Chapter 1
An Introduction to the Phylogenetic Comparative Method

Emmanuel Paradis

Abstract The phylogenetic comparative method (PCM) has an important place in evolutionary biology. This chapter aims at giving an overview on some selected topics. We first review briefly some important historical milestones including some early contributions and the relationships of comparative methods with phylogenetics. Some fundamental points on statistical inference, adaptation, and causality are then discussed. We also discuss briefly the application of the PCM to anthropology and conclude with some perspectives on its future development and applications.

1.1 Introduction

> A comparison of apples and oranges occurs when two items or groups of items are compared that cannot be practically compared. … However, apples are actually more closely related to pears (both are rosaceae) than to oranges.
>
> —Wikipedia[1]

The phylogenetic comparative method has undoubtedly been one of the most important phenomena of evolutionary biology during the last few decades. Comparative methods exist in many fields such as anthropology (Bock 1966), law (Kiekbaev 2003), linguistics (Forster et al. 1998), and evolutionary biology (Harvey and Pagel 1991). The concepts and uses of these different comparative methods vary widely. Since the present book is specifically concerned with biological evolution, it is thus useful to define our subject.

---

[1] http://en.wikipedia.org/wiki/Apples_and_oranges

E. Paradis (✉)
Institut de Recherche pour le Développement, Montpellier, France
e-mail: emmanuel.paradis@ird.fr

L. Z. Garamszegi (ed.), *Modern Phylogenetic Comparative Methods and Their Application in Evolutionary Biology*, DOI: 10.1007/978-3-662-43550-2_1,

We may define the *comparative method* as an analytical approach based on the comparison of different objects with the aim to elucidate the mechanisms at the origin of their diversity. From this, we can define the *phylogenetic comparative method* as the analytical study of species, populations, and individuals in a historical framework with the aim to elucidate the mechanisms at the origin of the diversity of life.

It is important to note that the phylogenetic comparative method (PCM) is distinct from but not independent of *phylogenetics*, the study and reconstruction of the historical relationships among species. For instance, in linguistics or in anthropology, the goal of the comparative method is the historical reconstruction of spoken languages or of human cultures (e.g., Forster et al. 1998, with some historical references therein; see Sect. 1.7 below).

The goal of this chapter is to give a general introduction to the PCM by examining some topics. The next section presents the main historical milestones of phylogenetics and the comparative method—since both have been tightly linked through their history. The following sections give some essential elements on statistical inference of evolutionary processes with comparative data. The last two sections aim to put the PCM in a broader perspective by looking at its relationships with anthropology and speculating about some of its current advances and its future.

1.2 History of Phylogenetics and the Comparative Method

1.2.1 Early Developments

In the nineteenth century, trees were essential graphical tools for the development of evolutionary ideas. Lamarck (1809) used a downward-growing tree to represent the relationships among the main groups of animals with a caption indicating that this “table displays the origin of the different animals.” History was central in Lamarck’s argumentation: “A strong reason prevents us to identify the changes that have successively diversified the animals as we know them today: we have never witnessed these changes.” This could be taken as a manifesto of today’s comparative method in evolutionary biology.

Cuvier was Lamarck’s great rival and strong opponent to the idea of evolution. However, Cuvier acknowledged that species are more or less closely related so that they can be classified in a hierarchical system and that different characters of these species are relevant at different levels, especially through his gradual characters (*caractères gradués*, Cuvier 1798). In spite of his backward ideas on fixism (Laurent 1986), Cuvier had a profound impact on comparative anatomy through the numerous illustrations and drawings included in his books—which could appear in a modern textbook on evolution after updating the captions.

It has been widely appreciated that Darwin (1859) used a phylogenetic tree as the only figure in the *Origin of Species*. He also used comparative data to support several of his points; for instance, “Genera which are polymorphic in one country seem to be, with some few exceptions, polymorphic in other countries, and likewise, judging from Brachiopod shells, at former periods of time.” Thus, Darwin characterized the patterns of diversity in space and in time and also used these facts to infer the processes of diversification of species: “…the larger genera also tend to break up into smaller genera. And thus, the forms of life throughout the universe become divided into groups subordinate to groups.”

The end of the nineteenth century has witnessed the wide acceptance of the idea of evolution, particularly with the contributions of Haeckel, the father of phylogenetics: “For the purpose of constructing a hypothetical genealogical tree of the Radiolaria, as of all other organisms, three sources of information are open to us, viz., palæontology, comparative ontogeny, and comparative anatomy.” (Haeckel 1887).

During the first half of the twentieth century, phylogenetics and biological comparative studies have followed separate paths. The discovery of the physical support of heredity (genes, chromosomes, and later DNA) led scientists to focus their interest on the genetic mechanisms of evolution. Fisher (1930) certainly best illustrates this change of paradigm where history was less important than previously thought: “For mutations to dominate the trend of evolution it is thus necessary to postulate mutation rates immensely greater than those which are known to occur…” For Fisher, mutations could not explain evolutionary novelties and we should rather look at other evolutionary forces such as selection or population structure to explain the diversity of life. At the same time, phylogenetics made fundamental contributions to evolutionary thinking. Paleontologists integrated phylogenetic ideas, mainly because of the historical nature of their data (Simpson 1944). Phylogenetic trees became the analytical tool of a school of systematists (cladistics), leading to the first numerical treatments of phylogenies (see a historical account in Felsenstein 2004).

1.2.2 Modern Developments

The late 1960s have witnessed some crucial turns. The development of statistical methods to reconstruct phylogenies from genetic data was a major step accomplished by Cavalli-Sforza and Edwards (1967). Because the approach they developed was statistical, it was possible to extend it to other kinds of data such as continuous characters. This next step was achieved by Felsenstein (1973) who proposed a method to calculate the likelihood of a tree for a set of continuous traits. The significance of this work was not obvious until the same author published a related method to calculate the phylogenetically independent contrasts (PICs), a major difference being that the calculations under this new method could be done with a hand calculator (Felsenstein 1985).

Until the 1970s, comparative biology developed its statistical tools independently of phylogenetic or historical ideas. Comparative data from *n* species used to be analyzed with standard statistical methods, assuming that they were *n* independent observations. This separation between comparative biology and the historical dimension of biological evolution seems surprising when considering that the idea of evolution, and particularly adaptation, was at the heart of most comparative studies (Clutton-Brock and Harvey 1979).

The 1980s can be seen as the golden age of PCMs when a great variety of methods were published (reviewed by Pagel and Harvey 1988). Two important papers were published in the same year: Cheverud et al. (1985), who proposed an approach based on auto-regression including the possibility to account for intraspecific variation, and Felsenstein (1985), already cited. A few years later, Grafen (1989), in a very rich and dense paper, proposed the use of generalized least squares (GLS) to derive a method now widely known as the phylogenetic generalized least squares (PGLS). Gittleman and Kot (1990) further developed the use of auto-correlation functions to assess phylogenetic signal in diverse settings, including using taxonomic levels when a phylogeny is not available. Nevertheless, the power of these methods to infer evolutionary models and parameters was not yet fully acknowledged, and the view that phylogeny was a confounding effect in comparative analyses still prevailed: "Confounding effects of phylogeny and other variables may lurk behind any comparative relationship, and they must be removed or controlled prior to considering adaptive arguments." (Pagel and Harvey 1988).

During the 1990s, the developments of the previous decade were confirmed and strengthened. Lynch (1991) made a link between models of quantitative genetics and phylogenetics. He developed a method to partition the variance of a trait into an environmental and a phylogenetic component. Importantly, the same decomposition can be done for the covariance between two traits, thus providing a formal way to quantify the historical component of the link between two characters. New methods were proposed for the analysis of discrete traits (Pagel 1994; Grafen and Ridley 1997). In two important papers, Hansen and Martins (1996) and Martins and Hansen (1997) showed how GLS can be used to address evolutionary questions beyond the basic Brownian motion model.

In the 2000s, some efforts were given to issues left temporarily aside such as fitting more complicated models combining continuous and discrete traits (Paradis and Claude 2002; Felsenstein 2005; Hadfield and Nakagawa 2010) or combining interspecific and intraspecific data (Felsenstein 2008; Garamszegi and Møller 2010; Stone et al. 2011; see Chap. 7). At the end of the decade, three papers by Revell (2009), Jombart et al. (2010), and Pavoine et al. (2010) defined a general framework for multivariate statistical analyses in a phylogenetic context. The concept of phylogenetic signal has also attracted significant interest with the aim of clarifying previous ideas on phylogenetic confounding effect (Blomberg et al. 2003; Ollier et al. 2006; Pavoine et al. 2008; Münkemuller et al. 2012). At the same time, PCMs have achieved maturity with some generalizations such as the development of a Brownian model with variable parameters (O'Meara et al. 2006)

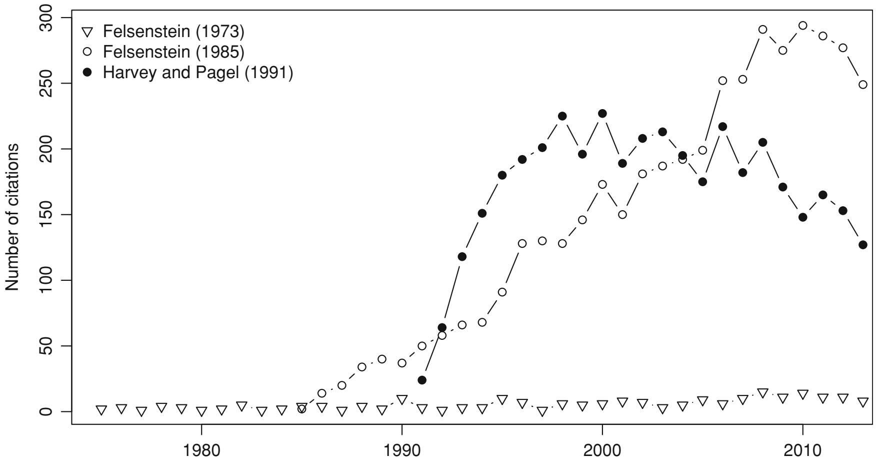

Fig. 1.1 The annual number of citations of three major contributions to the phylogenetic comparative method (*Source* Web of Science)

or the use of sophisticated model-fitting techniques such as Monte Carlo Markov chains (MCMC) to fit complicated models (Pagel et al. 2004; Pagel and Meade 2006; Hadfield and Nakagawa 2010).

Remarkable progress in phylogenetics also contributed to PCMs, particularly with the publication of more and more phylogenies, some of them being complete over a very large number of species (Bininda-Emonds et al. 2007; Smith et al. 2011; Jetz et al. 2012; see Chap. 3). Some methods have been developed to combine different sources of phylogenetic information in order to build trees for comparative analyses (Kuhn et al. 2011; Eastman et al. 2013; Thomas et al. 2013; see Chap. 2).

Figure 1.1 gives the number of citations of two earlier papers over the years together with another major contribution to the development of PCMs. After almost three decades, the range of applications of PCMs has grown to reach all branches of biological science: 6,533 citations of Felsenstein (1985) or Harvey and Pagel (1991) are found in 771 periodical titles. The PCM, through the development of a wide range of analytical tools, has contributed insights into many questions on evolution and the diversity of life.

1.3 The Covariance Structure of Comparative Data

A central issue with comparative data is the non-independence of observations. A similar problem is found in other fields such as geography (Cliff and Ord 1981), climatology (Tiao et al. 1990), ecology (Legendre 1993), or medical research (Houwing-Duistermaat et al. 1998).

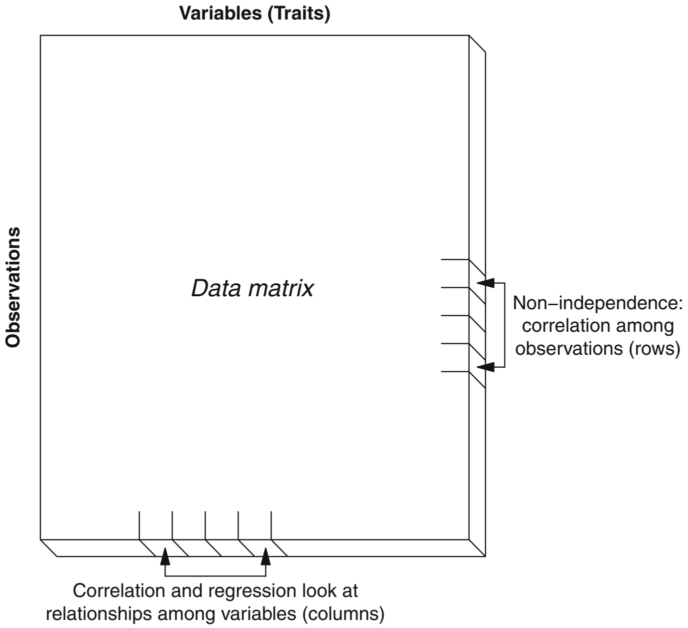

Fig. 1.2 A general depiction of a data set

In a very general way, a data set can be arranged in a matrix where the rows are the observations (individuals, populations, species, sequences, cells, etc.) and the columns are variables (size, area, nucleotide sites, RNA transcription levels, etc.). Data analyses seek for relationships among the columns of this matrix, and common statistical methods assume that the rows are independent observations; in other words, the values observed on a given row are not affected by the values at others (Fig. 1.2).

To statistically handle non-independence of observations, a general approach is to assume that two observations (rows), say i and j, are related through a covariance parameter denoted as σ_{ij}^2. This parameter specifies the strength of the relation between the values of the same variable (column) observed for these two observations. The way this parameter enters in the analyses depends on the method used, the kinds of variables, and the question asked. The covariance parameters are usually arranged in a symmetric matrix with the diagonal elements equal to the variances and the off-diagonal elements being the covariances (see Chap. 5). This matrix has n rows and n columns and so contains $n(n-1)/2$ off-diagonal elements.

There are many ways to define the values of σ_{ij}^2: they may be all equal or not, they may follow a specific distribution or may be related to another variable, they may be fixed or estimated from the data, etc. For instance, with spatial data, it is common to use a covariance function related to geographical distance.

In the case of comparative data from several species, it is possible to calculate a priori the covariances among species traits if we know how these traits have evolved. For instance, if we assume that a trait has evolved under a Brownian motion (BM) model, these covariances can be calculated from the phylogenetic tree linking these species without observing the trait itself. The PIC and PGLS methods were directly derived from this assumption. Both methods are identical though they are computationally very different (Blomberg et al. 2012). PGLSs directly use the covariances by calculating a correlation matrix among observations, which is simply a covariance matrix scaled to have values between -1 and 1 (see Chap. 5).

1.4 Statistical Inference

The covariance matrix is at the core of most PCMs. Fortunately, it is possible to calculate it for other models of trait evolution, in particular for the Ornstein–Uhlenbeck (OU) model which is appropriate to model evolution of traits under constraints (see Chaps. 13, 14 and 15). Using this and other models, it is thus possible to relax the assumption underlying the BM model. This feature of PCMs allows us to go beyond the paradigm that phylogeny is a confounding effect that must simply be corrected (see Rohlf 2006).

We can illustrate this point with a small simulation exercise. Taking the phylogeny in Fig. 1.3, we simulate two independent traits that evolve according to either a BM or an OU model. In this second model, the traits are constrained to evolve toward an optimal value with a strength controlled by the parameter denoted as α. The simulated traits were analyzed with two methods: a standard regression (assuming the species are independent) and a regression using the PICs calculated with the original phylogeny (which was thus assumed to be perfectly known). Table 1.1 shows the estimated rejection rates for both methods. Since both traits are independent, we expect these rates to be close to 5 %. The PIC-based analyses gave the correct answer with the data simulated from a BM model or from an OU model with a small value of α. On the other hand, for the large values of α, the PIC-based analyses had a high type I error rate, whereas the standard regression had a rejection rate close to 5 %.

Figure 1.4 shows the correlation matrices among the 20 leaves of the tree under different models of trait evolution. These matrices would be used in PGLS analyses (see Chap. 5). This shows clearly that an OU model with small α is close to a Brownian motion one, whereas when α is large, the observations are expected to be almost independent.

The critical point in a PCM-based analysis is to use the correct correlation structure among observations. The more distant the assumed correlation structure from the real one, the more biased the analysis will be. This property explains the statement that “in a comparative analysis a wrong phylogeny is better than no phylogeny at all” (Losos 1994; Martins 1996). Indeed, if the traits evolved on a

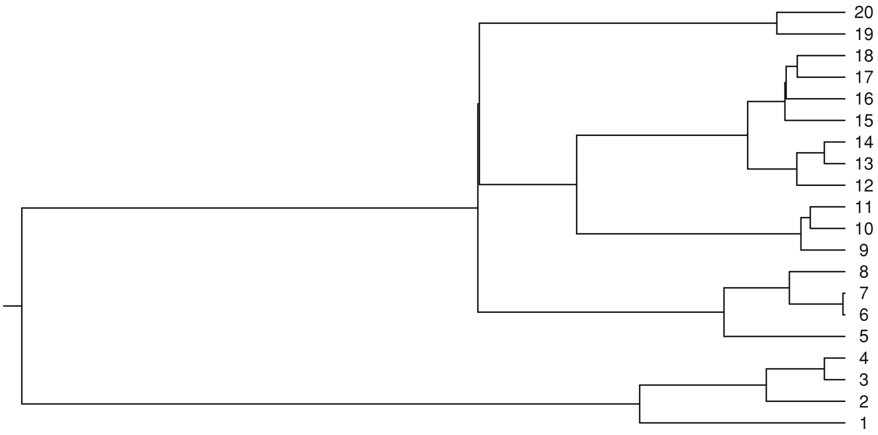

Fig. 1.3 A simulated phylogeny with $n = 20$

Table 1.1 Rejection rate of the test of correlation between two independent traits simulated on the phylogeny in Fig. 1.3 using the model indicated in the table

Simulated model	α	Standard regression	PIC regression
Brownian motion		0.396	0.051
Ornstein–Uhlenbeck	1	0.223	0.056
	10	0.065	0.120
	100	0.051	0.343

Simulations were replicated 10,000 times

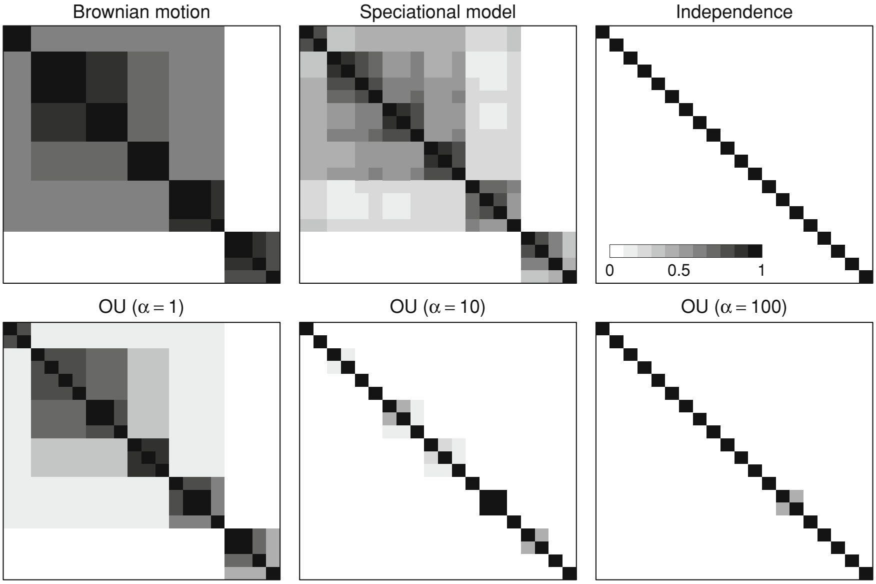

Fig. 1.4 Correlation matrices among the 20 tips of the tree in Fig. 1.3. The speciational model is one where change occurs only after a speciation event

phylogeny and another phylogeny is used for data analysis, the latter will result in a correlation structure closer to the correct one than assuming no correlation at all (i.e., independence of observations).

From the point of view of data analysis, one problem often encountered in published studies is that the phylogenetic correlation structure of the data is usually not assessed. This certainly comes from the view traditionally defended by most authors that only the phylogenetically controlled analyses are relevant. We now know that this can lead to wrong inference. This seems relatively easy to fix with tests of phylogenetic signal and model selection with information criteria such as the AIC (see Chap. 5). Remarkably, when different correlation structures are compared with real data, the Brownian motion model is rejected against more complex models such as the OU one (Whitney et al. 2011; Lapiedra et al. 2013).

1.5 Inferring Adaptation

Perhaps because of its history, the comparative method is most often used to infer adaptation. However, the scope and power of the PCM to reveal adaptation have been criticized several times over the years (e.g., Leroi et al. 1994; Martins 2000; Grandcolas et al. 2011). Such criticism is not really surprising: It has been discussed since a long time ago that characterizing the adaptative nature of a trait is a complicated endeavor (Bock 1959). Even the characterization of adaptation in viruses, which are far simpler than the organisms studied by most evolutionists, appears to be an arduous task (Pepin et al. 2010). The use of traits such as "habitat use" or "environment" with PCMs has been questioned because the analysis of such variables in a phylogenetic framework is meaningless (Grandcolas et al. 2011). On the other hand, it is hard to not consider these variables in evolutionary models since the assessment of the adaptive value of a trait cannot be separated from extrinsic variables such as habitat, resources, or climate (Bock 2003; Losos 2011; Watt 2013).

Some recent developments in PCMs provide a solution to the limitations underlined by the critiques cited above. As we have seen in the previous sections, the PCM does not simply aim at correcting for phylogenetic dependence or inferring repeated evolution of the same trait in different lineages, but rather to provide tools to analyze comparative data in a historical framework, and this includes fitting complex models of trait evolution that can handle various complications of the study design. For instance, some methods make possible to analyze several traits that evolve under different models: Bartoszek et al. (2012) developed a multi-trait model where traits can evolve following different processes of BM or OU.

One situation illustrated by Losos (2011) is the one of "incomplete convergence." Convergence toward similar phenotypes among distantly related species is often viewed as evidence for adaptation. However, adaptive evolution can proceed in different ways in different groups, and the patterns thus produced are likely to be masked or obscured by other variables (such as the taxonomical background). Losos (2011) gives the example of the head shape of lizards which is mainly related to phylogenetic relatedness; however, within distinct clades, some species evolved independently toward herbivory and share some similarities, but the convergence is incomplete as they retain their respective phylogenetic background. In this case, a standard comparative analysis will likely fail to characterize the limited convergence among species affected by similar selective forces. On the other hand, statistical methods in a historical framework, including models of trait evolution, are helpful to characterize such patterns of adaptation. The use of these and other recently developed models of trait evolution may help to solve this "paradox" of using non-heritable traits in comparative analyses.

1.6 Inferring Causality

Correlation is not causality, and PCMs do not escape this reality. In spite of the importance of causality in evolutionary theory (see Watt 2013, for a recent view), the application of PCMs is generally oblivious of this point. This has led to some debate about the applicability of the PCM in order to identify evolutionary mechanisms. The vast majority of publications do not elaborate much on correlation and causality in their predictions: A simple linear correlation is usually derived from the hypotheses under test.

In general statistical inference, the causal relationship between two variables (say x and y) can be assessed if one of them can be controlled and then used as a predictor in data analyses. With comparative data, x and y cannot be controlled: They are evolving traits (or intrinsic variables) which are measured "on the species" (or they are extrinsic variables, like habitat, which cannot generally be controlled). Therefore, in the situation of a PCM with two variables, it is not possible to determine which regression (x on y or y on x) best describes the data. In other words, we cannot infer the causal relationship between these two variables.

When three or more uncontrolled variables are analyzed, it is possible to assess alternative causal relationships among them with a method known as path analysis (Freedman 2009). This method considers explicitly the causal relationships among variables under alternative hypotheses. A causal relationship can be expressed as "the variation in y is caused by the variation in the value of x" and has the statistical consequence that the regression of y on x is meaningful. Under a given hypothesis of the causal relationships among variables, some regressions are meaningful, while others are not. Using a procedure called the d-sep, it is possible to test which hypothesis best describes the data (Shipley 2013). Santos and Cannatella (2011) and von Hardenberg and Gonzalez-Voyer (2013) proposed to extend the framework of path analysis to PCMs (see Chap. 8). In a traditional path analysis, the regressions are done assuming independence of observations. Therefore, it is straightforward to generalize this method to cases where the observations are not independent, using tools such as (P)GLS.

Causality in general, and in evolution in particular, is fundamental, but this is a difficult concept to apply in practice. Hopefully, future applications of PCMs will help to progress on this issue.

1.7 Phylogenetic Comparative Method and Anthropology

As mentioned above, the present book focuses on the uses of the comparative method in evolutionary biology. One reason for this restriction is that other scientists do not see the comparative approach in the same way than evolutionists do. For instance, Bock (1966) described the comparative method as follows (italics as original):

> It should be recalled at the outset that the primary objective of users of the comparative method is historical reconstruction. *What* history or *whose* history is by no means clear in the nineteenth century literature, and this question has hardly been resolved in recent controversy.

Thus, what anthropologists call “comparative method” seems close to what evolutionists call “phylogenetics.” Mace and Pagel (1994) revisited this issue by introducing a phylogenetic approach to anthropology directly inspired from evolutionary biology. Considering the links between comparative biology and phylogenetics, their message does not differ radically from the one formulated 28 years before by Bock.

In practice, the application of PCMs in anthropology differs substantially compared to evolutionary biology. A remarkable difference is that with anthropological data, the historical sequence of changes in traits (cultures, political systems, etc.) is often recorded—at least more often than in biology. For instance, Lindenfors et al. (2011) studied changes in political systems in the world between 1800 and 2008. Using several variables, they built a score ranging between -10 (total autocracy) and $+10$ (full democracy) and measured transitions among these different scores. They showed that most political changes occurred from autocratic systems (with a peak around -6) toward democratic ones (with a peak around $+8$). However, one interesting point about this study is their comment with respect to the historical dimension of the problem:

> A reconstruction of democracy as a political system on a language phylogeny would almost certainly indicate democracy as the ancestral state for large sections of the phylogeny. However, since we have exact information of all transitions, we know this not to be true.

In biological terms, there is a trend (or directional evolution) from autocracy toward democracy so that the second system is the most widespread today among countries. If we ignore this historical trend, we would make wrong inference. Here also, we see that using the wrong model of evolution can be misleading. Similar situations can be found with evolutionary data; for instance, if a trend exists in the evolution of a trait (say, increase in body size), then ancestral inference will likely be misleading if this trend is not taken into account (Grafen 1989). Anthropological data have other peculiarities, like the ubiquity of horizontal transfers (Borgerhoff Mulder et al. 2006), so that a full comparison between cultural and biological evolution would require a much longer discussion.

1.8 The Future of the Phylogenetic Comparative Method

The comparative method in biology has evolved through several centuries to reach its present status. Today, PCMs have attained a level of maturity and sophistication that the readers can appreciate in the chapters of this book. The directions of future progress are certainly multiple.

We have seen the importance of the evolutionary models in statistical inference with the PCM. Some researchers currently explore the possibility to analyze complex models with several variables and an explicit formulation of the relationships among them. Hadjipantelis et al. (2013) analyzed an evolutionary model of "function-valued traits" by combining dimensionality reduction and a "bagging" (bootstrap aggregating) procedure. Complex relational models fitted with structural equation models seem also a very promising approach for future comparative analyses (Chap. 8).

It has not been widely appreciated that some PCMs link a model of microevolution (random evolution through genetic drift or stabilizing selection) with the patterns of interspecific variation in a trait and thus with macroevolution. Further works in this direction will likely lead to some interesting investigations on evolutionary mechanisms.

During many decades, the fossil record has been considered as the only source of information about evolutionary change. This paradigm has been broken by two steps forward in evolutionary biology: phylogenetic methods which try to reconstruct the past from the present and observations of real evolutionary changes over recent years such as the spread of resistance alleles in pathogens. However, the divorce between paleobiology and PCMs does not seem natural, and several researchers try to reconcile them (Pennell and Harmon 2013). This task will surely be very difficult but considering the many contributions of fossils to evolutionary biology, this is worth the effort (Chap. 22).

A scientific discipline is sometimes judged by how it contributes to everyone's well-being. The PCM may well move very positively in this direction as comparative analyses could have concrete applications. Spreitzer et al. (2005) used simple comparisons between different plant and alga species to create new enzymes involved in photosynthesis by targeted mutations on "phylogenetic residues." The resulting enzyme is one with original characteristics, a kind of "phylogenetic chimaera." Such an approach of "phylogenetic engineering" may be promising to design new proteins or even new organisms based on predictions from evolutionary phylogenetic models.

Yan et al. (2012) used a phylogenetic analysis of a number of bacteria in order to propose cocktails of probiotic bacteria to reduce pathogens in food. Their approach is based on an investigation of a protein, MazF, which has an antimicrobial activity, and for which they propose an engineered variant. The phylogeny of the studied bacteria was instrumental in designing this new protein. The combination of molecular structure approaches with phylogenetic comparative analyses seems a promising venue to develop a variety of new molecules with desired properties.

Rich of its long history, the PCM seems to have a bright future both for addressing fundamental questions and for delivering applications.

Acknowledgments I am grateful to László Zsolt Garamszegi for inviting me to write this chapter. Many thanks to two anonymous reviewers for their positive comments.

References

Bartoszek K, Pienaar J, Mostad P, Andersson S, Hansen TF (2012) A phylogenetic comparative method for studying multivariate adaptation. J Theor Biol 314:204–215

Bininda-Emonds ORP, Cardillo M, Jones KE, MacPhee RDE, Beck RMD, Grenyer R, Price SA, Vos RA, Gittleman JL, Purvis A (2007) The delayed rise of present-day mammals. Nature 446:507–512

Blomberg SP, Garland T Jr, Ives AR (2003) Testing for phylogenetic signal in comparative data: behavioral traits are more labile. Evolution 57:717–745

Blomberg SP, Lefevre JG, Wells JA, Waterhouse M (2012) Independent contrasts and PGLS regression estimators are equivalent. Syst Biol 61:382–391

Bock KE (1966) The comparative method of anthropology. Comp Stud Soc Hist 8:269–280

Bock WJ (1959) Preadaptation and multiple evolutionary pathways. Evolution 13:194–211

Bock WJ (2003) Ecological aspects of the evolutionary processes. Zool Sci 20:279–289

Borgerhoff Mulder M, Nunn CL, Towner MC (2006) Cultural macroevolution and the transmission of traits. Evol Anthropol 15:52–64

Cavalli-Sforza LL, Edwards AWF (1967) Phylogenetic analysis models and estimation procedures. Am J Hum Genet 19:233–257

Cheverud JM, Dow MM, Leutenegger W (1985) The quantitative assessment of phylogenetic constraints in comparative analyses: sexual dimorphism in body weight among primates. Evolution 39:1335–1351

Cliff AD, Ord JK (1981) Spatial and temporal analysis: autocorrelation in space and time. In: Wrigley EN, Bennett RJ (eds) Quantitative geography: a british view. Routledge & Kegan Paul, London, pp 104–110

Clutton-Brock TH, Harvey PH (1979) Comparison and adaptation. Proc R Soc Lond B 205:547–565

Cuvier G (1798) Tableau élémentaire de l'histoire naturelle des animaux. Baudouin, Paris

Darwin C (1859) On the origin of species by means of natural selection. John Murray, London

Eastman JM, Harmon LJ, Tank DC (2013) Congruification: support for time scaling large phylogenetic trees. Meth Ecol Evol 4:688–691

Felsenstein J (1973) Maximum-likelihood estimation of evolutionary trees from continuous characters. Am J Hum Genet 25:471–492

Felsenstein J (1985) Phylogenies and the comparative method. Am Nat 125:1–15

Felsenstein J (2004) Inferring phylogenies. Sinauer Associates, Sunderland

Felsenstein J (2005) Using the quantitative genetic threshold model for inferences between and within species. Phil Trans R Soc Lond B 360:1427–1434

Felsenstein J (2008) Comparative methods with sampling error and within-species variation: contrasts revisited and revised. Am Nat 171:713–725

Fisher RA (1930) The genetical theory of natural selection (a complete variorum edition, 1999). Oxford University Press, Oxford

Forster P, Toth A, Bandelt HJ (1998) Evolutionary network analysis of word lists: visualising the relationships between Alpine romance languages. J Quant Linguist 5:174–187

Freedman DA (2009) Statistical models: theory and practice (revised edition). Cambridge University Press, Cambridge

Garamszegi LZ, Møller AP (2010) Effects of sample size and intraspecific variation in phylogenetic comparative studies: a meta-analytic review. Biol Rev 85:797–805

Gittleman JL, Kot M (1990) Adaptation: statistics and a null model for estimating phylogenetic effects. Syst Zool 39:227–241

Grafen A (1989) The phylogenetic regression. Phil Trans R Soc Lond B 326:119–157

Grafen A, Ridley M (1997) A new model for discrete character evolution. J Theor Biol 184:7–14

Grandcolas P, Nattier R, Legendre F, Pellens R (2011) Mapping extrinsic traits such as extinction risks or modelled bioclimatic niches on phylogenies: does it make sense at all? Cladistics 27:181–185

Hadfield JD, Nakagawa S (2010) General quantitative genetic methods for comparative biology: phylogenies, taxonomies and multi-trait models for continuous and categorical characters. J Evol Biol 23:494–508

Hadjipantelis PZ, Jones NS, Moriarty J, Springate DA, Knight CG (2013) Function-valued traits in evolution. J R Soc Interface 10(20121):032

Haeckel E (1887) Report on the Radiolaria collected by H.M.S. Challenger during the years 1873–1876. Her Majesty's Stationery Office, London

Hansen TF, Martins EP (1996) Translating between microevolutionary process and macroevolutionary patterns: the correlation structure of interspecific data. Evolution 50:1404–1417

Harvey PH, Pagel MD (1991) The comparative method in evolutionary biology. Oxford University Press, Oxford

Houwing-Duistermaat JJ, van Houwelingen HC, Terhell A (1998) Modelling the cause of dependency with application to filaria infection. Statist Med 17:2939–2954

Jetz W, Thomas GH, Joy JB, Hartmann K, Mooers AO (2012) The global diversity of birds in space and time. Nature 491:444–448

Jombart T, Pavoine S, Devillard S, Pontier D (2010) Putting phylogeny into the analysis of biological traits: a methodological approach. J Theor Biol 264:693–701

Kiekbaev DI (2003) Comparative law: method, science or educational discipline? Electronic journal of comparative law 7.3. url http://www.ejcl.org/73/art73-2.html

Kuhn TS, Mooers AO, Thomas GH (2011) A simple polytomy resolver for dated phylogenies. Meth Ecol Evol 2:427–436

Lamarck JB (1809) Philosophie zoologique. Flammarion (1994 edition), Paris

Lapiedra O, Sol D, Carranza S, Beaulieu JM (2013) Behavioural changes and the adaptive diversification of pigeons and doves. Proc R Soc Lond B 280(20122):893

Laurent G (1986) Cuvier et Lamarck: la querelle du catastrophisme. La Recherche 17:1510–1518

Legendre P (1993) Spatial autocorrelation: trouble or new paradigm? Ecology 74:1659–1673

Leroi AM, Rose MR, Lauder GV (1994) What does the comparative method reveal about adaptation? Am Nat 143:381–402

Lindenfors P, Jansson F, Sandberg M (2011) The cultural evolution of democracy: saltational changes in a political regime landscape. PLoS ONE 6:e28270

Losos JB (1994) An approach to the analysis of comparative data when a phylogeny is unavailable or incomplete. Syst Biol 43:117–123

Losos JB (2011) Convergence, adaptation, and constraint. Evolution 65:1827–1840

Lynch M (1991) Methods for the analysis of comparative data in evolutionary biology. Evolution 45:1065–1080

Mace R, Pagel M (1994) The comparative method in anthropology (with discussion). Curr Anthropol 35:549–564

Martins EP (1996) Conducting phylogenetic comparative studies when the phylogeny is not known. Evolution 50:12–22

Martins EP (2000) Adaptation and the comparative method. Trends Ecol Evol 15:296–299

Martins EP, Hansen TF (1997) Phylogenies and the comparative method: a general approach to incorporating phylogenetic information into the analysis of interspecific data. Am Nat 149:646–667 erratum vol 153, p 488

Münkemüller T, Lavergne S, Bzeznik B, Dray S, Jombart T, Schiffers K, Thuiller W (2012) How to measure and test phylogenetic signal. Meth Ecol Evol 3:743–756

Ollier S, Couteron P, Chessel D (2006) Orthonormal transform to decompose the variance of a life-history trait across a phylogenetic tree. Biometrics 62:471–477

O'Meara BC, Ané C, Sanderson MJ, Wainwright PC (2006) Testing for different rates of continuous trait evolution using likelihood. Evolution 60:922–933

Pagel M (1994) Detecting correlated evolution on phylogenies: a general method for the comparative analysis of discrete characters. Proc R Soc Lond B 255:37–45

Pagel M, Meade A (2006) Bayesian analysis of correlated evolution of discrete characters by reversible-jump Markov chain Monte Carlo. Am Nat 167:808–825

Pagel M, Meade A, Barker D (2004) Bayesian estimation of ancestral character states on phylogenies. Syst Biol 53:673–684

Pagel MD, Harvey PH (1988) Recent developments in the analysis of comparative data. Quart Rev Biol 63:413–440

Paradis E, Claude J (2002) Analysis of comparative data using generalized estimating equations. J Theor Biol 218:175–185

Pavoine S, Ollier S, Pontier D, Chessel D (2008) Testing for phylogenetic signal in phenotypic traits: new matrices of phylogenetic proximities. Theor Pop Biol 73:79–91

Pavoine S, Baguette M, Bonsall MB (2010) Decomposition of trait diversity among the nodes of a phylogenetic tree. Ecol Monogr 80:485–507

Pennell MW, Harmon LJ (2013) An integrative view of phylogenetic comparative methods: connections to population genetics, community ecology, and paleobiology. Ann NY Acad Sci 1289:90–105

Pepin KM, Lass S, Pulliam JRC, Read AF, Lloyd-Smith JO (2010) Identifying genetic markers of adaptation for surveillance of viral host jumps. Nat Rev Microbiol 8:802–813

Revell LJ (2009) Size-correction and principal components for interspecific comparative studies. Evolution 63:3258–3268

Rohlf FJ (2006) A comment on phylogenetic correction. Evolution 60:1509–1515

Santos JC, Cannatella DC (2011) Phenotypic integration emerges from aposematism and scale in poison frogs. Proc Natl Acad Sci USA 108:6175–6180

Shipley B (2013) The AIC model selection method applied to path analytic models compared using a d-separation test. Ecology 94:560–564

Simpson GG (1944) Tempo and mode in evolution. Columbia University Press, New York

Smith SA, Beaulieu JM, Stamatakis A, Donoghue MJ (2011) Understanding angiosperm diversification using small and large phylogenetic trees. Am J Bot 98:404–414

Spreitzer RJ, Peddi SR, Satagopan S (2005) Phylogenetic engineering at an interface between large and small subunits imparts land-plant kinetic properties to algal Rubisco. Proc Natl Acad Sci USA 102:17225–17230

Stone GN, Nee S, Felsenstein J (2011) Controlling for non-independence in comparative analysis of patterns across populations within species. Phil Trans R Soc Lond B 366:1410–1424

Thomas GH, Hartmann K, Jetz W, Joy JB, Mimoto A, Mooers AO (2013) PASTIS: an R package to facilitate phylogenetic assembly with soft taxonomic inferences. Meth Ecol Evol 4:1011–1017

Tiao GC, Reinsel GC, Xu DM, Pedrick JH, Zhu XD, Miller AJ, DeLuisi JJ, Mateer CL, Wuebbles DJ (1990) Effects of autocorrelation and temporal sampling schemes on estimates of trend and spatial correlation. J Geophys Res-Atmos 95:20507–20517 von Hardenberg A, Gonzalez-Voyer A (2013) Disentangling evolutionary cause-effect relationships with phylogenetic confirmatory path analysis. Evolution 67:378–387

Watt WB (2013) Causal mechanisms of evolution and the capacity for niche construction. Biol Philos 28:757–766

Whitney KD, Boussau B, Baack EJ, Garland T (2011) Drift and genome complexity revisited. PLoS Genet 7(e1002):092

Yan XH, Gurtler JB, Fratamico PM, Hu J, Juneja VK (2012) Phylogenetic identification of bacterial MazF toxin protein motifs among probiotic strains and foodborne pathogens and potential implications of engineered probiotic intervention in food. Cell Biosci 2:39