregiously bad, overly simplistic, or both. (For an example, see **Figure 2*a*** and **Supplemental Appendixes 1** and **2**.) A better approach is to fit the individual curves—the m_js—more flexibly, using a basis function expansion that is pliable enough to approximate complex curve shapes. The basic approach is to specify a set of functions—the basis functions—and fit the data using a linear (or weighted) combination of these functions. If the basis functions are $\phi_1, \phi_2, \ldots, \phi_K$, the basis function expansion representation of individual j's function m_j has the form

$$m_j(t) = \sum_{i=1}^{K} c_{ij}\phi_i(t), \qquad 1.$$

where the K coefficients $c_{1j}, c_{2j}, \ldots, c_{Kj}$ are the coefficients associated with individual j. Note that the line $m_j(t) = \alpha_j + \beta_j t$ can be recast as a basis function expansion with $K = 2$ and with basis functions $\phi_1(t) = 1$, $\phi_2(t) = t$ and coefficients $c_{1j} = \alpha_j$, $c_{2j} = \beta_j$. One can use higher-degree polynomials instead of lines, with, for instance, a quadratic polynomial fit using basis functions $\phi_1(t) = 1$, $\phi_2(t) = t$, and $\phi_3(t) = t^2$. Indeed, Morrissey & Liefting (2016) apply random regression with a quadratic polynomial basis to analyze variation in nonlinear thermal performance curve data. However, Meyer (2005) notes that while quadratic, cubic, and higher-order polynomials offer considerably more flexibility for fitting curves than straight lines, the fit in one part of the data can have a large and unwanted impact on the fit in other parts of the data. Schluter (1988), in a simpler context, also noted problems that might result if fitting a nonflexible function, such as a quadratic function. Meyer recommends instead the use of piecewise polynomials—splines—as basis functions, which behave better for statistical analyses. (See also Griswold et al. 2008 for a comparison of different analyses of the same functional data using alternative basis functions.)

Since the basis functions are specified, estimating an individual j's curve amounts to estimating the coefficients, the c_{ij}, in Equation 1. Furthermore, because Equation 1 is linear in these coefficients, analyses based on basis function expansions can be carried out using the standard statistical framework of linear mixed effects models, under normality assumptions. So not only does the use of a basis function expansion allow great flexibility in describing functions, but estimates and inferences are obtained using a standard and relatively familiar statistical approach.

Supplemental Material >

Supplemental Appendixes 1 and **2** work through detailed examples that contrast analyses based on simple lines [basis functions $\phi_1(t) = 1$ and $\phi_2(t) = t$] with analyses based on highly flexible continuous piecewise linear functions that more easily fit the local behavior of the data. In that analysis, we use so-called B-spline basis functions (e.g., De Boor 2001) because they are computationally efficient. For piecewise linear functions, the B-spline basis functions are (except for the constant function) triangular hat functions that are equal to zero outside of a small interval. A plot of these basis functions is provided in **Supplemental Appendix 1**. Higher-degree B-spline basis functions can be used for fitting piecewise quadratic or cubic functions or, indeed, any degree of polynomial; quadratic basis functions are shown in **Supplemental Appendix 1**. Note, too, that the random regression analysis accommodates any basis function expansion (Meyer 2005). In random regression, for a given fixed collection of basis functions $\{\phi_1, \phi_2, \ldots, \phi_K\}$ the set of coefficients $\{c_{1j}, c_{2j}, \ldots, c_{Kj}\}$ for individual j in the expansion in Equation 1 would be viewed as a random sample from a population with mean coefficient set $\{c_1, c_2, \ldots, c_K\}$.

2. FUNCTION-VALUED TRAIT VARIATION

Biological variation is ubiquitous and crucial for evolutionary change in populations and species (Lewontin 1974). As this applies to function-valued traits in particular, it is important to describe their variation in ways that highlight biologically meaningful features and that can be used to project the evolutionary dynamics of populations. With these goals in mind, this section reviews how variation in function-valued traits is described and analyzed.

2.1. Covariance Functions

A fundamental measure of function-valued trait variation is the variance-covariance function or, more simply, the covariance function. A covariance function is the natural extension of the covariance matrix used to describe patterns of phenotypic and genetic variability within and among the components of a multivariate trait. Indeed, a phenotypic or genotypic covariance function, as with a covariance matrix, includes the variance of each trait component and the covariances between trait component pairs with different index values. Specifically, a covariance function for a function-valued trait m with continuous index t is a bivariate function, say, C, defined as $C(t, t') = \text{cov}[m(t), m(t')]$. Note that, when $t = t'$, $C(t, t)$ is simply the variance of $m(t)$. **Supplemental Appendixes 1** and **2** have worked examples with real and simulated data showing how to estimate and visualize the covariance function using basis function expansions. **Figure 4** shows the estimated covariance and variance functions for the *Tribolium* growth data (**Supplemental Appendix 1**). Another popular method for estimating the covariance function is principal analysis by conditional expectation (PACE), based on smoothing; PACE is particularly suitable for sparse data on a large number of individuals (Yao et al. 2005).

Understanding variation and covariation of a trait in a population is an important part of understanding evolution of the trait. However, not all trait variation contributes to evolution, and indeed, only the heritable component of it fuels adaptive evolution. For quantitative traits, the heritable part of variation is the additive-genetic variance (Fisher 1930). Similarly, for multivariate and function-valued traits, the heritable part of covariation between pairs of trait components is the additive-genetic covariance (Falconer & Mackay 1996). For a function-valued trait m with index t, these additive-genetic variances and covariances are described by an additive-genetic covariance function G, which is defined such that $G(t, t')$ is the additive genetic covariance between $m(t)$ and $m(t')$, and $G(t, t)$ is the additive-genetic variance of $m(t)$. Below in Section 3.2 we show how G can be used to project the evolutionary response to selection.

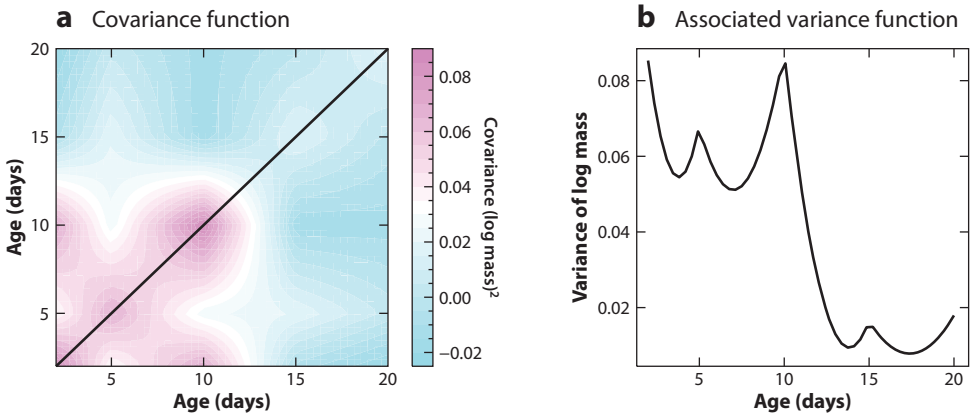

Figure 4

Covariance and variance functions estimated from the *Tribolium* growth trajectory data displayed in **Figures 1–3** and described in **Supplemental Appendix 1**. (*a*) Covariance function $C(t, t')$, defined as the covariance between size at age t and size at age t'. (*b*) Associated variance function $C(t, t)$ as a function of age t, that is, the elevations encountered along the diagonal transect shown in panel *a* from lower left to upper right.

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Additive-genetic covariance functions are estimated from function-valued trait measurements of relatives. The statistical methods are similar to those used for simple and multivariate quantitative traits (Falconer & Mackay 1996, Lynch & Walsh 1998). These methods require knowledge of the pedigree of individuals in the data set in order to account for the correlation between related individuals. The pedigree determines the numerator relationship matrix, a key element in the analysis. Except in simple cases, the statistical analysis must be carried out numerically, via packages such as WOMBAT (Meyer 2007) or ASReml (Gilmour et al. 2009). For further information, readers are directed to Kirkpatrick et al. (1994), Meyer & Hill (1997), Meyer (1998), Pletcher & Geyer (1999), Meyer & Kirkpatrick (2005), and Irwin & Carter (2013). For the theoretical foundations, readers are directed to Kirkpatrick & Heckman (1989) and Kirkpatrick et al. (1990).

Although the covariance function provides a general summary of function-valued trait variation, heritable or otherwise, biological analyses often require further modeling or narrower or specialized descriptions of trait variability. The following subsections discuss various approaches to understanding trait variability within and among species.

2.2. Principal Functions Analysis

Principal component analysis, in this context called principal functions analysis (PFA), uses the variance-covariance function to analyze modes of variability in curve data about the population mean curve. PFA yields a parsimonious description of curve variability by using the data to determine a few principal functions. These principal functions can then be employed as the ϕ_i's, the basis functions, in a slightly modified version of Equation 1: $m_j(t) = \mu(t) + \sum_{i=1}^{K} c_{ij}\phi_i(t)$, where $\mu(t)$ is the population mean curve at t. Like principal components for a multivariate trait, each principal function produces a principal function score, which is a linear combination of the original measurements, and the first principal function produces the scores that account for the most variation; subsequent principal functions are uncorrelated and account for successively less of the remaining variation. For many biological data sets, the first one or two principal functions suffice to capture most of the variability in the data. PFA also produces estimates of the c_{ij}'s, the individual-level coefficients, which are simply the principal function scores.

PFA has a potential shortcoming: The principal functions are defined purely on the basis of mathematical criteria and so their biological meaning can be challenging to interpret or even nonexistent. (The same is true of principal components for multivariate data.) Simple basis analysis (SBA), described in Section 2.3, provides a more interpretable method of viewing variation about the population mean (though SBA, like PFA, is founded on mathematical rather than biological criteria).

Another potential shortcoming of PFA is that principal functions capture a highly specific mode of variation. Other modes of variation may be present in the data, including modes that are of biological importance. PFA defines variation of a population of curves in terms of vertical shifts from the population mean function μ. For instance, consider data that consist of n individuals' growth curves (masses as a function of age). Often, PFA of growth data yields one principal function of interest, call it ϕ_1, so that an individual j's growth rate can be modeled as $\mu(t)+c_{1j}\phi_1(t)$, that is, each individual's growth curve differs from the population mean by $c_{1j}\phi_1(t)$, with the multiplier c_{1j} containing all (or most) of the individual-to-individual variation. But often, individual-to-individual variation occurs in the horizontal (age) direction, because different individuals have different biological clocks. Horizontal variation is best analyzed by registration—that is, alignment—techniques, described in Section 2.6. Even vertical and horizontal variation may be insufficient to describe certain types of biological variation. In this case, analysis via template mode variation (TMV), described in Section 2.4, should be used.

Despite these caveats, PFA of the additive-genetic covariance function is key to understanding and predicting adaptive evolutionary change. In particular, the first principal function of G describes what are called "genetic lines of least resistance" for a function-valued trait. As defined by Schluter (1996), the genetic lines of least resistance refers to the direction of greatest additive-genetic variance within populations. The basic idea is that adaptive phenotypic divergence within or among populations will occur most rapidly along these directions since they harbor the greatest supply of evolutionarily relevant genetic variation. It may be surprising at first to think of a function as a direction, but it may be helpful to recall that functions may be viewed as extensions of vectors, which are routinely used to describe evolutionary directions of multivariate traits (think Wright's adaptive landscape; Wright 1931, 1932). At the other extreme, PFA of the additive-genetic covariance function can also be used to identify directions along which populations would evolve very little or not at all in response to selection (see Section 3.3).

2.3. Simple Basis Analysis

Function-valued traits are sometimes referred to as infinite dimensional (e.g., Kirkpatrick & Heckman 1989) to emphasize the virtually limitless flexibility inherent to functions. Unfortunately, while the flexibility may be mathematically correct, much of it is likely to be biologically unrealistic and, with a completely unstructured model, not amenable to estimation with acceptable statistical confidence based on a finite sample. A new approach, called SBA (Gaydos et al. 2013), restricts decompositions of function-valued trait variability to relatively simple shapes. The approach focuses analyses on functions that are relatively easy to comprehend and limits the consideration of biologically implausible shapes.

SBA is similar to PFA (Section 2.2) in that the end result is K basis functions. In PFA, the basis functions are defined completely in terms of the data, without input from the analyst. In SBA, the basis functions depend on the independent variable values and on a user-selected quantitative measure of simplicity, such as the average magnitude of the function's first or second derivatives. In PFA, the first basis function is the function that accounts for maximal variation, whereas in SBA the first basis function is the simplest function in terms of the user-defined metric of simplicity.

Gaydos et al. (2013) define the simplicity of a function in terms of first divided differences of function evaluations, which approximate its first derivatives. This criterion yields a constant function as the simplest function. However, many other simplicity definitions are possible. Like principal functions, simple basis functions are perpendicular to one another. In mathematical terms, principal functions are eigenfunctions of the covariance function, whereas simple basis functions are eigenfunctions of a user-provided matrix that is used to quantify simplicity. However, unlike the principal scores in PFA, the regression coefficients corresponding to the simplicity basis are correlated. **Figure 5** shows a side-by-side comparison of principal and simple basis function modes of variation applied to the data set shown in **Figure 2**.

2.4. Template Mode of Variation Analysis

For some types of function-valued traits, biologists have identified particular directions or modes of variation that are of special interest. Some of these modes of variation are nonadditive and as a consequence are ill-described or effectively undetectable by principal function and simple basis methods. The TMV method is an alternative approach that can be used to decompose functional variation along predefined directions, including nonadditive ones (Izem & Kingsolver 2005, Izem & Marron 2007) that may be hypothesized by separate biological arguments.

The TMV method differs from PFA and SBA in two key ways. First, TMV describes variation around a common shape—the template—which need not be equal to the population mean shape. Second, TMV can simultaneously explore a range of types of variation of this template curve. Like PFA and SBA, TMV can be used to explore variability caused by vertical shifts from the template curve. In addition, TMV can be used to explore horizontal shifts. Thus, TMV is useful to ecological and evolutionary physiologists, who have a particular interest in detecting vertical and horizontal modes of variation among ectothermic organisms in thermal performance curves (Huey & Kingsolver 1989). Vertical shifts reflect faster-slower variation, whereas horizontal shifts are evidence of a hotter-colder pattern of variation. Vertical shifts are a simple kind of shift that can be explored by PFA and SBA, whereas horizontal shifts cannot be explored by either.

The method of TMV analysis provides an informative and manageable way to describe what mathematicians call nonlinear modes of variation. To date, the TMV approach has been developed only for thermal performance curves, but it seems reasonable to expect that the approach could be extended to other types of function-valued traits and nonlinear deformations of particular biological relevance. Current TMV methods allow estimation of the template function and evaluation of variation in curve elevation, width, and location (Izem & Kingsolver 2005, Izem & Marron 2007). Yamahira et al. (2007) present a maximum-likelihood method that uses, as they describe it, almost the same model as TMV methods. Their approach allows for among- and within-group differences in function parameters and assumes normally distributed deviations between each observation and the corresponding value of the function.

Knies et al. (2006) used TMV to analyze changes in temperature-dependent growth rate curves in a laboratory evolution experiment. The study subjected bacteriophage G4 to selection for increased growth at high temperatures. Their TMV analysis estimated that horizontal (hotter-colder) shifts accounted for the majority of evolutionary changes in thermal performance curve shape. Genome sequencing revealed strong associations between particular curve shapes and mutations at specific nucleotide sites, which are known to be polymorphic in nature. The study is an innovative use of laboratory evolution to understand evolution in the wild.

Drown et al. (2011) used TMV methods to compare performance curves over a salinity gradient of genotypes sampled from lakes and streams in invasive and native ranges of the New Zealand

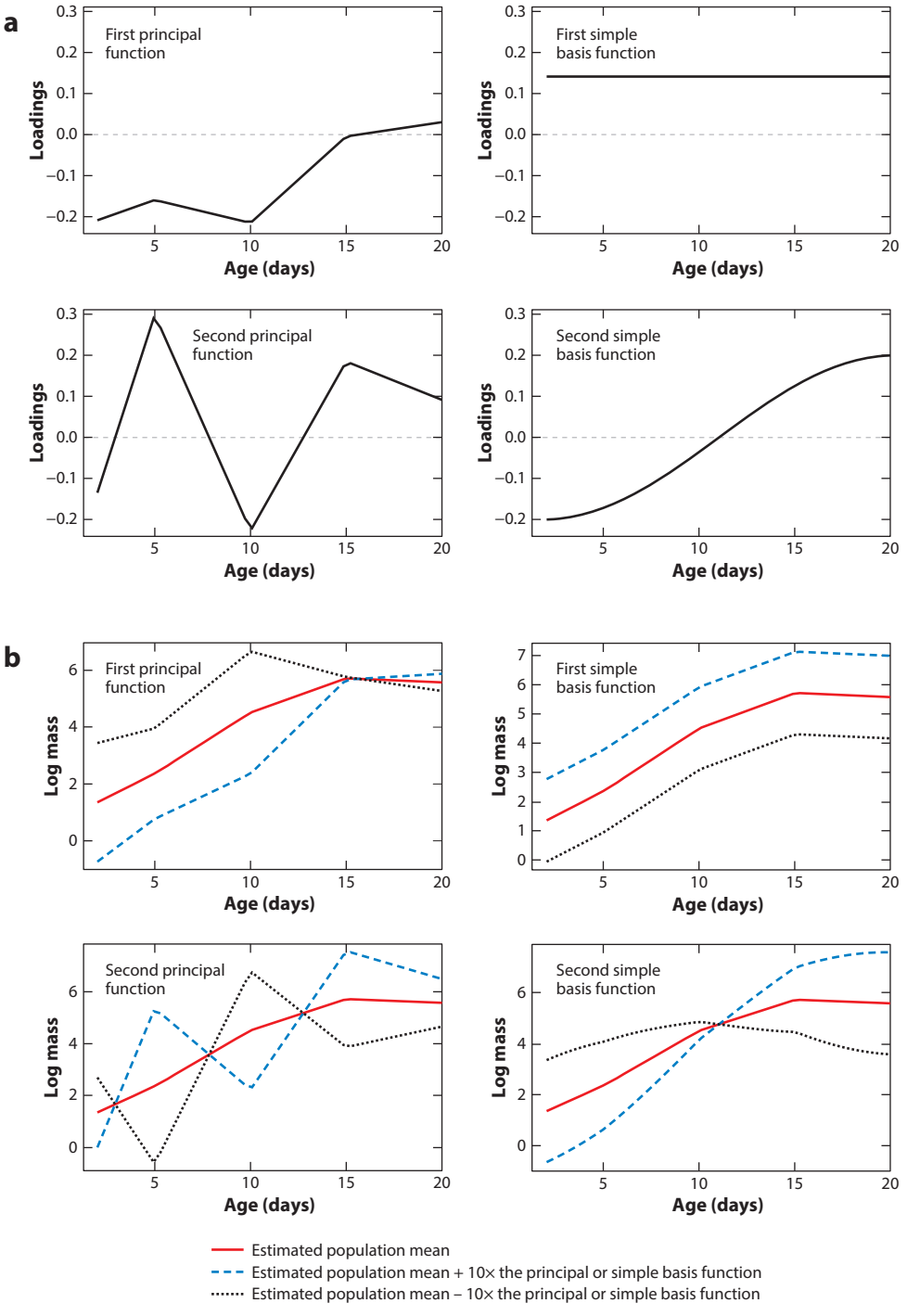

Figure 5

Modes of population variation for the *Tribolium* growth trajectory data used for **Figures 2** and **4** (see also **Supplemental Appendix 1**). (*a*) First two principal functions (*left column*) and first two simple basis functions (*right column*). The first principal function explains 74.43% of the variation, while the second principal function explains 17.82%. The first simple basis function explains 47.32% of the variability, while the second simple basis function explains 26.59%. The simple modes of variation are easier to interpret. (*b*) Variability about the population mean due to the particular function (mode) graphed in panel *a*.

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mudsnail, *Potamopyrgus antipodarum*, which is a worldwide invader. They raised juvenile snails over a range of salinity treatments and assessed two measures of performance that are closely related to invasive potential: finite growth rate (λ) and time of first reproduction. Their TMV analyses revealed that most of the variation among invasive and ancestral types could be attributed to horizontal shifts or to shifts in curve width. They concluded that these findings support a previously hypothesized invasive strategy called Jack-and-master but provide no evidence in support of two others, Jack-of-all-trades and master-of-some.

Note that while TMV allows one to probe function-valued trait variation along biologically motivated modes, to date there is no complementary theoretical framework for making specific predictions about how these genetic directions contribute to short-term evolutionary dynamics or if they might allow prediction of long-term patterns of adaptive divergence between populations. This is clearly a subject worthy of future study that will further clarify how TMV informs our understanding of evolution.

2.5. Comparative Methods

Biologists are increasingly interested in exploring among-species patterns of evolution and inferring potential causes of long-term diversification in evolutionary traits of interest that are inherently function-valued, including life histories, complex ecophysiological traits, and responses to environmental stressors (toxins, salinity, drought, etc.). Phylogenetic comparative methods provide sophisticated statistical approaches based on shared ancestry for inference and hypothesis testing of evolutionary history at and above the species level (Felsenstein 1985, Harvey & Pagel 1991, Martins & Hansen 1997). Due to a lack of tools for comparing curves, most phylogenetic comparative analyses have focused on one or a handful of function-valued trait characteristics, such as the LD50 value (dose level of a toxin that causes 50% expected mortality of exposed subjects) used to represent a species' entire dose-response curve. Another example is the total area under a thermal tolerance curve (e.g., Izem & Kingsolver 2005).

This analytical void has been filled recently by phylogenetic comparative methods that were developed specifically for function-valued traits. The method of phylogenetic Gaussian process regression (PGPR) allows estimation of the evolutionary history of function-valued traits (Aston et al. 2012, Hadjipantelis et al. 2013, Jones & Moriarty 2013). This approach is highly flexible in terms of the curve shapes, sources of uncertainty, and macroevolutionary models it can accommodate, but it is incompatible with standard comparative methods that rely on reconstruction of ancestral states. This incompatibility has been resolved by Goolsby (2015), who developed an extension of PGPR methods that includes estimation of ancestral states; the methods are implemented in the R package `phylocurve` (Goolsby 2017). The original and extended PGPR approaches basically compare finite collections of shape landmarks (i.e., registered or aligned x, y coordinates of the curves; see next section) among species and use sophisticated statistical methods to reconstruct the landmarks of their ancestors. We speculate that a rather different approach might also work well for phylogenetic comparisons of traits such as ontogenetic trajectories, tolerance profiles, and reaction norms; these function-valued traits can each be described by a curve whose y coordinate is a function of x [i.e., $y = f(x)$]. Comparisons between species could instead be made, we suggest, among the coefficients of their respective basis function representations (see Section 1.4), provided the same set of basis functions was used for fitting curves of all the given species. Imagine, for example, that the eight growth trajectories shown in **Figure 1*b*** represented eight different species; one could directly analyze the intercept-slope pairs, (α_j, β_j), of the straight-line fits of these species (**Figure 2*a***) using standard multivariate phylogenetic comparative methods.

2.6. Curve Registration

Sometimes a population of curves is similar except that each individual's curve requires a rescaling, warping, or horizontal shift of the independent variable in order to align the curves. For instance, for a population of growth curves, the independent variable, clock time, may not represent the more appropriate biological clock of each individual. The main mode of variation may be eliminated simply by transforming from clock time to biological time, viewing each curve as a function of biological time. This transformation from clock time to biological time is called a warping or registration function.

The population of warping functions can be of interest in its own right as a means to understand the associated variation in the population. In addition, ignoring warping functions in functional data analysis and proceeding with a function-valued trait analysis with unaligned curves can lead to incorrect conclusions. For instance, using nonaligned growth trajectories to estimate a population mean curve can dampen or completely mask biologically crucial periods with growth spurts. However, warping is not a panacea; some important biological questions, such as the absolute timing of growth events, can only be addressed using nonaligned curves.

Many registration methods exist in the statistical literature and were initially motivated by the analysis of the famous Berkeley Growth Study, where both the magnitude of growth spurts and their age of occurrence vary across subjects (Ramsay & Silverman 2005). Some registration methods use landmark registration, which aligns a few specified and well-defined landmarks such as the prepubescent growth spurt (Kneip & Gasser 1992, Gasser & Kneip 1995). Other methods use whole-curve criteria, basing alignment on a distance measure between two functions (Sakoe & Chiba 1978, Ramsay & Li 1998, Srivastava et al. 2011). All of these papers consider registration as a stand-alone analysis, so any further analysis would be an additional step. Recently, statisticians have considered blending registration and function-valued trait approaches into a unified analysis, placing the entire analysis on more solid statistical grounds (Brumback & Lindstrom 2004, Telesca & Inoue 2008, Raket et al. 2014, Chakraborty & Panaretos 2017, Fu & Heckman 2017). Gervini & Carter (2014) also blend registration and function-valued trait analysis into one analysis but consider the case of functional data sampled from families of related individuals, specifically half-siblings.

2.7. Statistical Uncertainty in Estimates and Depictions of Function-Valued Trait Variation

As mentioned in Section 1.4, assessing the variability of the estimate of the population mean is straightforward, with calculations based on variability of the estimate of the mean of the population regression coefficients. Consider the case where the function-valued trait is modeled as a straight line, with slopes and intercepts varying across the population. We can estimate the population mean intercept α and slope β and calculate standard errors of these estimates. However, to calculate a standard error for the estimated function-valued trait at, say, age t, that is, the standard error of $\hat{\alpha} + \hat{\beta}t$, we also need an estimate of the covariance between $\hat{\alpha}$ and $\hat{\beta}$. All of this information is available in a mixed model fit. See **Supplemental Appendixes 1** and **2** for examples, R code, and further details about these computations.

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Assessing the variability of the estimates of the population covariance structure is more challenging, as the covariance estimates depend on the data in a complex way. However, large-sample theory provides us with information about the accuracy of the estimates in the form of the estimates' asymptotic joint distribution. This joint distribution is not only useful for assessing the accuracy of the estimates themselves but can also be sampled to assess the accuracy of anything that depends on the estimates. Thus, the joint distribution can be used for inference of the covariance

function and things depending on the covariance function such as principal functions. Kingsolver et al. (2015b) take this approach by repeatedly simulating estimates that follow the asymptotic joint distribution and calculating quantities of interest in terms of the simulated estimates. Cabassi et al. (2017) take another inferential approach, testing the hypothesis of equality of covariance functions of different populations.

2.8. Molecular Genetic Approaches

An impressive literature of function-valued trait studies in biomedical and agricultural research has emerged in recent years (reviewed, for example, by Wu & Lin 2006, Huang et al. 2017). These functional mapping studies mostly seek to discover the molecular genetic basis of variation (quantitative trait loci, quantitative trait nucleotides, genome-wide association studies) for function-valued traits relevant to the goals of human health and agriculture. It is reasonable to expect that at least some of the empirical and statistical methods being developed in these applied fields could prove useful for addressing questions about evolution in wild populations. The Knies et al. (2006) study discussed in Section 2.4 exemplifies how genomics and experimental evolution approaches can be combined to illuminate how performance curves evolve adaptively in nature.

The general issue of how molecular genetic analyses inform our understanding of processes that drive phenotypic evolution and adaptation has recently been the subject of vigorous discussion (see, especially, Rockman 2012, Travisano & Shaw 2013, Rausher & Delph 2015). A central concern is that identifying a molecular source of variation for a trait involved in adaptive evolution may reveal little or nothing about why that change was adaptive. The caveats those articles raise have direct relevance for the evolution of function-valued traits.

3. FITNESS, SELECTION, AND EVOLUTION OF FUNCTION-VALUED TRAITS

Adaptive evolution is driven by heritable differences in individual fitness (Fisher 1930). The fitness of an individual is the number of descendants it is expected to leave at a specific point in time, and in a population with nonoverlapping generations, this is the number of offspring an individual is expected to directly produce (e.g., Lewontin 1974). To understand how phenotypes evolve adaptively, one must also associate phenotypic variation with variation in individual fitness (Robertson 1966, Price 1970). The same general components of the adaptive process apply to all kinds of phenotypes, including simple, multivariate, and function-valued traits. As discussed in this section, they differ in the degree of technical detail needed to describe the relationship between phenotype and fitness and to project the evolutionary response to selection that results from fitness differences among individuals.

3.1. Fitness Functionals

Phenotypes can evolve adaptively when they are associated with fitness. For simple and multivariate phenotypes, a fitness function describes the connection between fitness and phenotype mathematically. Similarly, a fitness functional quantifies the relationship between fitness and a function-valued trait. Fitness functions and functionals can be modeled using knowledge of key biological processes or can be inferred statistically from phenotype and fitness data (e.g., Schluter 1988).

Models of individual fitness range from phenomenological to derivations based on detailed mathematical descriptions of underlying biological processes. An example of the former is the use of optimizing functions to depict an individual's fitness as a function—usually a Gaussian or a quadratic polynomial—of its phenotype's distance from a designated optimal phenotype. The

Gaussian form in particular has been used in many contexts (e.g., Lande 1976, 1979; Via & Lande 1985; Kirkpatrick 1988; Beder & Gomulkiewicz 2007) partly because its form is flexible enough to encompass both directional and stabilizing selection. The optimal phenotype itself is in some cases inferred from data (e.g., Kingsolver et al. 2001) and in others based on biological first principles (e.g., how morphology affects flight performance or how the optimal metabolic rate changes with temperature; see Segev et al. 2011 for a prime illustration of this approach).

Fitness models that do not assume a single optimum phenotype are less common in the literature, most likely because they require more biological detail. For example, Kingsolver & Gomulkiewicz (2003) proposed a model for how daily temperature fluctuations experienced in the field by *Pieris rapae* determine the fitness of individual caterpillars with temperature-dependent growth rates, which is the function-valued trait of interest. By accounting for the entire distribution of temperatures experienced, the model can be used to project fitness changes that could result from, for example, global warming. A test of the fitness model (Kingsolver et al. 2007), however, gave a poor prediction of the evolutionary response to selection in an experimental population of *P. rapae* (see next section), which suggests that the fitness model lacks significant features (such as, perhaps, the influence of age or size on growth rates). Modeling the fitness associated with an entire curve is challenging enough that biologists usually resort to modeling the fitness consequences of a summary phenotype (e.g., the surface area of a morphological shape) or of a specific phenotypic value on the curve (e.g., thermal performance at the mean annual temperature). **Supplemental Appendix 3** has a worked example of how life history theory can be used to calculate the fitness of an entire growth curve without assuming an optimum.

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3.2. Selection Gradients and Evolutionary Responses

Positive or negative directional selection on a phenotype occurs when individual fitness increases with higher or, respectively, lower values of the trait. If phenotypic differences have a heritable genetic basis, then directional selection will result in a cross-generation evolutionary response in the mean phenotype of a population. For simple quantitative traits with polygenic inheritance, the evolutionary response can be computed using the breeder's equation (Falconer & Mackay 1996). Lande (1976, 1979) rewrote the breeder's equation in a form that is particularly valuable for studying natural populations and multiple correlated traits. In Lande's formulation, the sign and strength of directional selection on each trait is quantified by the selection gradient, and the evolutionary response to this selection can be projected using the additive-genetic variances and covariances of the traits in question.

Kirkpatrick & Heckman (1989) extended Lande's form of the breeder's equation to function-valued traits:

$$\Delta\bar{z}(t) = \int_{t_{\min}}^{t_{\max}} G(t,\xi)\beta(\xi)\mathrm{d}\xi, \qquad 2.$$

where $\Delta\bar{z}(t)$ is the between-generation change in the mean of the function-valued trait z at index value t, G is the additive-genetic covariance function, and β is the selection gradient function (see also Kirkpatrick et al. 1990, Beder & Gomulkiewicz 1998). Recall (Section 2.1) that $G(t,t)$ is the additive-genetic variance for the trait at index value t and $G(t_1,t_2)$ is the additive-genetic covariance between trait values at indices t_1 and t_2; $\beta(t)$ indicates the sign and strength of directional selection on $z(t)$, holding all other values of z fixed.

There are two distinct methods to compute a selection gradient. The first requires a model of the relationship between the function-valued trait and fitness (i.e., a fitness functional; see Section 3.1). Assuming that the distribution of function-valued traits in a population is normal

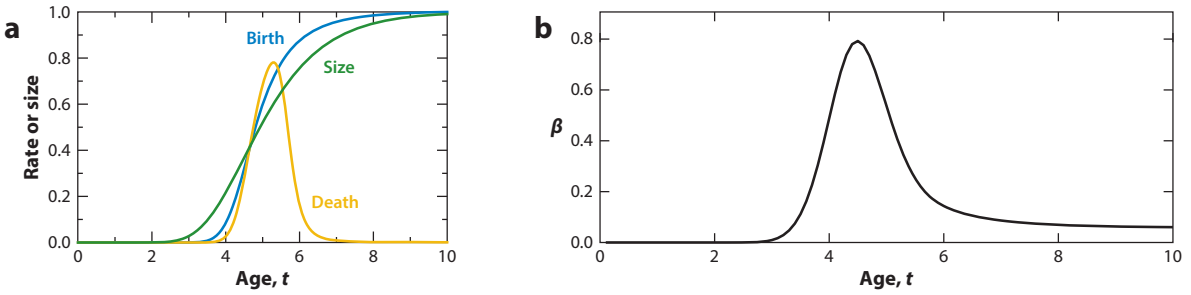

Figure 6

Mean growth trajectory and components of fitness (*a*) and the resulting selection gradient function (*b*) for a hypothetical prey species. Graphs are based on a life history model for an annual species whose main source of mortality is a visual predator with a gape width 60% of the prey's maximum size. Prey individuals avoid predation at young ages when their small size makes them difficult to detect and at older ages when they exceed the predator's gape size. Birth rates are assumed to increase sigmoidally with size once maturity is reached at age $t = 1$ (see **Supplemental Appendix 3** for computational details that were used to generate these graphs). (*a*) Growth trajectory (*green*) and associated per capita birth (*blue*) and death (*yellow*) rates of the mean individual in a population. Both vital rates depend on individual size at age t. Sizes and birth rates are shown scaled as proportions of their respective maximum values. (*b*) Selection gradient function derived from the fitness components and mean growth trajectory in panel *a* assuming growth curves are normally distributed around the mean at each age t. $\beta(t)$ is the strength of selection on size at age t.

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and individual fitness is frequency independent (i.e., does not depend on the distribution of traits in the population), then the corresponding selection gradient is the functional derivative[3] of the log-mean fitness functional computed with respect to the mean $\bar{z}$. This is Lande's Theorem for function-valued traits (Gomulkiewicz & Beder 1996). Although one could, in principle, use data to infer the form of the fitness functional (as has been done for simple and multivariate traits; Schluter 1988, Schluter & Nychka 1994), this approach to computing selection gradients has to date been applied only with theoretical versions of fitness functionals (Gomulkiewicz & Kirkpatrick 1992; Kirkpatrick & Lofsvold 1992; Beder & Gomulkiewicz 1998, 2007; Kingsolver & Gomulkiewicz 2003; Kingsolver et al. 2007). A selection gradient function, computed by applying Lande's Theorem to the fitness functional described for growth trajectories in **Supplemental Appendix 3**, is shown in **Figure 6**. Another interesting example can be found in Day et al. (2011), who derive a selection gradient and continuous version of the breeder's equation (Equation 2) for the evolution of pathogen infection life histories starting from immunological and epidemiological first principles.

The second way to compute a selection gradient function does not require a fitness functional but rather estimates β directly from data using regression methods. The approach is a direct extension of that used for simple and multivariate quantitative traits (Lande 1979, Lande & Arnold 1983). For a multivariate trait $\mathbf{z} = \{z_1, z_2, \ldots, z_n\}$ the selection gradient is a vector $\boldsymbol{\beta} = \{\beta_1, \beta_2, \ldots, \beta_n\}$ whose ith component β_i represents the direct strength of selection on z_i after removing phenotypic correlations among the traits; $\boldsymbol{\beta}$ can be readily estimated with partial regression analyses from population samples in which each individual's trait value and fitness have been measured (Lande & Arnold 1983; Arnold & Wade 1984a,b; Mitchell-Olds & Shaw 1987).

For a function-valued trait z measured at index values $t_1, t_2, \ldots, t_n$, these multivariate methods can be applied by identifying vector components $\beta_i = \beta(t_i)$ for $i = 1, \ldots, n$. In this case, β_i would describe directional selection on $z(t_i)$ after accounting for correlations with trait values at the other

[3]The functional derivative can be thought of as a function-valued extension of the more familiar vector-valued gradient of a multivariate function from multivariate calculus.

$n - 1$ index values of measurement. An estimate of the entire selection gradient function can then be generated by interpolating the n components of $\boldsymbol{\beta}$ (Kirkpatrick & Heckman 1989, Kirkpatrick et al. 1990). **Supplemental Appendix 3** includes a demonstration of this process. By passing through its points, an interpolated estimate effectively treats the values of $\boldsymbol{\beta}$ as exact. If, however, standard errors are available for the estimate of $\boldsymbol{\beta}$, then an estimate of the selection gradient function that avoids overfitting, that is, fitting the components of $\boldsymbol{\beta}$ exactly, can be computed using weighted least squares (Kirkpatrick et al. 1990).

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Despite a voluminous literature on selection gradients for multivariate traits (Kingsolver et al. 2012), very few studies have estimated selection using functional methods. Recently, however, Kulbaba et al. (2017) used penalized splines (Goldsmith et al. 2011, Randolph et al. 2012) to estimate selection gradient functions for two function-valued floral traits using data from studies of *Delphinium glaucum*. They analyzed a phenological trait (anthesis rate—number of new flowers opened per day—as a function of inflorescence age) and a morphological trait (lower sepal length as a function of relative flower position) using, respectively, total seed number and total fruit set to indicate individual plant fitness. Their analyses found that longer sepals are favored at the base and top of a flower, whereas shorter sepals are favored in between. Their results also showed that selection favored plants whose anthesis rates are highest when flowering first commences. Kulbaba et al. (2017) also used molecular genetic markers to infer genetic relatedness of the individual plants they sampled to estimate the heritability of anthesis rate. The results suggest that anthesis rates in this population of *D. glaucum* are evolving in response to natural selection. Were it possible to estimate the additive-genetic covariance function from these data, the specific form of evolutionary response in anthesis rates could be predicted using the breeder's equation (Equation 2).

3.3. Evolutionary Constraints

Evolutionary constraints exist when some evolutionary outcome, typically one related to adaptation such as a fitness optimum, cannot be reached within a particular time horizon. In artificial selection, constraints may be defined in terms of reaching a breeding objective within a cost limit. Constraints for natural populations are not always as clearly defined but usually refer to Darwinian fitness or phenotypic diversification.

So-called absolute constraints (Houle 2001) are relatively straightforward to define mathematically. In the context of the breeder's equation (Equation 2), an absolute constraint exists if the evolutionary response produced by a nonzero selection gradient function is identically zero, that is, if $\Delta\bar{z}(t) = 0$ for all values of the index t when $\beta(t) \neq 0$ for at least one value of t. Absolute constraints are identified quantitatively by such selection gradients, which may be visualized as directions of adaptive evolution in multivariate or function-valued space that are inaccessible to the population as long as it maintains its current patterns of additive-genetic variation and covariation. These constraints can be detected by PFA (Section 2.2). Alternatively, they may be detected by the method of selection skewers, which is, in essence, trial and error: the idea is to generate a set of selection gradients of unit strength (the skewers) and identify which of them results in negligible evolutionary responses when applied to the breeder's equation (Equation 2; see Ragland & Carter 2004, Calsbeek & Goodnight 2009). Absolute constraints are described collectively by the null space of the additive genetic covariance matrix or function, which is the set of directions in multivariate or function-valued phenotype space that are evolutionarily forbidden because there is no additive-genetic variation (Kirkpatrick 2009). In mathematical terms, the evolutionary null space is spanned by the eigenvectors (principal components) or eigenfunctions (principal functions) associated with zero eigenvalues of the additive-genetic covariance matrix or function (Kirkpatrick & Lofsvold 1992).

While absolute constraints are simple to define in theoretical terms, in practice their detection and biological interpretation can pose substantial challenges. Indeed, it is impossible to prove statistically that a quantity is exactly zero, including genetic variance (Kirkpatrick 2009). Even if evolutionary constraints are detected, it can be difficult to interpret them. Constraints can also be temporary, depending on the genetic polymorphisms present that can be altered by novel mutations and interactions with other loci. An example of this is provided by preexisting genetic variants in *Escherichia coli* that predisposed experimental lines to reverse the absence of heritable variation and evolve the innovative use of citrate in the presence of oxygen (Blount et al. 2012).

One way to address the problem of detecting constraints has been to relax the requirement of establishing the complete absence of genetic variation (Houle 2001, Mezey & Houle 2005, Kirkpatrick 2009, Gomulkiewicz & Houle 2009, Kingsolver et al. 2015b). The main rationale for this approach is that only negligible evolutionary responses would be achievable in real populations with small enough amounts of heritable variation except, perhaps, for extremely long timescales (see the final paragraph of this section). Houle (2001) refers to these as quantitative constraints; the corresponding set of directions in multivariate or function-valued trait space in which adaptive evolution is highly limited is called the nearly null space (Gomulkiewicz & Houle 2009, Kingsolver et al. 2015b), which may be imagined as a slight enlargement of the null space.

Of course, identifying constraints in terms of the nearly null space requires one to define in a biologically relevant way what is meant by "small enough" additive genetic variation. Gomulkiewicz & Houle (2009) (see also Duputié et al. 2012) showed that when adaptive evolution can be directly connected to demography (evo-demo), the nearly null space can be defined by using a nonzero cutoff equal to the minimum amount of heritable variance that a population would need to avoid going extinct in the face of either an abrupt or continuous environmental change. For systems lacking a clear demographic context, Kingsolver et al. (2015b) (see also Mezey & Houle 2005, Hansen & Houle 2008, Gaydos et al. 2013) proposed defining the nearly null space as the complement of the model subspace that represents at least 98% of the total genetic variance in the additive genetic covariance matrix or function; the nearly null space would thus represent less than 2% of the total genetic variance in all phenotypic dimensions. Mezey & Houle (2005) and Hansen & Houle (2008) suggest using a criterion based on the statistical power for detection with a given study design.

Similar to how a null space is described by the subspace spanned by eigenfunctions of the zero eigenvalue, the nearly null space is the subspace spanned by eigenfunctions of eigenvalues equal to or less than the lower bound for genetic variance, however chosen (Gomulkiewicz & Houle 2009, Kingsolver et al. 2015b). PFA (Section 2.2) can be used to estimate this subspace, though the result can be difficult to decipher. Gaydos et al. (2013) show how SBA (Section 2.3) can be used to probe for simple phenotypic directions within a nearly null space identified using PFA. Kingsolver et al. (2015b) applied this method using data sets from different species to interpret nearly null spaces for growth or thermal performance curves. They found, for many of the data sets, that the simplest direction in the nearly null space is relatively complex, which predicts substantial evolutionary resistance only to elaborate selection gradient functions that change sign several times across temperatures or ages. In a few cases, SBA revealed that even relatively simple patterns of selection, such as strong selection for increased size early in life and decreased size later in life (or the reverse) would result in little growth curve evolution. This same two-step approach combining PFA with SBA could also be used to explore the contents of phenotypic spaces with abundant additive-genetic variation, such as genetic lines of least resistance (see Section 2.2.)

Finally, note that constraints identified using the null or nearly null space of a genetic covariance matrix or function reflect standing levels of genetic variation of the current population under study. Such patterns of heritable variation and constraint are themselves subject to change—perhaps substantial change—over long periods of time due to any number of evolutionary processes,

including mutation, random genetic drift, genetic interactions, recombination, and selection (e.g., Jones et al. 2003, Griswold et al. 2007, Arnold et al. 2008).

SUMMARY POINTS

1. Curve thinking—regarding an entire curve as the fundamental object of biological interest—offers not only important conceptual advantages for understanding how function-valued traits are selected and evolve but also many benefits for empirical studies of evolution, including powerful tools for statistical analyses and considerable flexibility for designing informative and practical experiments.
2. Basis function expansions provide a highly adaptable framework for describing function-valued traits and for analyzing functional data employing standard statistical approaches. Because they combine information from different individuals in a study sample, random regression methods make the best statistical use of functional data.
3. Phenotypic and genotypic covariance functions are valuable summaries of function-valued trait variation for many evolutionary questions. PFA and SBA can be used to estimate and illuminate the evolutionary potential and constraint that covariance functions represent. Curve variation can also be explored using TMV analysis, curve registration, molecular-genetic approaches, and phylogenetic comparative methods.
4. The evolutionary dynamics of function-valued traits in natural populations can be projected by combining the selection gradient function, which describes the directions and strengths of directional selection on a curve, with the additive-genetic covariance function, which describes heritable patterns of trait variation and covariation.

FUTURE ISSUES

1. Many questions in evolutionary biology involve consideration of two or more function-valued traits expressed by single individuals, such as an individual's metabolic rate and growth rate, which could both be sensitive to ambient temperatures. Likewise, the expression of some function-valued traits can depend on more than one index; for instance, a plant's flowering time could be a function of both ambient light availability and temperature. It would be valuable to develop theory and statistical tools for studying the evolution of these more complicated versions of function-valued traits.
2. TMV analysis and curve registration methods are intriguing ways to decompose function-valued trait variation, but they are not as clearly connected to evolutionary processes as principal functions. Clarifying connections with adaptive evolution would increase the value of TMV and curve registration methods.
3. The breeder's equation (Equation 2) used to project the evolution of function-valued traits in response to selection assumes that phenotypes are the sum of additive-genetic and nongenetic components that are normally distributed in the population. Since many traits of interest to evolutionary biologists may not be normally distributed, it would be beneficial to develop methods for prediction that do not rely on that assumption. **Supplemental Appendix 3** describes one way this could be done in a relatively simple case of a population for which the distribution of growth trajectories is far from normal.

Supplemental Material >

4. The recent surge in biomedicine and agriculture of functional mapping studies that reveal the molecular genomic basis of function-valued trait expression and variation demonstrates the value of functional data analyses for research in those applied fields. Those methods, perhaps in modified form, may also prove useful for the study of function-valued trait evolution in the wild.

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