

Developmental Dynamics and G-Matrices: Can Morphometric Spaces be Used to Model Phenotypic Evolution?

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Abstract Modern morphometrics, especially geometric morphometrics, is a powerful tool for modeling the evolution and development of the phenotype. Complicated morphological transformations can be simulated by using standard evolutionary genetic equations for processes such as selection and drift in the same morphospaces that are used for empirical morphometric studies. Such applications appear to be consistent with the theory of quantitative evolution of the phenotype. Nevertheless, concerns exist whether simulations of phenotypic changes directly in morphospaces is realistic because trajectories traced in such spaces describe continuous gradations in the phenotype and because the gain and loss of structures is often impossible because morphospaces are necessarily constructed from variables shared in common by all the phenotypes being considered. Competing models of phenotypic change emphasize morphological discontinuity and novelty. Recently developed models of phenotypic evolution that introduce a “phenotypic landscape” between evolutionary genetic constructs like the adaptive landscape and morphospace may correct this shortcoming.

Keywords Adaptive landscapes · Geometric morphometrics · Morphospaces · Phenotypic evolution · Phenotypic landscapes

Introduction

Morphometrics is usually considered to be a tool for the quantitative description and statistical analysis of morphology. The variety of applications of morphometrics to evolutionary biology and the frequency with which they have been applied have increased notably in the past decade, thanks in part to the ease with which geometric methods for simultaneously analyzing and visualizing complicated phenotypes can now be performed (Bookstein 1991; Dryden and Mardia 1998; Richtsmeier et al. 2002; Zelditch et al. 2004; Hammer and Harper 2005).

Evolutionary studies for which morphometrics are central include phenotypic integration and modularity (e.g., Marroig et al. 2004; Goswami 2006; Richtsmeier et al. 2006; Mitteroecker and Bookstein 2007), quantitative trait locus (QTL) analysis (e.g., Klingenberg et al. 2004; Albert et al. 2008), study of the regulation of morphological variance through ontogeny (e.g., Cardini and O’Higgins 2005; Zelditch et al. 2006), assessing the genetic dimensionality of morphological traits (Mezey and Houle 2005), and measuring the tempo and mode of evolutionary change (e.g., Roopnarine et al. 2005; Hannisdal 2007; Hunt 2007; Wood et al. 2007; Drake and Klingenberg 2008). All of these studies use empirical data to determine associations among organisms or among the variables that represent their phenotypes.

Another class of evolutionary studies uses morphometric spaces, or *morphospaces*, to extrapolate trajectories, either through empty space between empirical data points

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or inside an empty morphospace that has been constructed with the mathematical properties that characterize a particular evolutionary hypothesis. This class of studies includes: (1) evolutionary quantitative genetic predictions of change in the phenotypic means and variances (e.g., Lande 1976, 1979; Arnold et al. 2001; Marroig et al. 2004; Jones et al. 2007; Hohenlohe and Arnold 2008); (2) “random skewers” methods for evaluating the evolutionary effects of a phenotypic covariance matrix by measuring the response to a series of random selection vectors (Cheverud 1996; Cheverud and Marroig 2007); (3) long-term modeling of phenotypic evolution over paleontological time scales (Polly 2004); (4) mapping phenotypes onto a phylogenetic tree and reconstructing ancestral phenotypes at the nodes (Felsenstein 1985; Grafen 1989; Maddison 1991; Martins and Hansen 1997; Rohlf 2001; Stepan 2004; Wiley et al. 2005; Corbin 2008; Polly 2008); and (5) building phylogenetic trees from quantitative phenotypic traits (Felsenstein 1973, 1988). Not all of these methods are self-described as involving evolutionary extrapolations through a morphospace, but the geometry of their equations allows them to be viewed as such.

A common feature of these methods is that they project mathematical trajectories through a morphospace based on statistical models derived from evolutionary quantitative genetic theory. These evolutionary transformations are interpreted as good estimates of evolutionary change given the assumptions implicit in the transforming equations and the geometry of the space. Such evolutionary transformations usually have the following properties: (1) they trace a continuous gradation of phenotypes; (2) they involve transformations in a fixed number of phenotypic variables, which are chosen as part of the study design; and (3) the geometry of the morphospace and the transforming equations involve only phenotypic variables, though in most cases they are based on theory that connects them to underlying genetic, environmental, or developmental processes. These properties are generally compatible with multivariate evolutionary quantitative genetic theory (e.g., Simpson 1944; Lande 1976, 1979; Arnold et al. 2001; Blows and Brooks 2003; Gavrillets 2004; Hansen 2006; Blows 2007). The evolutionary transformations listed above are founded explicitly or implicitly on this body of evolutionary quantitative genetic theory, which assumes that phenotypic change is continuous; that the direction of change is a function of genetic covariances (the **G** matrix), selection, itself a function of adaptive and fitness landscapes, selective covariances, and drift; and that the magnitude of change is a function of genetic variance, selection intensity, and population size.

Another body of theory, derived primarily from evolutionary developmental biology, suggests that such evolutionary transformations in morphospace may be

founded on unrealistic views of how phenotypic transformations are expected to occur (e.g., Alberch 1982, 1985; Gilchrist and Nijhout 2001; Salazar-Ciudad and Jernvall 2004; Salazar-Ciudad 2006, 2007). This literature emphasizes that development is the set of mechanisms by which the phenotype is constructed from genetic and epigenetic interactions, as well as the interactions between those and the environment: phenotypes are emergent products of these interactions. Continuous changes in underlying genetic and environmental parameters may not map additively into continuous transitions in the phenotype (Rice 2002, 2004a, b).

Developmental interactions of this kind have three consequences that may hamper the accurate prediction of evolutionary transformations in morphospace. One consequence is that evolutionary transitions in underlying genetic parameters—the rate of expression of developmental activators or inhibitors, for example—may be quasi-continuous, but the corresponding change in the phenotype may jump discontinuously from one point in morphospace to another without traversing intermediate points (Fig. 1). If so, then the same quantitative genetic equations cannot simultaneously describe changes in the phenotype and in the underlying factors. A second consequence is that

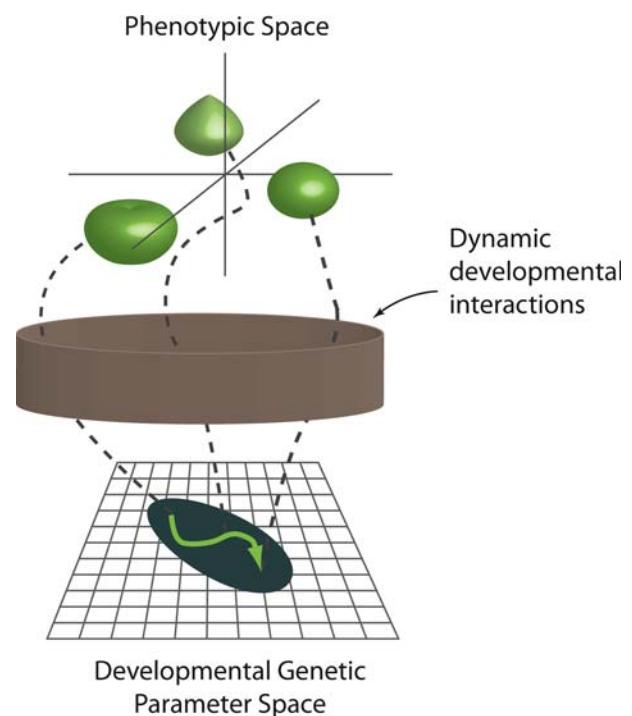


Fig. 1 Non-linear mapping of genetic-developmental parameter space onto phenotypic space. Continuous evolutionary changes developmental genetic parameter space, such as a change the rate of expression of activators or inhibitors of cellular division (bottom panel), may produce discontinuous changes in phenotypic space

developmental interactions may limit production of some phenotypic variants, biasing variation in certain directions that, in turn, bias the direction of evolutionary transformations (Alberch 1982; Goodwin 1994; Newman and Müller 2000; Arthur 2004). Some argue that these biases are adequately accounted for in evolutionary genetic theory by the structure of variances and covariances in the **G** matrix (e.g., Maynard Smith et al. 1985; Hansen 2006), whereas others argue that many of the biases come from non-additive interactions and so are not adequately described by **G** (e.g., Salazar-Ciudad 2007). The third consequence is that developmental interactions can produce novel structures or cause the loss of existing structures. By strict definition, a novel structure is one that is neither homologous to any structure in an ancestor nor equivalent to any other structure in the same organism (Müller and Wagner 1991). More loosely, a novel structure can also be the repetition of an already existing structure, such as a vertebra. The gain and loss of such features may be impossible to represent in some morphospaces because the dimensionality of the space is fixed and because the quantitative variables associated with the dimensions of the space may be mapped onto the phenotype in such a way that the gain or loss of phenotypic components is mathematically prohibited. Several authors have recently begun extending evolutionary quantitative genetic theory to represent these developmental phenomena (Johnson and Porter 2001; Rice 1990, 2000, 2002, 2004a, b; Wolf et al. 2001, 2004; Hunt et al. 2007).

This review explores the potential consequences of developmental interactions for modeling evolutionary transformations in morphospace. I will first review the mathematical properties of morphospaces that are relevant to such transformations. I will then review how evolutionary quantitative genetic theory is tied to existing methods for estimating evolutionary trajectories through morphospace and how those estimates may differ from predictions derived from evolutionary developmental biology. I will also review how the recent extensions of evolutionary quantitative genetic theory try to account for the non-linear developmental mapping of the phenotype onto genetic and environmental factors. The specific consequences of these issues for modeling evolutionary transformations in morphospace will be explored and a revised concept for modeling them based on the extended evolutionary quantitative genetics models will be considered.

Morphospaces and Their Properties

Morphometric spaces, or *morphospaces*, are mathematical constructions for the orderly arrangement of phenotypes using one or more variables as the criteria for the ordering. Morphospaces are often used for visualizing multivariate

phenotypic similarities and differences; for statistical analysis of phenotypes to one another or to external factors such as environment, sex, age, or geography; and for generating theoretical phenotypic models (Bookstein 1991; Dryden and Mardia 1998; McGhee 2007). Morphospaces can have one or more dimensions, each of which is defined by a phenotypic variable (such as the length of a structure or a Cartesian coordinate of a landmarks) or by a transformed combination of such variables. Each position within a morphospace represents a single, unique phenotype whose identity is determined by the geometry of the space and how the associated morphometric variables are mapped onto the phenotype.

Morphospaces are sometimes categorized as empirical or theoretical depending on whether their geometry, especially their coordinate system, is derived from real data or from the parameters of equations used to generate theoretical morphotypes (Raup 1966; McGhee and McKinney 2002; McGhee 1999, 2001, 2007). This distinction is useful in many contexts, though it is fairly arbitrary (MacLeod 2002; Polly 2004). For the purposes of this paper, however, the distinction between empirical and theoretical morphospaces will be ignored because my focus is on trajectories through empty parts of morphospace that are “theoretical” regardless of whether they are drawn in an empirical morphospace or not.

Morphospaces have several properties that relate directly to the question of evolutionary transformations within them: the criteria used to order the phenotypes, the coordinate system of the space, the scaling of the axes, the dimensionality of the space, and the methodological philosophy with which variables associated with the morphospace are mapped onto the phenotype.

Ordering of Phenotypes, Coordinates Systems, and Scaling in Morphospaces

The criteria used to order phenotypes within a morphospace, the coordinate system of the space, and the scaling of its axes are closely related to one another and to the variables used to characterize the phenotypes. The simplest morphospaces have the original variables as their axes, often log transformed if they are size variables (Fig. 2a). Phenotypes in these morphospaces are therefore ordered by the scale of the original variables and the coordinate system of the space is defined by the same variables. The distribution of phenotypes is often correlated on two or more of the axes, as is usually the case with size variables.

In multivariate morphometrics, the coordinate system of the space is often transformed to the principal components (PCs) of the covariance matrix of the original variables (Reyment 1984). The PC coordinate system is centered on the phenotypic mean and the primary axis runs through the

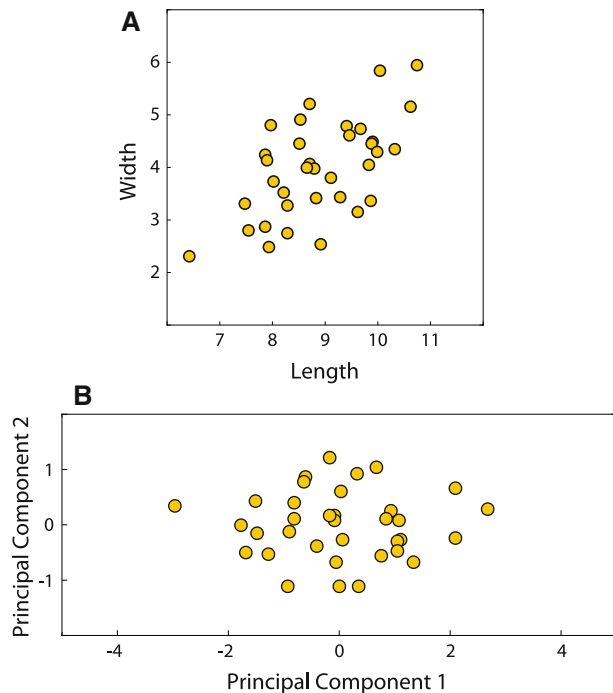


Fig. 2 (a) A simple morphospace with two measured variables, length and width, that form the axes, and therefore the coordinate system, of the space. Note that the length and width data are correlated. (b) A principal component (PC) morphospace, which is a transformation of the space in A by rigid rotation. Note that the distances among the data points are unchanged, but that there is no correlation in the data between PC 1 and PC 2

major axis of variation in the data with subsequent axes running at right angles through the minor axes of variation. This transformation, if based on the covariance matrix, is a simple rigid rotation of the original variable space: even though the axes and coordinate system are new, the ordering and spacing of phenotypes is unchanged (Fig. 2b). Evolutionary transformations within a covariance-based PC morphospace are exactly the same as in the original variable space, except for the coordinates used to describe the trajectory. If the PC system is based on a correlation matrix, the ordering of phenotypes is unchanged by the transformation, but their spacing is altered. Evolutionary transformations in this space would be different than in the original variable space.

Other transformations of scaling and coordinate systems are used in morphometrics, one of the most common being the canonical variates (CV), which maximizes differences among pre-specified groups (Reyment 1984). Technically speaking, the ordering of phenotypes is unchanged in a CV space, but the changes in scaling are so radical and so closely tied to the properties of a data set that they are not easily predictable. The nearest neighbor of an object in CV space can be considerably different from its nearest neighbor in the original variable space (Klingenberg and Monteiro 2005).

The ordering of phenotypes within a morphospace is thus normally the same regardless of the coordinate system or the scaling of the axes and is determined by the ordering of the original variables. The ordering of the phenotypes is preserved when the transformed axes are linear combinations of the original axes. The spacing between phenotypes is the same if the scaling of the original variables is preserved in the transformation of the axes, but it is changed if the scaling is altered. When a PC system is based on a correlation matrix, for example, the variance of the original variables is standardized to 1.0 prior to the rotation of the coordinate system.

The consequence of these properties is that evolutionary trajectories drawn between two particular phenotypes in a morphospace will pass through intermediate phenotypes in *approximately* the same order, regardless of changes in coordinate system or scaling. The scaling of phenotypic change along the trajectory depends heavily on the scaling of the axes of the morphospace, however, which has implications for methods that estimate distance between phenotypes or rates of change between one phenotype and another. The nearest neighbor to any particular phenotype also depends on the scaling of the axes, which has implications for tree-building in morphospaces. The effect of scale changes can have effects that are more complicated than what is described here (e.g., Rohlf 2000; Klingenberg and Monteiro 2005) and one should never presume that a linear evolutionary trajectory between two phenotypes in one space will pass through the *exactly* the same intermediate phenotypes in a transformed space unless the transformation is known to be a rigid rotation.

Dimensionality of Morphospaces

The dimensionality of a morphospace is fixed, either by the number of variables used in its construction or by the degrees of freedom in the data if the morphospace axes are based on an empirical sample (Reyment 1984; Bookstein 1991). Dimensionality places stringent limits on the variety of phenotypes that can be represented, limits that are determined by the choice of variables used to represent the phenotype. Imagine a morphospace where each axis represents a different phenotypic trait. An evolutionary trajectory drawn through that space can describe change in any one or more of the traits, but a new trait, an evolutionary novelty, cannot be added nor can a trait be lost because the number of traits is implicitly defined by the choice of variables. Thus, morphospaces cannot easily be used to model evolutionary transformations that involve the gain and loss of traits.

The limitation of dimensionality is not absolute, however, because the evolutionary gain and loss of features can be modeled in a morphospace if each axis represents an

independent feature and if the value of the phenotype on the axis can move to zero. In a morphospace with these properties, evolutionary loss of a feature could be modeled by restricting trajectories to a subspace that does not include the axis associated with that feature. The gain of that feature could then be modeled by allowing trajectories to move away from the zero point of that axis. This approach would still be limited because the number of features that can be gained or lost is predetermined by the choice of variable axes in the morphospace.

It should be noted, however, that all finite-dimensional morphospaces can be viewed as subspaces of an infinite dimensional Hilbert space. Such an infinite-dimensional space would allow modeling of the evolutionary gain and loss of any number of features, but the relation of each axis to a phenotype would have to be specified to make the model biologically meaningful.

Homology and Homology-Free Characterizations of the Phenotype

The mapping of morphometric variables onto the phenotype is important for modeling evolutionary transformations in morphospace. Even though the mapping is not directly related to the other properties of the morphospace, it determines how individual points in the space are translated into a picture of the phenotype. The choice of mapping will determine what kind of phenotypic transformations can be described by evolutionary trajectories through a morphospace and how the phenotypes are ordered in the space. Many classifications of kinds of morphometric variables exist (Reyment 1984; Bookstein 1991; Zelditch et al. 2004; Hammer and Harper 2005), but here I will concentrate on the distinction between homology and homology-free variables. I will also concentrate on geometric variables that can be used to graphically represent the phenotype, though some of this discussion could be extended to other types of variables.

Homology-based variables are ones that are associated directly with a particular biologically homologous structure. Landmark points that are applied to specific homologous substructures of the phenotype are the most familiar example (Fig. 3a). Regardless of whether such points are analyzed as Cartesian coordinates (Bookstein 1991) or as interpoint distances (Strauss and Bookstein 1986; Lele and Richtsmeier 1991), there is a fixed correspondence between variables and homologous substructures of the phenotype.

Homology-free variables are ones that are applied to the phenotype using a mathematical algorithm that is “homologous” in its orientation to place individual points at regularly specified intervals that may or may not fall on the same homologous substructure. Outlines (Younker and Erlich 1977; Lohmann 1983; MacLeod and Rose 1993) and

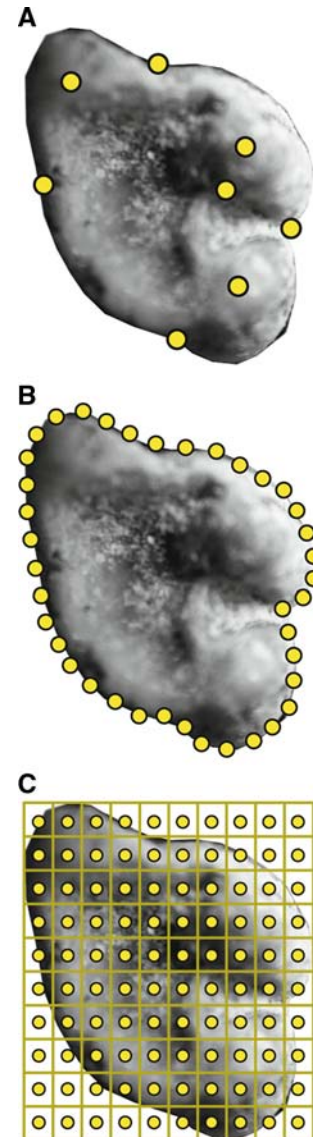


Fig. 3 (a) Homology-based mapping of landmark points on a lower third molar of *Marmota caligata* in occlusal view. (b) Homology-free outline coordinates around the perimeter of the same tooth. (c) Homology-free 3D grid-coordinates on the surface of the tooth

3D surfaces (Salazar-Ciudad and Jernvall 2004; Wiley et al. 2005; Polly 2008; McPeck et al. 2008), whether quantified as polynomial functions, Fourier descriptors, angular deformations, or Cartesian coordinates, are examples of homology-free variables (Fig. 3b, c). Homology-free characterizations have a fixed number of variables that help define the dimensions of the associated morphospace, but the number of homologous substructures is not necessarily fixed. This property of homology-free characterizations of the phenotype potentially allows structures to be gained or lost in evolutionary transformations in a morphospace, though the potential is limited to structures that are identifiable from the contours of a curve, an outline, or a surface.

Homology-free variables hold the most promise for modeling the evolution of novelty.

The pros and cons of homology-free variables have been discussed at length in the morphometric and systematics literature (e.g., Bookstein et al. 1982; Erlich et al. 1983; Bookstein 1991; Zelditch et al. 1995; MacLeod 1999). Homology-based variables are required if one wants to measure variation in particular homologous substructures (though some methods are better suited for this task than others (Lele and Richtsmeier 1992)), to maintain a one-to-one correspondence between morphometric structures and homologous characters in a phylogenetic analysis, or, arguably, to validly use morphometric variables as data for phylogeny reconstruction. Homology-free variables are required if one wants to characterize shape variation that includes the gain and loss of homologous substructures. Because of existing disagreements about the validity of homology-free methods for characterizing geometric shapes, three things are worth emphasizing: (1) the “homology-free” characterization I am describing is homology-based in that it is applied to biologically homologous structures in a biologically comparable orientation; (2) that relative morphometric distances between phenotypes as wholes are closely correlated, regardless of which characterization is used because both approaches are fundamentally measuring the same phenotype; and (3) homology-based and homology-free characterizations grade into one another because homologous landmarks can be used to restrict homology-free curves, semi-landmark constellations, or subsurfaces to particular homologous substructures (MacLeod 1999; Bookstein et al. 2003; Wiley et al. 2005). The difference between the approaches is really a matter of how variables are mapped onto substructures and which interpretations are possible given that mapping.

The potential for modeling evolutionary novelty is most fully realized with full three-dimensional characterizations of entire structures. Morphometric methods for the analysis of 3D surfaces are in their infancy and have logistical and mathematical issues waiting to be resolved. A handful of studies have appeared, however, that demonstrate the power of surface characterizations for representing some kinds of evolutionary gains and losses. Salazar-Ciudad and Jernvall (2004), for example, used a simple grid of 3D points whose x y base was placed on a mammalian tooth row and whose z heights were used to characterize the shape of the tooth row. This method is able to describe variation in the number of teeth, presence and absence of cusps and cingulae on individual teeth, as well as relative shape and proportions of teeth, cusps, and dentitions. Polly (2008) used a flexible grid of 3D points fit to the surface of the calcaneum to characterize variation across taxonomic and locomotor groups of the mammalian Carnivora. This system was able to capture the presence and absence of the

peroneal process, as well as the functional proportions of the bone and the curvature of articulating joints. Wiley et al. (2005) used a combination of homologous landmark coordinates, sliding semi-landmark curves, and surface patches of semi-landmarks to characterize entire primate skulls. McPeck et al. (2008) used 3D spherical Fourier harmonics to describe the entire surface structure of elements of the male genitalia in damselflies. Male and female structures interlock in these insects in a complicated way that is associated with prezygotic reproductive isolation. Transformations in the phenotype from one species to another are structurally dramatic. Each of the last three studies modeled evolutionary change in the respective phenotypes—including the gain, loss and transformation of substructures like the peroneal process—by applying statistical models derived from evolutionary quantitative genetics to extrapolate empirically measured phenotypes over a phylogenetic tree.

Linking Evolutionary Genetics and Development to Morphospaces

Evolutionary Quantitative Genetics of the Phenotype

Most existing models for mapping evolutionary transformations in phenotypic morphospaces are derived from multivariate evolutionary quantitative genetic theory. The theory for phenotypic evolution is extrapolated from the theory for allele frequencies and uses basically the same equations (Fisher 1930; Wright 1968; Lande 1976; Roff 1997). Simply put, change in phenotypic means is a function of drift, selection and the matrix of additive genetic variances and covariances, \mathbf{G} . Drift is a function of population size and \mathbf{G} , selection is a function of fitness, which can be described by an adaptive landscape (Lande 1976; Arnold et al. 2001; Gavrillets 2004). Long-term evolution of the phenotype is the summation of the changes in mean phenotype over many generations of selection and drift.

More specifically, the multivariate phenotype \mathbf{P} (or \mathbf{z} in some notations) is composed of two major components, genetic, \mathbf{G} , and environmental, \mathbf{E} . Change in mean multivariate phenotype is described by the multiplication of a vector of selection coefficients and the additive genetic covariance matrix, such that $\Delta\bar{\mathbf{z}}_s = \mathbf{G}\boldsymbol{\beta}$, where $\Delta\bar{\mathbf{z}}_s$ is change in the mean phenotype due to selection, \mathbf{G} is the additive genetic covariance matrix, and $\boldsymbol{\beta}$ is the vector of selection coefficients (Arnold et al. 2001; Lande 1979). Added to this is change in the mean phenotype due to drift: $\Delta\bar{\mathbf{z}}_d = \mathbf{G}/N_e$, where $\Delta\bar{\mathbf{z}}_d$ is change in the mean phenotype due to drift, and N_e is the effective population size (Lande 1979). The direction and magnitude of selection

coefficients is a function of reproductive fitness, which is represented by the shape of an adaptive landscape, $W(\bar{z})$ (Arnold et al. 2001). Selection on the adaptive landscape normally moves the mean phenotype toward the peak. The literature on quantitative phenotypic evolution is rich and deals with many issues not touched on here (see the succinct review by Arnold et al. 2001).

An important feature of these evolutionary quantitative genetic equations is they describe changes solely in terms of the phenotype. Genetic and developmental correlations are described by \mathbf{G} , which is estimated from phenotypes experimentally, perhaps with offspring-parent regression (Roff 1997). Likewise, selective and environmental correlations are described by $W(\bar{z})$ and β , which are estimated from phenotypes using an appropriate experimental design. These evolutionary genetic equations do not require specific knowledge of the mapping of the phenotype onto specific underlying genetic, developmental, or environmental factors, though the additive phenotypic effects of those factors are described by \mathbf{G} and so influence the direction and magnitude of evolutionary changes predicted by these equations (Maynard Smith et al. 1985; Steppan et al. 2002; Hansen 2006).

The fact that the evolutionary quantitative genetic equations are expressed exclusively in terms of the phenotype make them particularly applicable to modeling phenotypic transformations in morphospace in a theoretically informed, probabilistic manner (Fig. 4). Indeed, a morphospace can be constructed directly from \mathbf{G} if it is available, or from \mathbf{P} , which is autocorrelated with \mathbf{G} (Cheverud 1988; but see Willis et al. 1991) if \mathbf{G} is not known. All of the methods used to estimate evolutionary trajectories in morphospace—short and long-term modeling of phenotypic evolution, random skewers, phylogenetic character mapping, ancestral state reconstructions, and maximum likelihood phylogenetic reconstructions—are founded on these evolutionary genetic equations (e.g., Felsenstein 1988; Martins and Hansen 1997; Rohlf 2001; Polly 2004).

Alternative Developmental Models of Phenotypic Evolution

Despite the proven effectiveness of evolutionary quantitative genetic theory and the ease of applying it to evolution in morphospaces, the criticisms derived from developmental biology that phenotypic evolution does not necessarily behave according to the assumptions of this theory deserves consideration. Three issues deserve special attention: (1) the mapping of phenotypes onto underlying genetic, developmental, and environmental factors may be non-linear so that evolutionary transformations that are continuous at one level may not be continuous at the other; (2) developmental

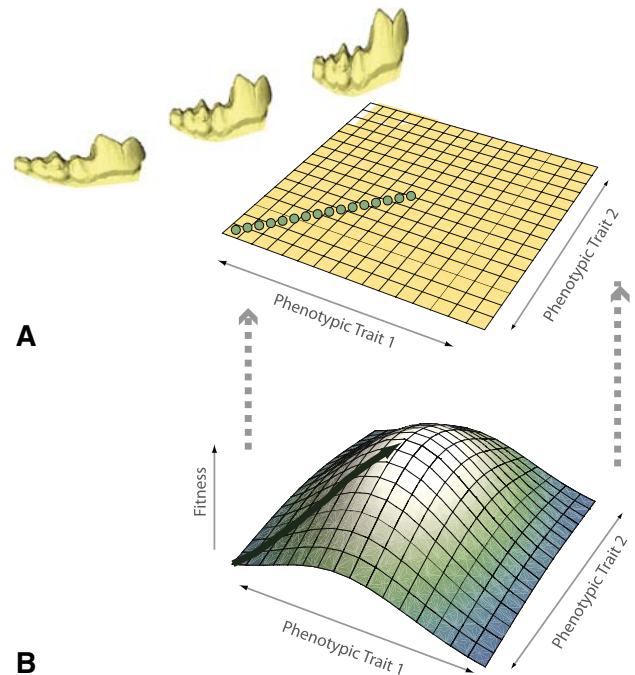


Fig. 4 Typical mapping of evolutionary genetic processes (**b**) into morphospace (**a**). Evolutionary quantitative genetic models of phenotypic evolution usually make a direct link between phenotype and fitness without intermediate consideration of interactions between molecular genetic, developmental, or environmental components of the phenotype. Evolutionary changes, such as movement of the mean phenotype up the slope of an adaptive landscape map linearly into morphospace because there is a one-to-one correspondence of phenotypic traits in the two systems. Any process that is continuous on the adaptive landscape produces continuous change in the phenotype

interactions may bias phenotypic variation in non-additive ways, perhaps prohibiting some variants altogether or making variation meristic instead of continuous; and (3) developmental interactions may produce novel phenotypic structures even though the underlying genetic, developmental, and environmental processes are not novel. (Novelty can, of course, arise from non-developmental transformations; I am not intending to imply that this last is the only source of novelty).

These issues have long been a part of debate about whether the developmental interactions play a role in evolution independent of adaptation and selection. The roots of developmental side of this debate extend back to Cope (1887), Bateson (1894), Morgan (1916), and Vavilov (1922), but have been elaborated recently by Riedl (1978), Alberch (1982, 1985), Gould (1985, 2002), Müller and Wagner (1991), Kauffman (1993), Raff (1996), Salazar-Ciudad et al. (2001), Salazar-Ciudad and Jernvall (2004), and Salazar-Ciudad (2006, 2007). The issues raised by these authors could once have been considered to be outside the domain of evolutionary quantitative genetics

because the transformations involved were difficult to express as quantitative traits. However, the heightened ability for geometric morphometrics to quantitatively describe complicated, multivariate phenotypes, the ease with which evolutionary transformations can be modeled using quantitative genetic equations, and the increase in knowledge about how genetic, developmental, and environmental interactions produce phenotypes make it worth reconsidering the consequences of the for modeling phenotypic evolution in morphospaces.

The developmental issues have three important consequences for modeling phenotypic change in morphospaces: (1) transitions in the phenotype often involve evolutionary gains or losses that can be quantitatively equivalent to the gain and loss of variables or morphospace dimensions, except possibly when homology-free variables are used; (2) evolutionary transitions within phenotypic space cannot be expected always to be continuous, even though the transitions in their underlying genetic parameters might be; and, therefore, (3) the equations that describe evolution of the phenotype may need to be fundamentally different from the equations that describe evolution of allele frequencies, molecular sequences, gene expression levels, or other factors that underlie the phenotype.

One key to understanding the potential conflict between developmental models of the phenotype and the expectation of phenotypic evolution inherent in evolutionary quantitative genetic models is that standing variation in the phenotype does not directly give information about the underlying developmental processes (Salazar-Ciudad 2007); any observed pattern of phenotypic covariance might be the product of one of several possible systems of interaction among underlying factors (Rice 2004a). Depending on the interaction of the underlying factors, evolutionary change might take the course predicted from the additive effects of **G** or it might not depending on the situation. Instead of proceeding continuously, phenotypic evolution may wander continuously in one region of morphospace before jumping discontinuously to another. Instead of *e* being able to take on all its possible values, a phenotypic variable may have limits that cannot be crossed because they describe developmentally prohibited phenotypes. Instead of a multivariate phenotype being composed of a fixed number of variables, structures may be gained and lost such that terms would have to drop into and out of modeling equations to describe the changes.

Mammalian teeth provide an example of how developmental interactions can produce such biased and discontinuous phenotypes even though the underlying changes in underlying molecular genetic factors may be continuously gradational (see reviews by Thesleff and Sharpe 1997; Jernvall and Thesleff 2002). Teeth form along the dental arch as a series of interactions between

ectodermal and neural-crest derived mesodermal layers, which are regionalized into incisors, canines, premolars and molars by HOX-like expression domains. Individual teeth start as buds in the ectodermal epithelium, which are surrounded by a proliferation of mesenchyme cells. Iterative signaling within and between these layers, initiated by the primary enamel knot cells in the epithelium, causes the bud to invaginate and fold into the rough shape of the tooth crown, after which mineralization forms the enamel and dentine structures that will later erupt into the mouth as a functional tooth. While involving many gene products, the developmental system that produces the crown shape can be characterized by the epithelial rate of cell division, the rate of expression of activator molecules, which signal affected epithelial cells to differentiate into new signaling centers when a threshold concentration is reached, inhibitor cells, which inhibit production of activator molecules and which stimulate growth in the mesenchymal layer, and diffusion coefficients for the activators and inhibitors (Salazar-Ciudad and Jernvall 2002). Small changes in any of these parameters can change the pattern of folding to increase or decrease cusp sharpness, increase or decrease the number of cusps, transform cusps into lophs, or to reorganize structures on the tooth crown. Changes in expression of signaling molecules can have dramatic effects on several structures in several teeth. Up or down regulation of ectodysplasia, for example can change the number of cusps, the position of cusps on the crown and the number of teeth in the tooth row (Kangas et al. 2004). These dramatic, discontinuous changes across the entire tooth row are possible because signaling happens by diffusion. Changes in growth of the developing tooth and the folding of its tissues can affect the outcome equally as much as actual changes in the level of expression of the signaling molecules. Change in one parameter thus can produce non-linear knock-on effects in the entire system.

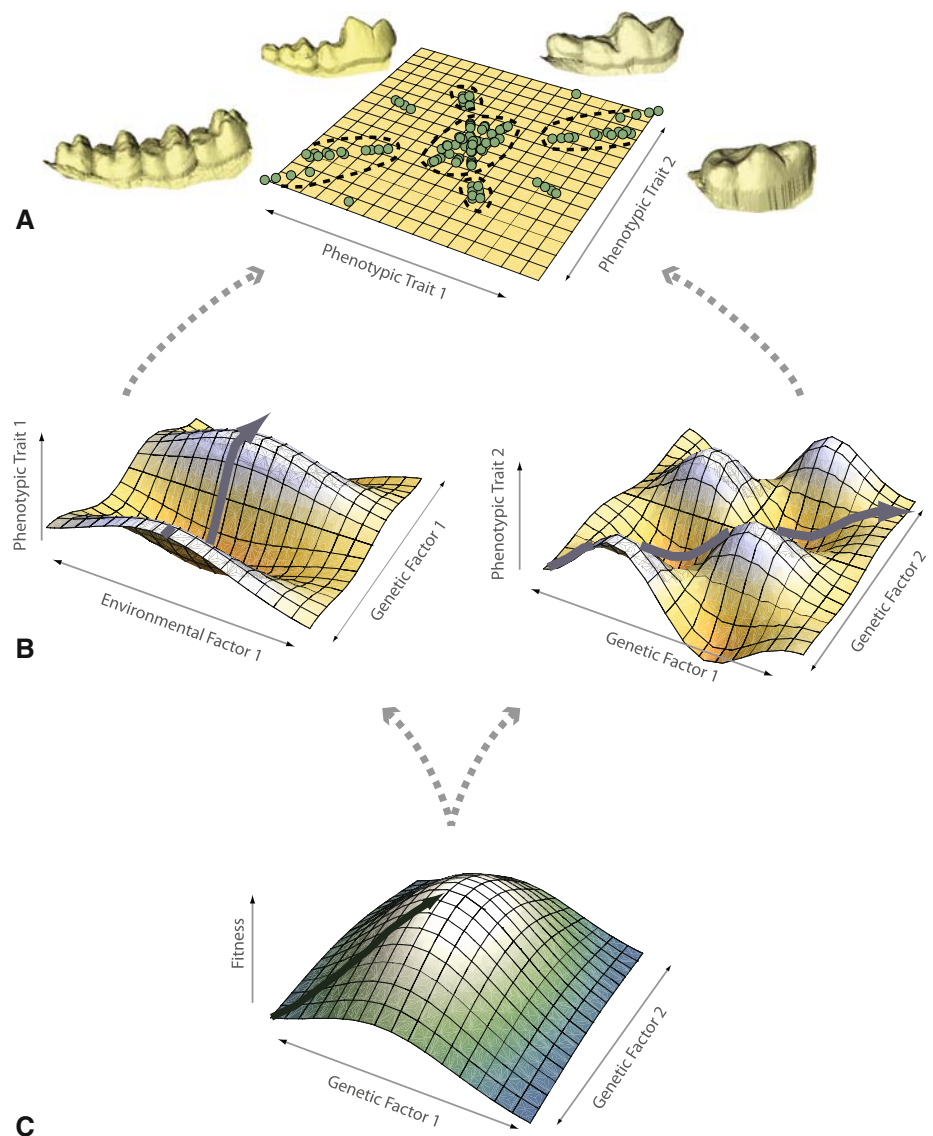
Phenotypic differences like the ones associated with ectodysplasia are characteristic of differences found among phylogenetically distant species, but also of variation within species (Wolsan 1989; Jernvall 1995, 2000; Szuma 2002). Differences in cusp number, tooth number, and the topography of features on the tooth crown are arranged in geographic clines similar to ones characteristic of body size, for example (Szuma 2007). Furthermore, continuous variation in underlying developmental parameters can produce patchy and discontinuous distributions of phenotypes in morphospace (Salazar-Ciudad and Jernvall 2002). It would clearly be of interest to be able to model population and evolutionary changes in such traits in a way that is consistent with these patterns, a goal that is not obviously obtainable from existing models of evolutionary transformations in morphospaces.

Evolutionary Quantitative Genetics Extended

Theoretical work has already begun to extend evolutionary quantitative models to link underlying genetic, developmental and environmental factors with the phenotype instead of treating both levels independently with the same equations (Johnson and Porter 2001; Rice 1990, 2000, 2002, 2004a, b; Wolf et al. 2001, 2004; Hunt et al. 2007). These approaches insert a quantitative level between the adaptive landscape, on which genetic parameters evolve in response to selection and drift, and the phenotypic level (Fig. 5). The new level is the phenotypic landscape, which describes how interactions between genetic, developmental, environmental are translated into phenotypes. Each phenotypic trait (or independent component of a multivariate phenotypic trait) has an equation that describes its relation to the underlying factors (Rice 2004a). The relationships may be additive,

pleiotropic (if the same factor appears in more than one equation), or non-additive as is appropriate. The equations that describe real phenotypic traits must be based on information from developmental, genetic, or environmental studies, though hypothetical equations could be used purely for the purposes of simulation (as was done to generate Fig. 5). The equations for the various components of the phenotype can be combined into a multivariate phenotypic landscape, which describes how the phenotype changes in response to changes in the underlying parameters (Rice 2004a). In situations when the effects of the underlying factors on the phenotype are purely additive, then the system behaves as expected under the more standard quantitative genetic equations reviewed above; however, when some effects are not additive, the system behaves in a more complicated manner that includes biased patterns of multivariate phenotypic variance, discontinuous transformations

Fig. 5 Alternative mapping of genetic processes (c) into morphospace (a) using phenotypic landscapes (b) as an intermediate step. The complicated, multivariate phenotypes described by the morphospace can be biologically decomposed into separate phenotypic traits, each of which has its own equation to describe its relationship to underlying environmental and genetic factors. The independent contribution of each equation to the complete phenotype, as well as non-linear terms in the equations, permits non-linear, discontinuous phenotypic transitions to result from continuous transitions on the adaptive landscape. If the morphospace is constructed from homology-free variables, the discontinuous phenotypic changes can include the gain and loss of structures, as well as transformations in their shape and relative size



of the phenotype in response to continuous transformations in the underlying factors, and the appearance of novel traits in response to changes in how the factors underlying the phenotype interact. Whether these extended quantitative genetics models can capture the morphodynamic aspects of development described by Salazar-Ciudad and Jernvall (2002) is not clear, but they certainly capture many of the properties of phenotypic variation considered to be important by evolutionary developmental biologists.

A Revised Approach to Morphospace Modeling?

Both the discontinuity in morphospace of phenotypic transitions and the evolution of novel features, which is another type of mathematical discontinuity, present challenges for modeling evolution in morphospace. Generally speaking, evolutionary genetic models of morphological evolution describe the effects of selection and drift completely in terms of changes in phenotypic means and variances. Quantitative constructs like the phenotypic adaptive landscape can be mapped directly into morphospace because there can be a one-to-one correspondence between variables in the two systems (Fig. 4). Continuous evolutionary transitions on an adaptive landscape map directly to continuous phenotypic transitions in morphospace, though it should be noted that the topography of the adaptive landscape can itself be complicated, perhaps including non-linear discontinuities (Gavrilets 2004).

One issue with the mapping of evolutionary process into morphospace is whether developmental interactions and other constraints can be realistically taken into account when evolutionary transformations are modeled. A strong argument has been made that developmental interactions that influence phenotypic variation are described by **G** (Maynard Smith et al. 1985; Hansen 2006). Processes that introduce biases or correlations in phenotypic variation will manifest themselves as correlations in the adult phenotype. Because **G** is derived from such phenotypic data, it incorporates the effects of developmental interactions even though those may not be known directly. Even the effects of morphodynamic processes are expected to be imprinted in **G**, making it possible to predict evolutionary transformations in the phenotype that allow for developmental interactions. One objection to this view is that heritable variance may exist for a trait in an existing population, but developmental interactions may inhibit the production of new variance for that trait outside the observed range. Standard evolutionary genetic equations would allow the phenotypic mean to move into a developmentally prohibited range because **G** describes variance in that direction. Furthermore, **G** only describes additive covariances. The non-additive effects of interactions among underlying

factors will not be represented in **G**, making it a poor predictor of evolutionary response in some situations (Rice 2004a).

The extended evolutionary quantitative genetic system of Rice and others could be used to revolutionize the way that evolutionary transformations are modeled in morphospace. Their new system models many of the properties of phenotypic variation considered important by the evolutionary developmental biologists listed above (Rice 2004a, b). Non-linear interactions at the level of the phenotypic landscape can result in phenotypic variances that are not necessarily even close to multivariate normal, but which can be biased in surprising ways by the topography of the phenotypic landscape. Novel features can arise as traits with no heritable variation become heritable due to changes in the underlying factors, after which the new feature will start to evolve over the landscape. Discontinuous transformations in the phenotype can result from continuous transformations in the underlying genetic factors. An example of such discontinuity is illustrated in Fig. 5, where the non-linear phenotypic landscapes transform the simple linear change in two genetic factors in response to selection on a Gaussian adaptive landscape into a series of jumps in morphospace. While the teeth associated with the phenotypic clusters in Fig. 5 are merely illustrative of the possibility of what those clusters represent, the clusters themselves result from the mathematics of the two underlying layers.

A homology-free method for characterizing the phenotype would be required for such a system to model evolutionary novelties (or the loss of phenotypic structures). Many of the interesting phenomena in evolution of the phenotype involve the gain and loss of features, the origin of novelty (Raff 1996; Nitecki 1990; Müller and Wagner 1991). Despite the desirable properties of the extended quantitative genetic system, the origin of novel features cannot be modeled if the variables used to describe the phenotype are exclusively tied to existing homologous structures. With homology-free variables novel features can be visually represented by particular combinations of points at the appropriate topographical position, just like new shapes can be created on a bitmap computer screen by changing the colors of particular combinations of pixels. Salazar-Ciudad and Jernvall (2004) used a simple version of such a homology-free system to assess disparity and complexity of tooth shapes generated by their computer model of tooth development. For phenotypes like the dentition, where the novel features are cusps, crests, and teeth (Salazar-Ciudad and Jernvall 2004), for phenotypes like the mammalian tarsus, where novel features are processes and bones, (Polly 2008), or for phenotypes like insect genitalia, where novel features are projections and invaginations (McPeck et al. 2008), homology-free

surfaces are capable of representing most of what one would need to describe the gain and loss of homologous substructures. Other kinds of evolutionary novelties, such as internal organs, may not be easy to capture with existing methods.

The primary challenge for using this system to model morphospace transformations is that the equations that map phenotypic traits onto underlying factors must be known from experimental studies, even though no such information is available for many of the phenotypic traits of interest to evolutionary biologists, systematists, or paleontologists. (One can, however, imagine a Bayesian estimation of the parameters of the phenotype equations from observations of phenotype, environment, and gene expression).

Conclusions

Morphometric spaces are based purely on variables that represent phenotypes, with no reference to factors that influence evolution of one phenotype to another, regardless of whether those factors are developmental interactions, genetic linkages, selection, or whatever. Nevertheless, morphospaces are often used in conjunction with evolutionary quantitative genetic equations to model the short or long-term course of phenotypic evolution, to map phenotypic traits onto phylogenetic trees, to reconstruct ancestral phenotypes at tree nodes, or even to reconstruct phylogenetic relationships from the quantitative traits that define the morphospace. All of these procedures rely on certain assumptions about continuity and direction of phenotypic change within the space in response to typical evolutionary processes such as drift and selection. Furthermore, the geometry of most morphospaces and the way that their associated variables are mapped onto the phenotype mean that evolutionary transformations in morphospace can only describe changes in a static set of features, but not the gain and loss of features.

The theoretical underpinnings of such transformations in morphospace are founded on evolutionary quantitative genetic theory of phenotypic evolution. Key features of this theory are that population means follow continuous trajectories through phenotypic space; the direction of change is a function of genetic covariances, selection (and selective covariances), drift; and the magnitude of change is function of genetic variance, selection intensity, and population size. Because this theory forms the basis for existing methods for projecting evolutionary trajectories through morphospace, these trajectories have the following properties: (1) changes in phenotype are continuous; (2) nothing except selection or additive variance prevent the phenotype from moving infinitely in a given direction; and (3) there is no obvious provision for gain or loss of features.

Nevertheless, studies of development have demonstrated that in many systems phenotypic variation may be discontinuous, it may be biased in certain directions, the interactions of genetic, developmental, and environmental factors may have non-linear effects on the phenotype, and “novelties” may arise from these non-linear interactions. Morphometric and quantitative genetic analysis of the phenotype are only indirectly indicative of the underlying developmental, genetic and environmental factors that channel variation in the phenotype. Some but not all of the underlying developmental factors are captured in measures of phenotypic variance and covariance.

A multi-level system for modeling evolutionary change in morphospaces using the extended evolutionary genetic equations developed by Rice and others for phenotypic landscapes deserves further attention. Of special interest would be integrating the phenotypic landscape equations with existing geometric morphospaces. While this elaboration is unnecessary for morphometric studies of existing phenotypic diversity, it could become very powerful tool for modeling long-term phenotypic evolution, including radiations involving evolutionary novelties, with the discontinuous, non-linear phenotypic transformations that characterize so many biological systems.

Does any of this matter? Are quantitative genetic extrapolations, such as random skewers simulations of phenotypic change over a single generation, likely to be dramatically altered by incorporating non-additive interactions of genetic, developmental and environmental factors? Are ancestral reconstructions based on extrapolating multivariate phenotypes across a phylogenetic tree likely to be dramatically different for having included these effects? Probably not. Most morphometric studies to date have self-selectively focused on systems where the assumptions of morphospace modeling are met, where the traits under consideration are consistently present across the taxa being studied, where the phenotypic changes are likely to have been fairly continuous, and where additive genetic variance for the range of phenotypes under consideration is possible. The non-additive effects of developmental interactions may be more important for long-term simulations of morphological change over paleontological timescales, though it should be remembered that evolutionary “novelty” can be an issue even within populations, as demonstrated by variation in the presence and absence of cusps and crests in mammalian teeth. But if geometric morphospace modeling can be extended to deal with discontinuous variance, with discontinuous evolutionary change, and with the origin of novelty, then these same powerful methods may in future be applied to new problems, such as the analysis of discontinuous variation or to phenotypic transitions in the early radiation of metazoan animals. Better methods for homology-free representation of phenotypic variation will be

required, as will sophisticated, non-linear algorithms for creating morphospaces, for drawing trajectories through them, and for ordinating extremely disparate morphologies in the same morphospace. Are these improvements possible, or necessary, in the near future? We shall see.

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References

- Alberch, P. (1982). Developmental constraints in evolutionary processes. In J. T. Bonner (Ed.), *Evolution and development* (pp. 313–332). Heidelberg: Springer.
- Alberch, P. (1985). Problems with the interpretation of developmental sequences. *Systematic Zoology*, 34, 46–58. doi:10.2307/2413344.
- Albert, A. Y. K., Saway, S., Vines, T. H., Knecht, A. K., Miller, C. T., Summers, B. R., et al. (2008). The genetics of adaptive shape shift in stickleback: Pleiotropy and effect size. *Evolution*, 62, 76–85.
- Arnold, S. J., Pfrender, M. E., & Jones, A. G. (2001). The adaptive landscape as a conceptual bridge between micro- and macro-evolution. *Genetica*, 112, 9–32. doi:10.1023/A:1013373907708.
- Arthur, W. (2004). The effect of development on the direction of evolution: Toward a twenty-first century consensus. *Evolution and Development*, 6, 282–288. doi:10.1111/j.1525-142X.2004.04033.x.
- Bateson, W. (1894). *Materials for the study of variation, treated with special regard to discontinuity in the origin of species*. London: MacMillan and Co.
- Blows, M. W. (2007). A tale of two matrices: Multivariate approaches in evolutionary biology. *Journal of Evolutionary Biology*, 20, 1–8. doi:10.1111/j.1420-9101.2006.01164.x.
- Blows, M. W., & Brooks, R. (2003). Measuring nonlinear selection. *American Naturalist*, 162, 815–820. doi:10.1086/378905.
- Bookstein, F. L. (1991). *Morphometric tools for landmark data: Geometry and biology*. Cambridge: Cambridge University Press.
- Bookstein, F. L., Gunz, P., Mitteroecker, P., Prossinger, H., Schaefer, K., & Seidler, H. (2003). Cranial integration in *Homo*: Singular warps analysis of the midsagittal plane in ontogeny and evolution. *Journal of Human Evolution*, 44, 167–187. doi:10.1016/S0047-2484(02) 00201-4.
- Bookstein, F. L., Strauss, R. E., Humphries, J. M., Chernoff, B., Elder, R. L., & Smith, G. R. (1982). A comment upon the uses of Fourier methods in systematics. *Systematic Zoology*, 31, 85–92. doi:10.2307/2413416.
- Cardini, A., & O'Higgins, P. (2005). Post-natal ontogeny of the mandible and ventral cranium in Marmota (Rodentia, Sciuridae): Allometry and phylogeny. *Zoomorphology*, 124, 189–203. doi:10.1007/s00435-005-0008-3.
- Cheverud, J. M. (1988). A comparison of genetic and phenotypic correlations. *Evolution*, 42, 958–968. doi:10.2307/2408911.
- Cheverud, J. M. (1996). Quantitative genetic analysis of cranial morphology in the cotton-top (*Saguinus oedipus*) and saddle-back (*S. fuscicollis*) tamarins. *Journal of Evolutionary Biology*, 9, 5–42. doi:10.1046/j.1420-9101.1996.9010005.x.
- Cheverud, J. M., & Marroig, G. (2007). Comparing covariance matrices: Random skewers method compared to the common principal components model. *Genetics and Molecular Biology*, 30, 461–469. doi:10.1590/S1415-47572007000300027.
- Cope, E. D. (1887). *Origin of the fittest: Essays on evolution*. New York: D. Appleton and Co.
- Corbin, C. E. (2008). Foraging ecomorphology within North American flycatchers and a test of concordance with southern African species. *Journal of Ornithology*, 49, 83–95. doi:10.1007/s10336-007-0221-6.
- Drake, A. G., & Klingenberg, C. P. (2008). The pace of morphological change: Historical transformation of skull shape in St Bernard dogs. *Proceedings – Royal Society B*, 275, 71–76. doi:10.1098/rspb.2007.1169.
- Dryden, I. L., & Mardia, K. V. (1998). *Statistical analysis of shape*. New York: Wiley.
- Erlich, R., Pharr, R. B., & Healy-Williams, N. (1983). Comments on the validity of Fourier descriptors in systematics: A reply to Bookstein et al. *Systematic Zoology*, 32, 202–206. doi:10.2307/2413281.
- Felsenstein, J. (1973). Maximum likelihood estimation of evolutionary trees from continuous characters. *American Journal of Human Genetics*, 25, 471–492.
- Felsenstein, J. (1985). Phylogenies and the comparative method. *American Naturalist*, 126, 1–25. doi:10.1086/284325.
- Felsenstein, J. (1988). Phylogenies and quantitative characters. *Annual Review of Ecology and Systematics*, 19, 445–471. doi:10.1146/annurev.es.19.110188.002305.
- Fisher, R. A. (1930). *The genetical theory of natural selection*. Oxford: Oxford University Press.
- Gavrilets, S. (2004). *Fitness landscapes and the origin of species*. Princeton, NJ: Princeton University Press.
- Gilchrist, M. A., & Nijhout, H. F. (2001). Nonlinear developmental processes as sources of dominance. *Genetics*, 159, 423–432.
- Goodwin, B. C. (1994). *How the leopard changed its spots*. London: Weidenfeld and Nicholson.
- Goswami, A. (2006). Morphological integration in the carnivoran skull. *Evolution*, 60, 122–136.
- Gould, S. J. (1985). *Ontogeny and phylogeny*. Cambridge, MA: Harvard Belknap Press.
- Gould, S. J. (2002). *The structure of evolutionary theory*. Cambridge, MA: Harvard Belknap Press.
- Grafen, A. (1989). The phylogenetic regression. *Philosophical Transactions of the Royal Society B*, 326, 119–157. doi:10.1098/rstb.1989.0106.
- Hammer, Ø., & Harper, D. A. T. (2005). *Paleontological data analysis*. London: Wiley-Blackwell.
- Hannisdal, B. (2007). Inferring phenotypic evolution in the fossil record by Bayesian inversion. *Paleobiology*, 33, 98–115. doi:10.1666/06038.1.
- Hansen, T. F. (2006). The evolution of genetic architecture. *Annual Review of Ecology Evolution and Systematics*, 37, 123–157. doi:10.1146/annurev.ecolsys.37.091305.110224.
- Hohenlohe, P. A., & Arnold, S. J. (2008). MIPoD: A hypothesis-testing framework for microevolutionary inference from patterns of divergence. *American Naturalist*, 171, 366–385. doi:10.1086/527498.
- Hunt, G. (2007). The relative importance of directional change, random walks, and stasis in the evolution of fossil lineages. *Proceedings of the National Academy of Sciences of the USA*, 104, 18404–18408. doi:10.1073/pnas.0704088104.
- Hunt, J., Wolf, J. B., & Moore, A. J. (2007). The biology of multivariate evolution. *Journal of Evolutionary Biology*, 20, 24–27. doi:10.1111/j.1420-9101.2006.01222.x.
- Jernvall, J. (1995). Mammalian molar cusp patterns: Developmental mechanisms of diversity. *Acta Zoologica Fennici*, 198, 1–61.
- Jernvall, J. (2000). Linking development with generation of novelty in mammalian teeth. *Proceedings of the National Academy*

- of Sciences of the USA, 97, 2641–2645. doi:10.1073/pnas.050586297.
- Jernvall, J., & Thesleff, I. (2000). Reiterative signalling and patterning during mammalian tooth morphogenesis. *Mechanisms of Development*, 92, 19–29. doi:10.1016/S0925-4773(99) 00322-6.
- Johnson, N. A., & Porter, A. H. (2001). Toward a new synthesis: Population genetics and evolutionary developmental biology. *Genetica*, 112–113, 45–58. doi:10.1023/A:1013371201773.
- Jones, A. G., Arnold, S. J., & Burger, R. (2007). The mutation matrix and the evolution of evolvability. *Evolution*, 61, 727–745. doi:10.1111/j.1558-5646.2007.00071.x.
- Kangas, A. T., Evans, A. R., Thesleff, I., & Jernvall, J. (2004). Nonindependence of mammalian dental characters. *Nature*, 432, 211–214. doi:10.1038/nature02927.
- Kauffman, S. A. (1993). *The origins of order: Self organization and selection in evolution*. Oxford: Oxford University Press.
- Klingenberg, C. P., Leamy, L. J., & Cheverud, J. M. (2004). Integration and modularity of quantitative trait locus effects on geometric shape in the mouse mandible. *Genetics*, 166, 1909–1921. doi:10.1534/genetics.166.4.1909.
- Klingenberg, C. P., & Monteiro, L. R. (2005). Distances and direction in multidimensional shape spaces: Implications for morphometric applications. *Systematic Biology*, 54, 678–688. doi:10.1080/10635150590947258.
- Lande, R. (1976). Natural selection and random genetic drift in phenotypic evolution. *Evolution*, 30, 314–334.
- Lande, R. (1979). Quantitative genetic analysis of multivariate evolution, applied to brain-body size allometry. *Evolution*, 33, 402–416. doi:10.2307/2407630.
- Lele, S., & Richtsmeier, J. T. (1991). Euclidean distance matrix analysis: A coordinate system free approach for comparing biological shapes using landmark data. *American Journal of Physical Anthropology*, 86, 415–417. doi:10.1002/ajpa.1330860307.
- Lele, S., & Richtsmeier, J. T. (1992). Statistical models in morphometrics: Are they realistic? *Systematic Zoology*, 39, 60–69. doi:10.2307/2992208.
- Lohmann, G. P. (1983). Eigenshape analysis of microfossils: A general morphometric method for describing changes in shape. *Mathematical Geology*, 15, 659–672. doi:10.1007/BF01033230.
- MacLeod, N. (1999). Generalizing and extending the eigenshape method of shape space visualization and analysis. *Paleobiology*, 25, 107–138.
- MacLeod, N. (2002). Systematic implications of a synthesis between theoretical morphology and geometric morphometrics. In L. Kandoff (Ed.), *Computations in science* (p. 7). Chicago, IL: Department of Physics, University of Chicago.
- MacLeod, N., & Rose, K. D. (1993). Inferring locomotor behavior in Paleogene mammals via eigenshape analysis. *American Journal of Science*, 293-A, 300–355.
- Maddison, W. P. (1991). Squared-change parsimony reconstructions of ancestral states for continuous valued characters on a phylogenetic tree. *Systematic Zoology*, 40, 304–314. doi:10.2307/2992324.
- Marroig, G., Vivo, M., & Cheverud, J. M. (2004). Cranial evolution in sakis (Pithecia, Platyrrhini) II: Evolutionary processes and morphological integration. *Journal of Evolutionary Biology*, 17, 144–155. doi:10.1046/j.1420-9101.2003.00653.x.
- Martins, E. P., & Hansen, T. F. (1997). Phylogenies and the comparative method: A general approach to incorporating phylogenetic information into the analysis of interspecific data. *American Naturalist*, 149, 646–667. doi:10.1086/286013.
- Maynard Smith, J., Burian, R., Kauffman, S., Alberch, P., Campbell, J., Goodwin, B., et al. (1985). Developmental constraints and evolution: A perspective from the mountain lake conference on development and evolution. *The Quarterly Review of Biology*, 60, 265–287. doi:10.1086/414425.
- McGhee, G. R. (1999). *Theoretical morphology: The concept and its applications*. New York: Columbia University Press.
- McGhee, G. R. (2001). Exploring the spectrum of existent, nonexistent and impossible biological form. *Trends in Ecology and Evolution*, 16, 172–173. doi:10.1016/S0169-5347(01) 02103-6.
- McGhee, G. R. (2007). *The geometry of evolution: Adaptive landscapes and theoretical morphospaces*. Cambridge: Cambridge University Press.
- McGhee, G. R., & McKinney, F. K. (2002). A theoretical morphologic analysis of ecomorphologic variation in *Archimedes* helical colony form. *Palaos*, 17, 556–570. doi:10.1669/0883-1351(2002)017<0556:ATMAOE>2.0.CO;2.
- McPeck, M. P., Shen, L., Torrey, J. Z., & Farid, H. (2008). The tempo and mode of 3-dimensional morphological evolution in male reproductive structures. *American Naturalist*, 171, E158–E178. doi:10.1086/587076.
- Mezey, J. G., & Houle, D. (2005). The dimensionality of genetic variation for wing shape in *Drosophila melanogaster*. *Evolution*, 59, 1027–1038.
- Mitteroecker, P., & Bookstein, F. (2007). The conceptual and statistical relationship between modularity and morphological integration. *Systematic Biology*, 56, 818–836. doi:10.1080/10635150701648029.
- Morgan, T. H. (1916). *A critique of the theory of evolution*. Princeton, NJ: Princeton University Press.
- Müller, G. B., & Wagner, G. P. (1991). Novelty in evolution: Restructuring the concept. *Annual Review of Ecology and Systematics*, 22, 229–256. doi:10.1146/annurev.es.22.110191.001305.
- Newman, S. A., & Müller, G. B. (2000). Epigenetic mechanisms of character origination. *Journal of Experimental Zoology*, 288, 304–317. doi:10.1002/1097-010X(20001215)288:4<304::AID-JEZ3>3.0.CO;2-G.
- Nitecki, M. H. (1990). *Evolutionary innovations*. Chicago, IL: University of Chicago Press.
- Polly, P. D. (2004). On the simulation of the evolution of morphological shape: Multivariate shape under selection and drift. *Palaeontologia Electronica*, 7(2), 7A, 1–28. http://palaeo-electronica.org/2004_2/evo/issue2_04.htm.
- Polly, P. D. (2008). Adaptive zones and the pinniped ankle: A 3D quantitative analysis of carnivoran tarsal evolution. In E. Sargis & M. Dagosto (Eds.), *Mammalian evolutionary morphology: A tribute to Frederick S. Szalay* (pp. 165–194). Dordrecht, The Netherlands: Springer.
- Raff, R. A. (1996). *The shape of life*. Chicago, IL: University of Chicago Press.
- Raup, D. M. (1966). Geometric analysis of shell coiling: General problems. *Journal of Paleontology*, 40, 1178–1190.
- Reyment, R. A. (1984). *Multivariate morphometrics*. London: Academic Press.
- Rice, S. H. (1990). A geometric model for the evolution of development. *Journal of Theoretical Biology*, 177, 237–245. doi:10.1006/jtbi.1995.0241.
- Rice, S. H. (2000). The evolution of developmental interactions: Epistasis, canalization, and integration. In J. B. Wolf, E. D. Brodie, & M. J. Wade (Eds.), *Epistasis and the evolutionary process* (pp. 82–98). Oxford: Oxford University Press.
- Rice, S. H. (2002). A general population genetic theory for the evolution of developmental interactions. *Proceedings of the National Academy of Sciences of the USA*, 99, 15518–15523. doi:10.1073/pnas.202620999.
- Rice, S. H. (2004a). Developmental associations between traits: Covariance and beyond. *Genetics*, 166, 513–526. doi:10.1534/genetics.166.1.513.
- Rice, S. H. (2004b). *Evolutionary theory: Mathematical and conceptual foundations*. Sunderland, MA: Sinauer and Associates.

- Richtsmeier, J. T., Aldridge, K., DeLeon, V. B., Panchal, J., Kane, A. A., Marsh, J. L., et al. (2006). Phenotypic integration of neurocranium and brain. *Journal of Experimental Zoology. Part B. Molecular and Developmental Evolution*, 306B, 360–378. doi:[10.1002/jez.b.21092](https://doi.org/10.1002/jez.b.21092).
- Richtsmeier, J. T., DeLeon, V. M., & Lele, S. R. (2002). The promise of geometric morphometrics. *Yearbook of Physical Anthropology*, 45, 63–91. doi:[10.1002/ajpa.10174](https://doi.org/10.1002/ajpa.10174).
- Riedl, R. (1978). *Order in living organisms: A systems analysis of evolution*. Chichester, England: Wiley-Interscience.
- Roff, D. A. (1997). *Evolutionary quantitative genetics*. New York: Springer.
- Rohlf, F. J. (2000). On the use of shape spaces to compare morphometric methods. *Hystrix*, 11, 1–17.
- Rohlf, F. J. (2001). Comparative methods for the analysis of continuous variables: Geometric interpretations. *Evolution*, 55, 2143–2160.
- Roopnarine, P. D., Murphy, M. A., & Buening, N. (2005). Micro-evolutionary dynamics of the early Devonian conodont Wurmiella from the Great Basin of Nevada. *Palaeontologia Electronica*, 8(2), 31A.
- Salazar-Ciudad, I. (2006). On the origins of morphological disparity and its diverse developmental bases. *BioEssays*, 28, 1112–1122. doi:[10.1002/bies.20482](https://doi.org/10.1002/bies.20482).
- Salazar-Ciudad, I. (2007). On the origins of morphological variation, canalization, robustness, and evolvability. *Integrative and Comparative Biology*, 47, 390–400. doi:[10.1093/icb/icm075](https://doi.org/10.1093/icb/icm075).
- Salazar-Ciudad, I., & Jernvall, J. (2002). A gene network model accounting for development and evolution of mammalian teeth. *Proceedings of the National Academy of Sciences of the USA*, 99, 8116–8120. doi:[10.1073/pnas.132069499](https://doi.org/10.1073/pnas.132069499).
- Salazar-Ciudad, I., & Jernvall, J. (2004). How different types of pattern formation mechanisms affect the evolution of form and development. *Evolution and Development*, 6, 6–16. doi:[10.1111/j.1525-142X.2004.04002.x](https://doi.org/10.1111/j.1525-142X.2004.04002.x).
- Salazar-Ciudad, I., Newman, S. A., & Solé, R. V. (2001). Phenotypic and dynamical transitions in model genetic networks. I. Emergence of patterns and genotype-phenotype relationships. *Evolution and Development*, 3, 84–94. doi:[10.1046/j.1525-142x.2001.003002084.x](https://doi.org/10.1046/j.1525-142x.2001.003002084.x).
- Simpson, G. G. (1944). *Tempo and mode in evolution*. New York: Columbia University Press.
- Steppan, S. J. (2004). Phylogenetic comparative analysis of multivariate data. In M. Pigliucci & K. Preston (Eds.), *Phenotypic integration: Studying the ecology and evolution of complex phenotypes* (pp. 325–344). Oxford: Oxford University Press.
- Steppan, S. J., Phillips, P. C., & Houle, D. (2002). Comparative quantitative genetics: Evolution of the G matrix. *Trends in Ecology and Evolution*, 17, 320–327. doi:[10.1016/S0169-5347\(02\)02505-3](https://doi.org/10.1016/S0169-5347(02)02505-3).
- Strauss, R. E., & Bookstein, F. L. (1982). The truss: Body form reconstructions in morphometrics. *Systematic Zoology*, 31, 113–135. doi:[10.2307/2413032](https://doi.org/10.2307/2413032).
- Szuma, E. (2002). Dental polymorphism in a population of the red fox (*Vulpes vulpes*) from Poland. *Journal of Zoology (London)*, 256, 243–253.
- Szuma, E. (2007). Geography of dental polymorphism in the red fox *Vulpes vulpes* and its evolutionary implications. *Biological Journal of the Linnean Society*, 90, 61–84. doi:[10.1111/j.1095-8312.2007.00712.x](https://doi.org/10.1111/j.1095-8312.2007.00712.x).
- Thesleff, I., & Sharpe, P. (1997). Signalling networks regulating dental development. *Mechanisms of Development*, 67, 111–123. doi:[10.1016/S0925-4773\(97\)00115-9](https://doi.org/10.1016/S0925-4773(97)00115-9).
- Vavilov, N. I. (1922). The law of homologous series in variation. *Journal of Genetics*, 12, 47–89.
- Wiley, D., Amenta, N., Alcantara, D., Ghosh, D., Kil, Y. J., Delson, E., et al. (2005). Evolutionary morphing. *Proceedings of the IEEE Visualization*, 2005, 431–438.
- Willis, J. H., Coyne, J. A., & Kirkpatrick, M. (1991). Can one predict the evolution of quantitative characters without genetics? *Evolution*, 45, 441–444. doi:[10.2307/2409678](https://doi.org/10.2307/2409678).
- Wolf, J. B., Allen, C. E., & Frankino, W. A. (2004). Multivariate phenotypic evolution in developmental hyperspace. In M. Pigliucci & K. Preston (Eds.), *Phenotypic integration: Studying the ecology and evolution of complex phenotypes* (pp. 366–389). Oxford: Oxford University Press.
- Wolf, J. B., Frankino, W. A., Agrawal, A. F., Brodie, E. D. III, & Moore, A. J. (2001). Developmental interactions and the constituents of quantitative variation. *Evolution*, 55, 232–245.
- Wolsan, M. (1989). Dental polymorphism in the Genus *Martes* (Carnivora: Mustelidae) and its evolutionary significance. *Acta Therapeutica*, 34, 545–593.
- Wood, A. R., Zelditch, M. L., Rountrey, A. N., Eiting, T. P., Sheets, H. D., & Gingerich, P. D. (2007). Multivariate stasis in the dental morphology of the Paleocene–Eocene condylarth *Ectocion*. *Paleobiology*, 33, 248–260. doi:[10.1666/06048.1](https://doi.org/10.1666/06048.1).
- Wright, S. (1968). *Evolution and the genetics of populations: Genetic and biometric foundations*. Chicago, IL: University of Chicago Press.
- Yunker, J. L., & Erlich, R. (1977). Fourier biometrics—Harmonic amplitudes as multivariate shape descriptors. *Systematic Zoology*, 26, 336–342. doi:[10.2307/2412679](https://doi.org/10.2307/2412679).
- Zelditch, M. L., Fink, W. L., & Swiderski, D. L. (1995). Morphometrics, homology, and phylogenetics: Quantified characters as synapomorphies. *Systematic Biology*, 44, 179–189. doi:[10.2307/2413705](https://doi.org/10.2307/2413705).
- Zelditch, M. L., Mezey, J., Sheets, H. D., Lundrigan, B. L., & Garland, T. (2006). Developmental regulation of skull morphology II: Ontogenetic dynamics of covariance. *Evolution and Development*, 8, 46–60. doi:[10.1111/j.1525-142X.2006.05074.x](https://doi.org/10.1111/j.1525-142X.2006.05074.x).
- Zelditch, M. L., Swiderski, D., Sheets, D. H., & Fink, W. (2004). *Geometric morphometrics for biologists*. London: Academic Press.